

Tailored Siloxane Nanocomposites: Synthesis and Applications as Nanocarriers for Drugs, Metal Particles, and Catalysts

by

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Abstract

Tailored Siloxane Nanocomposites: Synthesis and Applications as Nanocarriers for Drugs, Metal Particles, and Catalysts

By

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Inorganic/Organic (I/O) hybrid nanocomposites are a rapidly growing field of science in pursuit of novel materials with improved properties and performances. Owing to the remarkable combination of inorganic and organic segments into one material, I/O hybrid nanocomposites promise to have the potential for numerous useful applications, which are not offered by inorganic or organic materials alone. In our approach to synthesize such hybrid materials, we have used cyclic and cubic siloxanes as hydrophobic, inorganic cores and frameworks for the generation of I/O hybrid materials by introducing hydrophilic, organic arms such as polyethylene glycols. The reaction was accomplished via Rh-catalyzed dehydrogenative alcoholysis coupling reaction between a cyclic siloxane (D_4^H) or cubic siloxane ($Q_8M_8^H$) and polyethylene glycol (PEG). The resultant silicones were analyzed by various spectroscopy techniques such as IR and NMR (^1H , ^{13}C , ^{29}Si), which showed successful substitutions in quantitative yields. Our hypothesis was that the amphiphilic nature of the resultant alkoxy siloxanes would generate well-defined siloxane networks and micelles when dissolved in selective solvents above a certain concentration. We envisioned that the micelles can be employed as nanoreactors not only for generation of metal nanoparticles, but also as stabilizers for generated colloids. Secondly, hydrophilic polyethylene glycol addition on the siloxane

core may allow solubility of hybrid composites and self-assembly into micelles in aqueous media. This property of hybrid composites makes them potential candidates as drug delivery carriers. The micellization of synthesized I/O hybrid nanocomposites was monitored with transmission electron microscope (TEM), which revealed well-defined siloxane network micellar structures. Furthermore, we believe that hybrid nanocomposites can be expanded to further generations by introducing additional siloxane units through glycol bridges giving rise to dendrimers.

To establish their role as nanoreactors, I/O hybrid micellar networks of first and second generation were for preparation of nanosized metallic particles, via in-situ reduction of metal salts at mild laboratory conditions. Silver (Ag), palladium (Pd), and platinum (Pt) nanoparticles of size 1-5 nm were prepared in this way. Characterization of nanoclusters was carried out using a number of analysis techniques, such as TEM and UV-vis, which revealed non-aggregated metal nanoparticles with narrow size distributions confirming the role of hybrid composites as excellent reducing agents and effective stabilizers as well. Catalytic application of Pt-nanoclusters was demonstrated by using them as effective catalyst for hydrosilylation of Si-H bonds of heptamethyltrisiloxane (HMTS) with double bonds of various alkenes. In most of the cases, quantitative and selective attachment of alkenes was achieved under mild reaction conditions without any noticeable side reactions. The scope of I/O hybrid nanocomposites as drug carriers was probed by encapsulation of a fluorescent dye in micelles in water solutions. Microscopic studies of encapsulated samples confirmed the potential and efficiency of hybrid nanocomposites as excellent drug carriers in aqueous media. Furthermore, grafting of octakis (dimethylsiloxy)-T₈-silsesquioxane (Q₈M₈^H) with

various alcohols was carried out in order to establish a potential route to POSS (polyhedral oligomeric silsesquioxanes) materials. Spectroscopy techniques such as IR, and NMR (^1H , ^{13}C , ^{29}Si) spectroscopy were used to analyze the covalent attachments and quantitative grafting was achieved. TGA analysis showed that the resultant POSS materials had higher thermal stability.

This thesis is dedicated to my parents for their unconditional love and never ending encouragement, who were invaluable source of strength and inspiration and whose prayers were always with me. Daddy, I wish so much you were here to see my success. I love you. To my brothers Amir and Imran for their continuous encouragement, guidance and support in every step of my life and during my struggles over the years to finally reach my goal. Ammi, Amir bhai and Imran bhai, I love you so much. My thanks to my friends, who helped me at different stages during this experience. Thank you all for believing in me. I am thankful to God Almighty for His blessings and I pray for even more success and happiness in my future endeavors.

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CHAPTER 1

1 Introduction to Inorganic/Organic (I/O) Hybrid Nanocomposites and Their Applications

1.1 Hybrid Materials

The synthesis of novel materials with improved properties and performances is a rapidly expanding field of chemistry and material science. Materials are an important part of our everyday life and the utilization of materials became familiar to men at the very early stages of civilization. Natural materials e.g., stone, minerals, metals were used as a necessary part of daily life in different forms. As the civilizations grew, the curiosity and need of exploring new materials to make lives better grew with them. Human kind discovered new materials at every step and came to know of their numerous applications, uses, and advantages and several methods were invented to extract materials from natural sources. Extracting metals from their ores, using calcium salts from rocks as paint or plaster, or making pottery with clay are some examples. As time passed and people became familiar with different materials and their properties, they started categorizing them. In present age, solid materials are classified into three basic categories: Metallic materials, ceramics, and polymers or molecular materials¹. With increasing knowledge in chemistry, chemists and material scientists learned to manipulate existing resources and synthesize new engineered materials where one can add or eliminate desired properties by means of chemical reactions. Thus, many new

materials came into existence, which were either a replica of natural materials with desired changes or completely new materials. These new engineered materials were categorized into two major groups: Composites (combination of two or more materials) and Semiconductors (materials with unusual electric properties).¹

Composites have gained much attention in recent years and a rapidly growing field of materials under this category is Inorganic/Organic Hybrid Materials. Inorganic/Organic (I/O) hybrid materials are the result of remarkable combination of two domains of chemistry i.e. Inorganic and Organic. Such a combination is intended to develop hybrid materials having significant properties of each component and eliminating their drawbacks. Hence this combination of dissimilar components yields multifunctional I/O hybrid materials with unusual and complementary properties, which cannot be obtained with a single material. Such hybrids are obtained either by carrying a chemical reaction between I and O components to form a new compound with different properties, or by physical mixing of the components where physical interaction of the molecules of both components results in developing new properties and decreasing their drawbacks.

The production and use of Inorganic/Organic hybrid materials is not new and, in fact, mankind has been using these materials for centuries. One example of an ancient hybrid material is Maya blue color from Mesoamerican civilization. Maya blue color is found in many Mayan archeologist sites, used in pottery, murals, and ceremonial artifacts. Through centuries, Maya blue color has maintained its bright color and is resistant to dilute mineral acids, alkalis, solvents, oxidants, reducing agents, moderate heat and biocorrosion (Figure 1). These properties of Maya blue color are very different from any other blue color used in ancient paintings or artifacts from other civilizations. In

a study by Yacaman et al.², they found that Maya blue color is actually a hybrid material.

Maya blue contains clays, mainly palygorskite mixed with smaller amounts of sepiolite and montmorillonite. Yacaman et al.² studied the Maya blue paint with high resolution transmission electron microscopy (TEM), scanning electron microscopy (SEM), electron energy loss



Figure 1: Maya blue was used in this mural representing a quetzal obtained from the Cacaxtla (Mexico) archeological site. (ref: http://srs.dl.ac.uk/arch/posters/CHIARI/maya_bari_poster/sld001.htm)

spectroscopy (EELS), and electron diffraction. They found that it contains, in addition to palygorskite, iron (Fe) nanoparticles (in elemental form and oxides) supported in an amorphous SiO₂ substrate. Further studies revealed that heat treatment of clays mixed with pigments with metal particles as impurities produced Maya blue microstructure. The encapsulation of particles in substrate is the reason of its resistant towards acids and other mild chemicals and keeps its blue color. Thus the Maya blue color is a combination of clays and metallic and oxide nanoparticles supported on a substrate (clays), which is eventually an hybrid material like modern nanocomposites.

In recent years, considerable attention has been paid to the preparation, characterization, and applications of inorganic/organic hybrid materials. The extraordinary and remarkable features of these materials make them center of attention because conventional materials do not offer such unusual properties. Most of the I/O hybrid composites, unlike traditional macroscale composite materials, are nanoscopic

with a domain size between 1-100nm.³ Because of their nano size scale, these materials also got the name of “Inorganic/Organic Hybrid Nanocomposites”. Literature shows that the term “nanocomposites” was first proposed by Theng in 1970.^{4,5} Infact, this nanosize scale of I/O hybrid composites makes them a creative alternative for obtaining new materials with unusual features like their utility and potential as catalysts, sensors, optical and electronic applications, drug delivery carriers, etc.⁶⁻¹³ I/O hybrid composites are expected to combine the chemical and mechanical resistance of an inorganic phase with the compliance and enhanced processability of an organic phase, to produce materials that are more than simply the sum of the component parts (Figure 2). This can be done effectively by designing components that can be combined at the atomic or molecular (nano) scales. As a result, I/O hybrid nanocomposites not only exhibit better mechanical strength, chemical and thermal stability, but they also offer a better control over the property

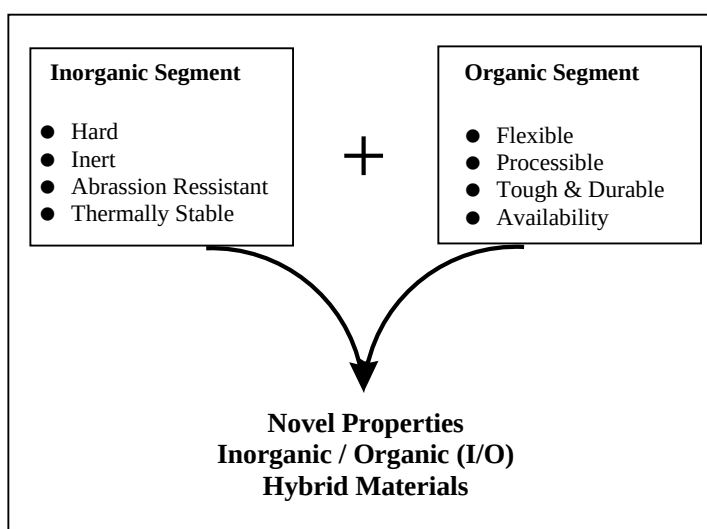


Figure 2: Schematic representation of combination of inorganic and organic segments to form I/O hybrid composites

profile of the material. Currently, several approaches exist for the preparation of I/O hybrid nanocomposites.¹⁴⁻¹⁸ The most common procedures to synthesize I/O hybrid nanocomposites are the following:⁵

1. The sol-gel method

2. Interaction of polymers and nanoparticles into layered structures
3. A combination of polymerization and formation of nanosized particles providing homogenous dispersion of an inorganic component in a polymeric matrix

Through a variety of combinations of different inorganic and organic components in conjunction with appropriate processing methods, various types of bonding can be achieved leading to new materials. The resulting hybrid composites can be quantum dots, fullerenes or metal nanoclusters dispersed in organic polymers, as well as, organic molecules, biomolecules, or enzymes embedded in inorganic matrices.¹⁹⁻²⁴ A classification of hybrid materials has been proposed according to the type of chemical interaction between the inorganic and organic components as Class I and Class II.²⁵ Class I materials are those where the interaction between inorganic and organic components is limited to weak bonds (ionic, hydrogen bonds, or van der Waals interactions), and Class II materials are the hybrids where the inorganic and organic components are linked together through strong chemical bonds (covalent, ionic-covalent or coordination bonds). Gomez-Romero, in a review, further classifies hybrid composites into three categories according to the nature of host and guest molecule.²⁶ Organic/Inorganic (O/I) materials are hybrids where the organic phase is the host to an inorganic guest, whereas inorganic/organic (I/O) composites are those with inorganic hosts and organic guests. The third category can be called as “Nanocomposite hybrids”, where none of the inorganic or organic components acts as the host or guest molecules but each part of the hybrid maintains its own structure with increased interfacial interaction due to the nanometric particle size. Based on above classifications, this thesis concentrates on

Inorganic/Organic (I/O) Hybrid Nanocomposites where organic components are incorporated as guests on an inorganic core (host).

1.2 Silicon based Inorganic/Organic (I/O) Hybrid Nanocomposites

Silicon is the second most abundant element in earth's crust (~27%). It is found in most of everyday materials around us like sand, minerals, clay, etc. The nature of the bonding that silicon makes with other elements and chemical characteristics of resulting compounds has made silicon based materials a center of attraction for chemists around the world in past decades.²⁷ Owing to unique property profile and applications of silicon based materials, a large number of groups around the globe has studied and investigated silicon chemistry extensively. Some key characteristics of silica and silicones are stability at high temperatures and resistance to age, sunlight, moisture, temperature extremes, and many solvents. Because of these characteristics, there is a widespread use of silicone materials in personal care, medical and industrial products like

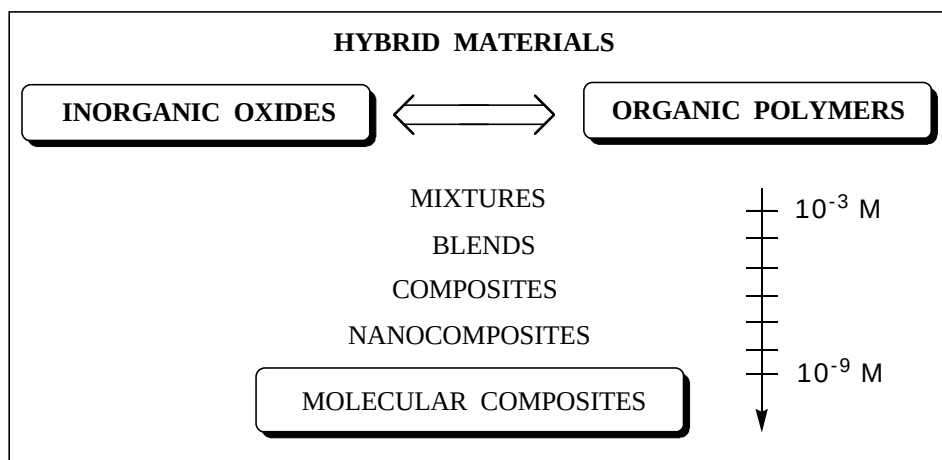
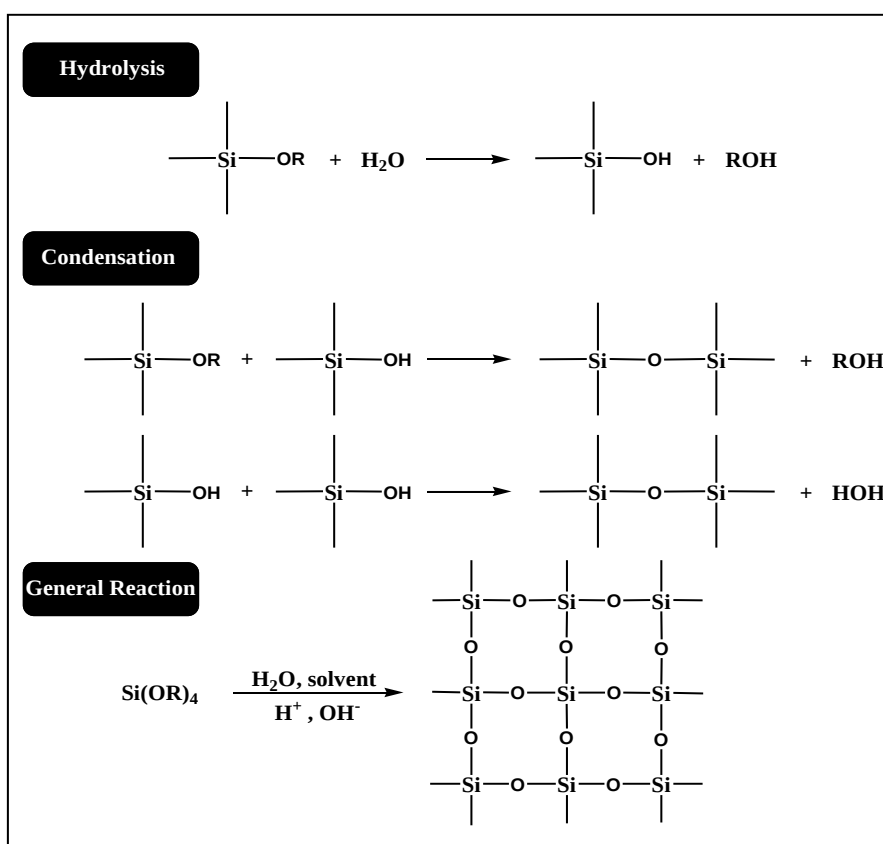


Figure 3: Illustration of the domain size in hybrid materials. (Reproduced from ref. 28)

cosmetics, medicine, medical devices, food processing, computers and chip making, waterproof coatings, lubricants etc.

The physical and chemical properties of inorganic compounds like silanes or siloxanes can be greatly enhanced by introducing organic groups into the inorganic framework. This can be achieved either in the form of physical mixtures of inorganic and organic molecules or macromolecules, or by covalently attaching the organic fragment to silicon. The properties of resulting inorganic/organic (I/O) hybrid composites are influenced by each of the components, their integration (physical or chemical), and their domain size.²⁸ By a reduction of the domain size, improved physical and chemical properties can be achieved as it increases the interfacial surface area. The demand for improved standards of performance triggered research in the area of nanocomposites, hybrid materials with domains on the nanometer scale. Figure 3 illustrates the range of domain size in hybrid materials. A widely used approach to achieve such nanocomposites is the sol-gel technique. The sol-gel method is a convenient procedure for the preparation of dispersed materials, which are often called “cереamers” and was initially used to prepare inorganic materials like glasses and ceramics. According to Hench and West,²⁹ interest in the sol-gel processing of inorganic ceramic and glass materials began as early as the mid-1800s with Ebelman’s^{30,31} and Graham’s³² studies on silica gels. They observed that the hydrolysis of tetraethyl orthosilicate (TEOS), $\text{Si}(\text{OC}_2\text{H}_5)_4$ under acidic conditions yielded SiO_2 in the form of a “glass-like material”. Fibers could be drawn from the viscous gel, and even monolithic optical lenses or composites formed. However, a major drawback of this technique was extremely long periods (~ one year) to dry the gels. In present time, with continuous research over the centuries, the drying period has

come down to weeks even days. The term “creeamer” was apparently first used by Wilkes et al.³³ and these materials were also termed as “ormosils” or “ormocers” by Schmidt et al.³⁴ The sol-gel method is based on polymerization of inorganic compounds at relatively low temperatures and involves the following stages: (1) preparation of a solution, (2) formation of a gel, (3) drying and (4) thermal treatment. The reaction is generally divided into two steps: hydrolysis of metal alkoxides to produce hydroxyl groups, followed by polycondensation of the hydroxyl groups and residual alkoxy groups to form a three dimensional network.^{29, 35-38} A general reaction path is shown in Scheme 1. Composites prepared in this way can vary from soft and flexible to brittle and hard



Scheme 1: A general reaction path of sol-gel approach (Reproduced from ref. 39)

materials depending on the chemical structure of the organic components and the overall composition ratio of organic to inorganic. Inorganic/Organic (I/O) hybrid gels prepared via sol-gel method have several uses in today's applicable technologies. Some current applications and properties of these materials are as follows:

1. Modified glasses and ceramics (Crucibles for high purity Si, Fiber optics etc.)
2. Scratch and abrasive resistant coatings for polymeric materials, metals, and glass surfaces
3. Thin films, adhesives and contact lens materials
4. Catalyst and porous supports, adsorbents
5. Chemical and biomedical sensors
6. Electrical and non linear optical materials

The research, results, and applications of sol-gel materials have been revised and reported by several groups and a special issue in ACS journal "*Chemistry of Materials*" was dedicated to this field.³⁹

Sol-gel chemistry offers versatile products with a number of very useful applications; however, it has some limitations. The gels produced via sol-gel route are highly cross linked networks, which offer very low or no control over further alteration or modification of these hybrid composites. Inorganic/organic (I/O) hybrid nanocomposites prepared in liquid form or solids, soluble in a variety of solvents (polar or non-polar) can be highly desirable for certain applications. A different approach can be used to synthesize such hybrid nanocomposites, where organic moieties (small molecules or oligomers) can directly be attached to inorganic cores through strong covalent bonds by chemical reactions in presence or an appropriate catalyst. This approach can allow the

formation of inorganic/organic hybrid molecules or macromolecules followed by a network formation via intermolecular physical attractive forces (hydrogen bonds, van der Waals interactions etc.). The hybrid nanocomposite networks synthesized by this direct method are flexible enough for further modification or functionalization as the molecules are connected through weak bonds.

The thrust of my research is to synthesize and analyze inorganic/organic hybrid materials by this direct approach and study their properties and possible applications. We chose siloxanes and polysiloxanes as the inorganic cores for formation of such hybrids. Siloxanes or polysiloxanes are silicon containing compounds or macromolecules, in other words silicones, referring to a structure that contains repeating silicon-oxygen groups in the backbone, side chains or cross links regardless of the substitution on the silicon atom. The presence of certain organic groups attached to the silicon atom in silicones or polysiloxanes enhances physical, chemical and mechanical properties.⁴⁰

This thesis focuses on synthesis, characterizations, and possible applications of inorganic/organic (I/O) hybrid nanocomposites, where siloxanes or polysiloxanes, mainly cyclic siloxanes, are used as inorganic cores. The choice of siloxanes as inorganic frameworks has a couple of reasons, which will be addressed in the next section and then again in later chapters.

1.2.1 Cyclic and cubic siloxanes as cores for I/O Hybrid Materials

Cyclic and cubic siloxanes offer the opportunity to develop a wide range of hybrid materials. Structural formulas of 1,3,5,7-Tetramethylcyclo-tetrasiloxane (D_4^H) and Octakis (dimethylsiloxy)-T8-silsesquioxane ($Q_8M_8^H$) are shown in Figure 4. *“They can act as a multidirectional core for the construction of silica network. Through their many Si vertices, these siloxanes may be covalently linked to a plethora of organic functional groups creating libraries of single-phase inorganic/organic hybrid composites”.*⁴⁰⁻⁴⁹ The organic component can be changed accordingly by means of an appropriate polymerizable R group. A further expansion of these molecules or oligomers can yield hybrid

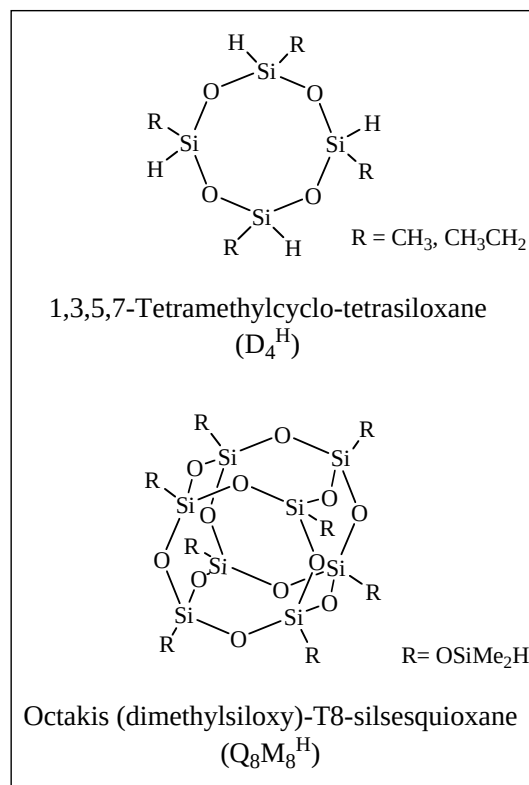


Figure 4: Structural formulas of D_4^H and $Q_8M_8^H$

polymers and dendrimers offering potential uses as structural materials for medical, dental, aerospace, electronic, magnetic recording, drug delivery (etc.) applications.

1.3 Applications of siloxane based I/O Hybrid Nanocomposites

The advantages and applications of siloxane based inorganic/organic (I/O) hybrid nanocomposites can be numerous. Their applications can range from coatings,

adhesives, adsorbents, membranes and films to electric and NLO materials, catalyst and porous supports, optical and contact lenses, biosensors, drug delivery carriers, and POSS materials. We synthesize and study these I/O hybrid nanocomposites for three major purposes: to use as nanoreactors for generation, characterization, and applications of transition metal nanoparticles, for their possible use as drug delivery carriers and as precursors to POSS materials. Therefore, only these applications of I/O hybrid materials produced by us will be discussed in details.

1.3.1 I/O Hybrid Nanocomposites as nanoreactors for generation of metal colloids

A significant application of siloxane based I/O hybrid materials is that they can be used as nanoreactors for the generation and stabilization of metal nanoparticles. Before going into details of this property, a brief introduction to nanotechnology and metal nanoparticles is necessary.

Nanotechnology is the ability to design and control the structure of an object at nanoscale. A nano refers to one-billionth of a unit. For example, one nanometer is approximately the length of three to six atoms placed side-by-side, or the width of a single strand of DNA. To get a simple and better idea of nanoscale, we can consider that the thickness of a human hair is between 50,000 and 100,000 nanometers. According to modern definitions, any material with a grain size range between 1-100 nm can be stated as nanomaterial. Much of today's nanoscale research is designed to reach a better understanding of how matter behaves on this small scale. Unlike most of today's conventional production methods, where desired materials are carved down from a bigger piece, nanotechnology builds from the molecular level up. Building atom by atom

enables increased product complexity, exact composition, and eliminates virtually all waste. Nanocrystalline materials and nanocomposites are subject of current interest because of their unusual properties.⁵⁰⁻⁵⁸ As mentioned above, the properties of nanocomposites often differ from their bulk properties. The reasons for these are confinement of electronic and vibrational excitation, quantum size effect and large surface to volume ratio.⁵⁹⁻⁶³ Although a great amount of research in nanoclusters has been carried out from both theoretical and experimental standpoints, the greatest challenge still is to find out an effective synthetic route. The fundamental challenges in nano-structured materials can be described as follows:

- Ability to control the scale (size) of the system
- Ability to obtain the required composition
- Correlation of the size of building blocks in nano-structured materials as well as the influence of microstructure on the physical, chemical and mechanical properties of this material.
- Transfer of developed technologies into industrial applications including the development of the industrial scale of synthesis methods of nanomaterials and nanostructured systems.

Metal particles in the nanometer range exhibit quantum mechanical properties that make them promising candidates for applications in nanotechnology.⁶⁴⁻⁷³ Today, metals are among the most important catalysts, being used on a large scale for refining of petroleum, conversion of automobile exhaust, hydrogenation of carbon monoxide, hydrogenation of fats, and many other processes. Transition metals are known to have very efficient catalytic properties for many important reactions. Since

nanoparticles have a large surface area as compared to their volume, their potential use in catalysis is obvious.⁷⁴⁻⁷⁸ The smaller the metal particles, the larger the fraction of the metal atoms that are exposed at surfaces, where they are accessible to reactant molecules and available for catalysis. Some drawbacks and challenges of metal nanoclusters are that the metals are often expensive and naked metal nanoclusters are highly unstable and tend to aggregate to form bulk, which eventually kills their catalytic efficiency. Therefore, they have to be kept in a finely dispersed form as particles on a high-surface area porous support to prevent aggregation. When this resultant material is applied as a catalyst, it may constitute only about 1 wt% of the catalytic material i.e. metal. The synthesis and patterning of nano-sized metal particles into organized structures is a potential route to stable and useful metal nanoclusters. Several approaches have been used to obtain three-dimensional aggregates of metal nano-particles.⁷⁹⁻⁸³ Considerable attention is now being focused on tailoring the chemical composition and morphological control of particles for possible applications.

In recent years, inorganic/organic hybrid composites have acquired a great interest for stabilization and controlling the morphology of nano-sized metal particles and as precursors for their self-assemblies.⁸⁴⁻⁸⁷ In solution, isolated nanoparticles with narrow size distribution can be synthesized in a classical way using low molecular mass molecules to stabilize the growing colloidal structure or in a more controlled way via the synthesis in confined reaction media such as microemulsions or block copolymer micelles. However, certain applications may require a solid polymeric matrix in order to combine the special colloidal effects with the mechanical properties of the surrounding polymer. In such case, solid polymeric materials such as polymer gels can be directly

used as a matrix for the formation of inorganic nanoparticles but the practical use of these composites has been elusive so far. The formation of inorganic colloids within the solid polymer matrices yields composite materials with exciting and promising properties, but it does not allow for an independent control of the number density or distribution and size of the inorganic particles. It is desirable to be able to create nanoparticles with a defined concentration and size inside a polymeric matrix and to be able to fully characterize the nanometer scale structure of such hybrid materials. The disadvantages of systems mentioned above can be overcome by the combination of a well-defined template and a polymer matrix prior to the synthesis of nanoparticles inside the whole system

A significant application of siloxane based I/O hybrid materials is that they can be used as versatile stabilizers for the stabilization of metal nanoparticles and cyclic and cubic siloxanes offer considerable potential as building blocks for such I/O hybrid materials or template matrix. With a choice of organic groups that can be attached

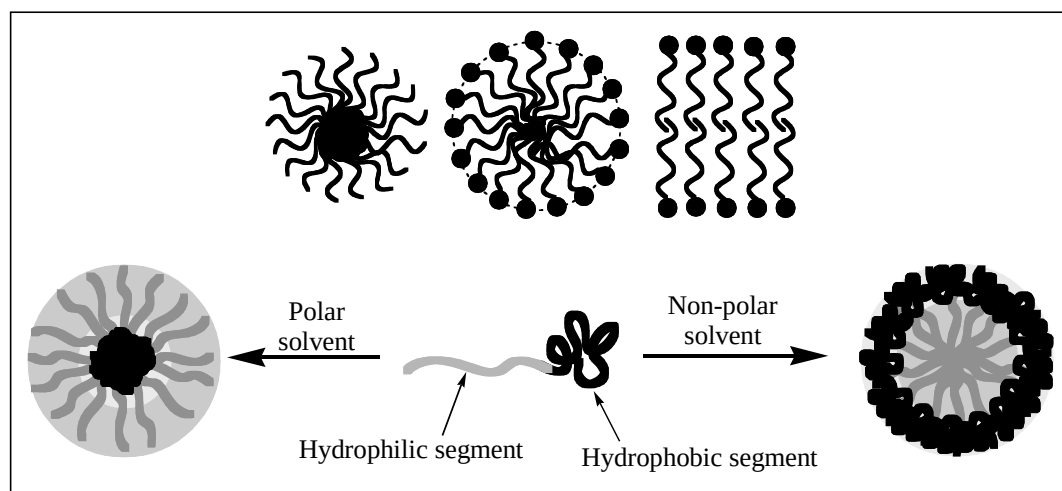


Figure 5: Classical schematic representation of spherical and lamellar micelles, and phenomena of micellization in polar and non-polar solvents

to siloxane cores, and an appropriate solvent, micelles can be formed acting as nanoreactors to confine the metal nanoparticles. Micellization is known to occur in

solutions of low molecular weight amphiphiles (or surfactants) above a concentration known as the critical micelle concentration (cmc).^{88, 89} The conventional micelles are usually produced by block copolymers. Block copolymers consist of two different types of polymer chains, which are covalently bonded together. When dissolved in a solvent, which is a good solvent for one block and a poor solvent for the other, micelles are formed, or we can say that block copolymers in a selective solvent have a tendency to self-assemble at surfaces and into micelles.⁹⁰⁻⁹⁶ A schematic representation of formation of a block copolymer micelle in selective solvent is shown in Figure 5. In an aqueous solution, the amphiphilic property of block copolymers composed of hydrophilic and hydrophobic segments causes the hydrophilic segments to extend into the aqueous solution collapsing the hydrophobic segments. As a result, micelles with core-shell structure are formed through the segregation of insoluble blocks into the core, which is surrounded by hydrophilic shell extended into the solution. Metal nanoparticles can be created within self-assembled nanoreactors, such as micelles or vesicles, and then patterned into superstructures through an additional self-organization step. For self-assembly to be possible, the forces between molecules must be much weaker than the covalent bonds between the atoms of a molecule. The weak intermolecular interactions responsible for molecular ordering include hydrogen bonds, coordination bonds in ligands and complexes, ionic interactions, dipolar interactions, van der Waals forces, and hydrophobic interactions.⁹⁷ Cyclosiloxane cores, with covalent addition of hydrophilic organic entities like ethylene glycol, can behave in the same way. The weak intermolecular attractions form a network, which acts as nanoreactors for preparation of

metal nanoparticles inside their micelles creating materials and templates of various distinct and useful properties.

1.3.2 I/O Hybrid Nanocomposites as Drug Delivery Carriers

In recent decades, considerable research has been focused on drug delivery systems. Controlled drug delivery technology represents one of the most rapidly advancing areas of science in which chemists and chemical engineers are contributing to human health care. Controlled drug delivery systems have several advantages over conventional dosage forms like improved efficiency, reduced toxicity, and improved patient compliance and convenience. Such systems often use synthetic polymers as carriers for the drugs.⁹⁸

Any drug administered to the body orally or by injections needs a carrier. The need of a carrier for drugs has a number of reasons. First, if the drug is toxic to the affected cells, it is toxic to the healthy cells of the body too and will damage the normal cells on its way. For example, acute renal toxicity is reported for doxorubicin (an anticancer drug) toxicity. The reason for this toxicity is that an intravenously administered anticancer drug is distributed throughout the body and only a small concentration is reached in the tumor tissue at the expense of massive contamination of the rest of the body. As cancer fighting drugs are toxic to both tumor and normal cells, they cause several important side effects. Secondly, a drug taken orally or by injections has to travel through the whole body before reaching the point of action. Without a proper protective carrier, the drug will be desolated by the body's immune system and will be excreted from the body through kidneys or digestive system as a waste. This is

true for almost any drug used to cure any kind of disease. Another important reason is that most drug molecules need to be dissolved in the aqueous environment of the body and freely diffuse within that medium before they can act on their target receptors. Carriers that can protect drug molecules from this aqueous living environment for a period of time are necessary to administer such drugs. Among different drug carriers used for drug delivery, self-assembled block copolymers are the most vastly studied and used class of synthetic materials.⁹⁹⁻¹⁰⁵ The reason for the rising interest in block copolymers as drug delivery carriers is their multifunctional nature that appears to fulfill several tasks required for an ideal carrier capable of selective drug delivery at different levels. For example, block copolymers can be functionalized by hydrophilic segments to facilitate the solubility in the aqueous environment of body and form core-shell micelles protecting drug molecules at the core. Furthermore, modification of block copolymers with “intelligent” functional groups that can respond to a change in their surroundings in a certain way can allow designing responsive carriers for some applications. Examples include thermo and pH responsive drug delivery carriers for anticancer drugs.¹⁰⁶⁻¹¹⁰ The small size of block copolymers (micro or even nano) is another key characteristic making the treatment possible at cellular levels. Despite all these magnificent properties, use of block copolymer as drug delivery carriers still has its limitations which are discussed in the next paragraph.

There is a significant clinical need for novel method for chemotherapy, which can offer improved sensitivity, specifitivity, and cost-effectiveness. Most animal cells are 10,000 to 20,000 nanometers in diameter. This means that nanoscale drug carriers (having at least one dimension less than 100 nanometers) can enter cells and the

organelles inside them to interact with DNA and proteins. Carriers developed through nanocomposites may be able to detect and cure disease in a very small amount of cells and tissues. Therefore, the potential for the nanostructures to enter and analyze single cells suggests that they could meet the need for necessary tools of being extremely sensitive to detect and cure molecular changes in a small percentage of cells. For chemotherapy, approaches that can kill affected cells while leaving non-target tissues unaffected are highly desirable.

A material has to meet many criteria to be an ideal drug delivery carrier. Among them, biocompatibility, hydrophilicity, stability, long circulation, and controlled release are some of the most important factors. An important consideration in designing drug delivery carriers for any controlled release mechanism is the fate of the carrier after drug release. Materials that are naturally excreted from the body are desirable for many controlled release applications. A carrier has to be biodegradable in order to break apart into smaller segments inside the body to be excreted out as waste after delivering the drug. These carriers may be excreted directly via the kidneys or may be biodegraded into smaller molecules that are then excreted. Not only the carrier is desired to be non-toxic for body tissues, but the smaller molecules that it degrades into should also be non-toxic. Most of the block copolymer carriers are either not biodegradable, or they degrade into smaller molecules that are toxic for the body. Moreover, due to poor stability of their micelles while circulating in the body causes a higher concentration of drug to be leaked out before reaching the point of action thus causing contamination of healthy tissues. An additional drawback of this poor stability is that they cannot be used for targeted and controlled drug delivery.

Siloxane based inorganic/organic (I/O) hybrid nanocomposites appear to be an exciting candidate for drug delivery carriers. Hydrophilic modification, particularly by introducing poly(ethylene glycol) by covalent linking of the carrier surfaces facilitates the micellization and solubility in aqueous environment of body, and drug can be loaded into the cores of these micelles. Such functionalization also prolongs the half-life of the carriers during circulation in blood by reducing opsonization and thus minimizing carrier clearance in RES organs such as liver, spleen, and lung. This provides the carriers a long-circulating stealth characteristic, which endows them a more valuable effect in cell targeting. These I/O hybrids can be further modified with pH or thermo responsive functional groups for the purpose of targeted delivery. Treatment of cancer can be taken

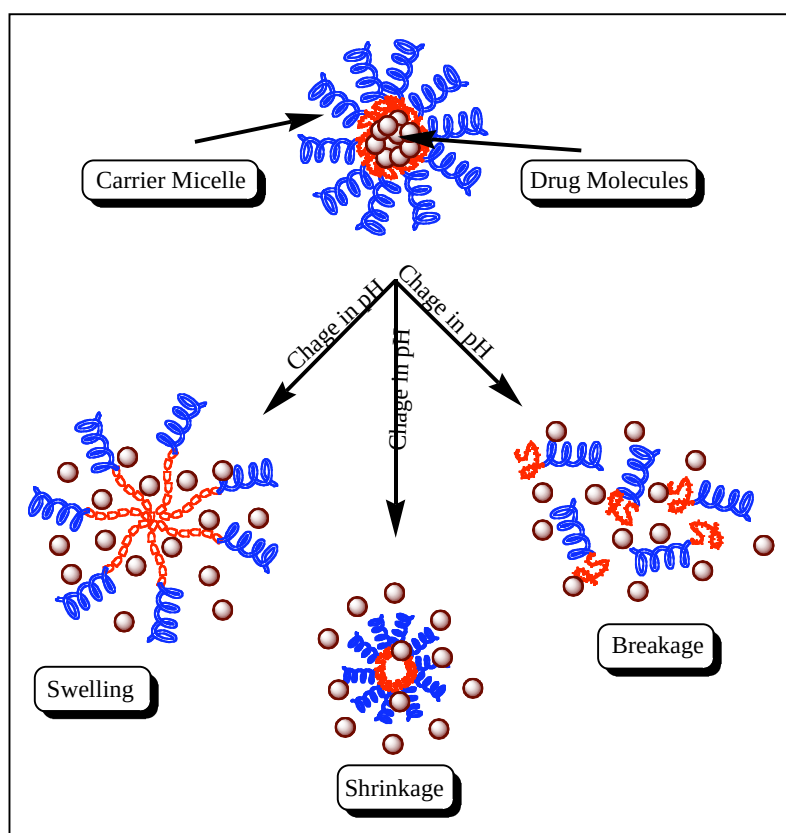


Figure 6: Release of drug molecules from the micelle core as a result of micelle swelling, shrinkage or collapse due to a change in pH of surrounding tissues

as an example here. The tumor extracellular pH is a consistently distinguishing phenotype of most solid tumors from surrounding normal tissues. The measured pH values of most solid tumors in patients, using invasive microelectrodes, range from pH 5.7 to 7.8 with a mean value of 7.0. More than 80% of these

measured values are below pH 7.2, while normal blood pH remains constant at 7.4.^{111, 112} The I/O hybrid drug carriers, with the addition of pH responsive groups that respond to a slight change in pH below 7.4 causing the carrier micelle to shrink, swell or collapse and thus change morphology and releasing the drug, can be used as targeted drug delivery carriers. A hypothetical example of such a release is illustrated in Figure 6. The ease and compliance of functionalization of siloxane based inorganic/organic (I/O) hybrid nanocomposites makes them interesting and potential precursors for constructing an exciting and useful class of drug delivery carriers. The biodegradability and non-toxicity of such carriers remain to be established.

