GIANT MOLECULAR SHAPE AMPHIPHILES

BASED ON POLYHEDRAL OLIGOMERIC SILSESQUIOXANE:

MOLECULAR DESIGN AND “CLICK” SYNTHESIS

A Thesis

Presented to

The Graduate Faculty of The University of Akron

In Partial Fulfillment

of the Requirements for the Degree

Master of Science

Chang Liu

May, 2013
GIANT MOLECULAR SHAPE AMPHIPHILES
BASED ON POLYHEDRAL OLIGOMERIC SILSESQUIOXANE:
MOLECULAR DESIGN AND “CLICK” SYNTHESIS

Chang Liu

Thesis

Approved: ____________________________________________  Accepted: ____________________________________________

Advisor
Dr. Stephen Z. D. Cheng

Dean of the College
Dr. Stephen Z. D. Cheng

Faculty Reader
Dr. Toshikazu Miyoshi

Dean of the Graduate School
Dr. George R. Newkome

Department Chair
Dr. Coleen Pugh

Date
ABSTRACT

Previous research in our group has revealed that the giant molecular shape amphiphiles (GMSAs) based on polyhedral oligomeric silsesquioxane (POSS) and polystyrene (PS) can self-assemble into various micro-phase separated ordered structures due to the shape imcommensurateness and chemical incompatibility between the molecular building blocks. In contrast to their block copolymer analogues, feature sizes of the formed nanostructures can reach sub-10 nm scales, which is still a challenging task for block copolymer based materials. To further investigate the micro-phase separation properties of POSS based GMSAs, the degree of shape imcommensurateness should be enlarged and the effect of molecular architecture should also be considered. Following a recently developed sequential “click” strategy combined the utilization of “click” adaptor molecules, two novel series of GMSAs, which are: (1) two functionalized POSS cages tethered to one PS chain end (2DPOSS-PS), and (2) one functionalized POSS cage tethered to the core of one star-PS with three identical arms (DPOSS-3PS), have been designed and synthesized in an efficient and modular manner. The work discussed here provides necessary topological variations to our current libraries of GMSAs and thus allows systematic study on the self-assembly behaviors of our GMSA systems.
ACKNOWLEDGEMENTS

I would like to thank my advisor, Dr. Stephen Z. D. Cheng, to offer me the opportunity to learn and to do research in his group. And thanks also give to Dr. Hui Li for her strong recommendations.

I would like to thank my mentor, Mr. Kan Yue, who trained me experimental skills which help me avoid many troubles and helped me in many aspects. Thanks also give to all the other group members for their discussions and suggestions. I would also like to thank Dr. Chrys Wesdemiotis and Ms. Kai Guo for their help in MS spectra, and Mr. Jon Page for GPC characterizations.

I would like to thank my family for their love and support.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIST OF FIGURES</td>
<td>viii</td>
</tr>
<tr>
<td>LIST OF SCHEMES</td>
<td>x</td>
</tr>
<tr>
<td>CHAPTER</td>
<td></td>
</tr>
<tr>
<td>I. INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>II. BACKGROUND</td>
<td>4</td>
</tr>
<tr>
<td>2.1 The self-assembly behaviors of small-molecule surfactants</td>
<td>4</td>
</tr>
<tr>
<td>2.2 The self-assembly behaviors of block copolymers</td>
<td>7</td>
</tr>
<tr>
<td>2.3 General rules of our design</td>
<td>9</td>
</tr>
<tr>
<td>2.4 Polyhedral oligomeric silsesquioxane</td>
<td>11</td>
</tr>
<tr>
<td>2.4.1 Introduction of POSS</td>
<td>11</td>
</tr>
<tr>
<td>2.4.2 Preparation of POSS derivatives</td>
<td>12</td>
</tr>
<tr>
<td>2.4.3 Synthesis of POSS-Polymer Hybrids</td>
<td>14</td>
</tr>
<tr>
<td>III. PREVIOUS INVESTIGATIONS OF SYNTHETIC METHODOLOGY</td>
<td>19</td>
</tr>
<tr>
<td>3.1 The preparation of mono-substituted POSS blocks</td>
<td>20</td>
</tr>
<tr>
<td>3.2 The “growing-from” and “grafting-to” strategies</td>
<td>21</td>
</tr>
<tr>
<td>3.3 “Click” chemistry</td>
<td>24</td>
</tr>
<tr>
<td>3.4 Building blocks bearing “click” functional groups and sequential “click”</td>
<td></td>
</tr>
</tbody>
</table>
strategy .................................................................................................................. 28