1.3.3 I/O Hybrid Nanocomposites as Precursors to POSS Technology

A new versatile and fast growing class of polymers in recent decades is Polyhedral Oligomeric Silsesquioxane (POSS) materials.^{6, 43, 113, 114} These are cage like hybrid molecules of silicon and oxygen ($\text{RSiO}_{1.5}$) with similarities to both silica (SiO_2) and silicone (R_2SiO).¹¹⁵ POSS molecules can be thought of as the smallest particles of silica possible. However, they have one advantage over silica that each POSS molecule contains covalently bonded reactive functionalities suitable for polymerization or grafting POSS monomers to polymer chains or dendrimers.

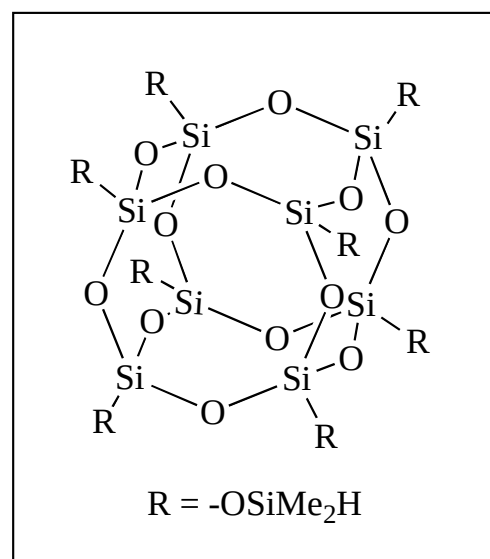


Fig. 7: Structural formula of Octakis (dimethylsiloxy)-T8-silsesquioxane ($\text{Q}_8\text{M}_8^{\text{H}}$)

Each POSS molecule may be decorated with a selection of nonreactive organic functionalities for solubility and compatibility of the POSS segments with the various polymer systems. The growing interest in POSS technology owes to the numerous novel characteristics of these materials when compared with conventional polymeric materials. POSS molecules can be mixed, chemically or physically, with conventional polymeric materials to highly enhance these properties. Enhancements in the physical properties of polymers incorporating POSS segments result from POSS's ability to control the motions of the chains while still maintaining the processability and mechanical properties of the base resin. This might be a direct result of POSS's nanoscopic size and its relationship to polymer dimensions. Following are some key enhancements in the property profile of materials that can be achieved by POSS materials:

- ◆ Higher Mechanical Stability
- ◆ Increased T_g
- ◆ Reduced Flammability
- ◆ Extended Temperature Range
- ◆ Lower Thermal Conductivity
- ◆ Higher Thermal Stability
- ◆ Thermoplastic or Curable
- ◆ Enhanced Blend Miscibility
- ◆ Oxidation Resistance

The chemical diversity of POSS technology is very broad and a large number of POSS monomers and polymers can be synthesized using cyclic and cubic siloxanes as cores. Organic functional groups, through an appropriate choice, can be

covalently attached to cyclic and cubic siloxanes to create a library of desired POSS materials expandable to higher generations.

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CHAPTER 2

2

Cyclic Siloxane (D_4^H) Based I/O Hybrid Composites and their Applications for Generation and Stabilization of Metal Nanoparticles

2.1 Synthesis of Nanoparticles

Synthesis of metal nanoparticles has gained a rapid increase in interest by scientists from different fields of sciences like chemistry, physics, and biology in the 20th century. The reason for this significant attention is the unique properties of nanoparticles and their fascinating potential use in various applications.¹⁻⁵ Metal nanoclusters acquire these unique properties due to their “nano” size, which enables them of “quantum size effect” and tremendously increases their surface area as compared to their volume. As the size of metal decreases from bulk metal to atomic level, the mobility of its electrons is restricted due to the confinement of available space.

The restriction in mobility and confinement of space causes a huge difference in excitation or transition energy levels between molecular metal and the bulk. The energy of electronic excitation of an isolated metal atom is considerably higher than the energy of intermolecular transition of corresponding macro metal. Therefore, due to the small size, metal nanoparticles acquire unique spectroscopic and optical properties, which are termed as “quantum size effect”, and nanoparticles having quantum size effect are called as quantum dots.^{1,2} Quantum dots can be used as fluorescent sensors in

biotechnology and diagnostic agents in medical technology.⁶⁻¹⁵ Nanoparticles are also bringing revolutionary enhancements to electronics and computer industry everyday. Owing to high surface area, metal nanoparticles act as efficient and highly active catalysts as compared to conventional metal complexes and supported metal catalysts. Moreover, metal nanoparticles can provide better control over selectivity of product and activity and recyclability of the catalyst.

There are two distinct ways to prepare metal nanoparticles, which are by subdivision of bulk metals (a physical method) and by the growth of particles starting from metal atoms, which are obtained from molecular or ionic precursors (a chemical method).¹⁶⁻¹⁸ The former method is also termed as “Top Down Method” and the later as “Bottom Up Method”. The latter preparative method is more suitable to obtain small and uniform nanoparticles than the former and is widely used. Figure 1 illustrates a graphical representation of the preparation of metal nanoparticles by above two methods. Synthesis of nanoparticles by bottom up method generally requires two steps. (1) The generation of zero valent metal nanoparticles and (2) the stabilization of these nanoparticles by some surfactant to prevent them from aggregation.

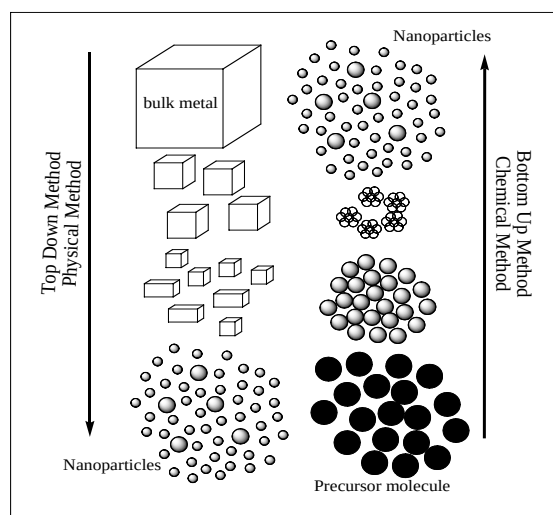


Figure 1: Graphical representation of preparation of metal nanoparticles by top-down and bottom-up methods. (Reproduced from ref. 16)

Synthesis of nanoparticles can be obtained by various methods leading to various particle size distributions. Nevertheless, whatever the method used, a stabilizing

agent is always necessary to prevent the aggregation of the colloids. Five general synthetic methods are mainly used in the literature to synthesize transition metal colloids:

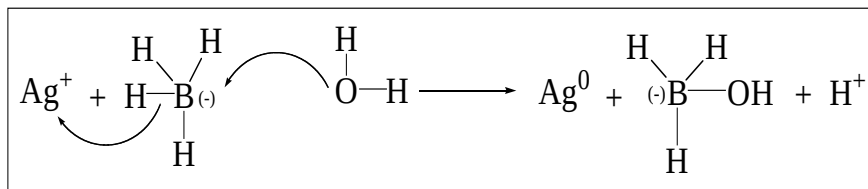
- i. Chemical reduction of transition metal salts.
- ii. Thermal, photochemical, or sonochemical decomposition.
- iii. Ligand reduction and displacement from organometallics.
- iv. Metal vapor synthesis.
- v. Electrochemical reduction.

The most widely used method to generate colloidal suspensions or colloidal powders of metals is the reduction of transition metal salts.

2.1.1 Chemical Reduction of Metal Salts

Reduction of metal salts in solution is generally a very simple method to implement in order to get narrow size distributed metal nanoparticles. A wide range of reducing agents can be used to obtain colloidal materials. These reducing agents may include gases such as hydrogen, carbon monoxide, or hydrogen sulfide; hydrides or salts such as sodium borohydride, potassium borohydride, or sodium citrate; or oxidable solvents such as alcohols or glycols.

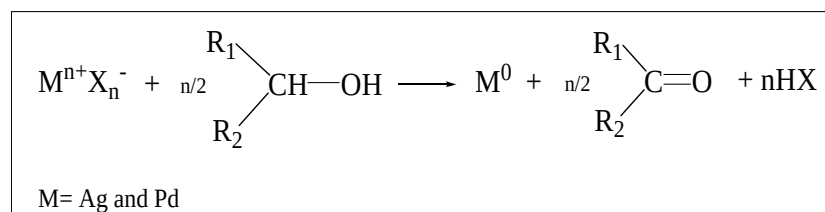
The most reliable and widely used method is reduction of metal salts by borohydrides (NaBH_4 or KBH_4) in aqueous medium in the presence of a stabilizing agent



Scheme 1: Reduction of silver ion to silver ions to silver colloids by sodium borohydride

such as water soluble polymers.¹⁹⁻²⁸ The water is then evaporated and the salt obtained is redispersed in organic solvent.²⁹ This method provides metal particles with a very narrow size distribution. Many groups use this method to synthesize nanoparticles of Au, Ag, Pt, Pd, or Cu.³⁰⁻³⁷ Scheme 1 shows a general route of reduction of metal salt by borohydride. Although this method produces very fine nanoparticles, it has some disadvantages. Boron contamination of the particles is one big disadvantage of this method. Another drawback of this method is the need of stabilizing agent in high concentrations, which limits the growth of generated nanoparticles and thus providing a poor control of particle size.

Reduction of metal salts to metal nanoparticles in aqueous alcohols is another extensively used method for generation of metal colloids. In this case, alcohol is used as a solvent, and as a reducing agent as well. Polymers or oligomers such as polyvinyl alcohol (PVA), polyvinylpyrrolidinone (PVP), or polyvinyl ether (PVE) are



Scheme 2: Formation of Metallic nanoparticles in alcohol media.

(Scheme reproduced from ref. 46)

used as the stabilizing agents for the metal particles.³⁸⁻⁴⁵ Most common used alcohols for this purpose are methanol, ethanol, or 2-propanol and synthesis of colloids is achieved by reducing the metal salt in alcohol by refluxing. Many groups have used this method to generate colloids of Rh, Pt, Pd, Os, or Ir.⁴⁶⁻⁵⁰ A general schematic representation is shown in Scheme 2.

Another method of chemical synthesis of metal nanoparticles is the chemical reduction of metal salts in liquid polyols under different reaction conditions by

polyol process. In the polyol process, a metallic compound is dissolved in a liquid polyol (usually ethylene-glycol), and then the experimental conditions are adjusted to achieve

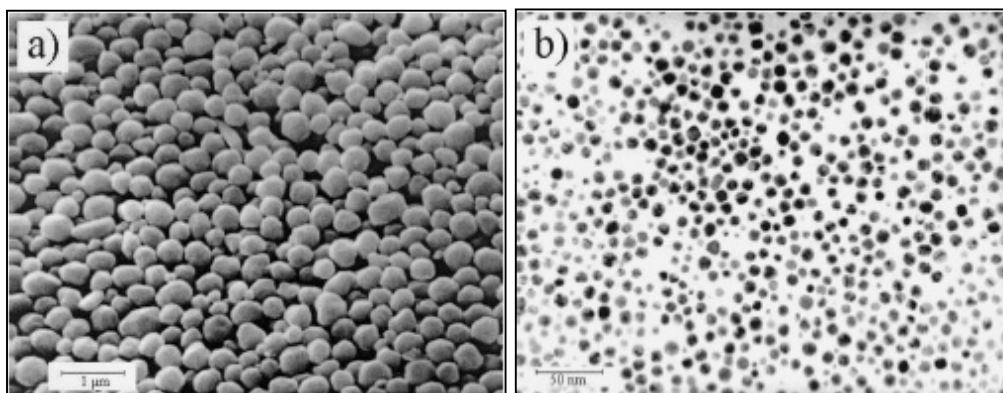


Figure 2: Micrographs of gold particles synthesized from HAuCl in ethylene glycol at

120 °C. (a) Submicronic gold and (b) colloidal gold. (Pictures taken from ref. 62)

the reduction of the metallic precursor by the polyol, atomic metal nucleation and metal particle growth.⁵¹⁻⁵⁵ A rigorous control of the different reaction parameters such as temperature, type, amount and order of addition of reactants, allows control of the size, shape and size distribution of the particles. Examples of metal particles synthesized in this way include Ag, Au, Ru, Rh, Cu.⁵⁶⁻⁶¹ Figure 2 shows spherical silver particles synthesized by polyol process by Bonet et. al.⁶²

2.1.2 Stabilization of Metal Nanoparticles

The biggest challenge in synthesizing metal nanoparticles is to prevent them from agglomeration. Naked metal particles have high surface energies and thus very unstable. The instability rises due to van der Waals forces among metal atoms that pull them together and cause them to aggregate into bulk metal. In order to stop the aggregation, some kind of repulsive force against van der Waals forces or a stabilizing source is essential. Stabilization of nanoparticles is generally achieved by two methods:

^{63,64} (1) electrostatic stabilization, in which stabilization of metal particles is achieved by electrostatic double layer formed by ions adsorbed at the particle surface and the corresponding counterions; (2) steric stabilization that can be achieved by coordination of a protective material on the particle surface. Examples of a protective material can be organic molecules or macromolecules, polymers, copolymers, ligands, solvents or surfactants. Such protective groups form a layer around the metal particle and keep them separated from each other thus preventing them from aggregation. The latter method is used extensively and it provides better control of particle size and shape with the proper choice of protective agent or in other words, stabilizer.

Ligands or polymers with some affinity for metals are often used as stabilizers. These substances also control both the reduction rate of metal ions and the aggregation process of metal atoms. In practice, reduction can be preceded or followed by the interaction between metallic species and polymers. If the reduction precedes the interaction, the structural properties of metal nanoparticles are determined only by the reduction conditions. However, if the interaction precedes the reduction, the interactive

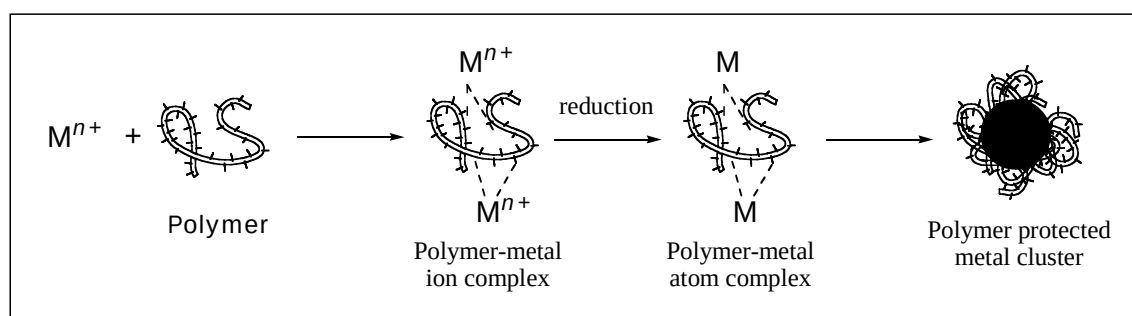


Figure 3: Schematic illustration of the reduction process of metal salt in presence of a stabilizing polymer

forces between polymers and metal ions may affect the size and structure of metal nanoparticles (Figure 3). The stabilization of metallic colloids and thus means to preserve their finely dispersed state is a crucial aspect to consider during their synthesis.

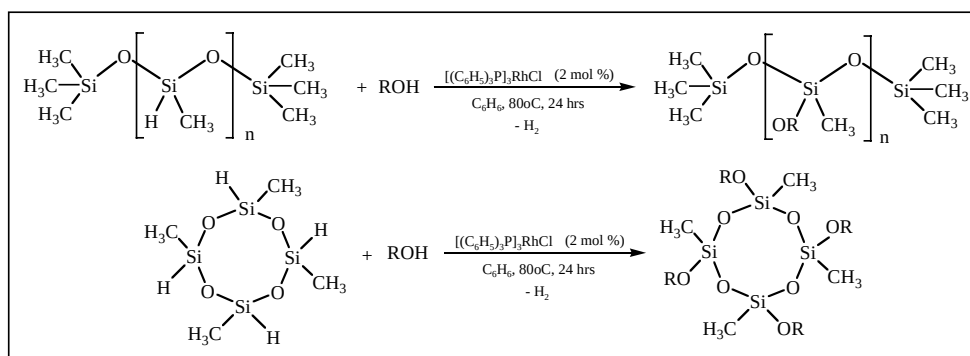
If these particles are agglomerated, this aggregation leads to the loss of the properties associated with their colloidal state. For example, during catalysis the coagulation of colloidal particles used as catalysts can lead to a significant loss of activity.

Silicon-based polymers are a very versatile class of polymers, which have been used as additives to enhance a number of physical properties such as thermal stability or water repellency, etc. Monomeric hydrosilanes and linear polymeric hydrosiloxanes have been successfully used as reducing agents for the generation of Ag, Au, Pt, Pd, and Rh nanosized particles.^{65,66} On the other hand, investigations of cyclic siloxanes as reducing and stabilizing agents for the generation of nanosized metal particles have not been much explored. In our approach, well-defined cyclic siloxane oligomers and polymers are envisioned to act as reducing agents, as well as templates to control the size, stability, and solubility of nanoparticles ranging in diameter from less than 1 up to 10 nm. The hybrid organic-inorganic materials, where cyclic siloxanes are used as the inorganic cores, may range from physical mixtures of inorganic and organic molecules or macromolecules to hybrid materials that utilize covalent attachment of the organic fragment to silicon. This can lead to highly cross-linked hybrid organic-inorganic materials containing a variable organic fragment attached to a multifunctional siloxane unit by silicon-oxygen-carbon bonds. The limited coordination of the organo-siloxane units, hydrophobicity of the siloxane core, the hydrophilicity of the organic segment, and the amphiphilic nature of the resulting organo-siloxane unit can facilitate formation of the micellar architecture through self-assembly and thus stabilize metallic nanoparticles.

2.2 Results and Discussions

2.2.1 Synthetic Strategy

In our synthetic strategy, the first step is the generation of alkoxy siloxanes by covalently attaching hydrophilic tails (polyethylene glycol) to hydrophobic cores (siloxanes). This method includes reacting a mono- or polyhydrosiloxane with a dihydric alcohol reactant such as glycols, to form alkoxy siloxanes. The reaction is carried out in the presence of a dehydrogenative coupling catalyst, such as those catalysts known to be useful for the dehydrogenative coupling of silanes. Our choice of the catalyst was the “Wilkinson catalyst ($\text{RhCl}(\text{PPh}_3)_3$)” due to its known efficiency for dehydrogenative coupling of siloxanes. This method of preparing alkoxy siloxane compounds provides for the selective alcoholysis of Si-H bonds. The dehydrogenative coupling of the hydrosiloxane occurs exclusively with the hydroxyl moiety of the alcohol

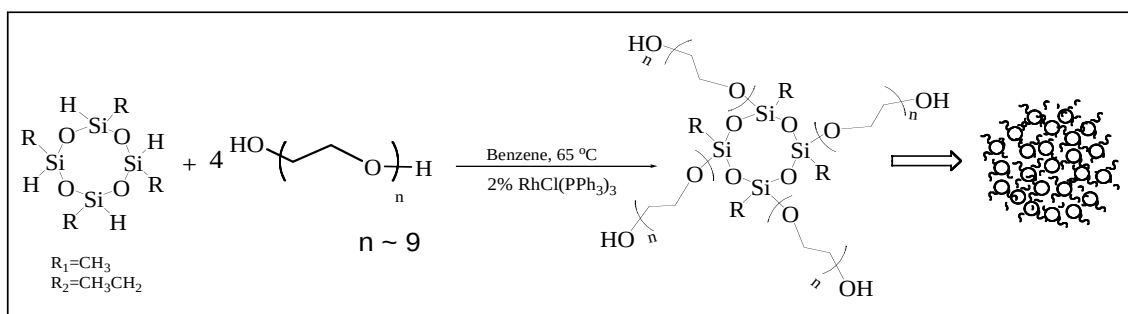


Scheme 3: Examples of alcoholysis of a linear polyhydrosiloxane and a cyclic siloxane.

reactant. So we can say that the formation of alkoxy siloxane is accomplished by the dehydrogenative alcoholysis coupling between the selectively activated Si-H bond of the hydrosiloxane and the alcohol. This reaction requires relatively anhydrous and deoxygenated conditions.

2.2.2 Formation of Alkoxy siloxanes and Siloxane Network

The reaction between 1,3,5,7-tetraethylcyclotetrasiloxane (TECTS) (0.297g, 1mmol) and polyethylene glycol (PEG) (1.6 g, 4 mmol; $M_w \sim 400$) was examined in presence of Wilkinson's catalyst $\text{RhCl}(\text{PPh}_3)_3$ (~ 0.002 g, 0.002 mmol) in benzene under positive pressure of nitrogen. Details of experimental procedures are given in the experimental part of this chapter. A general scheme of this reaction and idealized structure of the product is shown in scheme 4. The reaction mixture was heated at 65°C for about 30 hours. During the course of reaction, the reaction mixture became yellow and evolution of a gas (presumably H_2), was observed. After 30h of the reaction, complete consumption of 1,3,5,7-tetraethylcyclotetrasiloxane (TECTS) and formation of



Scheme 4: General synthetic route to poly(ethylene glycol) (PEG) substituted cyclic siloxanes. Idealized structure of the product shown.

polyethylene glycol substituted cyclic-siloxane (PEG_4TECTS) was observed in near quantitative yield by spectroscopic techniques (IR, NMR). The detailed product analysis was carried out by spectroscopic and microscopic techniques. In addition, methyl group substituted 1,3,5,7-tetraethylcyclotetrasiloxane (TMCTS) was also used in place of TECTS for such reaction under similar reaction conditions, and the resultant alkoxy siloxane i.e. polyethylene glycol substituted cyclic-siloxane (PEG_4TMCTS) produced almost similar results.

The reaction mixture was periodically monitored by IR, ^1H , and ^{29}Si NMR. ^{29}Si NMR of starting siloxane i.e. 1,3,5,7-tetraethylcyclotetrasiloxane (TECTS) shows two doublets of doublets centered at -31 ppm arising from D-type silicon (O-SiMeH-O-) units, where silicon atom is attached to two oxygen atoms. After glycolysis, the ^{29}Si NMR analysis of resulting product showed peaks centered at -56 to -57 ppm, reflecting the change in electronic environment of Si units due to the formation of new T-type (SiMe-OCH₂CH₂O) moieties, where silicon atom is attached to three oxygen atoms. No residual signals due to Si-H bonds were observed in ^{29}Si NMR of the product, indicating complete consumption of the Si-H bonds. The IR spectral analysis also confirmed the disappearance of the characteristic bands due to Si-H bonds around $\delta=2100\text{ cm}^{-1}$ region.¹¹

The resultant alkoxy siloxane was further analyzed by a number of

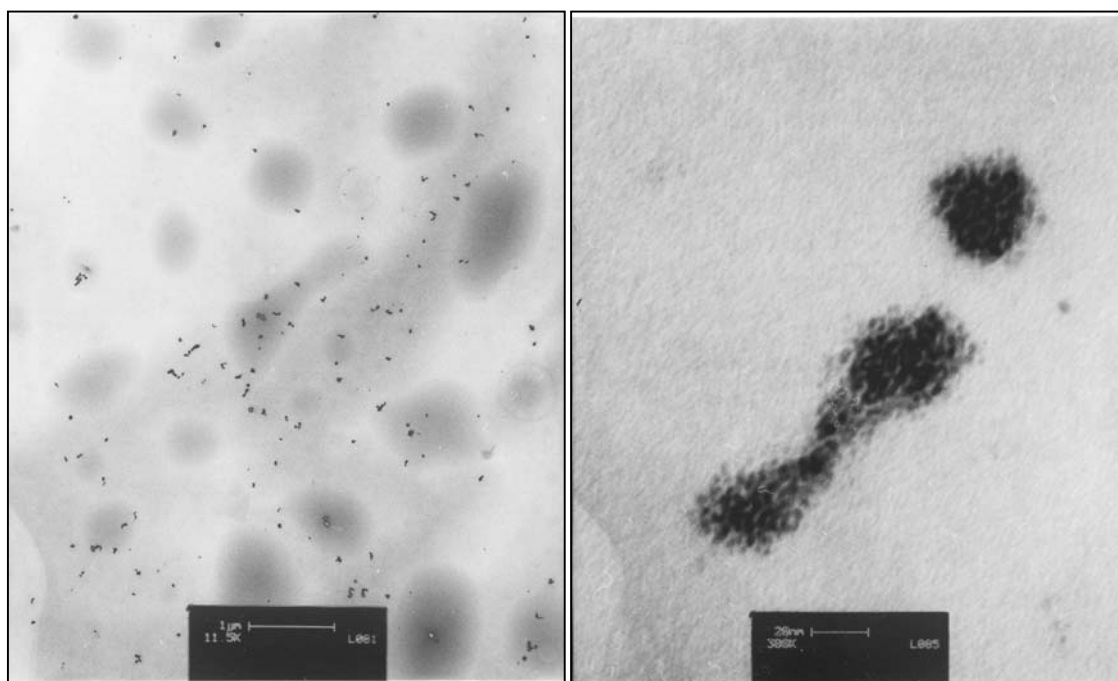


Figure 4: TEM images of siloxane network formed by using 1,3,5,7-tetraethylcyclotetrasiloxane (TETS) as core, coupled with polyethylene glycol units.

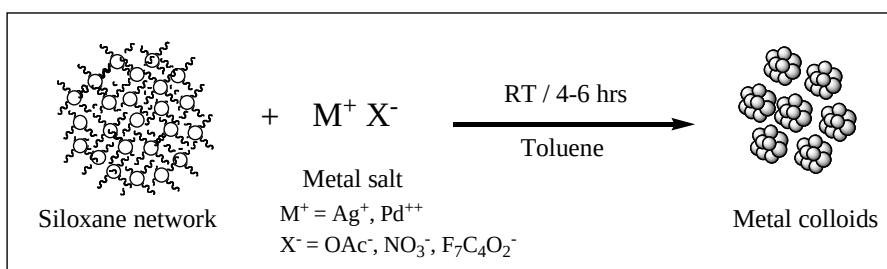
analytical techniques. The morphology of the generated polymers was investigated by Transmission Electron Microscopy (TEM) technique. The product PEG₄TECTS (0.188 gm, 0.2 mmol) was diluted in 20 ml of benzene. After stirring for 10 minutes in order to get a homogenous mixture, one drop of the solution was carefully dropped on formavar coated copper-carbon grid and solvent was allowed to evaporate at room temperature in open air. The TEM results are shown in Figure 3, which showed a well-defined micellar network with mono-dispersed particles. GPC analysis was also carried out of the acquired product. GPC plot showed multiple peaks, which corresponds to the decomposition of siloxane network on the GPC column. The reason for this decomposition may be due to the affinity or complexation of the siloxane with THF or the column.

We have used polyethylene glycol (PEG) of different chain lengths and molecular weights as the alcohol derivative for the preparation of cyclicsiloxane-polyether copolymers (alkoxy siloxanes). Our choice of polyethylene glycol has a couple of reasons. First is that the alcohol group at both ends of glycol provides a chance to expand the prepared alkoxy siloxane to further generation and thus synthesize well-defined polymers. This can be achieved by further dehydrogenative alcoholysis coupling by introducing more siloxane units to the system. Such a system may also allow the generation of dendritic structures. Second advantage of using polyethylene glycol is that the hydrophilicity and hydrophobicity of both ends of glycol can play an important role for the formation of micellar network, which can further act as a stabilizer for metallic nanoparticles.

2.2.3 Reduction of Metal Salts to Metal Nanoparticles

The PEG-substituted siloxane polymers were further used for the reduction of metal salts to metal nanoparticles. The reduction of metal salts to metal colloids in alcohol media is a known process. But the disadvantage of such system is that a surfactant or a stabilizer has to be introduced to the system in order to prevent the metal nanoparticles thus formed from agglomeration. Another disadvantage of reduction of metal salts to metal colloids in alcohols or polyols is that the reduction takes a long time and it requires harsh laboratory conditions such as high temperature or pressure. We envision that polyethylene glycol-substituted siloxane based macromolecules can not only act as the reducing agent for metal salts to metal nanoparticles, but they can also stabilize these metallic nanoparticles and create well defined self-assembled networks loaded with metal colloids. Reduction of silver acetate and palladium acetate to corresponding nanoparticles was examined using these macromolecules.

Silver acetate and palladium acetate were reduced to colloids using the product prepared by substitution of polyethylene glycol (MW=400) on a tetraethylcyclotetrasiloxane core (as mentioned in detail in section 2.2.2). The metal salts to product ratios were 1:4 (molar ratio). The reduction of metal salts to their colloids was



Scheme 5: General scheme of reduction and stabilization of metal salts to metal nanoparticles by siloxane network

monitored with UV-vis spectrometry. A general synthetic route for reduction of metal salts and their stabilization by siloxane network is shown in scheme 5. The silver acetate solution is colorless and shows a flat line in UV-vis spectrum. Silver acetate (0.05 mmol, 0.0083g) was suspended in toluene and the siloxane network was added to the reaction mixture in one shot at room temperature and followed by UV-vis spectroscopy. After 45 min of addition of polymer to silver acetate suspension in toluene, the solution color changed to light yellow. This

was the first evidence of silver colloids formation. During a period of four hours, the solution color changed to yellow and then to brown. UV-vis spectrum of the solution

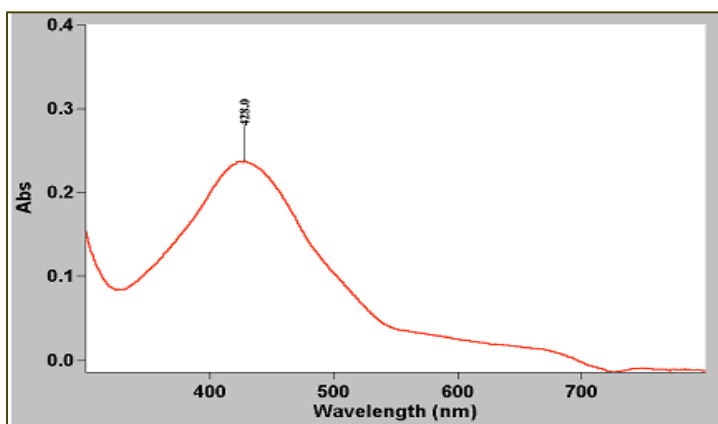


Figure 5: UV-vis spectrum of silver nanoparticles solution.

showed a peak at 423nm, which is a characteristic feature of silver nanoparticles (Figure 5). To our surprise, unlike known harsh conditions for polyol reduction process¹² of metal salts, the reduction took place under very mild reaction conditions in four hours.¹³

Palladium

acetate solution is light yellow and shows a peak around 396nm in UV spectrum. For about one hour, after addition of product to the solution, the color remained almost

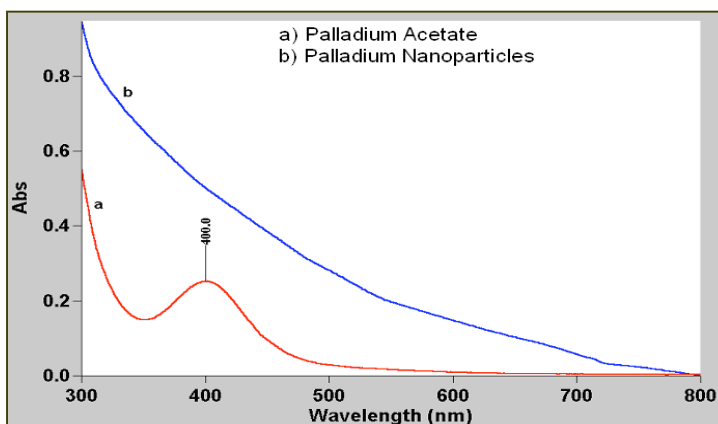


Figure 6: UV-vis spectra of a). Palladium acetate solution, b). Palladium nanoparticles solution

unchanged. Later on, after continuous stirring at room temperature, color started to change to brown. This was the first evidence of reduction of palladium acetate. During a period of about six hours, the solution color changed to brown and then to black, which was a strong evidence of palladium colloids formation. At this point, UV spectrum was taken and it showed a featureless absorption, a characteristic of palladium nanoparticles (Figure 6). The colloidal solutions of silver and palladium were quite stable. It was a strong proof that the siloxane network was not only acting as a reducing agent but also as a stabilizer, as no additional stabilizer or surfactant was added.

Colloidal solutions of silver and palladium were also analyzed by

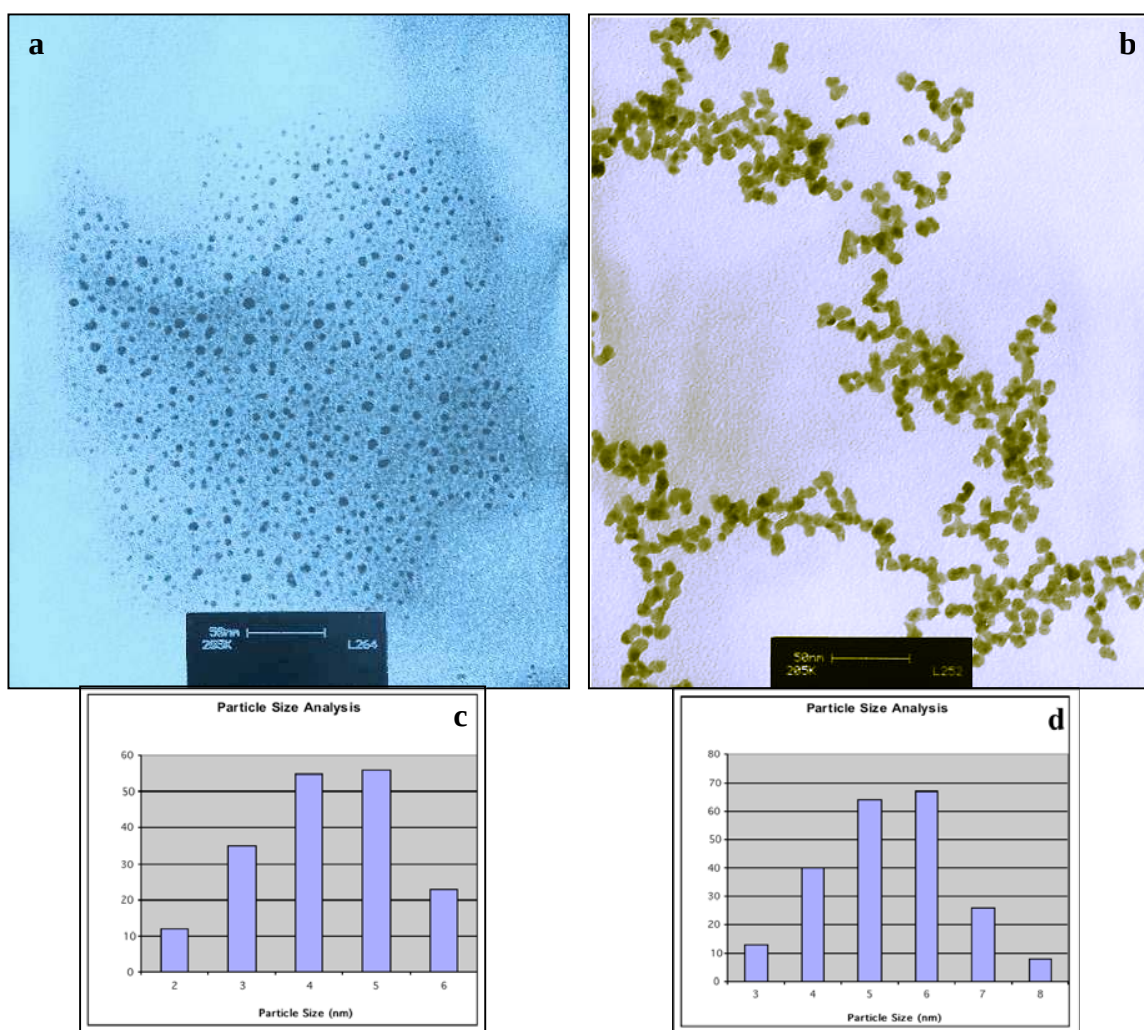


Figure 7: TEM images and particle size analysis of siloxane network stabilized a, c). Silver nanoparticles, b, d). Palladium nanoparticles respectively

transmission electron microscopy (TEM). The reaction mixtures were centrifuged for 10 min at 9000 rpm to remove un-reacted metal salt. One drop of the colloidal solution was carefully dropped on formavar coated copper-carbon grid. Solvent was allowed to evaporate at room temperature in open air for about 10 min. These images showed formation of spherical metal particles with narrow size distributions, which were stabilized by siloxane network, as no other stabilizer was added (Figure 7a, 7b). Particle size distribution analysis showed silver and palladium nanoparticles with an average size range of ~5 nm (Figure 7c, 7d). The nanoparticle solutions of silver and palladium were found to be stable for months, emphasizing the role of polyethylene glycol substituted cyclosiloxane networks as effective stabilizing agents. The resulting hybrids can be regarded as processable reservoirs of nanosized metal, which inherit the profitable solution behavior of silicon based polymers and the catalytic activity of metal colloids.

To examine the efficiency of nanoreactors, the reduction reactions were performed with varying amounts of polymers (1:4, 1:6, and 1:20; molar ratios). The

Table 1: A Comparison of Nanoreactor to Metal Salt Ratio effect on the Size of Resulting

Metal	Metal Salt to Polymer Ratio (mmol)	Reaction Time (h)	Particle Size ^b (nm)	UV-vis Absorption Maxima (nm)
Silver	1:4	4	4.7 (0.9)	428
Palladium	1:4	6	5.8 (0.9)	Featureless
Silver	1:6	2.5	4.2 (1.2)	425
Palladium	1:6	5.5	5.5 (0.9)	Featureless
Silver	1:20	2	2.6 (0.7)	434
Palladium	1:20	4	2.3 (0.5)	Featureless

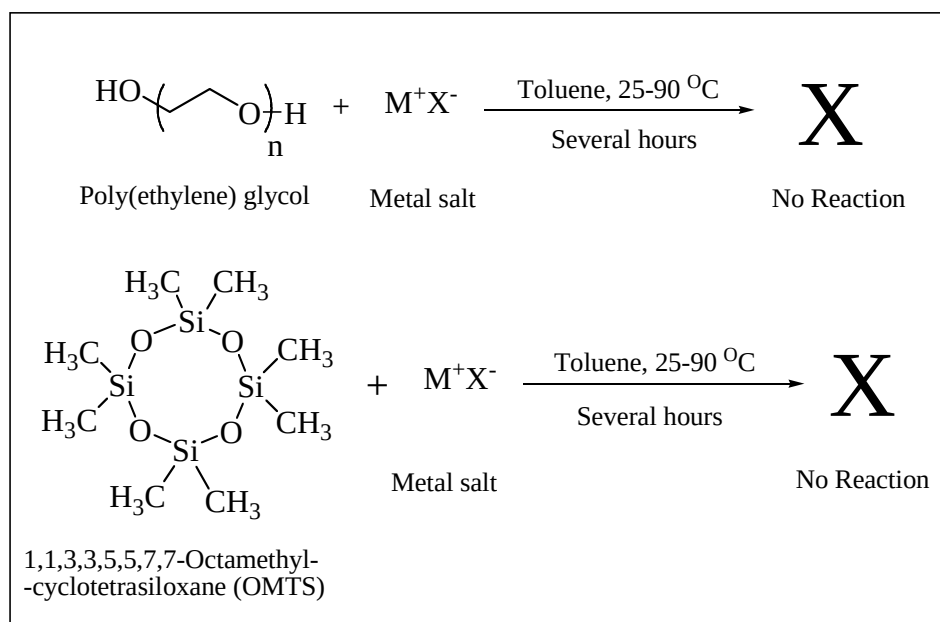
^a On average, 200 particles were counted for each particle size analysis study. ^b The figures in the parenthesis indicate the standard deviation.

results of TEM study and particles size analysis are summarized in Table 1. It was observed that with lower metal to polymer ratios, reduction reactions took longer time and visually did not produce much population of nanoparticles. By increasing polymer amounts, reduction time decreased, and a significant increase in the particle population was observed. Moreover, the particle size also decreased with higher polymer to metal salt ratios. At metal salt to polymer ratio of (1:20), reactions were very fast and led to formation of ~2.5 nm metal particles in two hours at room temperature. These studies indicate towards the potential of this methodology for generation of spherical metallic nanoparticles in various size regimes from the same nanoreactor (polymer).

The reduction of silver and palladium acetates in this manner led us to the assumption that this is a “polyol-like process”. The cyclosiloxane core was completely substituted by glycol units as confirmed by IR and NMR data spectroscopy. Therefore, hydrophilic tails of polyethylene glycol with –OH end groups could play an important role in reduction of metal salts. Literature shows that polyol process for reduction of metal salts to metal colloids usually requires harsh laboratory conditions.⁵³ Either it requires high temperatures or a long reaction time. To our surprise, the reduction of silver and palladium acetates by siloxane network took place at room temperature and over a short period of time. Various test reactions were carried out to investigate the role of polyethylene glycol substituted cyclic siloxanes in reduction of metal salts to metal nanoparticles.

2.2.4 Verification of Role of Siloxane Network in Reduction of Metal Salts

The structural features of the polymers play an important role in the reduction process. To verify this observation, separate reduction reactions of silver and palladium acetate were examined, where different compounds mimicking either the starting materials or the siloxane network products were used as reducing and stabilizing agents in place of siloxane networks. First, to similar solutions of silver and palladium acetates as mentioned earlier, polyethylene glycol in similar molar ratio was added and



Scheme 6: Reduction of metal salts to metal colloids by poly(ethylene) glycol and OMCTS respectively

reaction mixtures were stirred at room temperature. No change was observed even after continuous stirring for several hours. Later the reaction mixtures were heated at 80°C for 3-4 hours, but no color change as well as no change in UV spectrum was observed. In a second test reaction, 1,1,3,3,5,5,7,7-octamethylcyclotetrasiloxane (OMCTS) was used as the reducing agent. Again no evidence of metal salt reduction was observed either by a change in color or UV-vis spectroscopy even after continuously stirring for 8-12 hours at

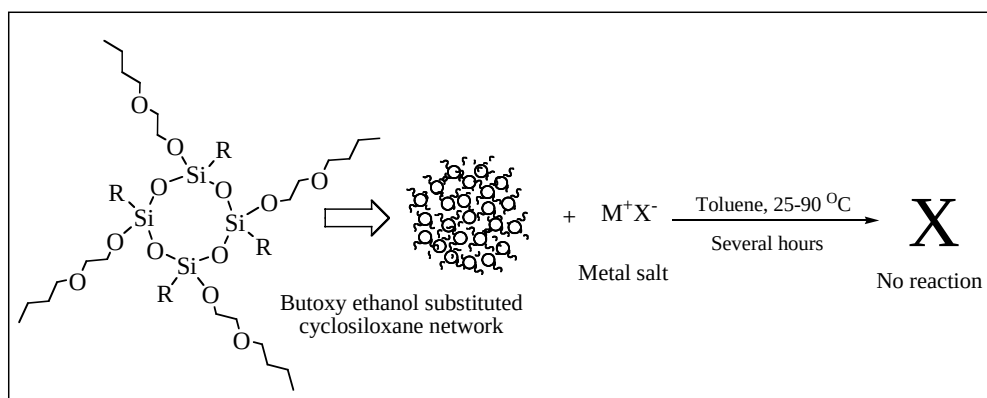
$$\begin{array}{c}
 \text{R}_1\text{---Si---H} \\
 | \quad | \\
 \text{O} \quad \text{O} \\
 | \quad | \\
 \text{H} \quad \text{R}_2
 \end{array}
 + 4 \text{ HOCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}
 \xrightarrow[\text{2\% RhCl(PPh}_3)_3]{\text{Benzene, 65 } ^\circ\text{C}}
 \begin{array}{c}
 \text{R}_1\text{---Si---O---CH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH} \\
 | \quad | \\
 \text{O} \quad \text{O} \\
 | \quad | \\
 \text{H} \quad \text{R}_2
 \end{array}
 \Rightarrow \text{Dendritic Polymer}$$

$\text{R}_1 = \text{CH}_3$
 $\text{R}_2 = \text{CH}_3\text{CH}_2$

shown in scheme 7. The reason to synthesize such an alkoxy siloxane was to investigate further the role of polyethylene glycol substituted cyclic siloxanes in reduction of metal

salts. The reaction between 1,3,5,7-tetramethylcyclotetrasiloxane (TMCTS) (0.297g, 1mmol) and butoxy ethanol (1.6 g, 4 mmol) was examined in presence of Wilkinson's catalyst $\text{RhCl}(\text{PPh}_3)_3$ (~0.002 g, 0.002 mmol) in benzene under positive pressure of Argon and was heated at 65 °C for about 30 hours. During the course of reaction, the reaction mixture became yellow and evolution of a gas (presumably H_2), was observed. Reaction progress was monitored by ^1H , and ^{29}Si NMR spectroscopy. After 30h of the reaction, complete consumption of 1,3,5,7-tetramethylcyclotetrasiloxane (TMCTS) and formation of butoxy ethanol substituted cyclic-siloxane (BE_4TMCTS) was observed in near quantitative yield.

This product was used to reduce silver and palladium acetates to their colloids. The reduction reactions were carried out under similar conditions as mentioned



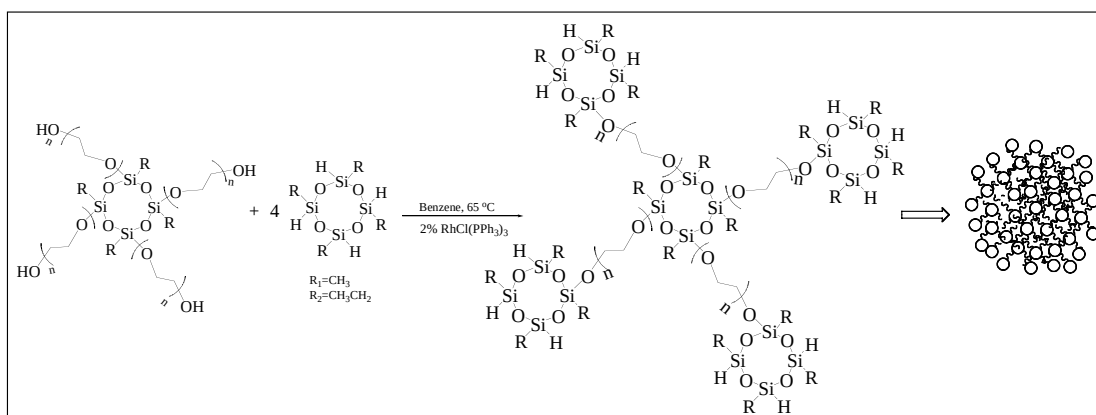
Scheme 8: Reduction of metal salts to metal colloids by butoxy ethanol substituted cyclosiloxane network

earlier with metal salts to product molar ratios as 1:4. The reduction reactions were monitored with UV-VIS spectrometry. A general synthetic route of for reduction of metal salts and their stabilization by siloxane network is shown in scheme 8. Formation of nanoparticles was not observed even after continuous stirring for several hours. Later, reaction mixtures were heated at 80 °C for 4 hours. The color as well as UV-vis spectra of silver and palladium acetate solutions remained unchanged.

These preliminary experiments indicate that substitution of glycol units to a cyclosiloxane core and formation of a micellar network plays an important role in reduction of metal salts by polyol like process. The resultant stable colloids with narrow size distribution further confirm that the network is not only acting as a reducing agent but also as an efficient host agent for nanoparticles.

2.2.5 Expansion of Alkoxy Siloxanes to Second Generation

The alkoxy siloxanes synthesized by substitution of poly(ethylene) glycols on a cyclic siloxane core can be expanded to further generation. As the end-groups of hydrophilic glycol tails on a cyclic siloxane core are $-OH$, another dehydrogenative alcoholysis coupling reaction can be carried out by selective alcoholysis of $Si-H$ bonds provided by adding additional units of cyclic siloxane (D_4^H). Expansion of alkoxy siloxanes in this manner allows the formation of macromolecules and dendrimers where cyclic siloxanes are attached to each other through polyethylene glycol units. The polyethylene glycol bridges may allow a control over the hydrophilicity of the resulting



Scheme 9: Expansion of siloxane network by covalently attaching additional cyclic siloxane units through polyethylene glycol bridges

materials and thus allowing a control over solubility in aqueous media or organic solvents. This control can be tailored accordingly by changing the lengths of polyethylene glycol units. These type of macromolecules and dendrimers promise to have the potential of being excellent drug delivery carriers and nanocomposites for the generation and stabilization of metal nanoparticles. Scheme 9 shows an illustration of expansion of such alkoxy siloxanes.

The reaction was carried out under similar conditions to those for the first generation alkoxy siloxanes. The catalyst used was Wilkinson catalyst ($\text{RhCl}(\text{PPh}_3)_3$). The theoretical molecular weight of alkoxy siloxane (PEG_4TMCTS) synthesized by substituting polyethylene glycol (MW-400) on 1,3,5,7-tetramethylcyclotetrasiloxane (TMCTS) was calculated which came out to be 1832.51 g/mole. Previously prepared alkoxy siloxane PEG_4TMCTS (0.92 g, 0.5 mmol) was dissolved in benzene along with Wilkinson's catalyst $\text{RhCl}(\text{PPh}_3)_3$ (~0.002 g, 0.002 mmol) and four equivalents of 1,3,5,7-Tetramethylcyclotetrasiloxane (TMCTS) (0.8 g, 2 mmol) were added to the reaction mixture. The reaction was carried out under positive pressure of Argon at 65 °C for about 32 hours. During the course of reaction, the reaction mixture became brownish and evolution of a gas (presumably H_2), was observed. After 32h of the reaction, complete consumption of 1,3,5,7-tetramethylcyclotetrasiloxane (TMCTS) and formation of second-generation alkoxy siloxane [$\text{TMCTS}(\text{PEG}_4)\text{TMCTS}_4$] was observed in near quantitative yield. The resultant was a very viscous liquid of brown color. A general synthetic route is illustrated in scheme 9.

The detailed product analysis was carried out by spectroscopic and microscopic techniques. The reaction mixture was periodically monitored by IR, ^1H , and

^{29}Si NMR. ^{29}Si NMR of starting siloxane i.e. PEG_4TMCTS shows two peaks centered at -56 to -57 ppm corresponding to T-type electronic environment of Si units ($\text{SiMe-OCH}_2\text{CH}_2\text{O}$), where silicon atom is attached to three oxygen atoms. After completion, two new peaks appeared centered at -32 ppm in ^{29}Si NMR. These new peaks correspond to D-type silicon (O-SiMeH-O-) units arising from the attachment of four equivalents of 1,3,5,7-tetramethylcyclotetrasiloxane (TMCTS). The ^1H NMR of the product also showed signals at 4.5 ppm as a result of new Si-H bonds

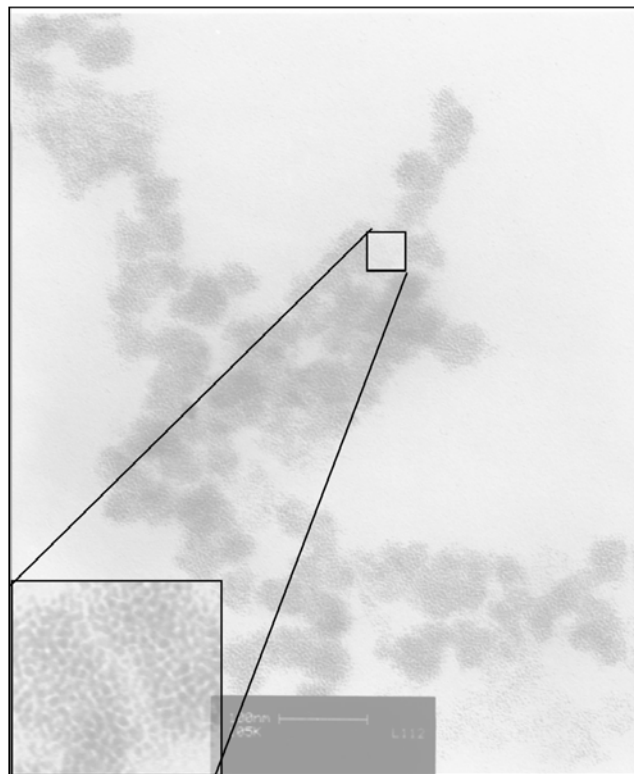


Figure 8: TEM image of second-generation siloxane network

present. The IR spectral analysis showed Si-H bonds characteristic bands around $\delta=2100\text{ cm}^{-1}$ region. The morphology of the generated polymers was investigated by Transmission Electron Microscopy (TEM) technique. The theoretical molecular weight of the product was calculated as 2786.55 g/mole. The product $[\text{TMCTS}(\text{PEG}_4)\text{TMCTS}_4]$ (0.56 gm, 0.2 mmol) was diluted in 20 ml of benzene. After stirring for 10 minutes in order to get a homogenous mixture, one drop of the solution was carefully dropped on formavar coated copper-carbon grid and solvent was allowed to evaporate at room temperature in open air. The TEM results are shown in Figure 8, which showed a well-defined micellar network with mono-dispersed particles.

The second-generation product was unstable in open air as it crosslinked and converted to a gel after coming in contact with oxygen. The reason for this is the presence of the catalyst, which facilitates naked Si-H bonds to react with oxygen and thus creating Si-O-Si linkage resulting in a cross-linked gel. In order to prevent the product from crosslinking and increase its stability, extra solvent i.e. benzene was added to reaction mixture after completion of the reaction while keeping it under positive pressure of Argon. The mixture was stirred for five minutes in order to get a homogenous solution followed by centrifuging at 9000 rpm for about 30 minutes. This was done to precipitate as much catalyst as possible out of the reaction mixture. The supernatant liquid part was carefully separated out and solvent was evaporated to get a light brown viscous liquid of product. It was assumed that some part of catalyst was still present in the product but it was a negligible amount as no further jellification was observed.

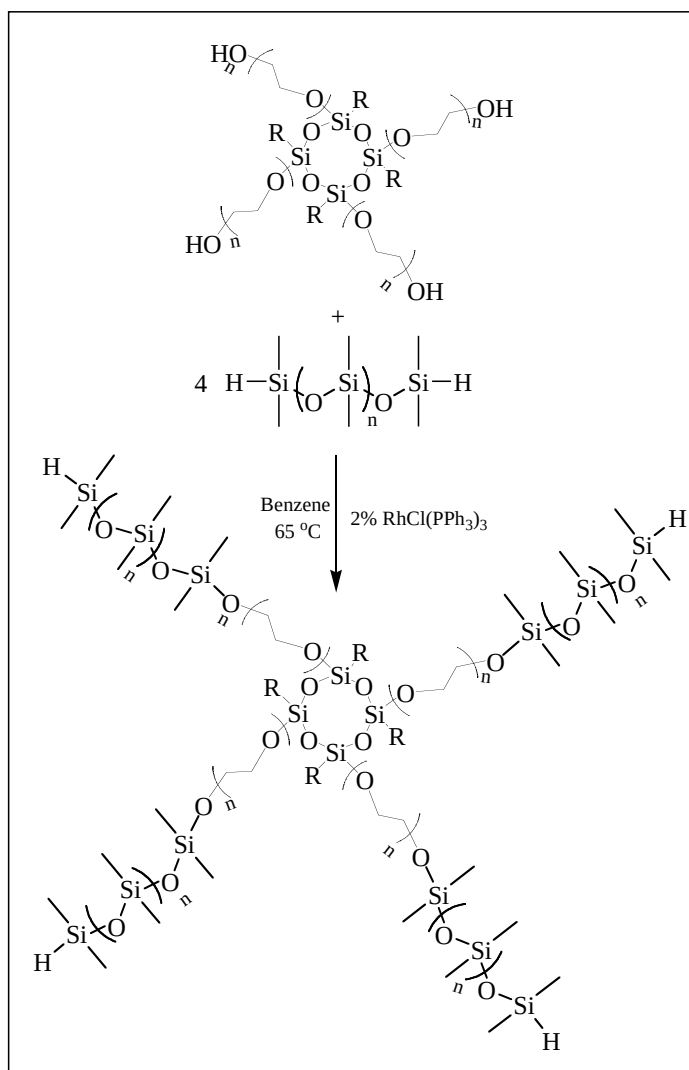
The second-generation alkoxy siloxane product was used to reduce platinum and palladium salts to generate corresponding nanoparticles. As expected, the second-generation polymer acted as an excellent reducing agent and it stabilized the nanoparticles to generate colloidal solutions of Pt and Pd. These nanoparticles were further used as catalysts in hydrosilylation and alcoholysis reactions respectively. The synthesis, characterization, and applications of these nanoparticles are discussed in detail in chapter four of this thesis.

2.2.6 Synthesis of Inorganic/Organic Hybrid Materials of Various Compositions

The dehydrogenative alcoholysis coupling of hydrophilic entities (polyethylene glycol) on hydrophobic cores (siloxanes) was further investigated by

synthesizing hybrid oligomers and polymers by a combination of linear and cyclic siloxanes attached through polyethylene glycol bridges. This approach may allow designing and synthesizing rod-block kind macromolecules with flexible and rigid units attached subsequently, which can lead to the generation of well-defined hybrid materials. We adopted two synthetic strategies to design such templates.

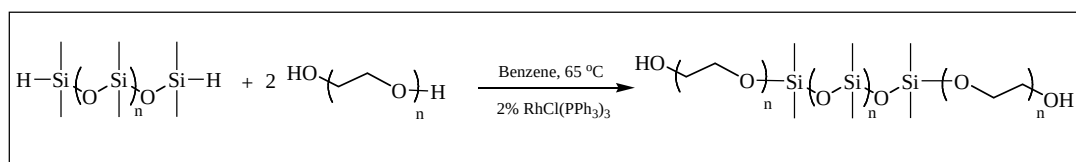
In first strategy, a cyclic siloxane was used as a core to which polyethylene glycol units were substituted via dehydrogenative coupling alcoholysis. The product thus formed was further expanded to second generation by addition of linear siloxane units. For this purpose, terminal Si-H functionalized poly(dimethylsiloxanes) (PDMS) with varying molecular weights and chain lengths ($M_w = 726, 1318, 2354$; $n = 8, 16, 30$) were chosen as precursors due to the availability of tunable side arms. Thus, to previously prepared alkoxy siloxane PEG₄TMCTS (0.92 g, 0.5



Scheme 10: Covalent attachment of poly(dimethylsiloxane) (PDMS) on a polyethylene glycol substituted cyclic siloxane core.

mmol) dissolved in benzene along with Wilkinson's catalyst $\text{RhCl}(\text{PPh}_3)_3$ (~ 0.002 g, 0.002 mmol), were added four equivalents of poly(dimethylsiloxane) (PDMS; MW = 726; $n = 8$) (1.45 g, 2.0 mmol). Reaction was carried out under a positive pressure of dry Argon at 65°C for about 30 hours. Scheme 10 describes the synthetic route adopted. The completion of reaction was confirmed by ^1H and ^{29}Si NMR, which showed gradual disappearance and then complete consumption of Si-H bonds peaks, associated with terminal Si-H protons and formation of desired product $[\text{TMCTS}(\text{PEG}_4)\text{PDMS}_4]$.

In the second synthetic strategy, a linear siloxane i.e. poly(dimethylsiloxane) (PDMS; MW = 726; $n = 8$) was used as the core and framework for the generation of micellar network by attaching cyclic siloxane units around it



Scheme 11: General synthetic route of attaching polyethylene glycol tails on a linear poly(dimethylsiloxane) core.

through polyethylene glycol bridges. The first step of the reaction was the addition of glycol units to the poly(dimethylsiloxanes) (PDMS). The reaction between Si-H terminated poly(dimethylsiloxanes) (PDMS) (0.73 g, 1mmol) and polyethylene glycol (PEG) (0.8 g, 2 mmol; Mw~400) was examined in presence of Wilkinson's catalyst $\text{RhCl}(\text{PPh}_3)_3$ (~ 0.002 g, 0.002 mmol) in benzene under positive pressure of Argon. A general scheme of this reaction and idealized structure of the product is shown in scheme 11. The reaction mixture was heated at 65°C for about 28 hours. During the course of reaction, the reaction mixture became yellow and evolution of a gas (presumably H_2), was observed. The complete substitution of glycol units was achieved in 28 hours, which

was confirmed by ^1H and ^{29}Si NMR and the resulting hybrid material (PEG₂PDMS) was a viscous liquid.

In the second step of the reaction, the product was further expanded by introducing cyclic siloxane units at both ends of polyethylene glycol bridges, which were attached to poly(dimethylsiloxanes) (PDMS) core. The theoretical molecular weight of

the product was

calculated as 1522

g/mole. The reaction

conditions were same as

for the first reaction. To

freshly prepared

PEG₂PDMS (0.76 g, 0.5

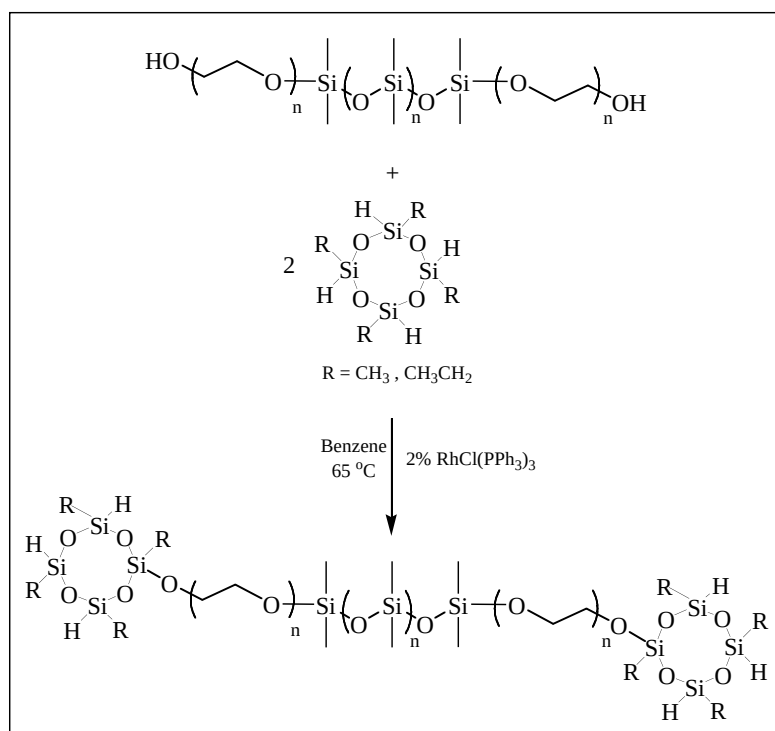
mmol) dissolved in

benzene along with

Wilkinson's catalyst

$\text{RhCl(PPh}_3)_3$ (~0.002 g,

0.002 mmol), were added



Scheme 12: Expansion of polyethylene glycol substituted linear poly(dimethylsiloxane) to further generation by attaching cyclic siloxane units at the glycol terminals.

two equivalents of 1,3,5,7-tetramethylcyclotetrasiloxane (TMCTS) (0.24 g, 1.0 mmol).

Reaction was carried out under a positive pressure of dry Argon at 65 °C for about 30

hours. The completion of reaction was confirmed by ^1H and ^{29}Si NMR. Scheme 12 shows the chemical pathway for the formation of second-generation macromolecules.

The successful synthesis of above mentioned hybrid materials led us to the assumption that such kind of macromolecules can act as templates for the generation of

hybrid networks of different morphologies and thus having unique properties. The macromolecules thus synthesized can be expanded to create hyperbranched polymers and dendrimers by proper choice of a variety of linear and cyclic siloxanes. We assume that tailoring of hydrophobic and hydrophilic units in such fashion can play a key role in the properties of the acquired networks. Introduction of rigid organic moieties onto linear siloxanes can result in chain-rod polymers, which can self assemble into a core-shell nanostructures in selective solvents. These networks can be used as reducing agents and stabilizers for the metal colloids and generate nanoparticles of different shapes and sizes. Such materials can also have very useful applications for drug delivery, magnetic recording, optical devices, and semi conductors etc.

2.3 Experimental Section

2.3.1 General Information

All reactions were carried out under a positive pressure of dry Argon or Nitrogen using standard Schlenk-tube technique.

Chemicals. All solvents were purchased from EM science (Merck) and distilled over sodium/benzophenone before use. Wilkinson's catalyst $\text{RhCl}(\text{PPh}_3)_3$, Polyethylene glycol (MW = 400, 600, 1000), and Butoxy ethanol were purchased from Aldrich Chemical Co. and used as received. 1,3,5,7-Tetramethylcyclotetrasiloxane (TMCTS), 1,3,5,7-Tetraethylcyclotetrasiloxane (TECTS), 1,1,3,3,5,5,7,7-Octamethylcyclotetrasiloxane were obtained from Gelest Inc. and used as received. Terminal Si-H poly(dimethylsiloxanes) (PDMS) were given by GE Silicones (now Momentive Performance Materials) and were used as received.

NMR Spectroscopy. ^1H NMR, ^{13}C NMR (200 MHz, 300 MHz), and ^{29}Si NMR (600 MHz) spectra were recorded in CDCl_3 or C_6D_6 on Varian Unity NMR instruments. ^{13}C NMR and ^{29}Si NMR spectra were referenced to Me_4Si . Proton spectra were referenced according to solvent proton shifts. All of the peaks in the NMR spectra were reported in ppm.

UV-vis Spectroscopy. UV-vis spectra were recorded on a Varian Cary Model 50 UV Spectrophotometer with 1-cm path length cells.

Infrared Spectroscopy. Infrared spectra were measured on the neat compounds with an FT Infrared Nicolet Mx-1 spectrophotometer by dropping 2-3 drops of compound to be analyzed dissolved in solvent on a KBr disc.

Transmission Electron Microscopy (TEM). Philips CM 100-transmission electron microscope (TEM) was used to probe the morphology of synthesized alkoxy siloxanes and nanoparticles of silver, palladium and platinum. Formavar coated copper-carbon grids were purchased from Electron Microscopy Sciences. Generally, the TEM grids were prepared under standard temperature and pressure and solvent was allowed to evaporate for 1-h before examination of the grid. To affirm the validity of the TEM results, images were taken at different magnifications and were examined thoroughly to rule out any “electron beam” induced modifications. The particle size analysis of metal nanoparticles was carried out manually on the EM images, using “Scion Image Software”. On average, 200-nanoparticles were measured before plotting the “Particle Size Analysis” graph.

2.3.2 Synthesis of Alkoxy Siloxanes

Synthesis of PEG₄TECTS:

Substitution of polyethylene glycol (PEG) on tetraethylcyclotetrasiloxane (TECTS) core. To a 50ml Schlenk tube equipped with a magnetic stirring bar, was added Wilkinson’s catalyst (0.002 g, 0.002 mmol). Schlenk tube was degassed and filled with nitrogen three times and polyethylene glycol (PEG) (1.4 ml, 4 mmol; MW: 400) was added to it. Reaction mixture was allowed to stir for 5 min in order to get a homogenous suspension of catalyst in PEG followed by addition of solvent (Benzene, 3 ml), which resulted in a brownish solution. At this juncture, Tetraethylcyclotetrasiloxane (TECTS) (0.3 ml, 1.0 mmol) was added to the reaction mixture. Reaction mixture immediately turned yellow and development of a gas (presumably H₂) was observed. Flask was degassed and filled

with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 30 hrs. Upon completion, reaction mixture was a dark brown viscous solution. Additional solvent was added to reaction mixture in order to separate the catalyst. Reaction mixture was centrifuged at 9000 rpm for about 30 minutes, which resulted in the precipitation of catalyst. The supernatant liquid was carefully separated and solvent was evaporated to get the product. The product was analyzed with FTIR, ^1H , ^{13}C , and ^{29}Si NMR, and transmission electron microscopy (TEM), which confirmed the formation of, desired product (PEG₄TECTS).

^1H NMR (δ , ppm): 0.627 (m), 0.992 (m), 3.594 (s), 3.655 (m), 3.707 (m), 3.877 (m); ^{13}C NMR (δ , ppm): 4.358 (m), 5.322 (m), 6.793 (m), 61.591 (s), 62.198 (s), 70.547 (s), 72.352 (s), 73.012 (s); ^{29}Si NMR (δ , ppm): -57.776 (m), -56.177 (m). Yield: 100%

Synthesis of PEG₄TMCTS:

Substitution of polyethylene glycol (PEG) on tetramethylcyclotetrasiloxane (TMCTS) core.

To a 50ml Schlenk tube equipped with a magnetic stirring bar, was added Wilkinson's catalyst (0.002 g, 0.002 mmol). Schlenk tube was degassed and filled with nitrogen three times and polyethylene glycol (PEG) (1.4 ml, 4 mmol; MW: 400) was added to it. Reaction mixture was allowed to stir for 5 min in order to get a homogenous suspension of catalyst in PEG followed by addition of solvent (Benzene, 3 ml), which resulted in a brownish solution. At this juncture, Tetramethylcyclotetrasiloxane (TMCTS) (0.24 ml, 1.0 mmol) was added to the reaction mixture. Reaction mixture immediately turned yellow and development of a gas (presumably H₂) was observed. Flask was degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under

a positive nitrogen pressure for 30 hrs. Upon completion, reaction mixture was a dark brown viscous solution. Additional solvent was added to reaction mixture in order to separate the catalyst. Reaction mixture was centrifuged at 9000 rpm for about 30 minutes, which resulted in the precipitation of catalyst. The supernatant liquid was carefully separated and solvent was evaporated to get the product. The product was analyzed with FTIR, ^1H , ^{13}C , and ^{29}Si NMR, and transmission electron microscopy (TEM), which confirmed the formation of, desired product (PEG_4TMCTS).

^1H NMR (δ , ppm): 0.082 (m), 3.475 (s), 3.532 (m), 3.591 (m), 3.779 (m); ^{13}C NMR (δ , ppm): -4.358 (m), 61.591 (s), 62.198 (s), 70.547 (s), 72.352 (s), 73.012 (s); ^{29}Si NMR (δ , ppm): -58.489 (m), -57.955 (m). Yield: 100%

Synthesis of BE_4TMCTS :

Substitution of butoxy ethanol (BE) on tetramethylcyclotetrasiloxane (TMCTS) core.

To a 50ml Schlenk tube equipped with a magnetic stirring bar, was added Wilkinson's catalyst (0.002 g, 0.002 mmol). Schlenk tube was degassed and filled with nitrogen three times and butoxy ethanol (BE) (0.52 ml, 4 mmol) was added to it. Reaction mixture was allowed to stir for 5 min in order to get a homogenous suspension of catalyst in PEG followed by addition of solvent (Benzene, 3 ml), which resulted in a brownish solution. At this juncture, Tetramethylcyclotetrasiloxane (TMCTS) (0.297 g, 2.0 mmol) was added to the reaction mixture. Reaction mixture immediately turned yellow and development of a gas (presumably H_2) was observed. Flask was degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 30 hrs. Upon completion, reaction mixture was a dark brown viscous solution. Additional solvent was added to reaction mixture in order to separate the

catalyst. Reaction mixture was centrifuged at 9000 rpm for about 30 minutes, which resulted in the precipitation of catalyst. The supernatant liquid was carefully separated and solvent was evaporated to get the product. The product was analyzed with FTIR, ^1H , ^{13}C , and ^{29}Si NMR, which confirmed the formation of, desired product (BE_4TMCTS).

^1H NMR (δ , ppm): 0.044 (m), 0.808 (m), 1.265 (m), 1.448 (m), 3.382 (m), 3.608 (s), 3.791 (m); ^{29}Si NMR (δ , ppm): -58.297 (m), -57.772 (m). Yield:100%

Synthesis of $[\text{TMCTS}(\text{PEG}_4)\text{TMCTS}_4]$:

Expansion of PEG_4TMCTS (polyethylene glycol substituted tetramethylcyclotetrasiloxane) to second generation.

For the expansion to second generation, theoretical molecular weight of . previously prepared alkoxy siloxane (PEG_4TMCTS) was calculated which came out to be 1832.51 g/mole. The alkoxy siloxane PEG_4TMCTS (0.92 g, 0.5 mmol) was dissolved in benzene along with Wilkinson's catalyst $\text{RhCl}(\text{PPh}_3)_3$ (~0.002 g, 0.002 mmol) and four equivalents of 1,3,5,7-Tetramethylcyclotetrasiloxane (TMCTS) (0.8 g, 2 mmol) were added to the reaction mixture. The reaction was carried out under positive pressure of Argon at 65°C for about 32 hours. During the course of reaction, the reaction mixture became brownish and evolution of a gas (presumably H_2), was observed. After 32h of the reaction, complete consumption of 1,3,5,7-tetramethylcyclotetrasiloxane (TMCTS) and formation of second-generation alkoxy siloxane $[\text{TMCTS}(\text{PEG}_4)\text{TMCTS}_4]$ was observed in near quantitative yield. The resultant was a very viscous liquid of brown color. In order to prevent the product from crosslinking and increase its stability, extra solvent (benzene) was added to reaction mixture after completion of the reaction while keeping it under positive pressure of Argon. The mixture was stirred for five minutes in

order to get a homogenous solution followed by centrifuging at 9000 rpm for about 30 minutes. This was done to precipitate as much catalyst as possible out of the reaction mixture. The supernatant liquid part was carefully separated out and solvent was evaporated to get a light brown viscous liquid of product. It was assumed that some part of catalyst was still present in the product but it was a negligible amount as no further jellification was observed.

^1H NMR: δ = 0.686 (m), 1.036 (m), 3.538 (s), 3.975 (m), 4.980 (m); ^{13}C NMR: δ = 4.525 (m), 5.215 (m), 6.869 (m), 8.522 (m), 61.796 (s), 62.342 (d), 70.578 (s), 70.911 (s), 72.519 (m), 72.966 (s); ^{29}Si NMR: δ = -57.62 (m, CH_2), -55.83 (m, CH_3), -31.73 (m, SiH), -29.680 (m, SiH). Yield: 98%

Synthesis of [TMCTS(PEG₄)PDMS₄]:

Substitution of poly(dimethylsiloxane) (PDMS) units on PEG₄TMCTS (polyethylene glycol capped tetramethylcyclotetra-siloxane).

To previously prepared alkoxy siloxane PEG₄TMCTS (0.92 g, 0.5 mmol) dissolved in benzene along with Wilkinson's catalyst $\text{RhCl}(\text{PPh}_3)_3$ (~0.002 g, 0.002 mmol), were added four equivalents of poly(dimethylsiloxane) (PDMS; MW = 726; n = 8) (1.45 g, 2.0 mmol). Reaction was carried out under a positive pressure of dry Argon at 65 °C for about 30 hours. The completion of reaction was confirmed by ^1H and ^{29}Si NMR, which confirmed the formation of desired product [TMCTS(PEG₄)PDMS₄].

^1H NMR: δ = -0.031(m), 3.538 (m), 3.701 (m), 4.603 (m); ^{29}Si NMR: δ = -56.758 (m), -21.532 (m), -11.461(m). Yield: 95%

Synthesis of PEG₂PDMS:

Substitution of polyethylene glycol (PEG) on poly(dimethylsiloxane) (PDMS) core.

The reaction between poly(dimethylsiloxanes) (PDMS) (0.73 g, 1mmol) and polyethylene glycol (PEG) (0.8 g, 2 mmol; Mw~400) was examined in presence of Wilkinson's catalyst $\text{RhCl(PPh}_3)_3$ (~0.002 g, 0.002 mmol) in benzene under positive pressure of Argon. The reaction mixture was heated at 65 °C for about 28 hours. During the course of reaction, the reaction mixture became yellow and evolution of a gas (presumably H_2), was observed. The complete substitution of glycol units was achieved in 28 hours, which was confirmed by ^1H and ^{29}Si NMR and the resulting hybrid material (PEG_2PDMS) was a viscous liquid.

^1H NMR: δ = -0.002 (m), 3.571 (m), 3.729 (m), 3.893 (m); ^{29}Si NMR: δ = -21.592 (m), -11.332 (m). Yield; 98%

Synthesis of $[\text{PDMS(PEG}_2\text{)TMCTS}_2]$:

Substitution of tetramethylcyclotetrasiloxane (TMCTS) units on PEG_2PDMS (polyethylene glycol capped poly(dimethylsiloxane)).

The theoretical molecular weight of previously prepared product PEG_2PDMS was calculated as 1522 g/mole. The reaction conditions were same as for the first reaction. To freshly prepared PEG_2PDMS (0.76 g, 0.5 mmol) dissolved in benzene along with Wilkinson's catalyst $\text{RhCl(PPh}_3)_3$ (~0.002 g, 0.002 mmol), were added two equivalents of 1,3,5,7-tetramethylcyclotetrasiloxane (TMCTS) (0.24 g, 1.0 mmol). Reaction was carried out under a positive pressure of dry Argon at 65 °C for about 30 hours. The completion of reaction was confirmed by ^1H and ^{29}Si NMR.

^1H NMR: δ = -0.026(m), 0.553 (m), 0.882 (m), 3.543 (m), 3.733 (m), 4.531 (s); ^{29}Si NMR: δ = -55.771 (m), -31.520 (m), -21.635 (m), -11.387 (s). Yield: 95%

2.3.3 Synthesis of Metal Nanoparticles

Synthesis of Silver Nanoparticles:

In a typical reduction procedure, silver acetate (0.0083 g, 0.05 mmol) was suspended in toluene (20 mL) in a 250 mL round bottom flask equipped with a vacuum inlet and a magnetic stirrer. After continuous stirring for about 10 min in order to achieve a homogeneous suspension, PEG₄TMCTS (polyethylene glycol substituted tetramethylcyclotetrasiloxane) (0.3665 g, 0.2 mmol) was added and resulting mixture was stirred at room temperature. After 45 min, the color of reaction mixture changed to light yellow. The color change indicated that the reduction of silver acetate to silver nanoparticles has ensued. In the course of four hours, the color changed to dark yellow and then to brown, indicating the complete reduction of silver acetate to silver colloids. The resulting nanoparticles solution was centrifuged at 9000 rpm for 10 min in order to remove un-reacted silver acetate. The formation of silver nanoparticles was confirmed by UV-vis and Transmission Electron Microscopy. In a similar fashion, reduction reactions with various ratios of polymer were examined. In case of palladium, stable black homogenous colloidal solution was obtained.

Synthesis of Palladium Nanoparticles:

For the synthesis of palladium nanoparticles, palladium acetate (0.0112 g, 0.05 mmol) was dissolved in toluene (20 mL) in a 250 mL round bottom flask equipped with a vacuum inlet and a magnetic stirrer. After stirring for about 5 min in order to achieve a homogeneous solution of yellow color, PEG₄TMCTS (polyethylene glycol substituted tetramethylcyclotetrasiloxane) (0.3665 g, 0.2 mmol) was added and resulting mixture was stirred at room temperature. Palladium acetate solution is light yellow and shows a peak

around 396 in UV spectrum. For about one hour, after addition of product to the solution, the color remained almost unchanged. Later on, after continuous stirring at room temperature, color started to change to brown. This was the first evidence of reduction of palladium acetate. During a period of about six hours, the solution color changed to brown and then to black, which was a strong evidence of palladium colloids formation. At this point, UV spectrum was taken and it showed a featureless absorption, a characteristic of palladium nanoparticles.

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CHAPTER 3

3 Grafting of Silsesquioxane ($\text{Q}_8\text{M}_8^{\text{H}}$) based Cubic Siloxanes. Another route to POSS Materials

3.1 Introduction

Considerable research efforts are being directed towards exploration and development of silicon based inorganic/organic hybrid composites and polyhedral oligomeric silsesquioxanes (POSS) are a growing class of such materials. The reason for this growing interest is the unusual properties that can be achieved from these materials. The flexibility of Si-O bond, the thermal and chemical stability, enhanced mechanical properties, control over structural profile, ease of use, low or no toxicity, and potential to create a library of hybrid macromolecules are the key features to name some. This rich property profile of silsesquioxanes provides the potential for their use in a large number of applications ranging from simple polymer blends to dental composites to aerospace materials. Cyclic siloxanes, where usually eight or more silicon atoms are linked with each other through oxygen bridges forming a cube-like structure are generally called silsesquioxanes.