IV. EXPERIMENTAL ................................................................................................. 33

4.1 Chemicals and solvents ................................................................................... 33

4.2 Molecular characterization .............................................................................. 34

4.3.1 Synthesis of 1yne-2Br ........................................................................... 36

4.3.2 Synthesis of 3yne-1Br ........................................................................... 36

4.3.4 General procedures for the azide substitution reaction ............................. 38

4.3.5 General procedures for the CuAAC “click” reaction between modified polymer-azide and VPOSS-alkyne ................................................................. 38

4.3.6 General procedures for the thiol-ene reaction ....................................... 39

4.3.7 Synthesis of PS-2Br ......................................................................... 39

4.3.8 PS-2N₃ .............................................................................................. 40

4.3.9 2VPOSS-PS ..................................................................................... 40

4.3.10 2DPOSS-PS ..................................................................................... 41

4.3.11 3PS-Br .............................................................................................. 42

4.3.12 3PS-N₃ .............................................................................................. 42

4.3.13 VPOSS-3PS ..................................................................................... 43

4.3.14 DPOSS-3PS ..................................................................................... 43

RESULTS AND DISCUSSIONS ................................................................................. 45

5.1 The molecular design, synthesis and characterization of 2DPOSS-PS ........ 45

5.2 The molecular design, synthesis and characterization of DPOSS-3PS ....... 56
## LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 A typical structure of surfactant</td>
<td>5</td>
</tr>
<tr>
<td>2.2 A typical structure of block copolymers</td>
<td>8</td>
</tr>
<tr>
<td>2.3 Four common POSS cages</td>
<td>11</td>
</tr>
<tr>
<td>3.1 Cartoons for various topologies for GMSAs</td>
<td>19</td>
</tr>
<tr>
<td>5.1 $^1$H NMR and $^{13}$C NMR spectra of 1yne-2Br</td>
<td>48</td>
</tr>
<tr>
<td>5.10 $^1$H NMR spectra of synthesis DPOSS-3PS</td>
<td>62</td>
</tr>
<tr>
<td>5.11 $^{13}$C NMR spectra of synthesis DPOSS-3PS</td>
<td>63</td>
</tr>
<tr>
<td>5.12 MALDI-TOF MS spectra of VPOSS-3PS</td>
<td>64</td>
</tr>
<tr>
<td>5.2 FT-IR spectra of the products in the synthesis of 2DPOSS-PS</td>
<td>49</td>
</tr>
<tr>
<td>5.3 GPC curves of the products in the synthesis of 2DPOSS-PS</td>
<td>50</td>
</tr>
<tr>
<td>5.4 $^1$H NMR spectra of synthesis 2DPOSS-PS</td>
<td>52</td>
</tr>
<tr>
<td>5.5 $^{13}$C NMR spectra of synthesis 2DPOSS-PS</td>
<td>53</td>
</tr>
<tr>
<td>5.6 MALDI-TOF MS spectra of 2VPOSS-PS</td>
<td>55</td>
</tr>
<tr>
<td>5.7 $^1$H NMR and $^{13}$C NMR spectra of 3yne-Br</td>
<td>59</td>
</tr>
<tr>
<td>5.8 FT-IR spectra of the products in synthesis of DPOSS-3PS</td>
<td>60</td>
</tr>
<tr>
<td>5.9 GPC curves of the products in synthesis of DPOSS-3PS</td>
<td>61</td>
</tr>
</tbody>
</table>
**LIST OF SCHEMES**