The name “silsesquioxanes” basically represents the silicon to oxygen ratio in the molecule. The name is derived from words *siloxane* (compounds of silicon and oxygen) and *sesqui* (Latin word meaning one and a half). Thus, basic ratio of silicon to oxygen atoms in silsesquioxanes is one (silicon) to one and a half (oxygen). The first

molecular structure determination of a silsesquioxane was made by Barry, et al¹ in 1955 using a single crystal x-ray diffraction method.

The silsesquioxane molecules are also called as the smallest sand (silica) particles. Octakis (dimethylsiloxy)-T₈-silsesquioxane (Q₈M₈^H) cube has eight terminal Si-H functionalities (Figure 1), which can be modified through a variety of reactions and

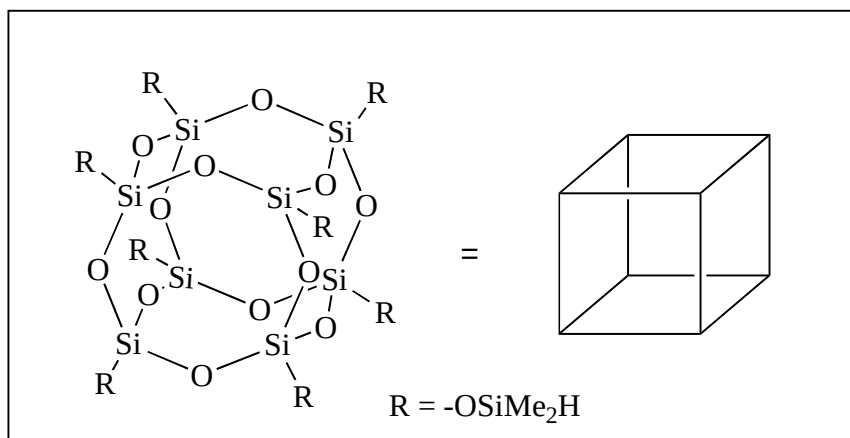


Figure 1: Chemical structure of a Octakis (dimethylsiloxy)-T₈-silsesquioxane (Q₈M₈^H) and its resemblance to a cube. (Reproduced from ref. 38)

selection of functional groups giving rise to multi-arm structures and macromolecules. With a selective modification by grafting functional groups and terminating the reactive functionalities, these macromolecules can be simply blended into elastomers using the usual mixing or compound processing, which enhances the stability profile of the resulting elastomer blends. This type of substitution, where the reactive functionalities are terminated, may provide with a better miscibility of silsesquioxanes with elastomers or polymers for better blending. Examples of substituted groups can be alkyls, alcohols, amines, and vinyl groups etc.² On the other hand, by grafting of reactive di-functional groups on the silsesquioxanes core; further expansion is possible, which can eventually allow one to create dendrimers of silsesquioxanes through organic functionalities' bridges, or highly cross-linked gels. Examples of such functional groups can be di-

alcohols, glycols, halides, amides, divinyls.³⁻¹⁵ Examples of silsesquioxane based dendrimers can be found out in work by Cole-Hamilton et al, where they have used silsesquioxanes as building blocks for dendrimers.¹⁶⁻¹⁹ Furthermore, by sol-gel processing of silsesquioxanes, highly cross-linked, porous materials can also be prepared.²⁰ The resulting macromolecules after grafting the silsesquioxanes with a library of functional groups are generally called polyhedral oligomeric silsesquioxanes (POSS) materials.

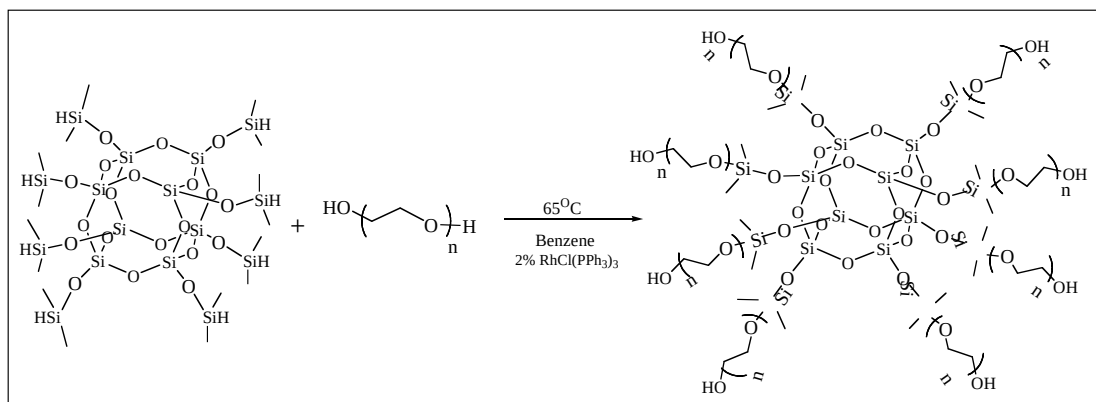
3.2 Results and Discussion

We have used octakis (dimethylsiloxy)-T₈-silsesquioxane (Q₈M₈) as the core for construction of POSS materials via covalent substitution of a variety of organic functional groups. Among different functionalities are ethylene glycols and polyethylene glycols, functional and non-functional alcohols and olefins. Substitution of glycols and alcohols was carried out via dehydrogenative alcoholysis coupling, whereas the olefins substitution was achieved by hydrosilylation of the double bond with Si-H functionality of Q₈M₈. The reactions were carried out in presence of a catalyst and Wilkinson's catalyst (RhCl(PPh₃)₃), palladium nanoparticles (Pd⁰), and platinum nanoparticles (Pt⁰) were used for glycolysis, alcoholysis and hydrosilylation respectively.

3.2.1 Grafting of Polyethylene Glycol (PEG)

First, polyethylene glycol (PEG) of different chain lengths and molecular weights were covalently attached to the Q₈M₈^H core. The reaction is a dehydrogenative alcoholysis coupling. For the covalent grafting of polyethylene glycol (PEG),

Wilkinson's catalyst (0.002 g, 0.002 mmol) and octakis(dimethylsiloxy)-T₈-Silsesquioxane (Q₈M₈^H) (0.2545 g, 0.25 mmol) were taken in a 50ml Schlenk tube equipped with a magnetic stirring bar. Schlenk tube was degassed and filled with nitrogen three times and solvent (benzene, 5 ml) was added which resulted in a brownish solution. At this juncture, polyethylene glycol (PEG) (0.8 g, 2 mmol; MW~400) was added to it that caused the reaction mixture to immediately turn yellow and formation of a gas (presumably H₂) was observed. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 32 hrs. Upon completion, reaction mixture was a light yellow viscous solution. In order to separate the catalyst, reaction mixture was taken in a test tube and was centrifuged at 9000 rpm for about 20 min, which resulted in catalysts



Scheme 1: Synthetic route to grafting of polyethylene glycol (PEG) on cubic siloxane (Q₈M₈). Idealized structure of product shown.

precipitation. Solvent was evaporated and product was analyzed with ¹H, and ²⁹Si NMR that confirmed the formation of desired product. Scheme 1 shows a general synthetic route and idealized structure of the product.

The reaction mixture was periodically monitored by ¹H, and ²⁹Si NMR (Figure 2). ²⁹Si NMR of octakis (dimethylsiloxy)-T₈-silsesquioxane (T₈) shows two peaks

centered at around -1ppm arising from eight side arm M-type silicon ($-\text{O}-\text{SiMe}_2\text{H}$) units, where silicon atom is attached to one oxygen atom; and second peak centered at around -

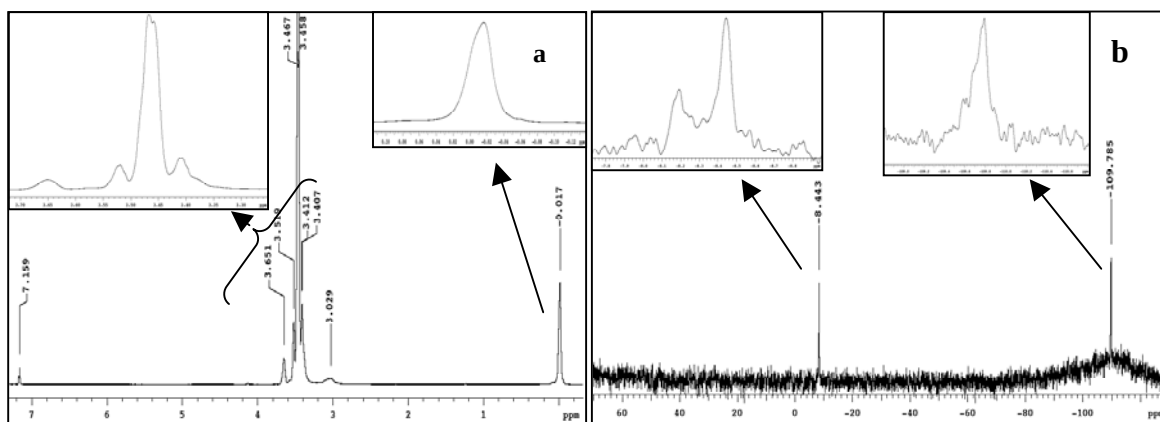


Figure 2: NMR analysis of polyethylene glycol grafted Q_8M_8 . (a) ^1H , (b) ^{29}Si

108ppm arising from eight central Q-type silicon units, where each silicon atom is attached to four oxygen atoms in the cage (Figure 3). After grafting of polyethylene glycol (PEG) on side arm silicon atoms, the ^{29}Si NMR analysis of resulting product showed a shift from -1ppm to -8ppm as a change in electronic environment of side arm Si units and formation of new D-type ($-\text{O}-\text{SiMe}_2-\text{OCH}_2\text{CH}_2\text{O}-$) moieties, where silicon atom is now attached to two oxygen atoms (Figure 4). No residual signals due to Si-H bonds were observed in ^{29}Si NMR of the product, indicating complete consumption of the Si-H bonds.

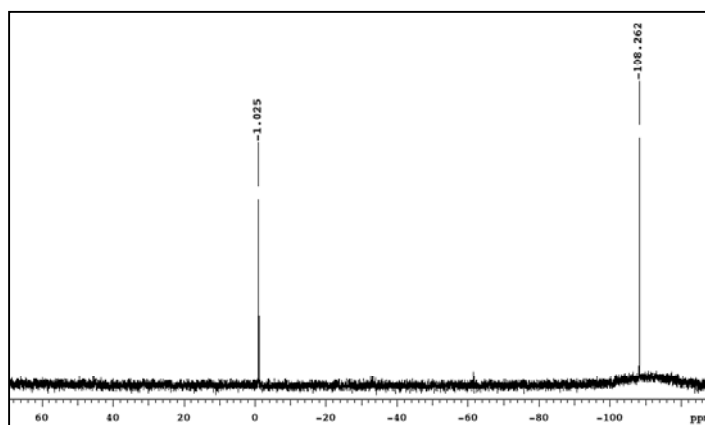


Figure 3: ^{29}Si NMR of octakis(dimethylsiloxy)- T_8 -Silsesquioxane

Among different glycols used were triethylene glycol and polyethylene glycols with varying chain lengths and molecular weights (MW=400, 1000). All the

products were almost clear, viscous liquids after solvent evaporation with the exception of polyethylene glycol (MW=1000), which resulted in a white waxy solid. Such glycol-substituted silsesquioxanes may have multiple uses. Due to the glycol modification on the surface, these silsesquioxane materials may be solubilized in water creating emulsions and giving rise to core-shell structures for possible uses in drug delivery. The active –OH functionality on the end of glycol chains may provide means of expansion of macromolecules to dendretic or highly cross-linked structures.

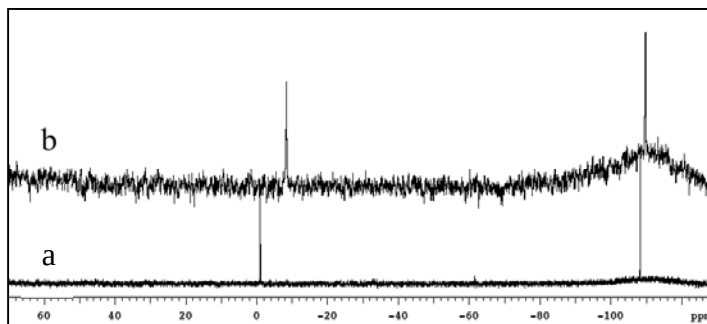


Figure 4: ^{29}Si NMR of octakis (dimethylsiloxy)- T_8 -Silsesquioxane (a) before PEG substitution, and (b) after PEG substitution

3.2.2 Substitution of Alcohols on a Cubic Siloxane Core

Grafting of octakis (dimethylsiloxy)- T_8 -silsesquioxane ($\text{Q}_8\text{M}_8^{\text{H}}$) with a range of alcohols was also carried out in pursuit of enhancement of physical and chemical properties of POSS materials. For this purpose, alcoholysis of octakis (dimethylsiloxy)- T_8 -silsesquioxane ($\text{Q}_8\text{M}_8^{\text{H}}$) was examined in presence of a number of alcohols with varying functionalities and structures. The catalyst used for such grafting was Palladium nanoparticles, which were prepared previously in our lab.²¹⁻²² Palladium nanoparticles turned out to be an excellent catalyst and gave comparatively high yields and were easy to isolate from the reaction mixture after the reaction was over.

The first step towards grafting of alcohols on a $Q_8M_8^H$ was the preparation of palladium nanoparticles. The synthesis of Pd-nanoparticles was carried out in a 500 ML round bottom flask, equipped with a magnetic stirring bar, at room temperature. Palladium acetate $[Pd(OAc)_2]$ was used as the precursor to generate Pd^0 colloids. In a typical procedure, $Pd(OAc)_2$ (0.0561 g, 0.25 mmol) was dissolved in 50 ml of dry toluene and a yellow solution was obtained. Upon stirring the mixture, polymethylhydrosiloxane (PMHS) (0.3 g, 5.0 mmol) was added to this yellow solution. The color of the reaction mixture started to change immediately from yellow to brown and in about 15 min, it changed further to dark brown and finally turned black. Evolution of gas (H_2 , presumably) was

observed along with the color change with continuous stirring. The progress of reaction was monitored by UV-vis analysis of the reaction mixture. Palladium acetate gives a peak around λ

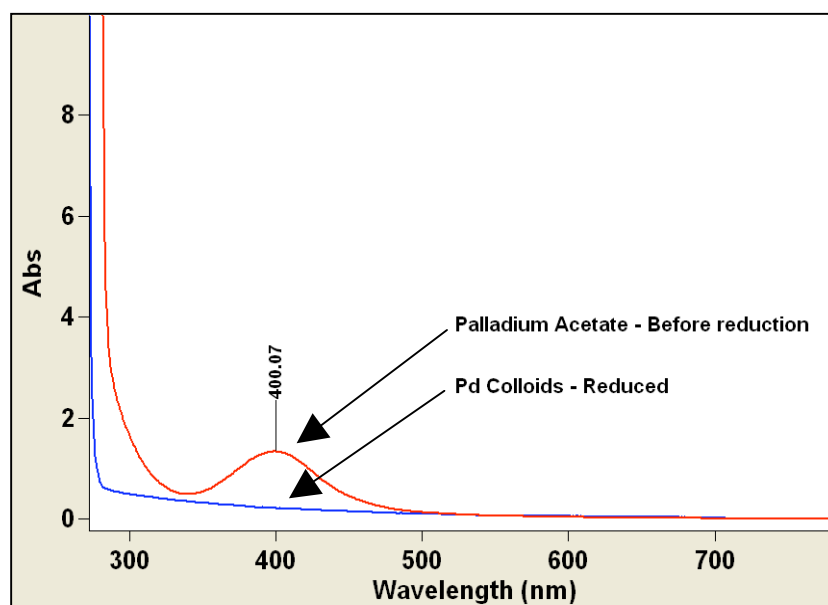
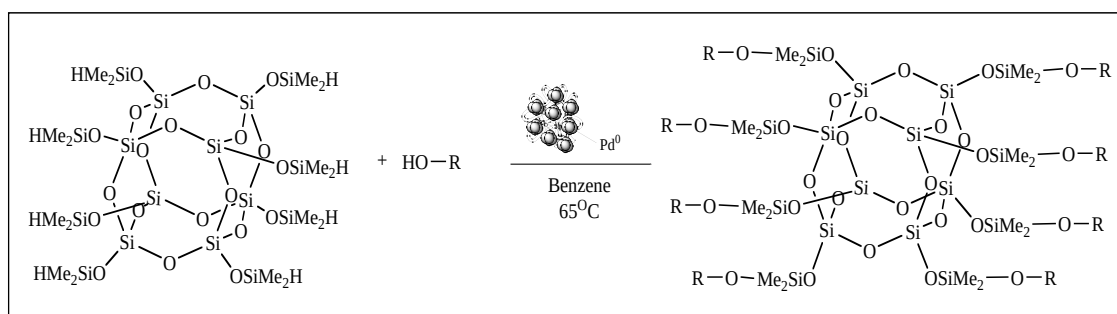


Figure 5: UV-vis spectra of palladium acetate before reduction and palladium colloids after reduction.

= 400 nm, which gradually disappeared and a featureless UV-vis spectra indicated conversion of $Pd(II)$ to $Pd(0)^{23}$ (Figure 5). After stirring the solution for about 2 hours at room temperature, a black solid began to precipitate and the reaction mixture turned colorless after next 3-4 hrs of stirring. At this juncture, black precipitate was filtered and

washed with excess of toluene and then dried overnight. The detailed analysis for the confirmation of formation of Pd^0 nanoclusters can be found reported elsewhere by our group.²¹⁻²²

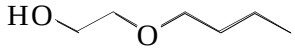
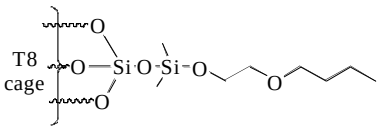
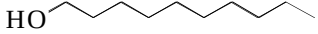
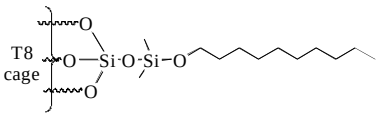
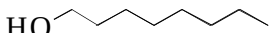
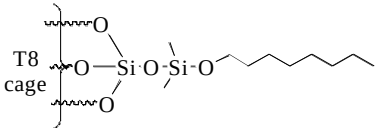
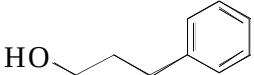
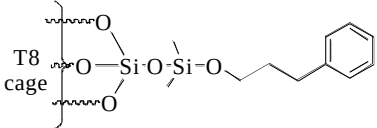
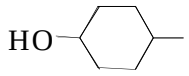
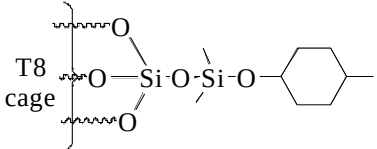
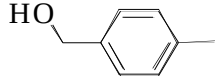
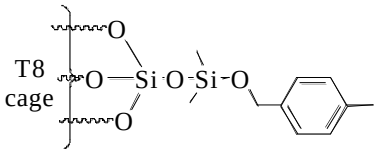
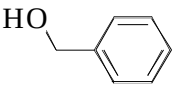
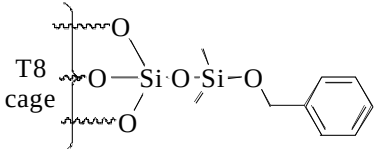
The black powder of palladium nanoparticles was used as a catalyst for the covalent addition of alcohols on a silsesquioxane core. In a typical alcoholysis experiment, Pd-nanoparticles (0.01 g) and octakis (dimethylsiloxy)- T_8 -Silsesquioxane (T_8) (0.1272 g, 0.125 mmol) were taken in a 50ml Schlenk tube equipped with a magnetic stirring bar. Schlenk tube was degassed and filled with nitrogen three times and solvent



Scheme 2: A general scheme of grafting of alcohols on a octakis (dimethylsiloxy)- T_8 -Silsesquioxane core and an idealized structure of product

(Benzene, 3 ml) was added to it. After stirring the mixture for 1 min and obtaining the homogeneity, 1-heptanol (0.14 ml, 1.0 mmol) was added to reaction mixture. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at 70°C under a positive nitrogen pressure for 32 hrs. A gradual change in the color of reaction mixture from colorless to homogeneous black colored solution was observed indicating the generation of soluble Pd-nanoclusters. Evolution of gas (H_2 , presumably) was also observed during the reaction. A general scheme of grafting of alcohols on a $\text{Q}_8\text{M}_8^{\text{H}}$ core is shown in scheme 2. ^1H NMR examination of the reaction mixture at regular intervals showed gradual disappearance of Si-H ($\delta = 4.5$) and $-\text{OH}$ ($\delta = 2.0$) signal associated with $\text{Q}_8\text{M}_8^{\text{H}}$ and 1-heptanol, respectively.

Table 1. Summary of alcohols grafted alcohols, resulted POSS materials and general conditions of the reactions.

Entry	Alcohols	Reaction Condition	Product	Yield (%)
1		32h/70°C		90
2		36h/70°C		90
3		32h/70°C		95
4		36h/70°C		85
5		39h/70°C		85
6		36h/70°C		70
7		42h/70°C		50

The ^{29}Si NMR spectra also confirmed complete consumption of Si-H bonds by disappearance of peak around $\delta = -1.019$ associated with Si-H and appearance

of a new peak at $\delta = -10.693$ due to formation of a new Si-O-R linkage. After complete substitution, reaction mixture was centrifuged at 9000 rpm for 20 minutes, which led to the isolation of Pd-nanoclusters at the bottom of centrifuge-tube. Filtration of the catalysts and subsequent evaporation of solvent under reduced pressure yielded a clear viscous liquid of 1-heptanol grafted Q_8M_8 . The alcoholysis of Q_8M_8 was examined in

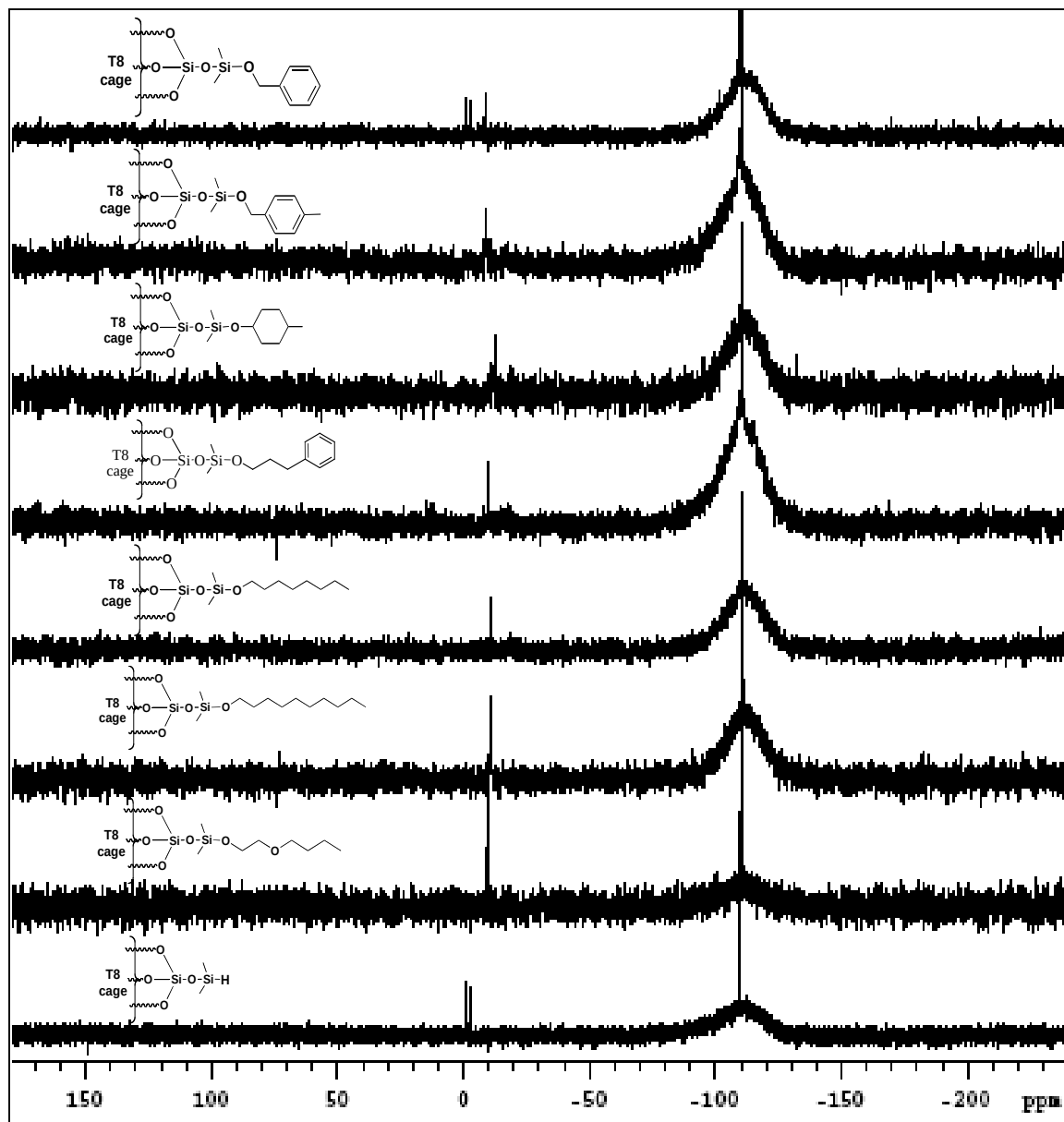


Figure 6: ^{29}Si NMR analysis comparison of Q_8M_8 before and after alcohol substitutions.

All the reactions and products were monitored with ^1H and ^{29}Si NMR and a shift in the peaks and/or appearance of new peaks were observed. Figure 6 shows ^{29}Si NMR comparison Q_8M_8 before and after substitution of alcohols.

The POSS materials obtained after substitutions of alcohols on octakis (dimethylsiloxy)- T_8 -Silsesquioxane were further analyzed for thermal property profile. TGA analysis of the products showed an enhanced thermal stability as compared to pure

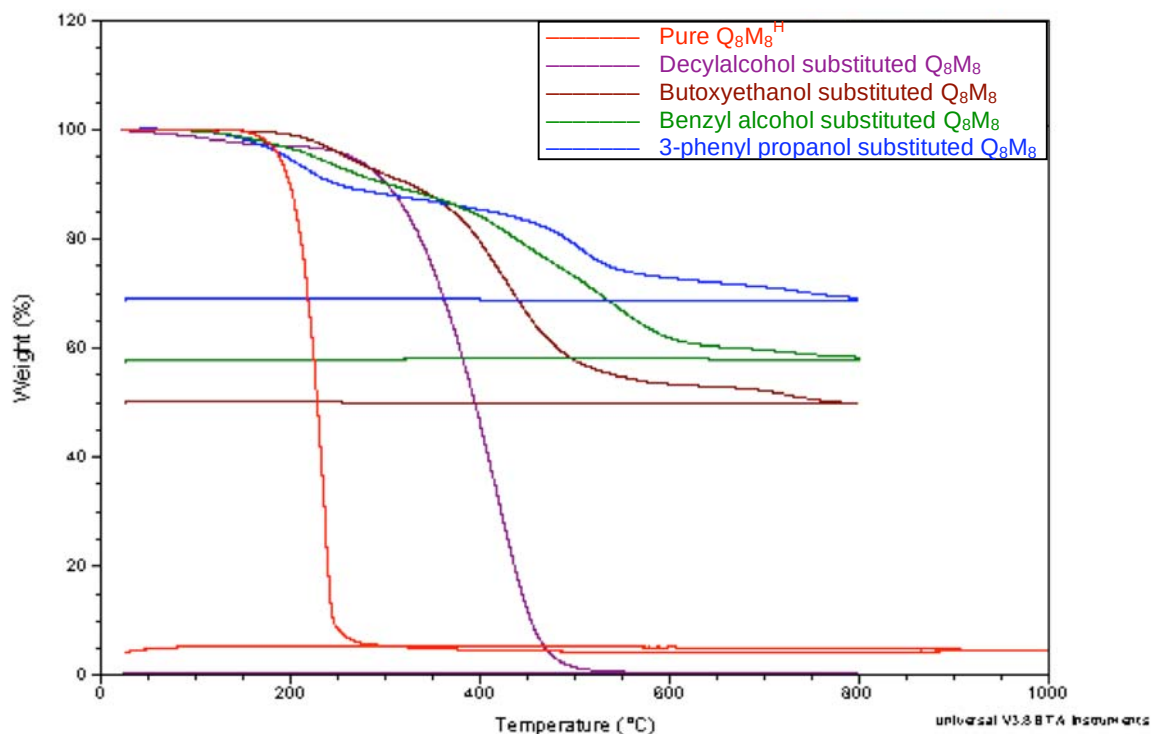


Figure 7: Thermal gravimetric analysis (TGA) of selected products

octakis (dimethylsiloxy)- T_8 -Silsesquioxane. Figure 7 shows the TGA analysis results of selected products.

3.2.3 Hydrosilylation of $\text{Q}_8\text{M}_8^{\text{H}}$ with Allyl Alcohol

One of the widely used methods for the production of silicon polymers is hydrosilylation, in which the hydrosilane unit (Si-H) is added to the double bond of an

alkene (C=C) to form an alkylsilane. This method enables the modification of silanes and siloxanes to create tailored macromolecules. Usually Rhodium or Platinum based catalysts are used for such addition.²⁴⁻²⁵ Hydrosilylation of alkenes with silsesquioxanes can be another approach for the generation of POSS materials and with careful choice of olefin groups and various degrees of functionalization, libraries of silsesquioxane based hybrid composites, oligomers and polymers can be created. Several groups have adopted this approach and examples of functionalization of silsesquioxanes can easily be found in literature.²⁶⁻⁴⁰ Attempts have also been made for the introduction of hydroxyl groups (OH) on silsesquioxanes surface, which is a potential route to create POSS materials that are amphiphilic in nature. Such hydrophilic addition on silsesquioxane surface provides with the means to create low-viscosity, easily curable, single-phase POSS materials. For this purpose, allyl alcohol is a favorable choice where double bond of allyl alcohol can be hydrosilylated across the hydrosilane (Si-H) functionality of silsesquioxane core for the fabrication of amphiphilic POSS composites. This approach has been probed in a great detail by Laine et al⁴¹. They used platinum divinyltetramethyldisiloxane complex (Pt(dvs)) as the catalyst, which provided with exclusive C-silylation but high concentrations of the catalyst and allyl alcohol were required. On the other hand, at low concentration of catalyst or allyl alcohol, O-silylation occurred simultaneously generating cross-linked or other side products. We chose platinum nanoparticles (Pt⁰) as the hydrosilylation catalyst, which yielded exclusive C-silylation with almost no or minute O-silylation traces even when used in low concentration. The platinum nanoparticles were prepared in our lab and details about the preparation and characterization can be found elsewhere.⁴²

Synthesis of Pt-nanoclusters was carried out by polymethylhydrosiloxane (PMHS) reduction of (cod)PtMe₂ complex. PMHS not only acted as an excellent reductant but also as a stabilizer for nanoparticles to prevent them from agglomeration. For the synthesis of Pt-nanoparticles, (cod)PtMe₂ (cod: 1,5 cyclo-octadiene) (0.25 mmol, 0.084 g) was taken in a 500 ML round bottom flask, equipped with a magnetic stirring bar and a vacuum inlet. Flask was degassed and filled with nitrogen and toluene (50 ml)

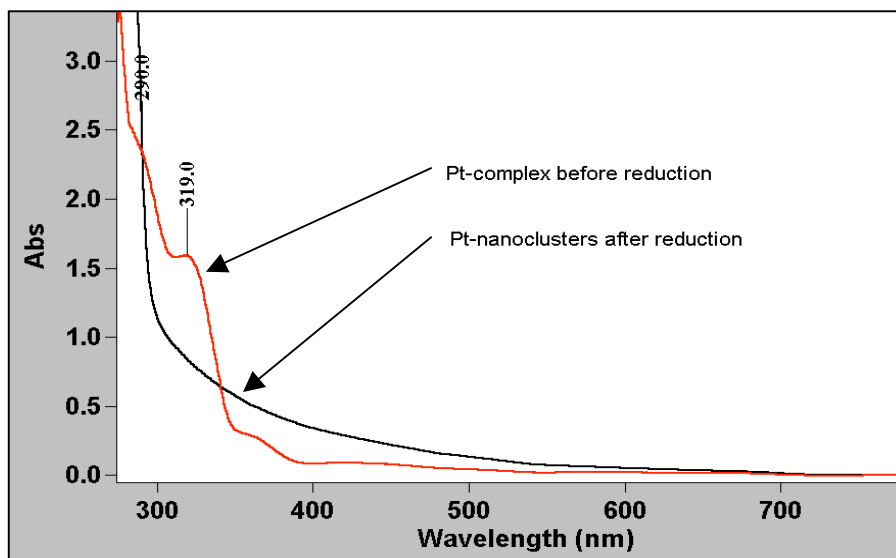
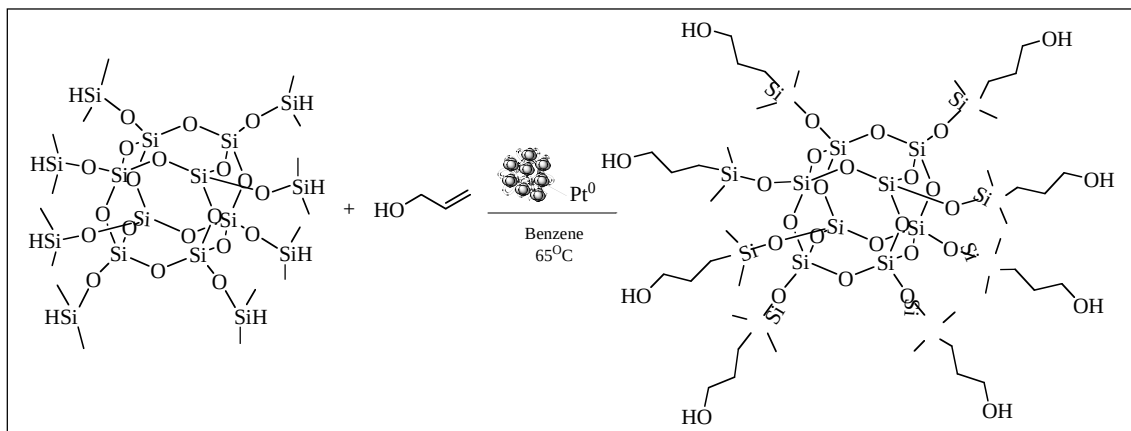


Figure 8: UV-vis analysis of (cod)PtMe₂ complex before reduction and Pt⁰ nanoparticles after reduction.

was added to it. After stirring for 5 min, polymethylhydrosiloxane (PMHS) (0.60 g, 10.0 mmol; MW ~ 2000) was added and reaction mixture was stirred at 80 °C for 24 hrs under positive pressure of nitrogen. Color of the reaction mixture turned yellow after 30 min, and thereafter gradually turned black. Reduction of (cod)PtMe₂ was monitored periodically with UV-vis spectroscopy, which disclosed a gradual disappearance of shoulders associated with (cod)PtMe₂, and finally leading to a featureless spectrum (Figure 8). This was the evidence of complete reduction of Pt(II) to Pt(0).⁴⁵ After confirming the reduction of (cod)PtMe₂, the solution was further characterized with

transmission electron microscopy (TEM) for the presence of nanoclusters. Later on, flow of nitrogen was stopped and the flask was exposed to air. Further stirring of solution for 6 to 12 hrs in open-air yielded a black gel-like solid. At this juncture, black gel-like solid was filtered and washed with excess of toluene and then dried overnight, which resulted in black powder of Pt-nanoclusters.

The black powder of platinum nanoparticles was used as a catalyst for the hydrosilylation of allyl alcohol with octakis (dimethylsiloxy)-T₈-silsesquioxane (Q₈M₈). Platinum nanoclusters (0.005 g) and octakis (dimethylsiloxy)-T₈-Silsesquioxane (T₈) (0.1272 g, 0.125 mmol) were taken in a 50ml Schlenk tube equipped with a magnetic stirring bar. Schlenk tube was degassed and filled with nitrogen three times and solvent (Benzene, 3 ml) was added to it. After stirring the mixture for 1 min and obtaining the



Scheme 3: Hydrosilylation of allyl alcohol with octakis (dimethylsiloxy)-T₈-silsesquioxane (Q₈M₈^H) in presence of platinum nanoparticles.

homogeneity, eight equivalents of allyl alcohol (0.07 ml, 1.0 mmol) were added to reaction mixture. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at room temperature under a positive nitrogen pressure for 4 hrs. A gradual change in the color of reaction mixture from colorless to dark brown was observed indicating the generation of soluble Pt-

nanoclusters. Evolution of gas (H_2 , presumably) was also observed during the reaction. A general scheme of grafting of alcohols on a Q_8M_8 core is shown in scheme 3.

Reaction mixture was analyzed by ^1H and ^{29}Si NMR. The gradual disappearance of Si-H signal at (^1H : $\delta = 4.5$; ^{29}Si : $\delta = -1$) associated with Q_8M_8 and

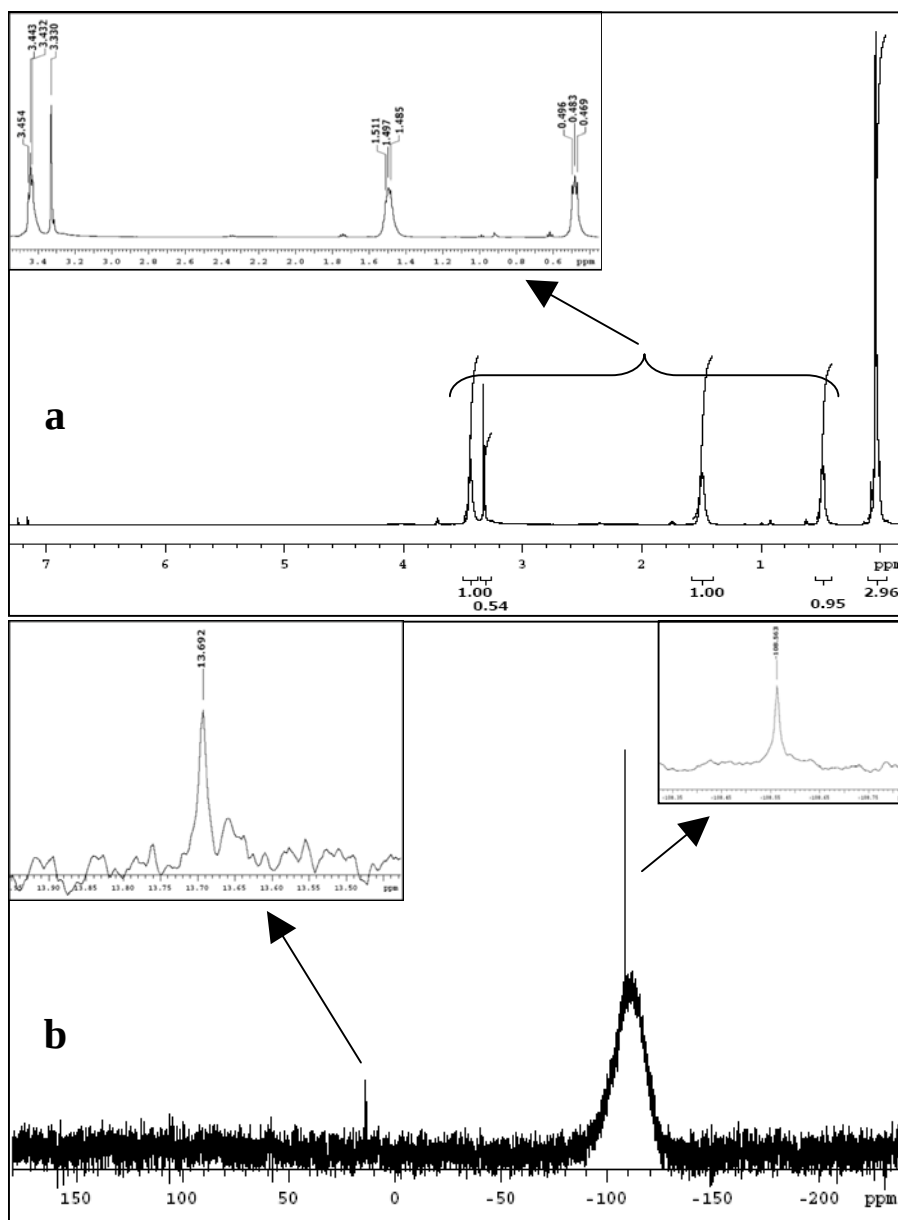


Figure 9: NMR analysis of allyl alcohol substitution on $Q_8M_8^H$ representing exclusive C-silylation. (a) ^1H , (b) ^{29}Si

appearance of new peaks centered at (^1H : $\delta = 0.483$, $\delta = 1.497$, $\delta = 3.443$; ^{29}Si : $\delta =$

13.692) confirmed the complete consumption of Si-H and formation of hydrosilylated product (Figure 9). The three triplets centered at $\delta = 0.483$, $\delta = 1.497$ and $\delta = 3.443$ in ^1H NMR was a confirmation of exclusive C-silylation as no or minute other signals were visible. Disappearance of vinyl signal centered at $\delta = 5.167$ and $\delta = 5.914$ in ^1H NMR was another confirmation of C-silylation and reaction completion. After complete substitution, reaction mixture was centrifuged at 9000 rpm for 20 minutes, which led to the

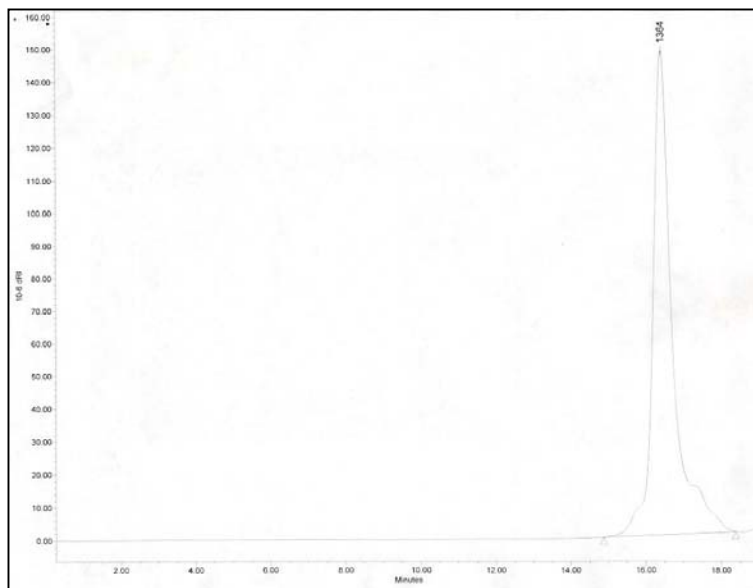


Figure 10: GPC analysis of allyl alcohol substituted Q_8M_8 .

isolation of Pt-nanoclusters in form of precipitate at the bottom of centrifuge-tube. Filtration of the catalysts and evaporation of solvent yielded a viscous liquid of allyl alcohol substituted Q_8M_8 . In addition to NMR analysis, the product was also analyzed by gel permeation chromatography (GPC) (Figure 10). If only C-silylation or O-silylation occurs, then the molecular weight of the resultant should be around 1450. Although GPC does not confirm the exclusive C-silylation, but a sharp peak does indicate a single major product, which can be confirmed as C-silylation with the help of other analysis such as NMR. If O-silylation would have occurred, then it could give a mixture of products including cross-linked macromolecules. This would result in multiple or a wide peak in GPC, as well as, in higher molecular weight larger than ~ 1450 .

3.3 Experimental Section

3.3.1 General Information

All reactions were carried out under a positive pressure of dry Argon or Nitrogen using standard Schlenk-tube technique.

Chemicals. All solvents were purchased from EM science (Merck) and distilled over sodium/benzophenone before use. Wilkinson's catalyst $\text{RhCl}(\text{PPh}_3)_3$, $(\text{cod})\text{PtMe}_2$, Palladium acetate, Polyethylene glycol (MW = 400, 1000), allyl alcohol, and all other alcohols were purchased from Aldrich Chemical Co. and used as received. Octakis (dimethylsiloxy)-T₈-Silsesquioxane ($\text{Q}_8\text{M}_8^{\text{H}}$) was obtained from Gelest Inc. and used as received.

NMR Spectroscopy. ^1H NMR (200 MHz, 300 MHz), and ^{29}Si NMR (600 MHz) spectra were recorded in CDCl_3 or C_6D_6 on Varian Unity NMR instruments. ^{29}Si NMR spectra were referenced to Me_4Si . Proton spectra were referenced according to solvent proton shifts. All of the peaks in the NMR spectra were reported in ppm.

Thermal Gravimetric Analysis (TGA). Thermal gravimetric analysis (TGA) was performed on Hi-Res TGA 2950 Thermogravimetric Analyzed from TA Instruments. The instrument was calibrated using standard aluminum/iron pan. The analysis was carried out under continuous flow of nitrogen. Temperature of the oven was ramped at 10.0 $^\circ\text{C}$ /min from 25.0 $^\circ\text{C}$ to 800.0 $^\circ\text{C}$.

Gel Permeation Chromatography (GPC) Analysis. An Alliance GPCV 2000 (water) equipped with two silica columns was used for Gel Permeation Chromatography (GPC) analysis. The two columns used were HRSE and HR-I with range of 100-5000 and 2000-4X10⁶, respectively. The instrument was calibrated using polystyrene standards. THF

was used as the solvent at a flow rate of 1.0 mL/min at 40.0 °C. A third order calibration curve was used to measure the molecular weight of unknown samples.

Transmission Electron Microscopy (TEM). Philips CM 100-transmission electron microscope (TEM) was used to probe the morphology of grafted silsesquioxane and synthesized nanoparticles. Formavar coated copper-carbon grids were purchased from Electron Microscopy Sciences. Generally, the TEM grids were prepared under standard temperature and pressure and solvent was allowed to evaporate for 1-h before examination of the grid. To affirm the validity of the TEM results, images were taken at different magnifications and were examined thoroughly to rule out any “electron beam” induced modifications.

3.3.2 Grafting of Ethylene glycols on $Q_8M_8^H$

Substitution of Triethylene glycol:

Substitution of triethylene glycol was carried out in the following way. To a 50ml Schlenk tube equipped with a magnetic stirring bar, were added Wilkinson’s catalyst (0.002 g, 0.002 mmol) and octakis(dimethylsiloxy)- T_8 -Silsesquioxane (T_8) (0.1272 g, 0.125 mmol). Schlenk tube was degassed and filled with nitrogen three times and solvent (Benzene, 3 ml) was added which resulted in a brownish solution. At this juncture, triethylene glycol (0.13 g, 1 mmol) was added to it that caused the reaction mixture to immediately turn yellow and development of a gas (presumably H_2) was observed. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 28 hrs. Upon completion, reaction mixture was a light yellow viscous solution. In order to

separate the catalyst, reaction mixture was taken in a test tube and was centrifuged at 9000 rpm for about 20 min, which resulted in catalysts precipitation. Solvent was evaporated and product was analyzed with ^1H , and ^{29}Si NMR that confirmed the formation of desired product.

^1H NMR (δ , ppm): -0.001 (m), 3.421 (m), 3.485 (m), 3.546 (m), 3.686 (s); ^{29}Si NMR (δ , ppm): -109.469 (m), -7.904 (m). Yield: 98%

Substitution of polyethylene glycol (PEG, MW=400)

Substitution of PEG (MW = 400) was carried out in the following way. To a 50ml Schlenk tube equipped with a magnetic stirring bar, were added Wilkinson's catalyst (0.002 g, 0.002 mmol) and octakis(dimethylsiloxo)- T_8 -Silsequioxane (T_8) (0.2545 g, 0.25 mmol). Schlenk tube was degassed and filled with nitrogen three times and solvent (Benzene, 5 ml) was added which resulted in a brownish solution. At this juncture, polyethylene glycol (PEG) (0.8 g, 2 mmol; MW~400) was added to it that caused the reaction mixture to immediately turn yellow and development of a gas (presumably H_2) was observed. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 32 hrs. Upon completion, reaction mixture was a light yellow viscous solution. In order to separate the catalyst, reaction mixture was taken in a test tube and was centrifuged at 9000 rpm for about 20 min, which resulted in catalysts precipitation. Solvent was evaporated and product was analyzed with ^1H , and ^{29}Si NMR that confirmed the formation of desired product.

^1H NMR (δ , ppm): 0.063 (m), 3.485 (m), 3.538 (m), 3.599 (m), 3.733 (m); ^{29}Si NMR (δ , ppm): -8.192 (m), -109.706 (s). Yield: 96%

Substitution of polyethylene glycol (PEG, MW=1000)

Substitution of PEG (MW = 1000) was carried out in the following way. To a 50ml Schlenk tube equipped with a magnetic stirring bar, were added Wilkinson's catalyst (0.002 g, 0.002 mmol) and octakis(dimethylsiloxy)-T₈-Silsesquioxane (T₈) (0.1272 g, 0.125 mmol). Schlenk tube was degassed and filled with nitrogen three times and solvent (Benzene, 5 ml) was added which resulted in a brownish solution. At this juncture, polyethylene glycol (PEG) (1.0 g, 1 mmol; MW~1000) was added to it that caused the reaction mixture to immediately turn yellow and development of a gas (presumably H₂) was observed. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 35 hrs. Upon completion, reaction mixture was a light yellow viscous solution. In order to separate the catalyst, reaction mixture was taken in a test tube and was centrifuged at 9000 rpm for about 20 min, which resulted in catalysts precipitation. Solvent was evaporated and product was analyzed with ¹H, and ²⁹Si NMR that confirmed the formation of desired product.

¹H NMR (δ, ppm): 0.067 (m), 3.480 (m), 3.535 (m), 3.598 (m), 3.727 (m); ²⁹Si NMR (δ, ppm): -8.023 (m), -109.680 (s). Yield: 96%

3.3.3 Alcoholysis of Octakis(dimethylsiloxy)-T₈-Silsesquioxane (Q₈M₈^H)

Reaction with Butoxy Ethanol (Entry 1, Table 1):

The alcoholysis reaction with butoxy ethanol was carried out in following way. Octakis(dimethylsiloxy)-T₈-Silsesquioxane (T₈) (0.1272 g, 0.125 mmol) and Pd-nanoparticles (0.01 g) and were taken in a 50ml Schlenk tube equipped with a magnetic stirring bar.

Schlenk tube was degassed and filled with nitrogen three times and solvent (Benzene, 3 ml) was added to it. After stirring the mixture for 1 min and obtaining the homogeneity, butoxy ethanol (0.13 ml, 1.0 mmol) was added to reaction mixture. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at 70°C under a positive nitrogen pressure for 32 hrs. Upon completion, solvent was evaporated and product was analyzed with ^1H , and ^{29}Si NMR that confirmed the formation of desired product.

^1H NMR (δ , ppm): 0.065 (m), 0.801 (m), 1.228 (m), 1.415 (m), 3.359 (m), 3.710 (m); ^{29}Si NMR (δ , ppm): -110.785 (s), -9.621 (s). Yield: 90%

Reaction with Decyl alcohol (Entry 2, Table 1):

The alcoholysis reaction with decyl alcohol was carried out in following way. Octakis (dimethylsiloxy)- T_8 -Silsesquioxane (T_8) (0.1272 g, 0.125 mmol) and Pd-nanoparticles (0.01 g) and were taken in a 50ml Schlenk tube equipped with a magnetic stirring bar. Schlenk tube was degassed and filled with nitrogen three times and solvent (Benzene, 3 ml) was added to it. After stirring the mixture for 1 min and obtaining the homogeneity, decyl alcohol (0.19 ml, 1.0 mmol) was added to reaction mixture. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at 70°C under a positive nitrogen pressure for 36 hrs. Upon completion, solvent was evaporated and product was analyzed with ^1H , and ^{29}Si NMR that confirmed the formation of desired product.

^1H NMR (δ , ppm): 0.035 (m), 0.765 (s), 1.151 (m), 1.417 (m), 3.528 (m); ^{29}Si NMR (δ , ppm): -110.641 (s), -10.802 (s). Yield: 90%

Reaction with 1-Heptanol (Entry 3, Table 1):

For the reaction with 1-heptanol, octakis (dimethylsiloxy)-T₈-silsesquioxane (T₈) (0.1272 g, 0.125 mmol) and Pd-nanoparticles (0.01 g) and were taken in a 50ml Schlenk tube equipped with a magnetic stirring bar. Schlenk tube was degassed and filled with nitrogen three times and solvent (Benzene, 3 ml) was added to it. After stirring the mixture for 1 min and obtaining the homogeneity, 1-heptanol (0.14 ml, 1.0 mmol) was added to reaction mixture. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at 70°C under a positive nitrogen pressure for 32 hrs. Upon completion, solvent was evaporated and product was analyzed with ¹H, and ²⁹Si NMR that confirmed the formation of desired product.

¹H NMR (δ, ppm): 0.040 (m), 0.773 (m), 1.183 (m), 1.428 (m), 3.570 (m); ²⁹Si NMR (δ, ppm): -110.644 (s), -10.693 (s). Yield: 95%

Reaction with 3-Phenyl-1-Propanol (Entry 4, Table 1):

The alcoholysis reaction with 3-phenyl-1-propanol was carried out in following way. Octakis (dimethylsiloxy)-T₈-Silsesquioxane (T₈) (0.1272 g, 0.125 mmol) and Pd-nanoparticles (0.01 g) and were taken in a 50ml Schlenk tube equipped with a magnetic stirring bar. Schlenk tube was degassed and filled with nitrogen three times and solvent (Benzene, 3 ml) was added to it. After stirring the mixture for 1 min and obtaining the homogeneity, 3-phenyl-1-propanol (0.14 ml, 1.0 mmol) was added to reaction mixture. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at 70°C under a positive nitrogen pressure for 36 hrs. Upon completion, solvent was evaporated and product was analyzed with ¹H, and ²⁹Si NMR that confirmed the formation of desired product.

^1H NMR (δ , ppm): 0.056 (m), 1.755 (m), 2.574 (t), 3.511 (t), 3.615 (m), 7.085 (m), 7.166 (m); ^{13}C NMR (δ , ppm): -4.310 (m), 60.066 (s), 69.037 (s), 69.250 (s), 71.510 (s); ^{29}Si NMR (δ , ppm): -110.420 (s), -10.005 (s). Yield: 85%

Reaction with 4-Methylcyclohexanol (Entry 5, Table 1):

For the alcoholysis with 4-methylcyclohexanol, octakis (dimethylsiloxy)- T_8 -Silsequioxane (T_8) (0.1272 g, 0.125 mmol) and Pd-nanoparticles (0.01 g) and were taken in a 50ml Schlenk tube equipped with a magnetic stirring bar. Schlenk tube was degassed and filled with nitrogen three times and solvent (Benzene, 3 ml) was added to it. After stirring the mixture for 1 min and obtaining the homogeneity, 4-methylcyclohexanol (0.13 ml, 1.0 mmol) was added to reaction mixture. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at 70°C under a positive nitrogen pressure for 39 hrs. Upon completion, solvent was evaporated and product was analyzed with ^1H , and ^{29}Si NMR that confirmed the formation of desired product.

^1H NMR (δ , ppm): 0.054 (m), 0.759 (m), 0.862 (m), 1.210 (m), 1.572 (m), 1.807 (m), 3.415 (m), 3.587 (m); ^{29}Si NMR (δ , ppm): -110.702 (s), -12.434 (s). Yield: 85%

Reaction with 4-Methylbenzyl alcohol (Entry 6, Table 1):

The alcoholysis reaction with 4-methylbenzyl alcohol was carried out in following way. Octakis (dimethylsiloxy)- T_8 -Silsequioxane (T_8) (0.1272 g, 0.125 mmol) and Pd-nanoparticles (0.01 g) and were taken in a 50ml Schlenk tube equipped with a magnetic stirring bar. Schlenk tube was degassed and filled with nitrogen three times and solvent (Benzene, 3 ml) was added to it. After stirring the mixture for 1 min and obtaining the homogeneity, 4-methylbenzyl alcohol (0.12 g, 1.0 mmol) was added to reaction mixture.

Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at 70°C under a positive nitrogen pressure for 36 hrs. Upon completion, solvent was evaporated and product was analyzed with ^1H , and ^{29}Si NMR that confirmed the formation of desired product.

^1H NMR (δ , ppm): 0.064 (m), 2.197 (s), 4.443 (m), 4.626 (m), 6.990 (m), 7.081 (m) ^{29}Si NMR (δ , ppm): -110.398 (s), -9.074 (s). Yield: 70%

Reaction with Benzyl alcohol (Entry 7, Table 1):

The alcoholysis reaction with benzyl alcohol was carried out in following way. Octakis (dimethylsiloxy)- T_8 -Silsequioxane (T_8) (0.1272 g, 0.125 mmol) and Pd-nanoparticles (0.01 g) and were taken in a 50ml Schlenk tube equipped with a magnetic stirring bar. Schlenk tube was degassed and filled with nitrogen three times and solvent (Benzene, 3 ml) was added to it. After stirring the mixture for 1 min and obtaining the homogeneity, benzyl alcohol (0.1 ml, 1.0 mmol) was added to reaction mixture. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at 70°C under a positive nitrogen pressure for 42 hrs. Upon completion, solvent was evaporated and product was analyzed with ^1H , and ^{29}Si NMR that confirmed the formation of desired product.

^1H NMR (δ , ppm): 0.098 (m), 2.733 (s), 4.503 (s), 4.644 (m), 7.226 (m); ^{29}Si NMR (δ , ppm): -110.465 (s), -109.338 (s), -9.003 (s), -1.108 (d). Yield: 50%

3.3.4 Hydrosilylation of allyl alcohol with $\text{Q}_8\text{M}_8^{\text{H}}$

Hydrosilylation of allyl alcohol with octakis (dimethylsiloxy)- T_8 -Silsequioxane (T_8) was carried out in the following way. Platinum nanoclusters (0.005

g) and octakis (dimethylsiloxy)-T₈-Silsesquioxane (T₈) (0.1272 g, 0.125 mmol) were taken in a 50ml Schlenk tube equipped with a magnetic stirring bar. Schlenk tube was degassed and filled with nitrogen three times and solvent (Benzene, 3 ml) was added to it. After stirring the mixture for 1 min and obtaining the homogeneity, eight equivalents of allyl alcohol (0.07 ml, 1.0 mmol) were added to reaction mixture. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at room temperature under a positive nitrogen pressure for 4 hrs. A gradual change in the color of reaction mixture from colorless to dark brown was observed indicating the generation of soluble Pt-nanoclusters. Evolution of gas (H₂, presumably) was also observed during the reaction. Upon completion, reaction mixture was analyzed by ¹H and ²⁹Si NMR.

¹H NMR (δ, ppm): 0.037 (m), 0.483 (t), 1.498 (t), 3.332 (s), 3.443 (t); ²⁹Si NMR (δ, ppm): -108.563 (s), 13.696 (s). Yield: 95%

3.3.5 Synthesis of metal nanoparticles

Synthesis of palladium nanoparticles:

The synthesis of Pd-nanoparticles was carried out in the following way. In a 500 ML round bottom flask, equipped with a magnetic stirring was taken palladium acetate [Pd(OAc)₂] (0.0561 g, 0.25 mmol) and 50 ml of dry toluene was added to it which resulted in a yellow solution. Reaction was carried out at room temperature. While stirring the mixture, polymethylhydrosiloxane (PMHS) (0.3 g, 5.0 mmol) was added to this yellow solution. The color of the reaction mixture started to change immediately from yellow to brown and in about 15 min, it changed further to dark brown and finally

turned black. Evolution of gas (H_2 , presumably) was observed along with the color change with continuous stirring. The progress of reaction was monitored by UV-vis analysis of the reaction mixture. Palladium acetate gives a peak around $\lambda = 400$, which gradually disappeared and a featureless UV-vis spectra indicated conversion of Pd(II) to Pd(0). After stirring the solution for about 2 hours, a black solid began to precipitate out and the reaction mixture turned colorless after next 3-4 hrs of stirring. At this juncture, black precipitate was filtered and washed with excess of toluene and then dried overnight, which eventually turned into a black powder.

Synthesis of platinum nanoparticles:

Synthesis of Pt-nanoclusters was carried out by polymethylhydrosiloxane (PMHS) reduction of (cod)PtMe₂ complex. For the synthesis of Pt-nanoparticles, (cod)PtMe₂ (cod: 1,5 cyclo-octadiene) (0.25 mmol, 0.084 g) was taken in a 500 ML round bottom flask, equipped with a magnetic stirring bar and a vacuum inlet. Flask was degassed and filled with nitrogen and toluene (50 ml) was added to it. After stirring for 5 min, polymethylhydrosiloxane (PMHS) (0.60 g, 10.0 mmol; MW ~ 2000) was added and reaction mixture was stirred at 80 °C for 24 hrs under positive pressure of nitrogen. Color of the reaction mixture turned yellow after 30 min, and thereafter gradually turned black. Reduction of (cod)PtMe₂ was monitored periodically with UV-vis spectroscopy, which disclosed a gradual disappearance of shoulders associated with (cod)PtMe₂, and finally leading to a featureless spectrum. Later on, flow of nitrogen was stopped and the flask was exposed to air. Further stirring of solution for 6 to 12 hrs in open-air yielded a black gel-like solid. At this juncture, black gel-like solid was filtered and washed with excess of toluene and then dried overnight, which resulted in black powder of Pt-nanoclusters.

3.4 References

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CHAPTER 4

4

Applications of Inorganic/Organic

Hybrid materials in Catalysts Generation and Catalysis

4.1 Introduction

In chemical and biological sciences, catalysis has a significant importance. Most of the important and everyday reactions involve catalysis, whether it's a small-scale reaction in a chemical laboratory or industrial production of an important chemical or a reaction in human body. The example of earliest important catalytic process on a commercial level is the Haber process for ammonia synthesis. Research into catalysis is a major field in applied science, and involves many fields of chemistry notably in organometallics chemistry and synthesis of novel materials with improved properties and performances. The choice of a proper catalyst is the key step for any chemical reaction involving catalysis as the catalyst not only increases the speed of the reaction but it also influences the quantity and quality of the product. The quality of the product may mean many things in chemical terms, such as stereoselectivity, regioselectivity, no side reactions, no or minimum by-products, easy isolation of the catalyst etc. Most of the conventional catalysts used are metal complexes or acidic or basic in nature.¹⁻⁹ Therefore separation of the catalyst from the reaction mixture and isolation of clean product is necessary, as any remaining catalyst in the system is regarded as contamination. This contamination may cause for the product to be toxic and hazardous or it simply may

cause further side reactions making the product impure. From commercial and industrial point of view, recyclability of the catalyst is another important factor as it plays an important role in cost effectiveness of the product. Most of the conventional catalysts lack these features and thus such limitations of catalytic systems prompted scientists to formulate new catalytic systems, which can overcome the drawbacks of conventional catalysis.

In recent years, transition metal nanoparticles have gained a growing interest in pursuit of new and efficient catalysts. The highly active surfaces of transition metal nanoclusters make them interesting candidates for catalysis and a great deal of research has been focused on the study of their catalytic properties.¹⁰⁻¹⁴ Nanoparticles have high surface areas, consequently more surface atoms are available to the substrate making the surface highly active. Thus the large surface to volume ratio of nanoparticles provides them with unusual features, which differ greatly from their bulk states.¹⁵⁻¹⁹ Examples can be found in literature where a number of catalytic reactions were reported such as hydrogenation, hydroformylation, hydrosilylation, C-C cross coupling, oxidation reactions etc, where metal nanoparticles were used as active catalysts.²⁰⁻²⁴

Despite all the research and efforts in fabricating new and efficient metal nanocluster catalysts, there are still many challenges facing the scientific community. The synthesis of metal nanoparticles active for catalysis, long term stability, preparation on commercial scale, cost effectiveness, particle size control, control over shape, accessibility of particle surface are some of the key aspects that need continuous development in coming future. It has been observed that the stability, particle size, and properties of metal nanoparticles strongly depend on the specific method of preparation

and the stabilizer used. As the metal nanoparticles are extremely active and thus very unstable, a stabilizer is necessary to be introduced in order to prevent them from agglomeration. In most cases, nanoparticles are stabilized with strong coordinating surfactants to prevent the agglomeration. The major drawback of conventional stabilizers is that they passivate most of the particle surface thus decreasing or totally killing the catalytic activity. Therefore, it is desirable to develop synthetic strategies and stabilizers that will allow one to prepare nanoparticles have better stability, long-term activity and maximum available surface area for efficient catalytic transformations.

4.2 Results and Discussion

The choice of a good reducing agent and a proper stabilizer is important in metal nanoparticle generation in order to attain maximum catalytic activity of nanoclusters. In our approach to achieve this goal, we utilized cyclic siloxanes based inorganic/organic hybrid composites of second generation. The alkoxy siloxanes were prepared by polyethylene glycol modification on cyclic siloxane core. The reason to use the I/O hybrid alkoxy siloxanes is their potential dual property of acting as reducing and stabilizing agents at the same time. Silanes and polysiloxanes containing Si-H bonds have been reported to be excellent reductants.²⁵ The involvement of Si-H bonds produces hydrogen in the presence of certain metal complexes and this property is most likely responsible for reducing the metal complexes into zero oxidation state. We envision that further unique properties of alkoxy siloxanes such as flexibility of Si-O bonds, hydrophobicity siloxanes, amphiphilic nature of resulting hybrids, tendency to create micelles in selective solvents etc may provide with means of excellent stabilization and

minimum passivation of nanoparticles' surfaces without the need of an additional surfactant. Using this approach, nanoparticles of platinum and palladium metals were synthesized and catalytic activity of platinum nanoparticles was investigated further in hydrosilylation reactions.

4.2.1 Synthesis of Alkoxy Siloxanes to be utilized as Stabilizer for Nanoparticles

The first step in our synthetic strategy was the preparation of alkoxy siloxanes of second generation. The synthesis was carried out in similar fashion as also described in earlier chapters. A cyclic siloxane 1,3,5,7-tetramethylcyclotetrasiloxane (TMCTS) also referred to as D_4^H was used as the core for the generation of alkoxy siloxane macromolecules. The reaction was carried in a 50 ml Schlenk tube equipped with a magnetic stirring bar. All the substrates i.e. Wilkinson's catalyst $RhCl(PPh_3)_3$ (~0.002 g, 0.002 mmol), polyethylene glycol (PEG) (1.6 g, 4 mmol; $M_w \sim 400$), and 1,3,5,7-tetramethylcyclotetrasiloxane (TMCTS) (0.24 g, 1 mmol) were taken in the Schlenk tube followed by addition of solvent (Benzene 5 ml) and tube was degassed and filled with nitrogen three times. The reaction mixture was heated at $65^\circ C$ for about 30 hours with continuous stirring. During the course of reaction, the reaction mixture became yellow and evolution of a gas (presumably H_2), was observed. After 30h of the reaction, complete consumption of Si-H bonds of TMCTS and formation of polyethylene glycol was observed in near quantitative yield by means of NMR spectroscopy. For this purpose, 1ml of the reaction mixture was taken out with the help of a syringe. ^{29}Si NMR of starting siloxane TMCTS shows four peaks centered at $\delta = -31$ ppm arising from D-type silicon (O-SiMeH-O-) units, where silicon atom is attached to two oxygen atoms.

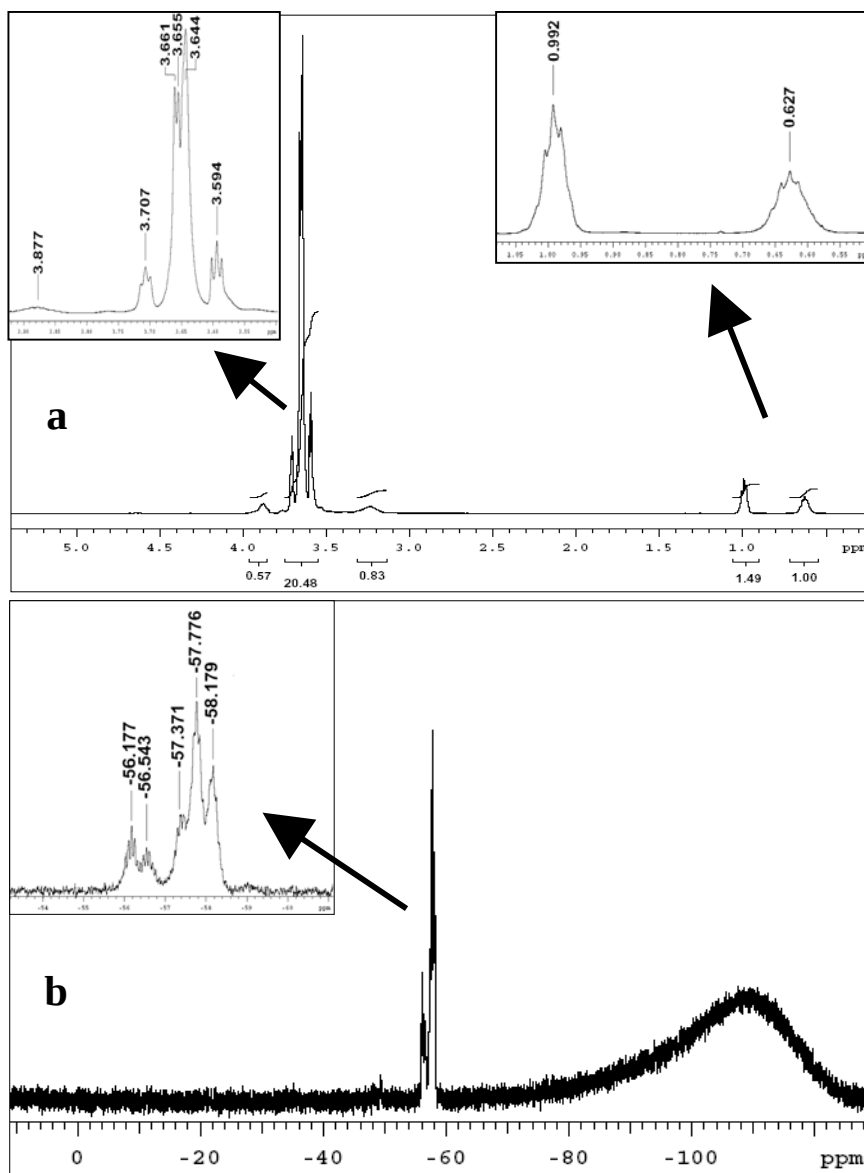


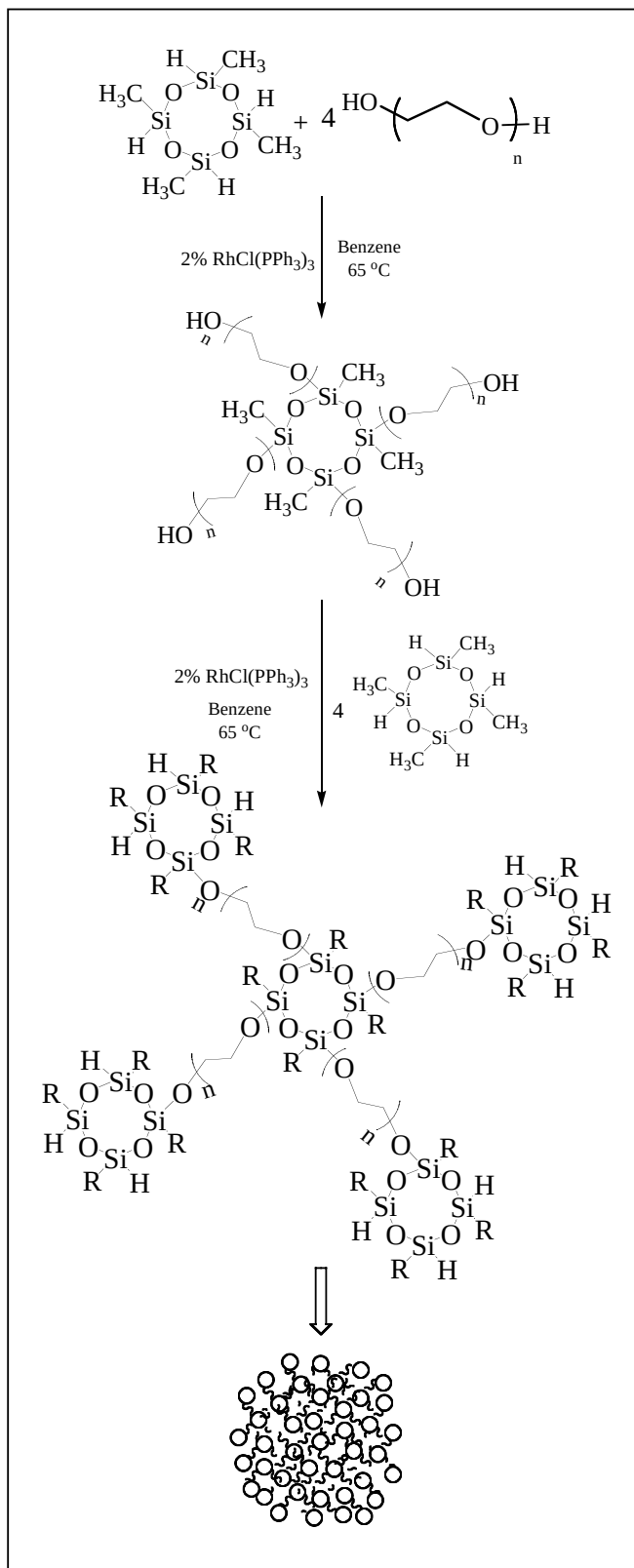
Figure 1: ^1H (a) and ^{29}Si (b) NMR spectra of polyethylene glycol substituted cyclosiloxane

After glycolysis, the ^{29}Si NMR analysis of resulting product showed peaks centered at $\delta = -56$ to -57 ppm, reflecting the change in electronic environment of Si units due to the formation of new T-type ($\text{SiMe-OCH}_2\text{CH}_2\text{O}$) moieties, where silicon atom is attached to three oxygen atoms. No residual signals due to Si-H bonds were observed in ^{29}Si NMR of the product, indicating complete consumption of the Si-H bonds. (Figure 1) Similarly, Si-H functionality of TMCTS shows a peak at $\delta \sim 4.5$ ppm in ^1H NMR. After completion,

no residual peak at this position was observed.

After confirmation of complete substitution, reaction was further continued to synthesize the second generation. The remaining amount of the product was calculated and four additional equivalents of 1,3,5,7-tetramethylcyclotetrasiloxane

(TMCTS) (0.77 g, 3.2 mmol) were added to the reaction mixture in order to cap the four hydroxyl end groups of substituted polyethylene glycol tails. Additional amount of Wilkinson's catalyst $\text{RhCl}(\text{PPh}_3)_3$ (~0.001 g, 0.001 mmol) was also added. Schlenk tube was degassed and filled with nitrogen three more times and reaction was allowed to continue at 65 °C for about 32 hours with continuous stirring. The reaction mixture was periodically



Scheme 1: General synthetic route to second generation alkoxy siloxanes and the idealized structure of product.

monitored with ^1H , and ^{29}Si NMR. Upon completion, reaction mixture was a viscous liquid of dark brown color. Scheme 1 represents a general synthetic route of the reaction. Additional solvent was added to reaction mixture in order to decrease the viscosity and mixture was centrifuged at 9000 rpm for about 30 min in order to separate the catalyst. Supernatant was carefully decanted and solvent was evaporated to obtain the viscous product of light yellow color. Product was kept in a nitrogen atmosphere and the long-

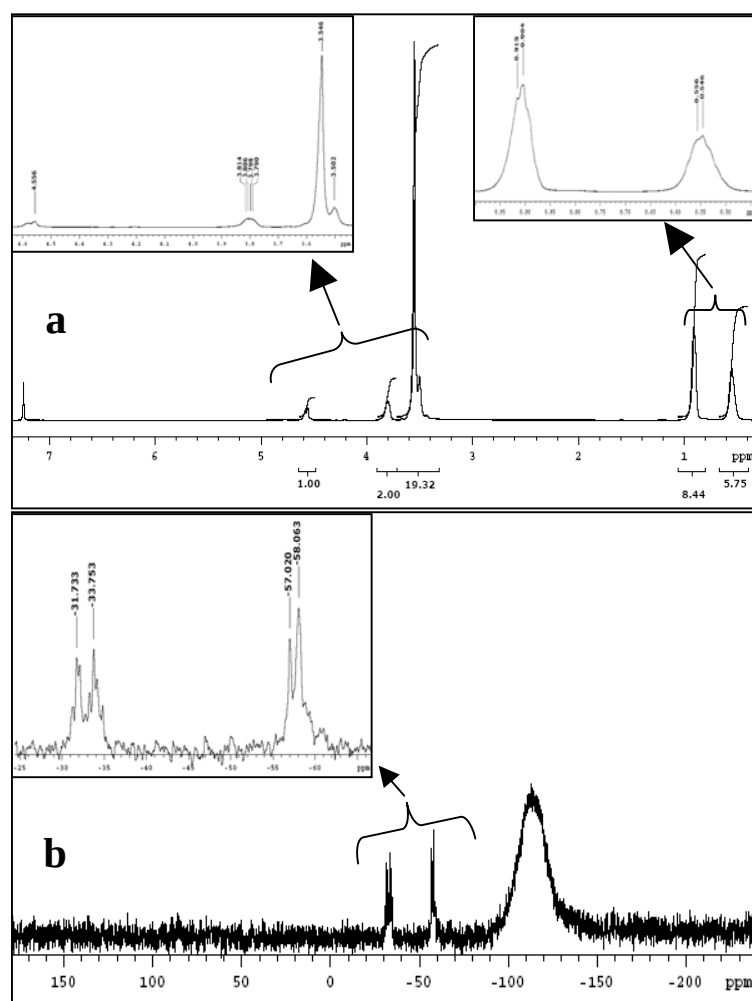


Figure 2: NMR spectra of second generation alkoxy siloxane. (a) ^1H and (b) ^{29}Si .

term exposure to oxygen and moisture caused cross-linking of product and ended up in a gel form. ^{29}Si NMR of product showed appearance of two new peaks centered at $\delta = -32$ ppm. These new peaks correspond to D-type silicon (O-SiMeH-O-) units arising from the attachment of four equivalents of 1,3,5,7-tetramethylcyclotetrasiloxane (TMCTS). The ^1H NMR of the product also showed new signals at $\delta = 4.5$ ppm as a

result of new Si-H bonds present. Figure 2 shows the NMR spectra of product. The

second generation alkoxy siloxane material prepared was further used as a reducing and stabilizing agent for the generation of platinum and palladium nanoparticles.

4.2.2 Generation of Metal Nanoparticles

Synthesis of nanoclusters was carried out by reduction of metal salts in organic solvent utilizing second generation alkoxy siloxane as the reducing and stabilizing agent. For the synthesis of platinum nanoclusters was performed in a 500 ML round bottom flask, equipped with a magnetic stirring bar and a vacuum inlet. Platinum complex (cod)PtMe₂ (cod: 1,5 cyclo-octadiene) (0.024 g, 0.075 mmol) was taken in the flask and flask was degassed and filled with nitrogen followed by addition of toluene (20 ml). After stirring for 5 min, second generation alkoxy siloxane product (2.09 g, 0.75 mmol) was added and reaction mixture was stirred at 80 °C for 24 hrs under positive pressure of nitrogen. Color of the reaction mixture turned yellow after 30

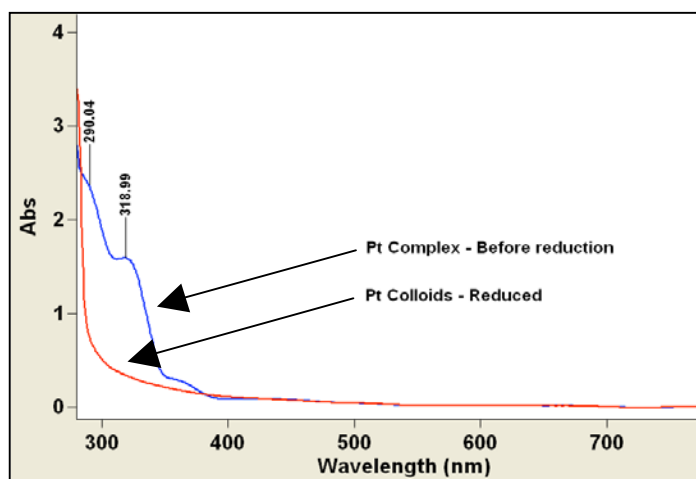


Figure 3: UV-vis spectra of platinum complex before reduction and platinum nanoparticles after reduction.

min, and thereafter gradually turned dark brown. Reduction of (cod)PtMe₂ was monitored periodically with UV-vis spectroscopy, which disclosed a gradual disappearance of shoulders associated with (cod)PtMe₂, and finally leading to a featureless spectrum, which was the evidence of complete reduction of Pt(II) to Pt(0) (Figure 3). After confirming the reduction of (cod)PtMe₂, the solution was further characterized with

transmission electron microscopy (TEM) for the presence of nanoclusters. One drop of the solution was deposited on a carbon-formvar coated copper grid at room temperature. The solvent was allowed to evaporate from the grid under normal temperature and pressure for about one hour before the TEM examination of the grid. TEM analysis of the solution revealed platinum nanoclusters with a narrow size distribution. Figure 4 shows the platinum nanoparticles present in the colloidal solution. The colloidal solution was collected in a glass vial and it was stable and catalytically active for almost a couple of months. Scheme 2 represents a general route to synthesis of platinum and palladium nanoparticles.

In a similar fashion, palladium nanoparticles were synthesized reducing palladium acetate by second generation alkoxy siloxane product, which also acted as the

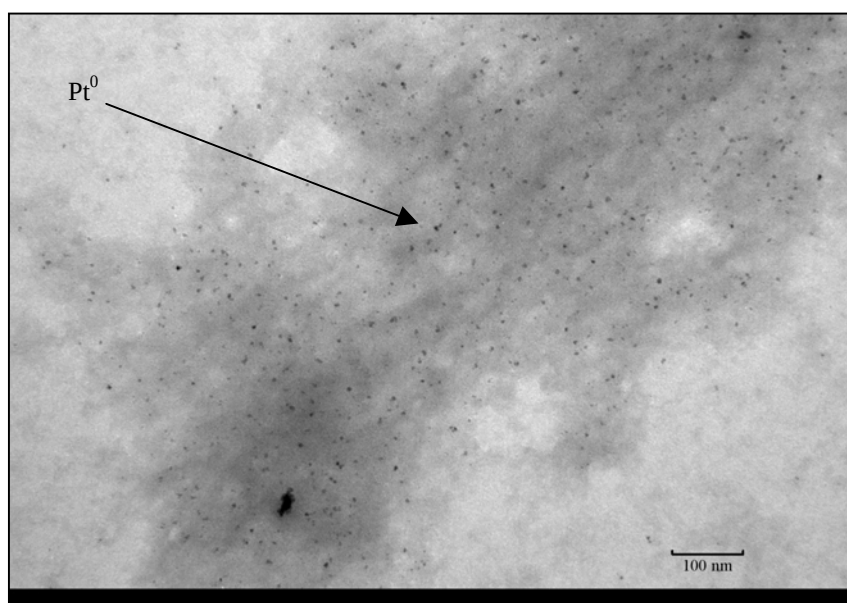
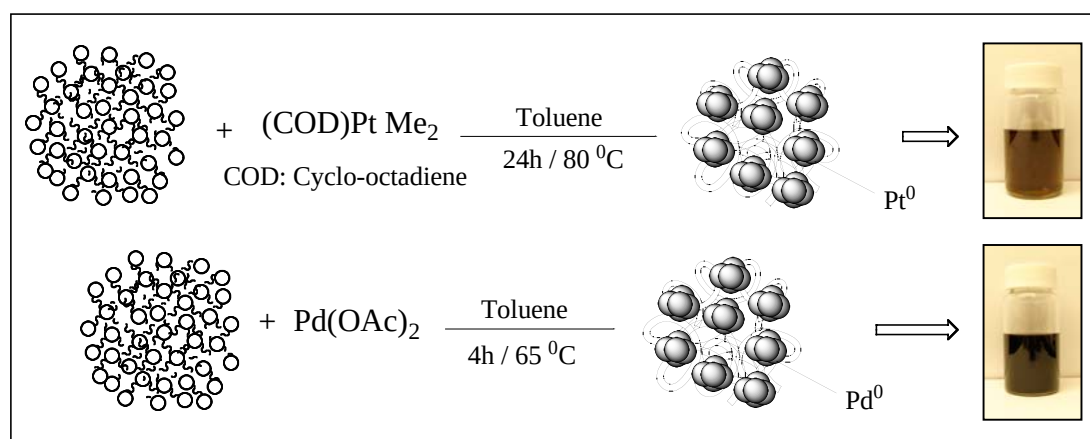


Figure 4: Platinum nanoparticles present in colloidal solution.

stabilizer for the particles. In a 500 ML round bottom flask, equipped with a magnetic stirring bar, palladium acetate [Pd(OAc)₂] (0.017 g, 0.075 mmol) was dissolved in 20 ml of dry toluene and a yellow solution was obtained. While stirring the mixture, second

generation alkoxy siloxane product (2.09 g, 0.75 mmol) was added to this yellow solution. The color of the reaction mixture started to change immediately from yellow to brown and in about 15 min, it changed further to dark brown and finally turned black. Evolution of gas (H_2 , presumably) was observed along with the color change with continuous stirring. The progress of reaction was monitored by UV-vis analysis of the reaction mixture. Palladium acetate gives a peak around $\lambda = 400$, which gradually disappeared in about two hours and a featureless UV-vis spectra indicated conversion of Pd(II) to Pd(0). At this point, stirring was stopped and solution was collected in a glass vial and further analysis was carried out by examining the solution under transmission electron microscope. For this purpose, one drop of the solution was deposited on a



Scheme 2: Reduction of metal salts to metal nanoparticles using second generation alkoxy siloxane and generation of colloidal solutions.

carbon-formvar coated copper grid at room temperature. The solvent was allowed to evaporate for about one hour under normal temperature and pressure conditions. TEM analysis of the solution revealed palladium nanoclusters with a narrow size distribution. Results of TEM and UV-vis spectroscopy are shown in Figure 5. The colloidal solution was stable for almost a couple of months. To verify the catalytic activity of the colloidal

solutions, platinum nanoparticle solution was used as catalyst in hydrosilylation reactions, which showed excellent catalytic activity and selectivity.

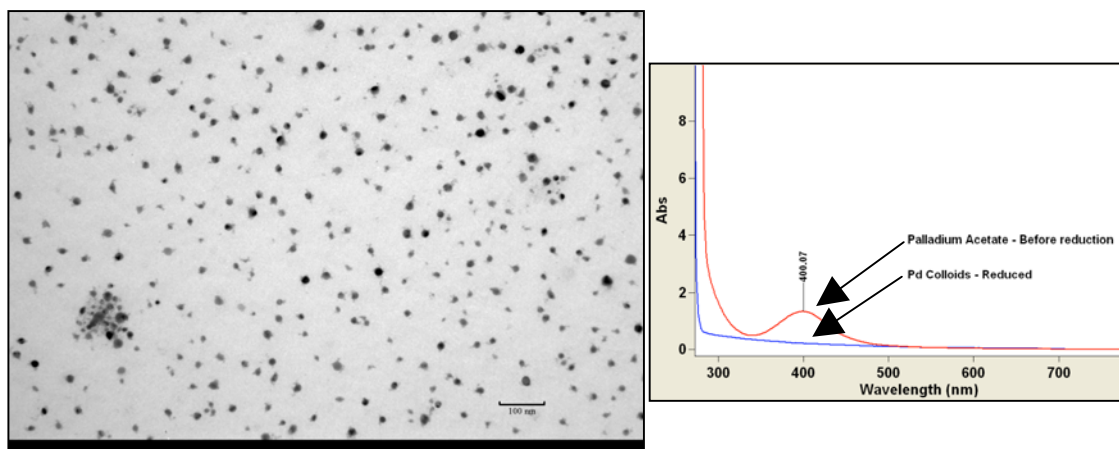


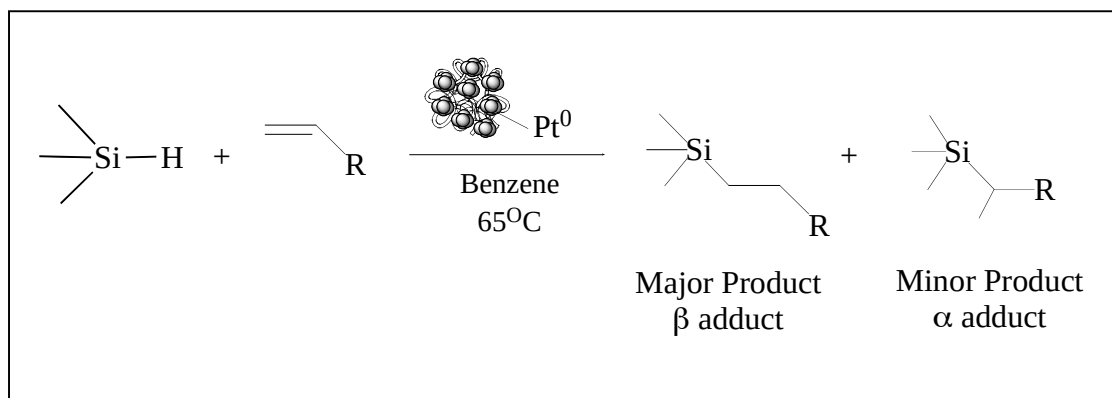
Figure 5: TEM analysis of colloidal solution. (b) UV-vis spectroscopy of palladium acetate and palladium colloids before and after reduction.

4.2.3 Hydrosilylation Reactions using Pt-nanoclusters as Catalyst

Hydrosilylation reactions are the addition of Si-H bonds across the unsaturated carbon-carbon double bonds of alkenes. This type of addition allows for the synthesis of organosilicon materials by introduction of organic functional groups into inorganic silicon based frameworks. Organosilicon materials are an important class of hybrid materials having enhanced and refined properties when compared with organic materials. Some of the key properties of organosilicon materials are high thermal stability, low toxicity, biocompatibility, high oxygen permeability, poor wettability, low surface tension, low glass-transition temperature, and radiation resistance etc.²⁶⁻²⁸

The first hydrosilylation reaction was reported by Speier²⁹ where he used H_2PtCl_6 as the catalyst. Later on, complexes of several other metals such as Pt, Pd, Ni,

Ru, Rh, Cu, Ir were used for hydrosilylation reactions as catalysts. The most widely used catalyst for such reactions is, however, the Karstedt catalyst. The major drawback of using these catalysts was the lack of control over regioselectivity, which resulted in a mixture of α and β products. Scheme 3 shows a general synthetic route of hydrosilylation reaction and possible products. Another challenge was to gain quantitative yields and the

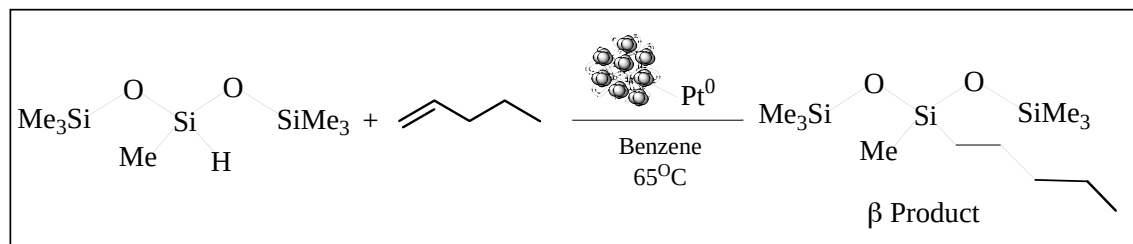


Scheme 3: General scheme of hydrosilylation of heptamethyltrisiloxane (HMTS) with alkenes and two possible products.

recyclability of the catalyst. As most of the transition metal complexes used for hydrosilylation are expensive, cost effectiveness is a major hurdle at industrial scale production. Therefore, generation of a hydrosilylation catalyst that can overcome these obstacles is highly desirable. Lewis and coworkers reported in 1980's the possible involvement of metal colloids for hydrosilylation and better control over regioselectivity.³⁰⁻³⁵ Since then, a lot of research has been focused on to investigate the potential of metal nanoparticles for hydrosilylation reactions.

We used the platinum colloidal solution as the catalyst for hydrosilylation of Si-H bonds with the unsaturated carbon-carbon double bonds of alkenes. To probe the catalytic activity, heptamethyltrisiloxane (HMTS) was chosen as the precursor due to the availability of central tunable Si-H group, which can be hydrosilylated with organic

functionalities. In a typical procedure, platinum colloidal solution (1 ml) was taken in a 50 ml Schlenk tube equipped with a magnetic stirring bar, followed by the addition of heptamethyltrisiloxane (HMTS) (0.27 ml; 1 mmol). Tube was degassed and filled with nitrogen three times and solvent (Benzene 3ml) along with 1-pentene (0.11 ml, 1 mmol) was introduced to the reaction mixture. Reaction was continued for 24 hrs at room temperature. The progress of the reaction was monitored with ^1H NMR spectroscopy, which revealed gradual disappearance of peaks associated with Si-H ($\delta = 4.5\text{ppm}$) and olefinic- protons ($\delta = 4.8\text{-}6.0\text{ ppm}$) and appearance of the new triplet peaks in the

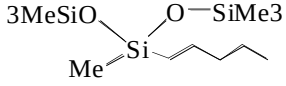
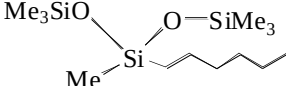
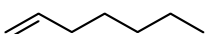
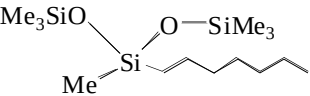
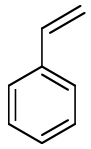
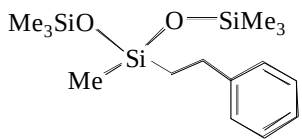
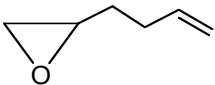
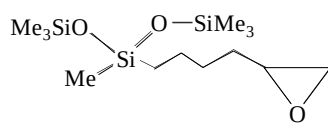
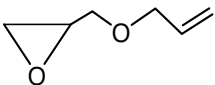
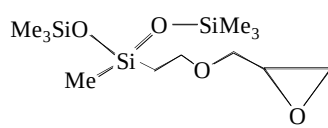
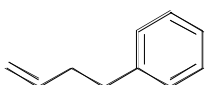
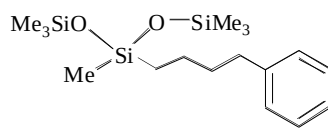


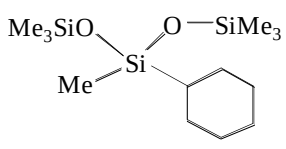
Scheme 4: Hydrosilylation of heptamethyltrisiloxane (HMTS) with 1-pentene and formation of exclusively β product.

methylene region. Moreover, ^{29}Si NMR of the product showed single peaks supporting selective substitution of pentyl group. A general synthetic scheme of hydrosilylation of 1-pentene with heptamethyltrisiloxane (HMTS) is shown in scheme 4.

A number of alkenes were used for hydrosilylation with heptamethyltrisiloxane (HMTS) and almost all the substrates produced β adduct as the major product. The exception was in case of styrene, which produced a 40:60 % ratio of α and β products. Table 1 summarizes the different alkenes used, general reaction conditions, percentage of α to β products, and yields of the products. All the product ratios were calculated using multinuclear spectroscopic analysis of crude reaction mixture and represent ratio of α to β products.

Table 1: Summary of hydrosilylation of heptamethyltrisiloxane (HMTS) with different alkenes and product details.

Entry	Alkenes	Reaction Condition	Major Product	Ratio $\alpha:\beta$	Yield (%)
1		18h/RT		0:100	98
2		20/RT		0:100	98
3		24h/70°C		0:100	98
4		24h/70°C		40:60	98
5		28h/70°C		20:80	95
6		28h/70°C		20:80	95
7		28h/70°C		20:80	85

8		42h/70°C		100	80
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Product yields represent the mixture of regioselective products and was calculated using multinuclear spectroscopic technique. All the reactions and products were monitored with ^1H and ^{29}Si NMR and a shift in the peaks and/or appearance of new peaks were observed. Figure 6 shows ^{29}Si NMR comparison of heptamethyltrisiloxane (HMTS) before and after hydrosilylation with selected alkenes.

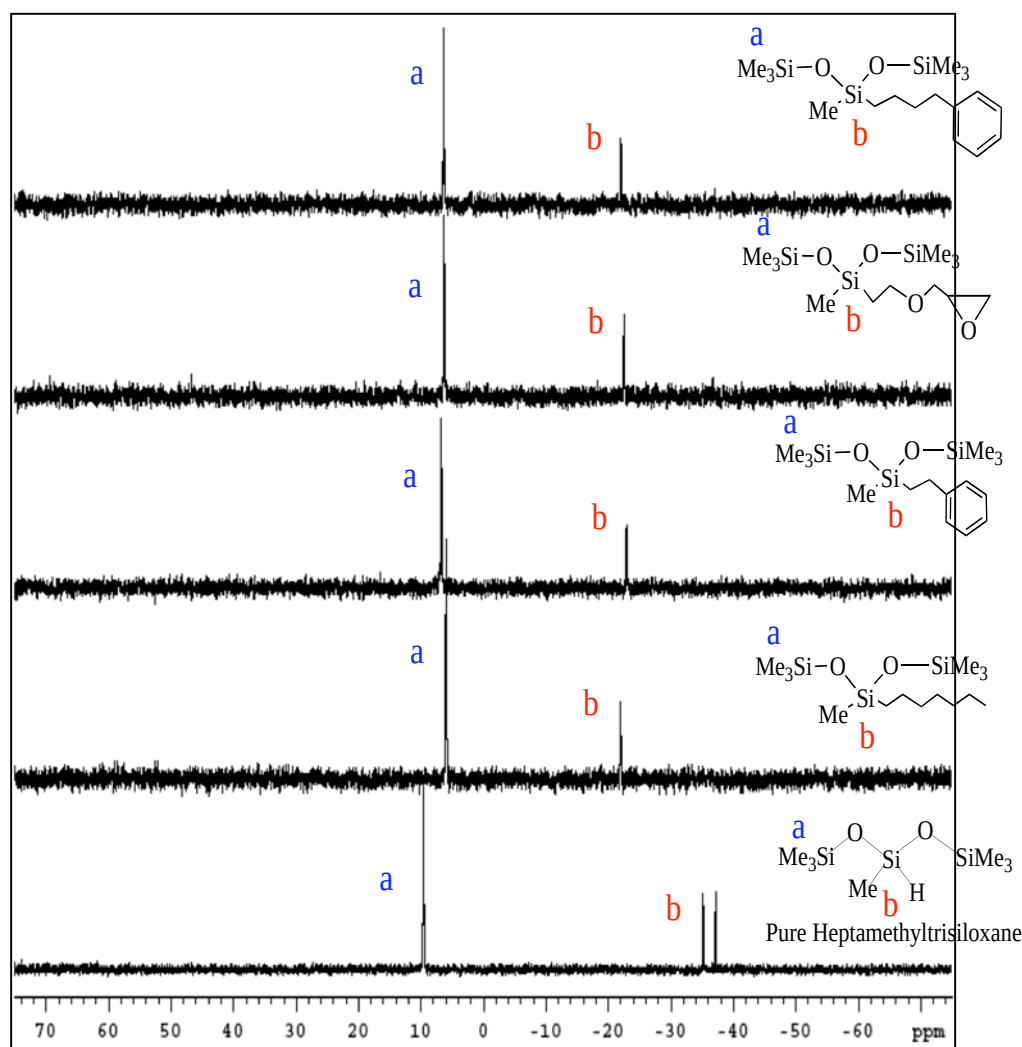


Figure 6: NMR analysis of selected hydrosilylated products.

4.3 Experimental Section

4.3.1 General Information

All reactions were carried out under a positive pressure of dry Argon or Nitrogen using standard Schlenk-tube technique.

Chemicals. All solvents were purchased from EM science (Merck) and distilled over sodium/benzophenone before use. Wilkinson's catalyst $\text{RhCl}(\text{PPh}_3)_3$, $(\text{cod})\text{PtMe}_2$, Palladium acetate, Polyethylene glycol (MW = 400), heptamethyltrisiloxane (HMTS), and all alkenes except 4-phenyl-1-butene were purchased from Aldrich Chemical Co. and used as received. 4-Phenyl-1-butene was purchased from GFS Chemicals and used as received. 1,3,5,7-tetramethylcyclotetrasiloxane (TMCTS) was obtained from Gelest Inc. and used as received.

NMR Spectroscopy. ^1H NMR (200 MHz, 300 MHz), and ^{29}Si NMR (600 MHz) spectra were recorded in CDCl_3 or C_6D_6 on Varian Unity NMR instruments. ^{29}Si NMR spectra were referenced to Me_4Si . Proton spectra were referenced according to solvent proton shifts. All of the peaks in the NMR spectra were reported in ppm.

Transmission Electron Microscopy (TEM). Philips CM 100-transmission electron microscope (TEM) was used to study the metal nanoparticle presence in colloidal solutions. Formavar coated copper-carbon grids were purchased from Electron Microscopy Sciences. Generally, the TEM grids were prepared under standard temperature and pressure and solvent was allowed to evaporate for one hour before examination of the grid. To affirm the validity of the TEM results, images were taken at different magnifications and were examined thoroughly to rule out any "electron beam" induced modifications.

4.3.2 Synthesis of second generation alkoxy siloxane

The reaction was carried in the following day. In a 50 ml Schlenk tube equipped with a magnetic stirring bar, all the substrates i.e. Wilkinson's catalyst $\text{RhCl}(\text{PPh}_3)_3$ (~0.002 g, 0.002 mmol), polyethylene glycol (PEG) (1.6 g, 4 mmol; $M_w \sim 400$), and 1,3,5,7-tetramethylcyclotetrasiloxane (TMCTS) (0.24 g, 1 mmol) were taken followed by addition of solvent (Benzene 5 ml) and tube was degassed and filled with nitrogen three times. The reaction mixture was heated at 65°C for about 30 hours with continuous stirring. During the course of reaction, the reaction mixture became yellow and evolution of a gas (presumably H_2), was observed. After 30hrs, stirring was stopped and 1ml of reaction mixture was taken out with a syringe to analyze with NMR for complete substitution of polyethylene glycol on cyclosiloxane core. After confirmation of complete substitution, reaction was further continued to synthesize the second generation alkoxy siloxane. The remaining amount of the product was calculated and four additional equivalents of 1,3,5,7-tetramethylcyclotetrasiloxane (TMCTS) (0.77 g, 3.2 mmol) were added to the reaction mixture. Additional amount of Wilkinson's catalyst $\text{RhCl}(\text{PPh}_3)_3$ (~0.001 g, 0.001 mmol) was also added. Schlenk tube was degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C for another 32 hours with continuous stirring. The reaction mixture was periodically monitored with ^1H , and ^{29}Si NMR. Upon completion, reaction mixture was a viscous liquid of dark brown color.

Synthesis of 1st generation: ^1H NMR (δ , ppm): 0.627 (m), 0.992 (m), 3.594 (s), 3.655 (m), 3.707 (m), 3.877 (m); ^{29}Si NMR (δ , ppm): -57.776 (m), -56.177 (m). Yield: 100%

Synthesis of 2nd generation: ¹H NMR (δ, ppm): 0.686 (m), 1.036 (m), 3.538 (s), 3.975 (m), 4.980 (m); ²⁹Si NMR (δ, ppm): -57.62 (m), -55.83 (m), -31.73 (m), -29.680 (m).

Yield: 98%

4.3.3 Synthesis of metal nanoparticles

Platinum nanoparticles:

Synthesis of platinum nanoclusters was performed in the following way. In a 500 ML round bottom flask, equipped with a magnetic stirring bar and a vacuum inlet, platinum complex (cod)PtMe₂ (cod: 1,5 cyclo-octadiene) (0.024 g, 0.075 mmol) was taken and flask was degassed and filled with nitrogen followed by addition of toluene (20 ml). After stirring for 5 min, second generation alkoxy siloxane product (2.09 g, 0.75 mmol) was added and reaction mixture was stirred at 80 °C for 24 hrs under positive pressure of nitrogen. Color of the reaction mixture turned yellow after 30 min, and thereafter gradually turned dark brown. Reduction of (cod)PtMe₂ was monitored periodically with UV-vis spectroscopy, which disclosed a gradual disappearance of shoulders associated with (cod)PtMe₂, and finally leading to a featureless spectrum, which was the evidence of complete reduction of Pt(II) to Pt(0). After confirming the reduction of (cod)PtMe₂, the solution was further characterized with transmission electron microscopy (TEM) for the presence of nanoclusters.

Platinum nanoparticles:

In a 500 ML round bottom flask, equipped with a magnetic stirring bar, palladium acetate [Pd(OAc)₂] (0.017 g, 0.075 mmol) was dissolved in 20 ml of dry toluene and a yellow solution was obtained. While stirring the mixture, second generation alkoxy siloxane

product (2.09 g, 0.75 mmol) was added to this yellow solution. The color of the reaction mixture started to change immediately from yellow to brown and in about 15 min, it changed further to dark brown and finally turned black. Evolution of gas (H_2 , presumably) was observed along with the color change with continuous stirring. The progress of reaction was monitored by UV-vis analysis of the reaction mixture. Palladium acetate gives a peak around $\lambda = 400$, which gradually disappeared in about two hours and a featureless UV-vis spectra indicated conversion of Pd(II) to Pd(0). At this point, stirring was stopped and solution was collected in a glass vial and further analysis was carried out by examining the solution under transmission electron microscope.

4.3.4 Hydrosilylation of heptamethyltrisiloxane (HMTS) with alkenes

Reaction with 1-Pentene (Entry 1, Table 1):

For reaction with 1-pentene, platinum colloidal solution (1 ml) was taken in a 50 ml Schlenk tube equipped with a magnetic stirring bar, followed by the addition of heptamethyltrisiloxane (HMTS) (0.27 ml; 1 mmol). Tube was degassed and filled with nitrogen three times and solvent (Benzene 3ml) along with 1-pentene (0.11 ml, 1 mmol) was introduced to the reaction mixture. Reaction was continued for 24 hrs at room temperature. The progress of the reaction was monitored with ^1H and ^{29}Si NMR spectroscopy and complete substitution of pentyl group was confirmed.

^1H NMR (δ , ppm): 0.024 (m), 0.356 (m), 0.785 (m), 1.227 (m); ^{29}Si NMR (δ , ppm): –20.87 (s), 7.11 (s).

Reaction with 1-Hexene (Entry 2, Table 1):

For reaction with 1-pentene, platinum colloidal solution (1 ml) was taken in a 50 ml Schlenk tube equipped with a magnetic stirring bar, followed by the addition of heptamethyltrisiloxane (HMTS) (0.27 ml; 1 mmol). Tube was degassed and filled with nitrogen three times and solvent (Benzene 3ml) along with 1-hexene (0.13 ml, 1 mmol) was introduced to the reaction mixture. Reaction was continued for 24 hrs at room temperature. The progress of the reaction was monitored with ^1H and ^{29}Si NMR spectroscopy and complete substitution of hexyl group was confirmed.

^1H NMR (δ , ppm): -0.02 (m), 0.37 (m), 0.80 (m), 1.21 (m); ^{29}Si NMR (δ , ppm): -20.9 (s), 7.1 (s).

Reaction with 1-Heptene (Entry 3, Table 1):

For reaction with 1-pentene, platinum colloidal solution (1 ml) was taken in a 50 ml Schlenk tube equipped with a magnetic stirring bar, followed by the addition of heptamethyltrisiloxane (HMTS) (0.27 ml; 1 mmol). Tube was degassed and filled with nitrogen three times and solvent (Benzene 3ml) along with 1-heptene (0.14 ml, 1 mmol) was introduced to the reaction mixture. Reaction was continued for 24 hrs at room temperature. The progress of the reaction was monitored with ^1H and ^{29}Si NMR spectroscopy and complete substitution of heptyl group was confirmed.

^1H NMR (δ , ppm): -0.08 (m), 0.002 (m), 0.37 (m), 0.80(m), 1.20(m); ^{29}Si NMR (δ , ppm): -20.90 (s), 7.05 (s).

Reaction with Styrene (Entry 4, Table 1):

For reaction with 1-pentene, platinum colloidal solution (1 ml) was taken in a 50 ml Schlenk tube equipped with a magnetic stirring bar, followed by the addition of heptamethyltrisiloxane (HMTS) (0.27 ml; 1 mmol). Tube was degassed and filled with

nitrogen three times and solvent (Benzene 3ml) along with styrene (0.11 ml, 1 mmol) was introduced to the reaction mixture. Reaction was continued for 24 hrs at room temperature. The progress of the reaction was monitored with ^1H and ^{29}Si NMR spectroscopy and reaction completion was confirmed.

^1H NMR (δ , ppm): 0.074 (m), 0.800 (t), 1.279 (d), 2.023 (q), 2.606 (t), 3.575 (s); ^{29}Si NMR (δ , ppm): -21.7 (s), 7.95 (s).

Reaction with 1,2-Epoxy-5-hexene (Entry 5, Table 1):

For reaction with 1-pentene, platinum colloidal solution (1 ml) was taken in a 50 ml Schlenk tube equipped with a magnetic stirring bar, followed by the addition of heptamethyltrisiloxane (HMTS) (0.27 ml; 1 mmol). Tube was degassed and filled with nitrogen three times and solvent (Benzene 3ml) along with 1,2-epoxy-5-hexene (0.11 ml, 1 mmol) was introduced to the reaction mixture. Reaction was continued for 24 hrs at room temperature. The progress of the reaction was monitored with ^1H and ^{29}Si NMR spectroscopy and reaction completion was confirmed.

^1H NMR (δ , ppm): 0.12, -0.01, 0.37(m), 1.35(m), 2.25(m), 2.53(m), 2.71(m); ^{29}Si NMR (δ , ppm): -21.62 (s), 6.97 (s).

Reaction with Allyl glycidyl ether (Entry 6, Table 1):

For reaction with 1-pentene, platinum colloidal solution (1 ml) was taken in a 50 ml Schlenk tube equipped with a magnetic stirring bar, followed by the addition of heptamethyltrisiloxane (HMTS) (0.27 ml; 1 mmol). Tube was degassed and filled with nitrogen three times and solvent (Benzene 3ml) along with allyl glycidyl ether (0.12 ml, 1 mmol) was introduced to the reaction mixture. Reaction was continued for 24 hrs at room

temperature. The progress of the reaction was monitored with ^1H and ^{29}Si NMR spectroscopy and reaction completion was confirmed.

^1H NMR (δ , ppm): 0.39 (m), 1.52 (m), 2.46 (m), 2.67 (t), 3.05 (m), 3.56 (m), 3.62 (m);

^{29}Si NMR (δ , ppm): -21.32 (s), 7.56 (s).

Reaction with 4-Phenyl-1-butene (Entry 7, Table 1):

For reaction with 1-pentene, platinum colloidal solution (1 ml) was taken in a 50 ml Schlenk tube equipped with a magnetic stirring bar, followed by the addition of heptamethyltrisiloxane (HMTS) (0.27 ml; 1 mmol). Tube was degassed and filled with nitrogen three times and solvent (Benzene 3ml) along with 1-phenylbutene (0.15 ml, 1 mmol) was introduced to the reaction mixture. Reaction was continued for 24 hrs at room temperature. The progress of the reaction was monitored with ^1H and ^{29}Si NMR spectroscopy and reaction completion was confirmed.

^1H NMR (δ , ppm): 0.037 (m), 0.458 (t), 0.869 (t), 1.330 (m), 1.583 (m), 2.533 (t), 7.073 (m), 7.164 (m); ^{29}Si NMR (δ , ppm): -22.05 (s), 6.31 (s).

Reaction with Cyclohexene (Entry 8, Table 1):

For reaction with 1-pentene, platinum colloidal solution (1 ml) was taken in a 50 ml Schlenk tube equipped with a magnetic stirring bar, followed by the addition of heptamethyltrisiloxane (HMTS) (0.27 ml; 1 mmol). Tube was degassed and filled with nitrogen three times and solvent (Benzene 3ml) along with cyclohexene (0.10 ml, 1 mmol) was introduced to the reaction mixture. Reaction was continued for 24 hrs at room temperature. The progress of the reaction was monitored with ^1H and ^{29}Si NMR spectroscopy and reaction completion was confirmed.

^1H NMR (δ , ppm): 0.15 (m), 1.31 (m), 1.65(m), 2.03 (m), 2.4 (m); ^{29}Si NMR (δ , ppm): –
21.78 (s), 7.56 (s).

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CHAPTER 5

5 Applications of Inorganic/Organic (I/O) Hybrid Nanocomposites in Drug Delivery

** Some of the work presented in this chapter was part of a collaborative project with Becton, Dickenson and Company (BD Technology). A patent was filed based on techniques described in this chapter.*

5.1 Introduction

In recent decades, drug discovery and drug development has gained a rapid growth due to improvements in technologies that have given rise to new and novel methods for drug discovery. As a result, drugs have been developed that are more effective and have better solubility profile in aqueous media of human body. With this increase in drug development and birth of new and more effective drugs everyday, the need for better drug delivery methods and materials for an efficient and precise drug delivery to the targeted areas has also increased. As a result, a lot of research is being focused on drug delivery systems. Controlled drug delivery technology represents one of the most rapidly advancing areas of science in which scientists are contributing to human health care. In comparison with conventional dosage forms, these delivery systems not only provide several advantages such as improved efficiency and reduced toxicity, but they also offer improved patient compliance and convenience.¹ Such systems use supports or shells as carriers for the drugs. Examples of these carriers include liposomes, synthetic polymers, polymeric micelles, microspheres, nano-composites etc.²⁻⁹ If synthetic polymers can be designed, which can prevent the drug molecules from leaking

and thus increase the circulation times, they can act as carriers and a source of drug delivery at the point of action via intravenous or oral dosage without the need of surgery or catheter insertions. Moreover, polymeric particles responsive to subtle changes in environmental conditions also stand out as potential excipients, where the structural conformation is altered by certain changes in the polymer environment such as a change in temperature or pH. Such polymers are called stimuli-responsive polymers or simply responsive delivery carriers.¹⁰⁻²³

The responses of polymers can be manifold, for example dissolution, precipitation, degradation, swelling, collapse, shrinkage, change in shape, conformational change, etc. An example of such a system is treatment of diabetes. For diabetes treatment,

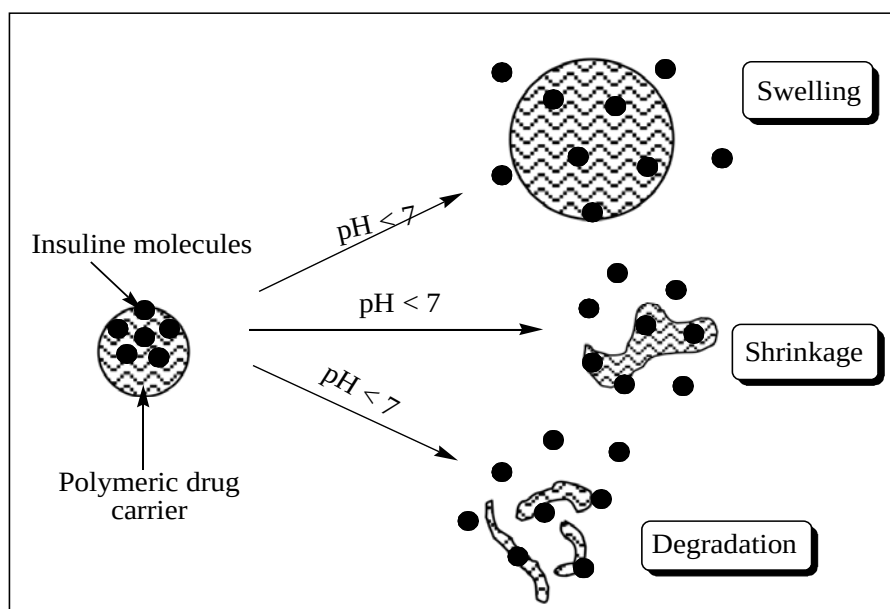


Figure 1: Delivery of Insulin as a result of swelling, shrinkage or degradation of carrier.

responsive drug delivery systems have been proposed that use the enzyme glucose oxidase as the sensor. When blood sugar levels rise, glucose oxidase converts glucose to gluconic acid resulting in lowered pH. This pH decrease is then used as the signal for

insulin release. Release is achieved by pH-sensitive polymers that shrink, swell, or degrade in acidic environments (Figure 1).^{1, 24, 25}

For the treatment of any disease, approaches that kill affected cells while leaving non-target tissues unaffected are highly desirable. Furthermore, preventing the drug from any side reactions and delivering the maximum amount to the targeted cells is also highly desirable. When a drug is administered in the body, the drug is distributed throughout the body via blood stream. A pharmacologically active concentration is reached in the targeted tissue at the expense of massive contamination of the rest of the body. As drugs are toxic not only to affected cells, they are as toxic for the normal cells too. Therefore, the efficiency of drug is often limited by important side effects. Moreover, as the drug travels throughout the body, a large part of it is lost before it reaches the target and only a very small percentage of drug is delivered to the point of action, thus decreasing the efficiency. The acidic environment in the stomach is another hurdle in acquiring the maximum efficiency of the drug. The drug molecules may be ionized in the acidic environment, preventing their diffusion across cellular membrane. All these obstacles lead to the need of development of new drug delivery methods and novel materials that can be used as effective drug delivery carriers that can distribute the therapeutically active drug molecule only to the site of action, without effecting healthy organs and tissues.

Another key element for a successful cure of vital diseases is to detect and treat them at earliest changes. One example of a vital disease is cancer. If cancer is not detected and treated at its earliest stages, it spreads to the other parts of body making the cure impossible and thus resulting in death of the patient. Therefore, scientists and

doctors must be able to detect changes at a molecular level and cure them before they spread and attack other parts of the body. This demands for the necessary tools to be extremely sensitive and small. Most animal cells are 10000 to 20000 nanometer in diameter, which means that nanoscale carriers (having at least one dimension less than 100 nanometer) can enter cells and the organelles inside them to interact with DNA and proteins. Delivery vehicles developed at nano-scales maybe able to enter and analyze single cells and cure disease in a very small amount of cells and tissues. Thus the potential for the nanostructures suggests that they could meet the need for necessary tools of being extremely sensitive carriers to deliver the drug at molecular levels.

The drug delivery carriers at nanoscale have several enviable attributes. For example, encapsulating drugs in nano-sized carriers reduces their volumes of distribution. It causes a decrease in drug toxicity as a consequence of preferential accumulation of drug molecules at target sites and lower concentration in healthy tissues, which results in improved efficacy.²⁶⁻³¹ Literature shows that normal vasculature is impermeable to drug-associated carriers larger than 2 to 4 nm compared to free, unassociated drug molecules.^{26, 32, 33} So if delivery carriers are produced, which are larger than 4 nm in size, the encapsulation and delivery of drugs in such carriers may offer the opportunity to reduce the drug distribution and toxicity to normal tissues and increase drug accumulation and local concentration in target sites such as tumor or inflamed sites by extravasation.

Several approaches have been adopted to produce nanocomposites for utilization as drug delivery carriers and a number of different families of materials have been synthesized for this purpose. For example, liposomes have been used as drug

delivery systems since the 1960s.³⁴ Liposomes are defined as vesicles in which an aqueous volume is entirely surrounded by a phospholipid membrane.³⁵ Many groups have used liposomes for drug delivery and applied various approaches for their surface modifications in order to increase the circulation half-lives of liposomes for

effective drug action.³⁶⁻⁵² Another type of drug delivery systems are nanoemulsions. Nanoemulsions are dispersions of oil and water where the dispersed phase droplets are in the nanosize range and stabilized with a surface-active film composed of surfactant and co-surfactant.^{26, 44-48} Concentration plays an important role in micelle formation as the amphiphiles have to exceed a certain concentration in order to self assemble into micelles. This is called the critical micelle concentration (CMC). For aqueous solutions, hydrophobic interactions are the predominant driving force in the assembly of the amphiphiles when their concentrations exceed the critical micelle concentration (CMC).⁵³ Figure 2 illustrates a general scheme of synthesis of block copolymers and their self-

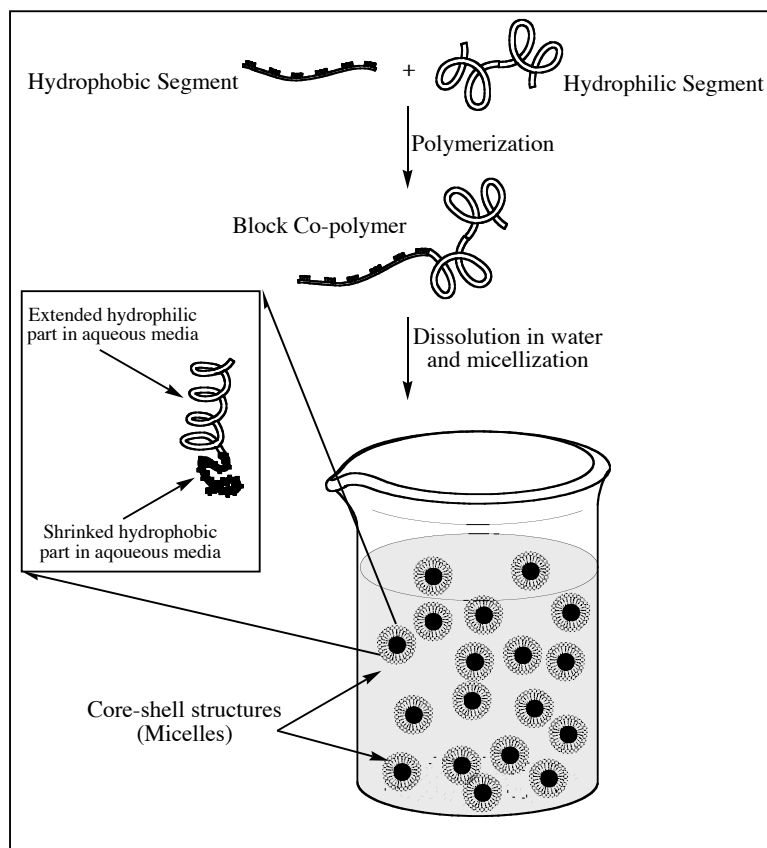


Figure 2: Graphical representation of block-copolymer synthesis and micellization in water solution.

assembly into micelles in aqueous solution. As hydrophobic part of copolymer shrinks and hydrophilic part extends out in aqueous solutions, aggregation of such particles give form to core-shell structures (micelles) and any hydrophobic drug can be attached to the hydrophobic core of these micelles through physical attractions. This phenomenon facilitates the drug dissolution in aqueous media and also helps circulate drug for extended periods of times in the body with minimal toxicity to healthy tissues. Furthermore, as explained earlier, fabrication of responsive carriers can further facilitate the release of drug at the point of action.

Cyclic and cubic siloxane based inorganic/organic hybrid materials, discussed in earlier chapters of this thesis, can be applied as efficient drug delivery carriers. The hybrid materials prepared by grafting of hydrophilic organic moieties on hydrophobic silica core self assemble into core-shell structures (micelles) upon dissolution in water. Changing the size and nature of grafted organic groups can control the solubility and the size of micelles. We have chosen polyethylene glycol (PEG) and its derivatives as the hydrophilic organic parts. Micelles of size 100nm up to 1000 nm can be prepared by changing the size of polyethylene glycol (PEG) chains. A drug can be loaded in the cores of these micelles and used for targeted delivery. Siloxanes and polyethylene glycol (PEG) both are biodegradable and non-toxic to human bodies, which degrade into smaller molecules during and after the delivery process and excreted out from the body as waste materials.

5.2 Results and Discussion

The synthesis of delivery carriers was accomplished via covalently attaching polyethylene glycol (PEG) and its derivatives to a cyclic or cubic siloxane core in a dehydrogenative alcoholysis coupling reaction. There are a number of reasons to choose polyethylene glycol (PEG) and its derivatives as the organic part. First, polyethylene glycol (PEG) is a biodegradable polymer and is available in different chain lengths and molecular weights. This variation in chain length size provides a possibility to tailor the solubility profile of the micelles, as well as the size of the micelles. Secondly, polyethylene glycol (PEG) is a di-alcohol, which means it has terminal hydroxyl groups on both ends. After grafting PEG on a siloxane core, the terminal hydroxyl group on the loose end of PEG chain provides the flexibility to further modify the carrier according to certain needs. Another key feature of polyethylene glycols (PEG) is their chemical inertness and immunogenicity. Particulates of delivery carriers in nano-size range usually have short circulation half-lives due to natural defense systems of the body. The body's immune system recognizes them as foreign bodies and eliminates them after opsonization by the mononuclear phagocyte system (MPS).⁵⁴ In order to prevent the carrier from opsonization, their surface needs to be modified making them "stealth" for the body immune system. Polyethylene glycol (PEG) is an excellent choice for such modification due to its low degree of immunogenicity and antigenicity, chemical inertness and hydrophilicity.⁵⁵ The flexibility, hydrophilicity and variation in sizes of polyethylene glycol (PEG) chains grafted on a hydrophilic siloxane core create micelles in aqueous media at CMC in micromolar and millimolar range. This facilitates the physical association of drug molecules of different polarities within the micelles without drug

modification and thus preventing drug efficiency, reducing its toxicity, and increasing its solubility in aqueous media.

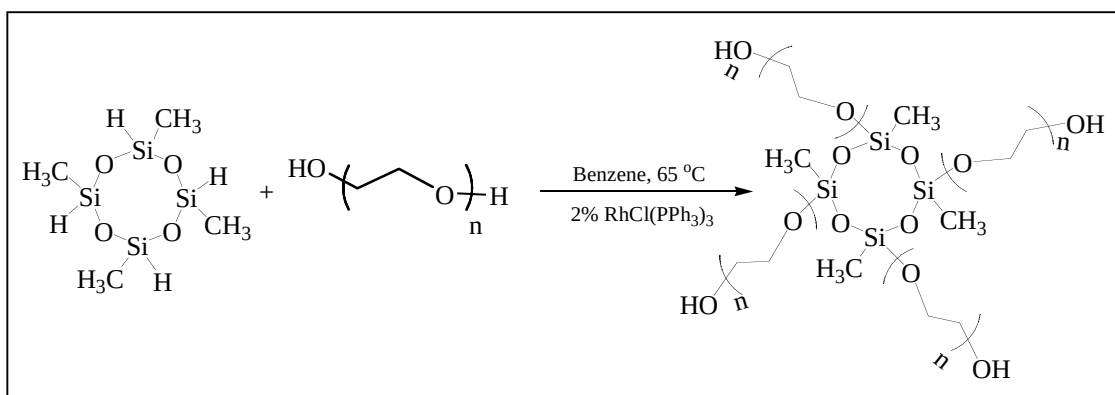
5.2.1 Synthesis of delivery carriers

Delivery vehicles were synthesized with varying sizes of siloxanes (cyclic and cubic) and with varying chain lengths of polyethylene glycols (PEG) and its derivatives. The siloxanes used as cores are cyclic siloxanes 1,3,5,7-tetramethylcyclotetrasiloxane (TMCTS) or also abbreviated as D₄, Pentamethylcyclopentasiloxane (PMCPs) or also abbreviated as D₅, and cubic siloxane Octakis (dimethylsiloxy)-T8-silsesquioxane, abbreviated as (Q₈M₈). Polyethylene glycol (PEG) was used with different molecular weights and chain lengths ranging from MW=400 to MW=4600. All the delivery carriers synthesized were named using the abbreviations of their constituent parts by first writing the organic chain abbreviation in brackets followed by the abbreviation of the siloxane core part. For example, a delivery carrier synthesized by grafting polyethylene glycol having molecular weight MW=400 grafted on a 1,3,5,7-tetramethylcyclotetrasiloxane (D₄) is named as (PEG400)₄D₄. All the delivery carriers synthesized are named in this fashion throughout the rest of this chapter for ease of writing and readability.

5.2.2 Synthesis of cyclic siloxane based drug carrier: (PEG400)₄D₄

The delivery vehicle (PEG400)₄D₄ was prepared in the following way. To a 50ml Schlenk tube equipped with a magnetic stirring bar, was added Wilkinson's catalyst (0.002 g, 0.002 mmol). Schlenk tube was degassed and filled with nitrogen three

times and polyethylene glycol (PEG) (3.2 g, 8 mmol; MW~400) was added to it. Reaction mixture was allowed to stir for 5 min in order to get a homogenous suspension of catalyst in PEG followed by addition of solvent (Benzene, 5 ml), which resulted in a brownish solution. At this juncture, 1, 3, 5, 7-tetramethylcyclotetrasiloxane (D_4^H) (0.48 g, 2 mmol) was added to the reaction mixture. Reaction mixture immediately turned yellow



Scheme 1: Synthetic route to drug carrier (PEG400)₄D₄. Idealized structure of the product shown.

and development of a gas (presumably H₂) was observed. Schlenk tube was degassed and filled with nitrogen three more times and reaction was allowed to continue at 65⁰C under a positive nitrogen pressure for 30 hrs. Upon completion, reaction mixture was a dark brown viscous solution. Solvent was evaporated and product was analyzed with ¹H, ¹³C, and ²⁹Si NMR, which confirmed the formation of desired product (PEG400)₄D₄. Synthetic scheme for the reaction is shown in scheme 1.

The reaction mixture was periodically monitored by ¹H, and ²⁹Si NMR. ²⁹Si NMR of starting siloxane i.e. 1,3,5,7-tetramethylcyclotetrasiloxane (D_4^H) shows four peaks centered at -31ppm arising from D-type silicon (-O-SiMeH-O-) units, where silicon atom is attached to two oxygen atoms. After grafting of polyethylene glycol (PEG), the ²⁹Si NMR analysis of resulting product showed peaks centered at -56 to -57ppm,

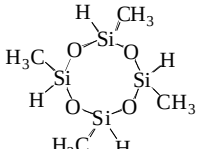
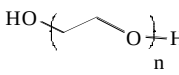
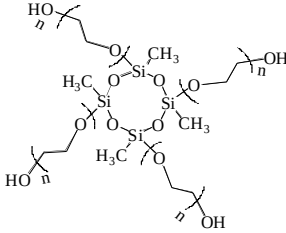
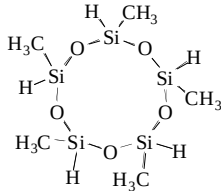
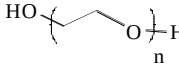
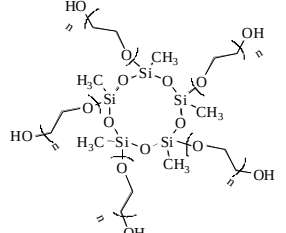
reflecting the change in electronic environment of Si units due to the formation of new Q-type ($\text{SiMe-OCH}_2\text{CH}_2\text{O-}$) moieties, where silicon atom is attached to three oxygen atoms. No residual signals due to Si-H bonds were observed in ^{29}Si NMR of the product, indicating complete consumption of the Si-H bonds.

Catalyst separation is crucial in any drug delivery carrier's preparation. Even a small fraction of metal/catalyst remained in the product can immensely increase the cytotoxicity of carrier. In order to separate the catalyst, reaction mixture was taken in a 250ml round bottom flask equipped with a magnetic stirring bar and ~30ml cyclohexane was added to it. Solution was stirred vigorously for 10 min and water (~10ml) was added which resulted in a milky color solution. Solution was vigorously stirred for an additional 20 min and then collected in a separatory funnel and allowed to sit for one hour. Catalyst was separated at the interphase of water and cyclohexane layers in form of precipitate. The bottom water layer containing delivery vehicle was separated and centrifuged for 10 min at 9000 rpm in order to get rid of any remains of the catalyst. The water was evaporated in a rotary evaporator under vacuum at 95°C for two hours. The resultant was a clear viscous solution of delivery vehicle $(\text{PEG400})_4\text{D}_4$. Product was analyzed with ^1H , ^{13}C , and ^{29}Si NMR again, which showed a slight shift to up field and a new small-unidentified peak at around -66 in ^{29}Si NMR was observed. This could be the result of water treatment and formation of Si-OH or Si-O-Si bonds.

Various versions of drug carriers were synthesized in this fashion with varying size of polyethylene glycol (PEG) chains, as well as, with increasing size of cyclic siloxane core. The general synthesis path was similar as in case of $(\text{PEG400})_4\text{D}_4$

with corresponding amounts and molar ratios and the catalyst was separated in the same way.

Table 1: Details of different synthesized carriers with varying sizes of polyethylene glycols and cyclic siloxanes

No	Siloxane	Polyethylene glycol (PEG)	Product	Product physical state	Solubility in water
1	 Tetramethyl-cyclotetra-siloxane (D₄)	 Polyethylene glycol MW = 400 n = ~9	 (PEG400)₄D₄	Clear viscous liquid	Perfectly soluble
2	Same as above	Polyethylene glycol MW = 1000 n = ~22	(PEG1000)₄D₄ Similar product structure as above	White waxy solid	Perfectly soluble
3	Same as above	Polyethylene glycol MW = 4600 n = ~105	(PEG4600)₄D₄ Similar product structure as above	White solid	Perfectly soluble
4	 Pentamethyl-cyclopenta-siloxane (D₅)	 Polyethylene glycol MW = 400 n = ~9	 (PEG400)₅D₅	Clear viscous liquid	Perfectly soluble

Varying molecular weights and chain lengths of polyethylene glycols used were PEG400 (MW = 400; n ~ 9), PEG1000 (MW = 1000; n ~ 22), and PEG4600 (MW = 4600; n ~ 105). In addition to D₄^H, a bigger cyclosiloxane i.e. pentamethylcyclotetrasiloxane (D₅^H) was also used as the core. All the reactions and

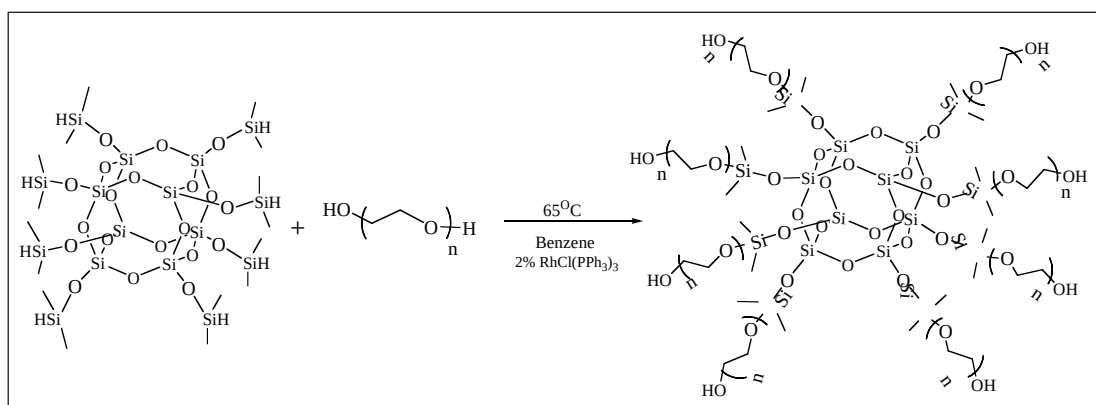
products achieved were analyzed with ^1H , ^{13}C , and ^{29}Si NMR, which showed spectra similar to $(\text{PEG})_4\text{D}_4$, before and after the catalyst separation and produced quantitative yields. All carriers had excellent solubility in water. In case of $(\text{PEG}4600)_4\text{D}_4$, ^1H NMR analysis confirmed the formation of desired product, whereas no peaks were observed in ^{29}Si NMR. The reason for this maybe that polyethylene glycol chains are very big having a very high molecular weight in comparison to siloxane D_4 core. Therefore, the siloxane core was completely dominated by PEG and no signal was observed in ^{29}Si NMR. Although ^1H NMR confirmed the formation of desired product, the difference between ratios of peaks associated with PEG and peaks associated with D_4 was huge. Table 1 summarizes different precursors used and products achieved, their ideal structures and major physical properties.

5.2.3 Synthesis of cubic siloxane based drug carrier: $(\text{PEG}400)_8\text{T}_8$

Cubic siloxane based delivery vehicles were also synthesized to investigate the improvements in encapsulation and stability of drug. Octakis(dimethylsiloxyl)- T_8 -Silsequioxane ($\text{Q}_8\text{M}_8^{\text{H}}$ – referred to as T_8 throughout rest of this chapter for ease of writing) is a cubic structure and has eight Si-H vertices as compared to four Si-H vertices in D_4^{H} . The carrier was synthesized by taking Wilkinson's catalyst (0.001 g, 0.001 mmol) and octakis(dimethylsiloxyl)- T_8 -Silsequioxane (T_8) (0.2545 g, 0.25 mmol) in a 50ml Schlenk tube equipped with a magnetic stirring bar. Schlenk tube was degassed and filled with nitrogen three times and solvent (Benzene, 5 ml) was added which resulted in a brownish solution. At this juncture, polyethylene glycol (PEG) (0.8 g, 2 mmol; MW~400) was added to it and reaction mixture

immediately turned yellow and development of a gas (presumably H_2) was observed. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 32 hrs. Upon completion, reaction mixture was a light yellow viscous solution. Solvent was evaporated and product was analyzed with ^1H , and ^{29}Si NMR that confirmed the formation of desired product $(\text{PEG400})_8\text{T}_8$. Scheme 2 shows a general synthetic route and idealized structure of the product.

The reaction mixture was periodically monitored by ^1H , and ^{29}Si NMR. ^{29}Si NMR of octakis(dimethylsiloxy)- T_8 -Silsesquioxane (T_8) shows two peaks centered



Scheme 2: Synthetic route to PEG400 substituted cubic siloxane and idealized structure of the product

at -1ppm arising from eight side arm M-type silicon ($-\text{O}-\text{SiMe}_2\text{H}$) units, where silicon atom is attached to one oxygen atom; and second peak centered at -108ppm arising from eight central Q-type silicon units, where each silicon atom is attached to four oxygen atoms in the cage. After grafting of polyethylene glycol (PEG) on side arm silicon atoms, the ^{29}Si NMR analysis of resulting product showed a shift from -1ppm to -8ppm as a change in electronic environment of side arm Si units and formation of new D-type ($-\text{O}-\text{SiMe}_2-\text{OCH}_2\text{CH}_2\text{O}-$) moieties, where silicon atom is now attached to two oxygen atoms.

No residual signals due to Si-H bonds were observed in ^{29}Si NMR of the product, indicating complete consumption of the Si-H bonds.

Catalyst separation was also carried out in a similar fashion as before. Reaction mixture was taken in a 250ml round bottom flask equipped with a magnetic stirring bar and ~30ml cyclohexane was added to it. Solution was stirred vigorously for 10 min and water (~10ml) was added which resulted in a milky color solution. Solution was vigorously stirred for an additional 20 min and then collected in a separatory funnel and allowed to sit for one hour. Catalyst was separated at the interphase of both layers in form of precipitate. The bottom water layer containing delivery vehicle was separated and centrifuged for 10 min at 9000 rpm in order to get rid of any remains of the catalyst. The water was evaporated in a rotary evaporator under vacuum at 95°C for two hours. The resultant was a clear viscous solution of delivery vehicle $(\text{PEG400})_8\text{T}_8$. Product was analyzed with ^1H , and ^{29}Si NMR again which showed a slight shift to up field and in some cases a new small unidentified peak appeared at around -18 in ^{29}Si NMR. This could be the result of water treatment and formation of Si-OH bonds.

In addition to PEG400, polyethylene glycol with MW=1000 and $n\sim 22$ was also grafted on a T_8 core. The reaction was carried out with similar synthetic route as described above in corresponding amounts and molar ratios. NMR analysis of the product showed comparable spectra and a quantitative yield of the product $(\text{PEG1000})_8\text{T}_8$ was achieved. Catalyst was separated in a like-wise fashion and product was collected in a clear waxy solid form, which had excellent solubility in water. A further NMR analysis of the product, after catalyst separation, revealed a slight shift to up field and in some cases a new small-unidentified peak appeared at around -18 in ^{29}Si NMR. This, as well,

could be explained as the result of water treatment and formation of Si-OH bonds in a small quantity.

The drug carriers prepared by grafting of polyethylene glycols (PEGs) on cyclic or cubic siloxanes form micelles when dissolved in an appropriate solvent above critical micelle concentration (CMC). Transmittance Electron Microscopy (TEM) technique was used to investigate the morphology of the micellar structures. For this purpose, drug carrier (PEG400)₄D₄ (0.188 gm; 0.2 mmol) was diluted in 20 ml of benzene. After stirring for 10 min in order to get a homogenous mixture, one drop of this solution was carefully dropped on a formavar coated copper-carbon grid. Solvent was

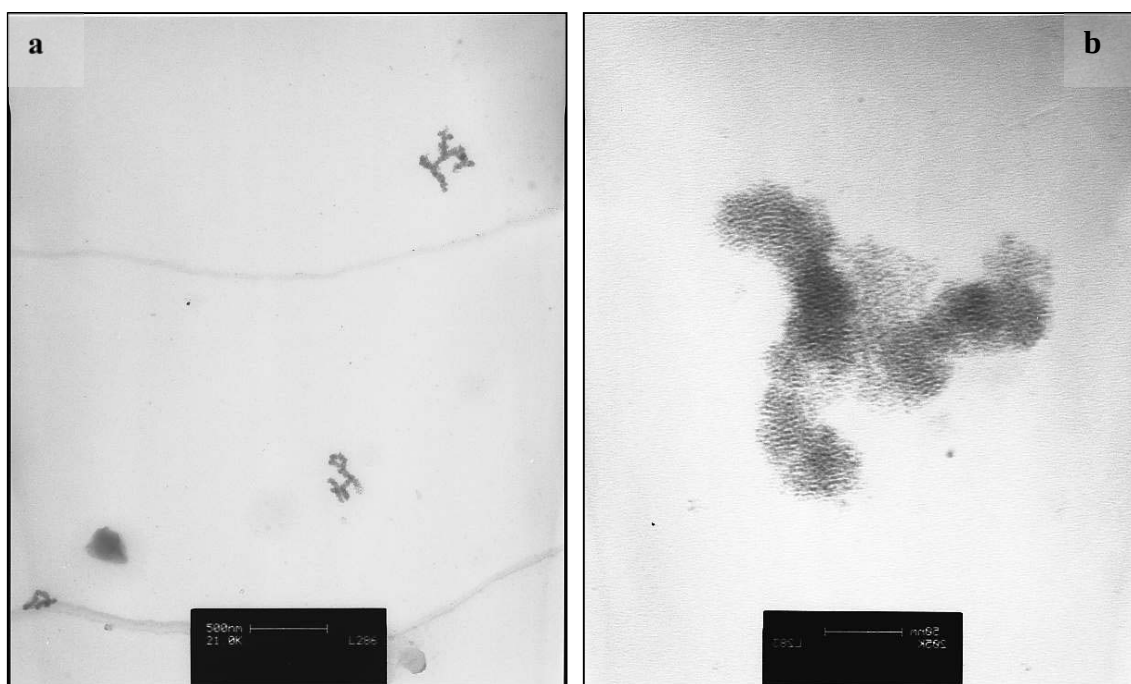


Figure 3: TEM images of delivery vehicle (PEG400)₄D₄. Scale bars are (a) 1 μ , and (b) 50 nm.

allowed to evaporate at room temperature in open air for about 10 min. TEM pictures showed a well-defined micellar network with monodispersed particles. The TEM captions are shown in figure 3.

All the carriers were examined by Transmittance Electron Microscopy (TEM) in a similar fashion and similar morphology was found in each case with a slight difference in particle size.

5.2.4 Drug loading/encapsulation efficiency studies

In drug delivery, a major concern is to establish new methods to determine the encapsulation and loading efficiency of the drug into the carrier micelles. In order to investigate the encapsulation efficiency of the carriers, a microscopic study was carried out. A fluorescence active dye, acridine orange was used in place of a drug in order to monitor the encapsulation. A dye solution was prepared by dissolving 1 mg of acridine orange dye in 20 ml of water. The solution was further diluted by taking 1 ml of dye solution and adding another 20 ml of water to it. The delivery vehicle (PEG400)₄D₄ (50 mg) was taken in a glass vial and 20 ml water was added to it. The carrier dissolved immediately upon mildly shaking the vial. The vial with carrier water solution was suspended in an ultrasonic cleaner water bath. One milliliter of diluted dye solution was slowly added to carrier solution drop-wise while sonicating. After complete addition of dye solution in about 2 min, sonication was stopped and sample was allowed to sit for one hour in order to achieve the complete encapsulation of dye in the carrier micelles. One drop of the diluted dye solution was deposited on a glass slide, and on another similar glass slide was placed one drop of carrier solution with encapsulated dye in it. Both slides were monitored under microscope with and without fluorescence light.

First, the dye solution was monitored. Figure 4 shows that the dye makes a homogenous solution in water, which is evident in the image. In the image without

fluorescence filter (Figure 4a), the black line is the boundary between the solution drop and empty glass slide. When the fluorescence filter is put on (Figure 4b), the area with dye solution drop emits green color whereas empty space shows a blank spot. It is evident from the green space, which is the dye solution in water, that dye is dissolved homogenously in water.

Secondly, the (PEG400)₄D₄ carrier solution with encapsulated dye in it

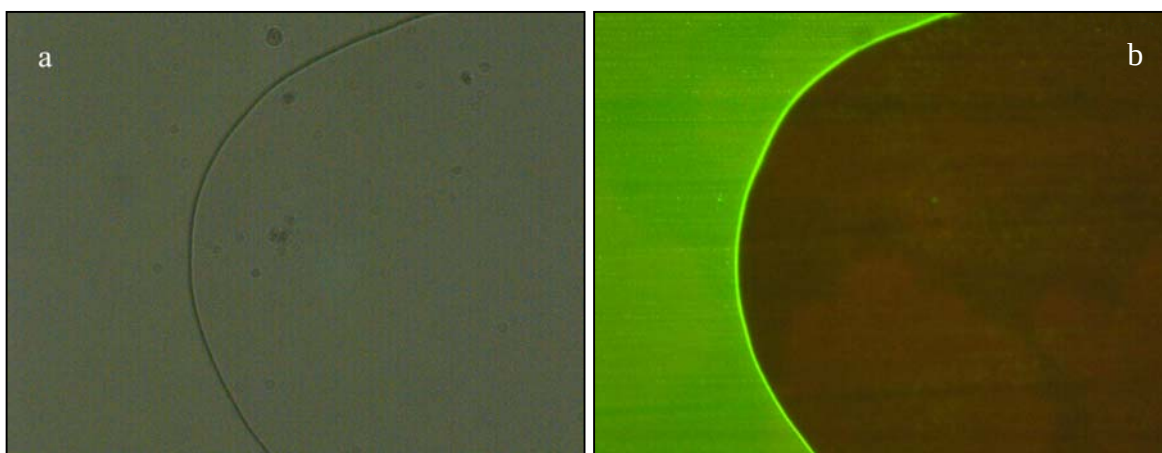
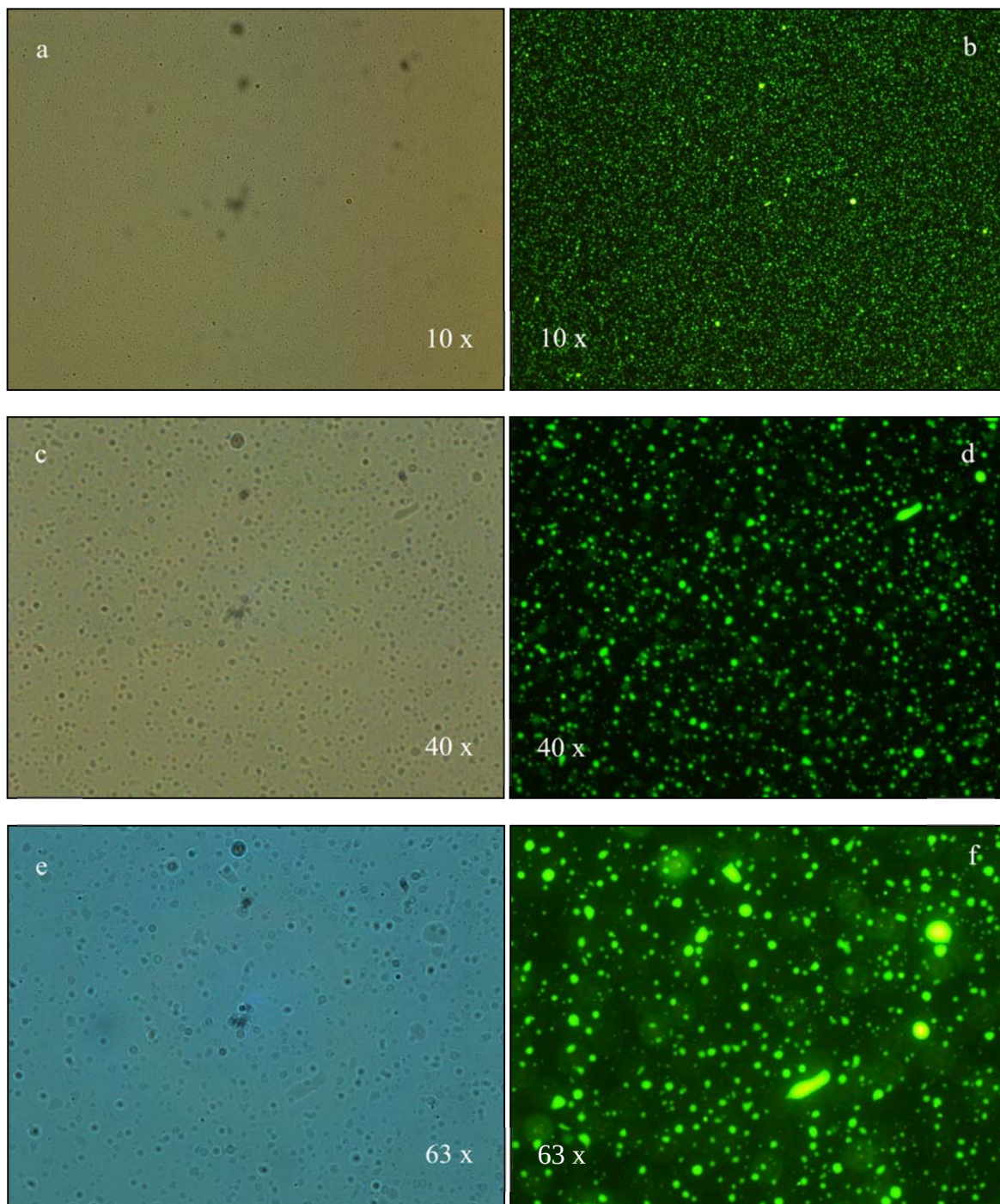


Figure 4: Acridine orange dye solution in water (a) without fluorescence light filter, and (b) with fluorescence light filter. The magnification in both images is 40x.

was monitored under the microscope with and without fluorescence light filter. Without the fluorescence light filter, the particles/micelles of carrier were visible as goblets in water solution. Upon turning the fluorescence light filter on, only the vehicle micelles were visible as green particles whereas water background was blank. This accounts for the fact that all the dye molecules were encapsulated in vehicle micelles and no dye was present in water. Following are the images. The microscope results are shown in figure 5, where a, c, e, and g are the images without fluorescence light filter and b, d, f, and h are the images with fluorescence light filter on.



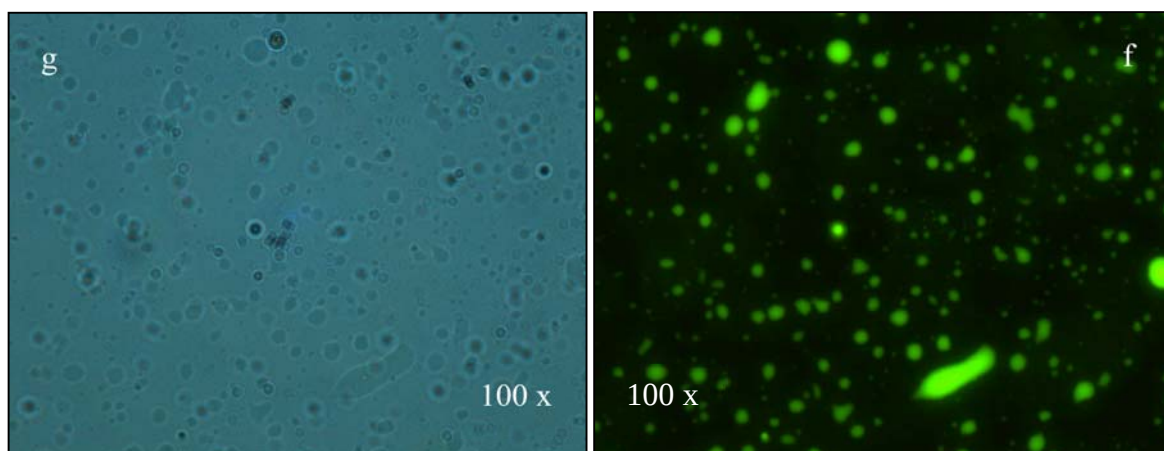


Figure 5: Water solution of encapsulated acridine orange dye in drug carrier (PEG400)₄D₄. Microscopic images at different magnification (a, c, e, g) without fluorescence light filter, and (b, d, f, h) with fluorescence light filter.

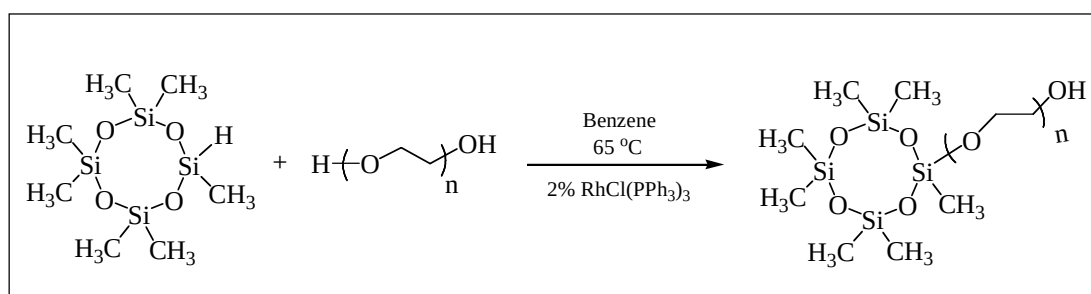
All the carriers were studied for the encapsulation using above method and similar results were achieved in each case with the exception of (PEG4600)₄D₄. In (PEG4600)₄D₄ case, no micellar structure formation was observed. The reason for this can be explained by the predominance of hydrophilic segment. The hydrophilic segment i.e. PEG in this case is much larger than the hydrophobic core i.e. siloxane. This hydrophilic predominance of PEG fails to attain a hydrophobic-hydrophilic balance and thus no micelles are formed. It is more likely dissolved completely in water. The encapsulation study affirms that cyclic and cubic siloxane based micellar networks can be successfully synthesized, which self-assemble into micelles in water solutions. A drug maybe be loaded in the cores of such micelles through physical association without modifying the drug and theses carriers can be used for targeted drug delivery and may provide long circulation times.

5.2.5 Preparation of model compounds mimicking the drug carriers. Study of solubility control and encapsulation ability

A drug carrier has to be readily dissolvable in the aqueous environment of human body for targeted and successful delivery. Choice of polyethylene glycols as the hydrophilic segment of drug carriers prepared by our methodology plays an important role in controlling the solubility profile of the carrier. Furthermore, it is also responsible for tailoring the micelle size and the encapsulation ability. In order to investigate these properties, a number of model compounds were prepared that mimicked the delivery carriers. In place of tetramethylcyclotetrasiloxane (D_4), a different siloxane i.e. heptamethylcyclotetrasiloxane (D_3D') was used as the core for the preparation of delivery carrier. The difference between D_4 and D_3D' is that latter has only one hydrogen (H) atom attached to one of the four silicon (Si) atoms and rest are methyl groups (CH_3) in contrast to four hydrogen (H) atoms on four silicon (Si) atoms in D_4 . This stands for the fact that only one polyethylene glycol (PEG), or for that matter any functional group, can be chemically attached to the core as compared to four PEG's on D_4 (in D_4 , all four Silicon atoms have hydrogen atoms attached to them). Thus the product (PEG_1D_3D') has only one PEG tail on the core.

The carrier was prepared by covalently attaching polyethylene glycol (MW~400) on D_3D' core. For this purpose, to a 50ml Schlenk tube equipped with a magnetic stirring bar, was added Wilkinson's catalyst (0.002 g, 0.002 mmol). Schlenk tube was degassed and filled with nitrogen three times and PEG (0.71 ml, 2 mmol; MW~400) was added to it. Reaction mixture was allowed to stir for 5 min in order to get a homogenous suspension of catalyst in PEG followed by addition of solvent (Benzene, 3 ml), which resulted in a brownish solution. At this juncture,

heptamethycyclotetrasiloxane D_3D' (0.6 ml, 2 mmol) was added to the reaction mixture. Reaction mixture immediately turned yellow and development of a gas (presumably H_2) was observed. Schlenk tube was degassed and filled with nitrogen three more times and reaction was allowed to continue at $65^\circ C$ under a positive nitrogen pressure for 28 hrs. Reaction was monitored with ^1H , and ^{29}Si NMR, which confirmed the formation of desired product by a shift in NMR signals due to the change in silicon environment after substitution. Upon completion, reaction mixture was a dark brown viscous solution. Catalyst was separated in a likewise manner as described for other carriers and solvent was evaporated which resulted in a clear viscous liquid of PEG_1D_3D' . The chemical structure of the product and a general synthesis scheme is shown in scheme 3.

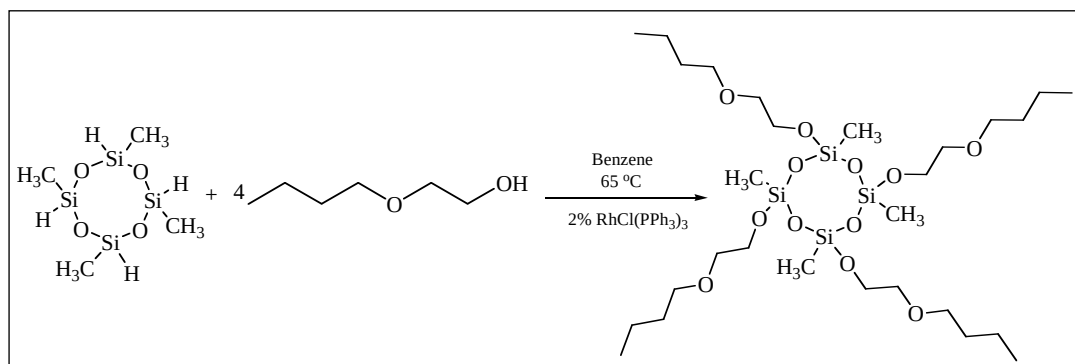


Scheme 3: Synthetic route to substitution of polyethylene glycol (PEG) on a heptamethycyclotetrasiloxane (D_3D') core.

The water solubility of this product PEG_400D_3D' was compared to delivery carrier $(PEG_400)_4D_4$. In contrast to $(PEG_400)_4D_4$, this product was completely insoluble in water. This confirms that an increase in PEG tails plays a significant role in raising the hydrophilicity of delivery vehicle. Based on this, it can be concluded that an increase in PEG tails, as well as the PEG size can improve the solubility, stability, and encapsulation properties of the delivery vehicle. These properties were further investigated by synthesizing additional model compounds mimicking the carriers by attaching polyethylene glycol derivatives on a D_4 core.

5.2.5.1 Butoxy ethanol substitution on D₄^H core

First, butoxy ethanol was grafted on a D₄ core as a derivative of polyethylene glycol. The structure of butoxy ethanol is similar to diethylene glycol with the difference that one terminal hydroxyl (OH) group is replaced with a methyl (CH₃) group. In other words, it's a monomeric form of polyethylene glycol with only one terminal hydroxyl (OH) group. To facilitate the synthesis, reaction was carried out in a 50ml Schlenk tube equipped with a magnetic stirring bar. Wilkinson's catalyst (0.002 g, 0.002 mmol) was added to the Schlenk tube. Tube was degassed and filled with nitrogen three times and butoxy ethanol (BE) (1.05 ml, 8.0 mmol) was added to it. Reaction mixture was allowed to stir for 5 min in order to get a homogenous suspension of catalyst in alcohol followed by addition of solvent (Benzene, 4.0ml), which resulted in a brownish solution. At this juncture, tetramethylcyclotetrasiloxane (D₄) (0.49 ml, 2.0 mmol) was added to the reaction mixture. Reaction mixture immediately turned yellow and development of a gas (presumably H₂) was observed. Tube was degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 28 hrs. Upon completion, reaction mixture was almost a clear

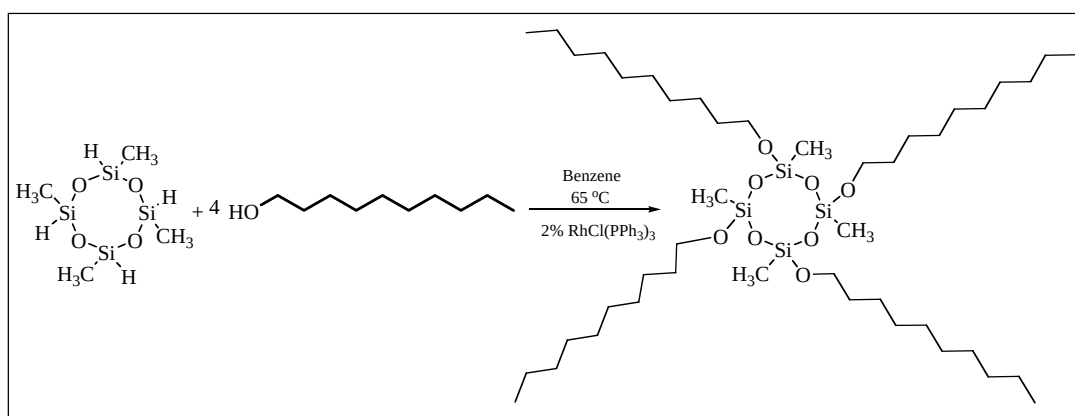


Scheme 4: Substitution of butoxy ethanol (BE) on a tetramethylcyclotetrasiloxane (D₄^H) core. Idealized structure of product shown.

solution. Catalyst was separated by centrifuging the reaction mixture for 20 min at 9000 rpm, which resulted in precipitation of the catalyst. The supernatant was carefully separated and solvent was evaporated to obtain the product BE_4D_4 in a clear liquid form. A general synthetic path and idealized structure of product is shown in scheme 4. Product was analyzed with IR, ^1H , ^{13}C , and ^{29}Si NMR, which confirmed the formation of desired product.

5.2.5.2 Decyl alcohol substitution on D_4^{H} core

As a second replica of PEG, a long chain alcohol i.e. decyl alcohol was used. It differs with PEG by having no oxygen atoms in its backbone. The reaction was carried out by adding Wilkinson's catalyst (0.002 g, 0.002 mmol) to a 50ml Schlenk tube equipped with a magnetic stirring bar followed by degassing and filling the tube with nitrogen three times. Decyl alcohol (1.53, 8.0 mmol) was added to it and reaction mixture was stirred gently for homogenous suspension of catalyst in alcohol followed by addition of solvent (Benzene, 4.0 ml), which resulted in a brownish solution. Subsequently, tetramethylcyclotetrasiloxane D_4 (0.49 ml, 2.0 mmol) was added to the reaction mixture and an immediate color change to light yellow along with development of a gas



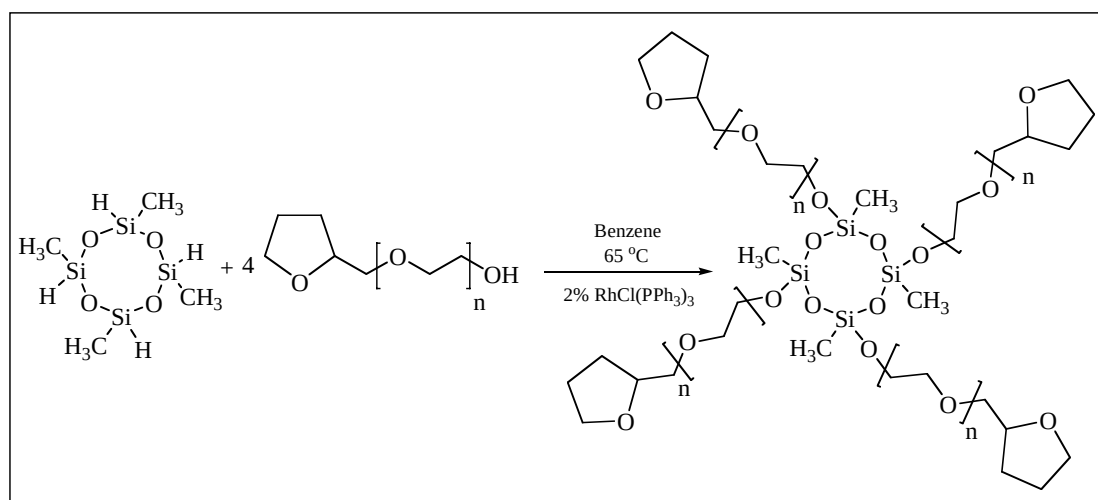
Scheme 5: Synthetic route to decyl alcohol (DA) substituted cyclic siloxane (D_4^{H}) and idealized structure of the product

(presumably H_2) was observed. Tube was degassed and filled with nitrogen three more times and reaction was allowed to continue at $65^{\circ}C$ under a positive nitrogen pressure for 28 hrs. Upon completion, reaction mixture was a yellowish solution. Centrifuging the reaction mixture for 20 min at 9000 rpm precipitated out catalyst and solvent was evaporated to obtain a clear liquid of DA_4D_4 . Product was analyzed with ^1H , ^{13}C , and ^{29}Si NMR, which confirmed the formation of desired product. Scheme 5 represents a general synthetic route and idealized structure of product.

5.2.5.3 Poly(ethylene glycol)-tetrahydrofurfuryl ether substituted D_4^H

Poly(ethylene glycol)-tetrahydrofurfuryl ether (PEGTHFE) was used as a polymeric derivative of PEG in preparation of model compounds. Poly(ethylene glycol)-tetrahydrofurfuryl ether (PEGTHFE) has a similar structure to PEG with a difference that one terminal hydroxyl (OH) group is replaced with a tetrahydrofuran (THF) ring. The number of repeating units of the polymer is approximately four ($n \sim 4$; $MN \sim 200$). For covalent addition of this polymer on a D_4 core, Wilkinson's catalyst (0.002 g, 0.002 mmol) was added to a 50ml Schlenk tube equipped with a magnetic stirring bar. Schlenk tube was degassed and filled with nitrogen three times and Poly(ethylene glycol) tetrahydrofurfuryl ether (0.86 ml, 4.0 mmol) was added to it. Reaction mixture was allowed to stir for 5 min in order to get a homogenous suspension of catalyst in polymer followed by addition of solvent (Benzene, 4.0ml). The resultant was a brownish solution. Addition of tetramethylcyclotetrasiloxane D_4 (0.24 ml, 1.0 mmol) to reaction mixture, at this point, immediately turned it into yellow color and development of a gas (presumably H_2) was observed. Tube was degassed and filled with nitrogen three more times and

reaction was allowed to continue at 65°C under a positive nitrogen pressure for 36 hrs. Upon completion, reaction mixture was almost a yellowish solution. Catalyst was separated by centrifuging the reaction mixture for 20 min at 9000 rpm and solvent was evaporated which resulted in a clear liquid of Poly(ethylene glycol) tetrahydrofurfuryl ether substituted D₄. ¹H, ¹³C, and ²⁹Si NMR analysis confirmed the formation of desired product (PEGTHFE)₄D₄.



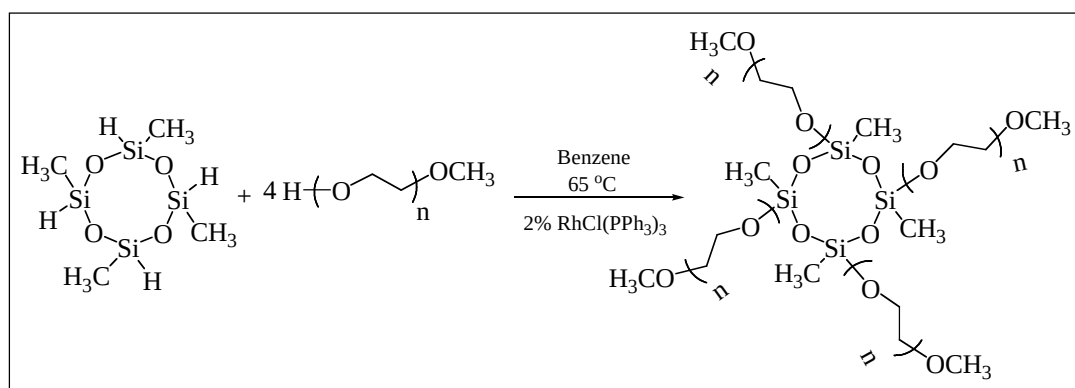
Scheme 6: Synthetic route to substitution of poly(ethylene glycol) tetrahydrofurfuryl ether (PEGTHFE) on a tetramethylcyclotetrasiloxane (D₄^H) core. Idealized structure of product shown

5.2.5.4 Substitution of poly(ethylene glycol) methyl ether (PEGME) on D₄^H core

The next polymer replica of PEG used was poly(ethylene glycol) methyl ether (PEGME). The structural disparity between PEG and PEGME is that in PEGME, the hydrogen atom (H) of one terminal hydroxyl group (OH) is substituted by methyl functionality. Poly(ethylene glycol) methyl ether (PEGME) with two different molecular weights (MW=350, n~8; and MW=550, n~12) were used for this purpose. Reaction was carried out in a 50ml Schlenk tube equipped with a magnetic stirring bar. Wilkinson's catalyst (0.002 g, 0.002 mmol) was added to the tube and tube was degassed and filled

with nitrogen three times followed by addition of poly(ethylene glycol) methyl ether (2.6 ml, 8.0 mmol; MW=350). Mild stirring of reaction mixture for 5 min produced a homogenous suspension of catalyst in polymer. Later, 4.0 ml of solvent (benzene) was added to reaction mixture, which resulted in a brownish solution. At this juncture, tetramethylcyclotetrasiloxane D_4 (0.49 ml, 2.0 mol) was added to the reaction mixture and an immediate color change to yellow with development of a gas (presumably H_2) was observed. Tube was degassed and filled with nitrogen three more times and reaction was allowed to continue at $65^\circ C$ under a positive nitrogen pressure for 32 hrs. ^1H , and ^{29}Si NMR spectroscopy was used as tools to confirm the reaction completion and formation of desired product by monitoring a shift in peaks associated with silicon centers due to a change in silicon environment. Upon completion, reaction mixture was almost a yellowish solution. The idealized structure of the product and a general synthesis scheme is shown in scheme 7.

In order to separate the catalyst, reaction mixture was taken in a 250ml round bottom flask equipped with a magnetic stirring bar and ~30ml cyclohexane was



Scheme 7: Substitution of poly(ethylene glycol) methyl ether (PEGME) on tetramethylcyclotetrasiloxane (D_4^H). Idealized structure of product shown

added to it. Solution was stirred vigorously for 10 min followed by addition of water (~10ml), which resulted in a milky color solution. Solution was vigorously stirred for an

additional 20 min, collected in a separatory funnel and allowed to sit for one hour. Catalyst was separated at the interphase of water and cyclohexane layers in form of precipitate. The bottom water layer, containing product was separated and centrifuged for 10 min at 9000 rpm in order to get rid of any remains of the catalyst. The water was evaporated in a rotary evaporator under vacuum at 95°C for two hours. The resultant was a clear viscous solution of (PEGME350)₄D₄. Product was analyzed again with ¹H and ²⁹Si NMR and no significant changes were observed. In a likewise fashion, a longer chain poly(ethylene glycol) methyl ether (MW=550, n~12) was also substituted on D₄^H with relative amounts and molar ratios, which produced similar results.

Table 2: Summary of various PEG derivatives substituted on D₄^H and their physical properties

No.	PEG Derivative	Product	Physical Appearance of Product	Solubility in Water
1	Butoxy Ethanol (BE)	(BE) ₄ D ₄	Clear Liquid	Moderate
2	Decyl alcohol (DA)	(DA) ₄ D ₄	Clear Liquid	Insoluble
3	Poly(ethylene glycol)-tetrahydrofurfuryl ether (PEGTHFE)	(PEGTHFE) ₄ D ₄	Clear Liquid	Moderate
4	Poly(ethylene glycol)-methyl ether 350 (PEHME350)	(PEGME350) ₄ D ₄	Clear Liquid	Excellent
5	Poly(ethylene glycol)-methyl ether 550 (PEHME550)	(PEGME550) ₄ D ₄	Clear Liquid	Excellent

All the above mentioned model compounds mimicking delivery carriers were studied further to investigate the effects of structural changes on solubility, micellization and encapsulation abilities. Table 2 summarizes the different model

compounds synthesized, resultant product, product's physical appearance and their solubility profile in water.

We observed that with a change in the organic segment attached to a D₄ core, the hydrophilicity of the carrier changed drastically. This has a direct effect on the micellization of carrier in water and thus altering its encapsulation efficiency. Based on these observations, it was concluded that polyethylene glycol (PEG) is a better choice for the fabrication of drug delivery carriers for an effective controlled delivery.

5.3 Experimental Section

5.3.1 General Information

All reactions were carried out under a positive pressure of dry Argon or Nitrogen using standard Schlenk-tube technique.

Chemicals. All solvents were purchased from EM science (Merck) and distilled over sodium/benzophenone before use. Wilkinson's catalyst $\text{RhCl}(\text{PPh}_3)_3$, Polyethylene glycol (MW = 400, 600, 1000, 4600), Poly(ethylene glycol) methyl ether (MW=350, 550), Poly(ethylene glycol) tetrahydrofurfuryl ether, Decyl alcohol, Butoxy ethanol, and Acridine orange dye were purchased from Aldrich Chemical Co. and used as received. 1,3,5,7-Tetramethylcyclotetrasiloxane (D_4^{H}), Pentamethylcyclopentasiloxane (D_5^{H}), Heptamethylcyclotetrasiloxane ($\text{D}_3\text{D}'$), and Octakis(dimethylsiloxy)- T_8 -Silsequioxane ($\text{Q}_8\text{M}_8^{\text{H}}$) were obtained from Gelest Inc. and used as received.

NMR Spectroscopy. ^1H NMR, ^{13}C NMR (200 MHz, 300 MHz), and ^{29}Si NMR (600 MHz) spectra were recorded in CDCl_3 or C_6D_6 on Varian Unity NMR instruments. ^{13}C NMR and ^{29}Si NMR spectra were referenced to Me_4Si . Proton spectra were referenced according to solvent proton shifts. All of the peaks in the NMR spectra were reported in ppm.

UV-vis Spectroscopy. UV-vis spectra were recorded on a Varian Cary Model 50 UV Spectrophotometer with 1-cm path length cells.

Sonication. A Branson Ultrasonic Cleaner (115v, 50/60HZ, 40 Hz transducer) with a 9 L water tank was used to sonicate any samples. Sonication of samples was performed in glass vials by suspending them in sonicator water tank with the help of clamps.

Microscopic Studies. All microscopic images were captured by using a ZEISS Axioskop2*plus* microscope equipped with X-Cite 120 EXFO fluorescence light source and an AxioCam MRc5 digital camera. Slides were prepared by dropping one drop of sample on a pre-cleaned glass slide. In some cases, samples were analyzed by microscope in a liquid form as a drop on glass slide, whereas, in other cases sample drop was allowed to dry on the glass slide and later was covered with a pre-cleaned cover slide before analyzing under microscope. The glass slides and cover glass were cleaned with ethanol wipes. Dry objectives were used for magnification of liquid samples and oil, or water objectives were used for magnifications of dry, covered samples.

Transmission Electron Microscopy (TEM). Philips CM 100-transmission electron microscope (TEM) was used to probe the morphology of synthesized delivery carriers and their micelles/nanoparticles. Formavar coated copper-carbon grids were purchased from Electron Microscopy Sciences. Generally, the TEM grids were prepared under standard temperature and pressure and solvent was allowed to evaporate for 1-h before examination of the grid. To affirm the validity of the TEM results, images were taken at different magnifications and were examined thoroughly to rule out any “electron beam” induced modifications.

5.3.2 Synthesis of Drug Delivery Carriers

Synthesis of delivery carrier (PEG400)₄D₄:

Substitution of polyethylene glycol (PEG, MW=400) on tetramethyclotetrasiloxane (D₄^H) core.

To a 50ml Schlenk tube equipped with a magnetic stirring bar, was added Wilkinson's catalyst (0.002 g, 0.002 mmol). Schlenk tube was degassed and filled with nitrogen three times and polyethylene glycol (PEG) (2.84 ml, 8 mmol; MW~400) was added to it. Reaction mixture was allowed to stir for 5 min in order to get a homogenous suspension of catalyst in PEG followed by addition of solvent (Benzene, 6 ml), which resulted in a brownish solution. At this juncture, 1, 3, 5, 7-tetramethylcyclotetrasiloxane (D_4^H) (0.49 ml, 2.0 mmol) was added to the reaction mixture. Reaction mixture immediately turned yellow and development of a gas (presumably H_2) was observed. Schlenk tube was degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 32 hrs. Upon completion, reaction mixture was a dark brown viscous solution. The product was analyzed with ^1H , ^{13}C , and ^{29}Si NMR, and transmission electron microscopy (TEM), which confirmed the formation of, desired product $(PEG400)_4D_4$.

Catalyst was separated in the following way. Reaction mixture was taken in a 250ml round bottom flask equipped with a magnetic stirring bar and ~30ml cyclohexane was added to it. Solution was stirred vigorously for 10 min and water (~10ml) was added which resulted in a milky color solution. Solution was vigorously stirred for an additional 20 min and then collected in a separatory funnel and allowed to sit for one hour. Catalyst was separated at the interphase of water and cyclohexane layers in form of precipitate. The bottom water layer containing delivery vehicle was separated and centrifuged for 10 min at 9000 rpm in order to get rid of any remains of the catalyst. The water was evaporated in a rotary evaporator under vacuum at 95°C for two hours. The resultant carrier $(PEG400)_4D_4$ was analyzed with ^1H , ^{13}C , and ^{29}Si NMR again.

Before catalyst separation.

^1H NMR (δ , ppm): 0.082 (m), 3.475 (s), 3.532 (m), 3.591 (m), 3.779 (m); ^{13}C NMR (δ , ppm): -5.236 (m), 60.824 (s), 69.659 (s), 69.872 (s), 71.965 (s); ^{29}Si NMR (δ , ppm): -58.489 (m), -57.955 (m). Yield: 98%

After catalyst separation.

^1H NMR (δ , ppm): -0.315 (m), 3.121 (s), 3.185 (m), 3.230 (m), 3.652 (m); ^{29}Si NMR (δ , ppm): -66.618 (m), -57.865 (m), -57.126 (m). Yield: 70%

Synthesis of delivery carrier (PEG1000) $_4\text{D}_4$:

Substitution of polyethylene glycol (PEG, MW=1000) on tetramethylcyclotetrasiloxane (D_4^{H}) core.

To a 100ml round bottom flask equipped with a magnetic stirring bar and vacuum inlet, was added Wilkinson's catalyst (0.004 g, 0.004 mmol). Flask was degassed and filled with nitrogen three times and polyethylene glycol (PEG) (8 g, 8 mmol; MW~1000) was added to it followed by addition of solvent (Benzene, 15 ml). Reaction mixture was allowed to stir for 5 min in order to get a homogenous brownish solution. At this juncture, 1, 3, 5, 7-tetramethylcyclotetrasiloxane (D_4^{H}) (0.49 ml, 2.0 mmol) was added to the reaction mixture. Reaction mixture immediately turned yellow and development of a gas (presumably H_2) was observed. Flask was degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 35 hrs. Upon completion, reaction mixture was a dark brown viscous solution. The product was analyzed with ^1H , ^{13}C , and ^{29}Si NMR, and transmission electron microscopy (TEM), which confirmed the formation of, desired product (PEG1000) $_4\text{D}_4$.

Catalyst was separated in the following way. Reaction mixture was taken in a 250ml round bottom flask equipped with a magnetic stirring bar and ~30ml cyclohexane was added to it. Solution was stirred vigorously for 10 min and water (~10ml) was added which resulted in a milky color solution. Solution was vigorously stirred for an additional 20 min and then collected in a separatory funnel and allowed to sit for one hour. Catalyst was separated at the interphase of water and cyclohexane layers in form of precipitate. The bottom water layer containing delivery vehicle was separated and centrifuged for 10 min at 9000 rpm in order to get rid of any remains of the catalyst. The water was evaporated in a rotary evaporator under vacuum at 95^oC for two hours. The resultant carrier (PEG1000)₄D₄ was a white waxy solid and was analyzed with ¹H, ¹³C, and ²⁹Si NMR again.

Before catalyst separation.

¹H NMR (δ, ppm): 0.065 (m), 3.264 (s), 3.380 (m), 3.514 (m), 3.633 (m); ¹³C NMR (δ, ppm): -4.310 (m), 60.066 (s), 69.037 (s), 69.250 (s), 71.510 (s); ²⁹Si NMR (δ, ppm): -56.854 (m). Yield: 98%

After catalyst separation.

¹H NMR (δ, ppm): -0.215 (m), 3.225 (m), 3.288 (s), 3.332 (m), 3.455 (m); ¹³C NMR (δ, ppm): -5.425 (m), 60.733 (s), 69.598 (s), 69.818 (s), 71.942 (s); ²⁹Si NMR (δ, ppm): -57.135 (m). Yield: 70%

Synthesis of delivery carrier (PEG400)₅D₅:

Substitution of polyethylene glycol (PEG, MW=400) on pentamethycyclopentasiloxane (D₅^H) core.

To a 50ml Schlenk tube equipped with a magnetic stirring bar, was added Wilkinson's catalyst (0.002 g, 0.002 mmol). Schlenk tube was degassed and filled with nitrogen three times and polyethylene glycol (PEG) (1.77 ml, 5 mmol; MW~400) was added to it. Reaction mixture was allowed to stir for 5 min in order to get a homogenous suspension of catalyst in PEG followed by addition of solvent (Benzene, 6 ml), which resulted in a brownish solution. At this juncture, pentamethylcyclopentasiloxane (D_5^H) (0.3 ml, 1.0 mmol) was added to the reaction mixture. Reaction mixture immediately turned yellow and development of a gas (presumably H_2) was observed. Schlenk tube was degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 36 hrs. Upon completion, reaction mixture was a dark brown viscous solution. The product was analyzed with ^1H , ^{13}C , and ^{29}Si NMR, and transmission electron microscopy (TEM), which confirmed the formation of, desired product (PEG400) $_5D_5$.

Catalyst was separated in the following way. Reaction mixture was taken in a 250ml round bottom flask equipped with a magnetic stirring bar and ~30ml cyclohexane was added to it. Solution was stirred vigorously for 10 min and water (~10ml) was added which resulted in a milky color solution. Solution was vigorously stirred for an additional 20 min and then collected in a separatory funnel and allowed to sit for one hour. Catalyst was separated at the interphase of water and cyclohexane layers in form of precipitate. The bottom water layer containing delivery vehicle was separated and centrifuged for 10 min at 9000 rpm in order to get rid of any remains of the catalyst. The water was evaporated in a rotary evaporator under vacuum at 95°C for two hours. The resultant carrier (PEG400) $_5D_5$ was analyzed with ^1H , ^{13}C , and ^{29}Si NMR again.

Before catalyst separation.

^1H NMR (δ , ppm): 0.070 (m), 3.470 (m), 3.532 (s), 3.580 (m), 3.767 (m); ^{29}Si NMR (δ , ppm): -58.860 (m), -59.296 (m). Yield: 98%

After catalyst separation.

^1H NMR (δ , ppm): -0.325 (m), 3.087 (m), 3.160 (s), 3.198 (m), 3.898 (m); ^{29}Si NMR (δ , ppm): -57.027 (m), -65.703 (m). Yield: 70%

Synthesis of delivery carrier (PEG400) $_8$ T $_8$:

Substitution of polyethylene glycol (PEG, MW=400) octakis(dimethylsiloxy)-T $_8$ -Silsesquioxane (Q $_8$ M $_8^{\text{H}}$) core.

The carrier was synthesized by taking Wilkinson's catalyst (0.001 g, 0.001 mmol) and octakis(dimethylsiloxy)-T $_8$ -Silsesquioxane (Q $_8$ M $_8^{\text{H}}$) (0.2545 g, 0.25 mmol) in a 50ml Schlenk tube equipped with a magnetic stirring bar. Schlenk tube was degassed and filled with nitrogen three times and solvent (Benzene, 5 ml) was added which resulted in a brownish solution. At this juncture, polyethylene glycol (PEG) (0.8 g, 2 mmol; MW~400) was added to it and reaction mixture immediately turned yellow and development of a gas (presumably H $_2$) was observed. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 32 hrs. Upon completion, reaction mixture was a light yellow viscous solution. Solvent was evaporated and product was analyzed with ^1H , and ^{29}Si NMR that confirmed the formation of desired product (PEG400) $_8$ T $_8$

For catalyst separation, reaction mixture was taken in a 250ml round bottom flask equipped with a magnetic stirring bar and ~30ml cyclohexane was added to it. Solution

was stirred vigorously for 10 min and water (~10ml) was added which resulted in a milky color solution. Solution was vigorously stirred for an additional 20 min and then collected in a separatory funnel and allowed to sit for one hour. Catalyst was separated at the interphase of both layers in form of precipitate. The bottom water layer containing delivery vehicle was separated and centrifuged for 10 min at 9000 rpm in order to get rid of any remains of the catalyst. The water was evaporated in a rotary evaporator under vacuum at 95^oC for two hours. The resultant was a clear viscous solution of delivery vehicle (PEG400)₈T₈. Product was analyzed with ¹H, and ²⁹Si NMR again which showed a slight shift to up field and in some cases a new small unidentified peak appeared at around -18 in ²⁹Si NMR. This could be the result of water treatment and formation of Si-OH bonds.

Before catalyst separation.

¹H NMR (δ, ppm): 0.063 (m), 3.485 (m), 3.538 (m), 3.599 (m), 3.733 (m); ²⁹Si NMR (δ, ppm): -8.192 (m), -109.706 (s). Yield: 96%

After catalyst separation.

¹H NMR (δ, ppm): 0.062 (m), 3.487 (m), 3.549 (m), 3.600 (m), 3.734 (m); ²⁹Si NMR (δ, ppm): -9.253 (m), -110.711 (s). Yield: 70%

Synthesis of delivery carrier (PEG1000)₈T₈:

Substitution of polyethylene glycol (PEG, MW=1000) octakis(dimethylsiloxy)-T₈-Silsesquioxane (Q₈M₈^H) core.

The carrier was synthesized by taking Wilkinson's catalyst (0.001 g, 0.001 mmol) and octakis(dimethylsiloxy)-T₈-Silsesquioxane (Q₈M₈^H) (0.1272 g, 0.125 mmol) in a 50ml Schlenk tube equipped with a magnetic stirring bar. Schlenk tube was degassed and filled

with nitrogen three times and solvent (Benzene, 5 ml) was added which resulted in a brownish solution. At this juncture, polyethylene glycol (PEG) (1.0 g, 1 mmol; MW~1000) was added to it and reaction mixture immediately turned yellow and development of a gas (presumably H₂) was observed. Reaction mixture was further degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 35 hrs. Upon completion, reaction mixture was a light yellow viscous solution. Solvent was evaporated and product was analyzed with ¹H, and ²⁹Si NMR that confirmed the formation of desired product (PEG1000)₈T₈. For catalyst separation, reaction mixture was taken in a 250ml round bottom flask equipped with a magnetic stirring bar and ~30ml cyclohexane was added to it. Solution was stirred vigorously for 10 min and water (~10ml) was added which resulted in a milky color solution. Solution was vigorously stirred for an additional 20 min and then collected in a separatory funnel and allowed to sit for one hour. Catalyst was separated at the interphase of both layers in form of precipitate. The bottom water layer containing delivery vehicle was separated and centrifuged for 10 min at 9000 rpm in order to get rid of any remains of the catalyst. The water was evaporated in a rotary evaporator under vacuum at 95°C for two hours. The resultant was a clear viscous solution of delivery vehicle (PEG1000)₈T₈. Product was analyzed with ¹H, and ²⁹Si NMR again which showed a slight shift to up field and in some cases a new small unidentified peak appeared at around -18 in ²⁹Si NMR. This could be the result of water treatment and formation of Si-OH bonds.

Before catalyst separation.

^1H NMR (δ , ppm): 0.067 (m), 3.480 (m), 3.535 (m), 3.598 (m), 3.727 (m); ^{29}Si NMR (δ , ppm): -8.023 (m), -109.680 (s). Yield: 96%

After catalyst separation.

^1H NMR (δ , ppm): 0.082 (m), 3.473 (m), 3.529 (m), 3.594 (m), 3.751 (m); ^{29}Si NMR (δ , ppm): -9.314 (m), -18.752 (m), -110.487 (s). Yield: 70%

5.3.3 Fluorescence Microscopic Studies

Acridine orange dye solution was prepared by dissolving 1 mg of acridine orange dye in 20 ml of water. The solution was further diluted by taking 1 ml of dye solution and adding another 20 ml of water to it. The delivery vehicle (PEG400) $_4\text{D}_4$ (50 mg) was taken in a glass vial and 20 ml water was added to it. The carrier was dissolved by shaking the vial gently. The vial with carrier water solution was suspended in ultrasonic cleaner water bath. One milliliter of diluted dye solution was slowly added to carrier solution drop-wise while sonicating over a period of 2 min. Sonication was stopped and sample was allowed to sit for one hour in order to achieve the complete encapsulation of dye in the carrier micelles. One drop of the diluted dye solution was deposited on a glass slide, and on another similar glass slide was placed one drop of carrier solution with encapsulated dye in it. Both slides were monitored under microscope with and without fluorescence light.

5.3.4 Synthesis of Model Compounds

Synthesis of model compound PEG400D $_3\text{D}'$

Substitution of polyethylene glycol (PEG) on heptamethylcyclotetrasiloxane (D $_3\text{D}'$) core.

To a 50ml Schlenk tube equipped with a magnetic stirring bar, was added Wilkinson's catalyst (0.002 g, 0.002 mmol). Tube was degassed and filled with nitrogen three times and polyethylene glycol (PEG) (0.71 ml, 2 mmol; MW=400) was added to it. Reaction mixture was allowed to stir for 5 min in order to get a homogenous suspension of catalyst in PEG followed by addition of solvent (Benzene, 3 ml), which resulted in a brownish solution. At this juncture, Heptamethycyclotetrasiloxane D₃D' (0.6 ml, 2 mmol) was added to the reaction mixture. Reaction mixture immediately turned yellow and development of a gas (presumably H₂) was observed. Flask was degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 28 hrs. Upon completion, reaction mixture was a dark brown viscous solution. Catalyst was separated by centrifuging the reaction mixture at 9000 rpm for 10 min and solvent was evaporated which resulted in a clear viscous liquid of PEG400D₃D'. Product was analyzed with ¹H, and ²⁹Si NMR that confirmed the formation of desired product.

¹H NMR (δ, ppm): 0.002 (m), 3.492 (m), 3.545 (m), 3.605 (m), 3.748 (m); ¹³C NMR (δ, ppm): -4.616 (s), 0.238 (m), 61.090 (s), 69.875 (s), 70.118 (s), 71.729 (s), 72.185 (s); ²⁹Si NMR (δ, ppm): -57.423 (m), -519.565 (m). Yield: 100%

Synthesis of model compound (BE)₄D₄

Substitution of butoxy ethanol (BE) on tetramethylcyclotetrasiloxane (D₄) core.

To a 50ml Schlenk tube equipped with a magnetic stirring bar, was added Wilkinson's catalyst (0.002 g, 0.002 mmol). Tube was degassed and filled with nitrogen three times and butoxy ethanol (BE) (1.05 g, 8 mmol) was added to it. Reaction mixture was allowed to stir for 5 min in order to get a homogenous suspension of catalyst in BE followed by

addition of solvent (Benzene, 4 ml), which resulted in a brownish solution. At this juncture, 1,3,5,7-tetramethylcyclotetrasiloxane (D₄) (0.49 ml, 2 mmol) was added to the reaction mixture. Reaction mixture immediately turned yellow and development of a gas (presumably H₂) was observed. Flask was degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 28 hrs. Upon completion, reaction mixture was a dark brown viscous solution. Catalyst was separated by centrifuging the reaction mixture at 9000 rpm for 20 min and solvent was evaporated which resulted in a clear viscous liquid of (BE)₄D₄. Product was analyzed with ¹H, and ²⁹Si NMR that confirmed the formation of desired product.

¹H NMR (δ, ppm): 0.044 (m), 0.808 (m), 1.265 (m), 1.448 (m), 3.382 (m), 3.608 (s), 3.791 (m); ²⁹Si NMR (δ, ppm): -58.297 (m), -57.772 (m). Yield: 100%

Synthesis of model compound (DA)₄D₄

Substitution of decyl alcohol (DA) on tetramethylcyclotetrasiloxane (D₄) core.

To a 50ml Schlenk tube equipped with a magnetic stirring bar, was added Wilkinson's catalyst (0.002 g, 0.002 mmol). Tube was degassed and filled with nitrogen three times and decyl alcohol (DA) (1.53 ml, 8 mmol) was added to it. Reaction mixture was allowed to stir for 5 min in order to get a homogenous suspension of catalyst in DA followed by addition of solvent (Benzene, 4 ml), which resulted in a brownish solution. At this juncture, 1,3,5,7-tetramethylcyclotetrasiloxane (D₄) (0.49 ml, 2 mmol) was added to the reaction mixture. Reaction mixture immediately turned yellow and development of a gas (presumably H₂) was observed. Flask was degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 28 hrs. Upon completion, reaction mixture was a dark brown viscous solution. Catalyst

was separated separated by centrifuging the reaction mixture at 9000 rpm for 20 min and solvent was evaporated which resulted in a clear viscous liquid of (DA)₄D₄. Product was analyzed with ¹H, and ²⁹Si NMR that confirmed the formation of desired product.

¹H NMR (δ, ppm): 0.060 (m), 0.795 (s), 1.185 (s), 1.474 (s), 3.666 (m); ²⁹Si NMR (δ, ppm): -59.878 (m), -58.982 (m). Yield: 98%

Synthesis of model compound (PEGTHFE)₄D₄

Substitution of poly(ethylene glycol) tetrahydrofufuryl ether (PEGTHFE) on tetramethylcyclotetrasiloxane (D₄) core.

To a 50ml Schlenk tube equipped with a magnetic stirring bar, was added Wilkinson's catalyst (0.002 g, 0.002 mmol). Tube was degassed and filled with nitrogen three times poly(ethylene glycol) tetrahydrofufuryl ether (PEGTHFE) (0.86 ml, 4 mmol) was added to it. Reaction mixture was allowed to stir for 5 min in order to get a homogenous suspension of catalyst in PEGTHFE followed by addition of solvent (Benzene, 4 ml), which resulted in a brownish solution. At this juncture, 1,3,5,7-tetramethylcyclotetrasiloxane (D₄) (0.24 ml, 1 mmol) was added to the reaction mixture. Reaction mixture immediately turned yellow and development of a gas (presumably H₂) was observed. Flask was degassed and filled with nitrogen three more times and reaction was allowed to continue at 65⁰C under a positive nitrogen pressure for 36 hrs. Upon completion, reaction mixture was a dark brown viscous solution. Catalyst was separated separated by centrifuging the reaction mixture at 9000 rpm for 10 min and solvent was evaporated which resulted in a clear viscous liquid of (PEGTHFE)₄D₄. Product was analyzed with ¹H, and ²⁹Si NMR that confirmed the formation of desired product.

^1H NMR (δ , ppm): 0.064 (m), 1.509 (m), 1.774 (m), 1.839 (m), 3.386 (s), 3.483 (s), 3.543 (s), 3.649 (m), 3.763 (m), 3.936 (m); ^{29}Si NMR (δ , ppm): -57.996 (m). Yield: 98%

Synthesis of model compound (PEGME350) $_4$ D $_4$

Substitution of poly(ethylene glycol) methyl ether (MW=350) (PEGME350) on tetramethylcyclotetrasiloxane (D $_4$) core.

To a 50ml Schlenk tube equipped with a magnetic stirring bar, was added Wilkinson's catalyst (0.002 g, 0.002 mmol). Tube was degassed and filled with nitrogen three times poly(ethylene glycol) methyl ether (PEGME350) (2.6 ml, 8 mmol, MW ~ 350) was added to it. Reaction mixture was allowed to stir for 5 min in order to get a homogenous suspension of catalyst in PEGME350 followed by addition of solvent (Benzene, 6 ml), which resulted in a brownish solution. At this juncture, 1,3,5,7-tetramethylcyclotetrasiloxane (D $_4$) (0.49 ml, 2 mmol) was added to the reaction mixture. Reaction mixture immediately turned yellow and development of a gas (presumably H $_2$) was observed. Flask was degassed and filled with nitrogen three more times and reaction was allowed to continue at 65 $^{\circ}\text{C}$ under a positive nitrogen pressure for 32 hrs. Upon completion, reaction mixture was a dark brown viscous solution. Catalyst was separated by centrifuging the reaction mixture at 9000 rpm for 10 min and solvent was evaporated which resulted in a clear viscous liquid of (PEGME350) $_4$ D $_4$. Product was analyzed with ^1H , and ^{29}Si NMR that confirmed the formation of desired product.

^1H NMR (δ , ppm): -0.228 (m), 2.998 (s), 3.183 (m), 3.215 (m), 3.274 (m), 3.322 (m), 3.564 (s); ^{29}Si NMR (δ , ppm): -57.327 (m), -55.298 (m). Yield: 98%

Synthesis of model compound (PEGME550) $_4$ D $_4$

Substitution of poly(ethylene glycol) methyl ether (MW=550) (PEGME550) on tetramethylcyclotetrasiloxane (D₄) core.

To a 50ml Schlenk tube equipped with a magnetic stirring bar, was added Wilkinson's catalyst (0.002 g, 0.002 mmol). Tube was degassed and filled with nitrogen three times poly(ethylene glycol) methyl ether (PEGME550) (3.03 ml, 6 mmol; MW ~ 550) was added to it. Reaction mixture was allowed to stir for 5 min in order to get a homogenous suspension of catalyst in PEGME550 followed by addition of solvent (Benzene, 6 ml), which resulted in a brownish solution. At this juncture, 1,3,5,7-tetramethylcyclotetrasiloxane (D₄) (0.36 ml, 1.5 mmol) was added to the reaction mixture. Reaction mixture immediately turned yellow and development of a gas (presumably H₂) was observed. Flask was degassed and filled with nitrogen three more times and reaction was allowed to continue at 65°C under a positive nitrogen pressure for 35 hrs. Upon completion, reaction mixture was a dark brown viscous solution. Catalyst was separated by centrifuging the reaction mixture at 9000 rpm for 10 min and solvent was evaporated which resulted in a clear viscous liquid of (PEGME550)₄D₄. Product was analyzed with ¹H, and ²⁹Si NMR that confirmed the formation of desired product.

¹H NMR (δ, ppm): -0.325 (m), 2.917 (s), 3.102 (m), 3.126 (m), 3.193 (m), 3.236 (m), 3.551 (s); ²⁹Si NMR (δ, ppm): -57.590 (m), -57.097 (m). Yield: 98%

5.4 References

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