<table>
<thead>
<tr>
<th>Scheme</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.2 Synthesis scheme of homo-substituted POSS</td>
<td>12</td>
</tr>
<tr>
<td>2.3 Synthesis scheme of hetero-substituted fluorinated POSS derivatives with nine silicon atoms in the cage framework</td>
<td>13</td>
</tr>
<tr>
<td>2.4 Synthesis of a monohydroxylheptavinyl substituted POSS derivative (VOSS-OH)</td>
<td>14</td>
</tr>
<tr>
<td>2.5 Polymerization scheme of macro-monomers containing POSS</td>
<td>14</td>
</tr>
<tr>
<td>2.6 “Growing-from” synthesis of POSS-end-capped PS by ATRP initiated by a POSS derivative</td>
<td>15</td>
</tr>
<tr>
<td>2.7 “Growing-from” synthesis of POSS-end-capped polycaprolactone by ROP initiated by a hydroxyl-POSS derivative</td>
<td>16</td>
</tr>
<tr>
<td>2.8 “Grafting-to” synthesis of POSS-end-capped PS by urethane linkage</td>
<td>17</td>
</tr>
<tr>
<td>2.9 “Grafting-to” synthesis of POSS-end-capped PEO in both chain ends by urethane linkage</td>
<td>17</td>
</tr>
<tr>
<td>3.1 Functionalization on POSS surface</td>
<td>20</td>
</tr>
</tbody>
</table>
3.2 Synthesis scheme of VPOSS-diOH.................................................................21
3.3 Synthesis scheme of VPOSS-alkyne...............................................................21
3.4 “Growing-from” synthesis scheme of VPOSS-PLLA .................................22
3.5 “Growing-from” synthesis of PS-VPOSS-PS...............................................22
3.6 “Growing-from” synthesis scheme of PCL-VPOSS-PCL ............................23
3.7 “Grafting-on” synthesis scheme of PS-POSS-PDMS by hydrosilylation......23
3.8 “Grafting-on” synthesis scheme of PS-VPOSS by hydrosilylation..............24
3.9 Synthesis scheme of PS-VPOSS-PCL ..........................................................24
3.10 Cu-catalyzed azide-alkyne cycloaddition....................................................25
3.11 A complex structure synthesized via CuAAC reaction ..............................26
3.12 Synthesis of tethered-nanoparticle by CuAAC “click” chemistry...............27
3.13 Scheme of thiol-ene reaction.......................................................................28
3.14 Post-polymerization functionalization at chain end....................................29
3.15 The sequential “click” approach .................................................................30
3.16 Synthesis of 3DPOSS-PS and 2DPOSS-2PS by sequential “click” approach and molecular “click” adaptors

5.1 Molecular design and synthesis scheme of 2DPOSS-PS

5.2 Synthesis scheme of molecular “click” adaptor 1yne-2Br

5.3 Molecular design and synthesis of DPOSS-3PS

5.4 Synthesis of 3yne-Br
CHAPTER I

INTRODUCTION

It is well known that the macroscopic properties of materials are not only determined by their compositions but also the microscopic structures. In the history of human civilization, development of new materials largely depends on the compositional discoveries, from the woods and stones to metal and alloys, and finally to various kinds of artificial components. Nowadays, traditional materials with relatively monotonous and stiff microscopic structures cannot satisfy the requirements of achieving both high-performance and low costs. Inspired by bio-structures in nature, the formation of hierarchical structures at different length scales under various conditions plays an important role in realizing optimal functionalities.

Self-assembly is a “bottom-up” approach to construct such complex structures, and is especially unparalleled at the nanometer length scale, say, 1 to 100 nm, which is challenging or even beyond the reach of traditional processing techniques. Various non-covalent interactions, through which different blocks on molecules recognize each other and form ordered aggregations, trigger the self-assembly process. At the same time, the positional, orientational and conformational effects complementarily
determine the details of ordered-structures by packing the building blocks in a proper way to induce cooperative interactions and increase the overall stability of the whole system.

Aiming at novel synthetic self-assembled systems, previous research in our group has systematically designed and constructed a library of molecules based on molecular nano-particles and synthetic polymers, which is named as the giant molecular shape amphiphiles (GMSAs). One prototype structure of this design, composed of a molecular nanoparticle tethered with a polymer tail, can be regarded as ether as an amplified small-molecule surfactant, or as a low-molecular-weight diblock copolymer with one block replaced by the molecular nano-particle. The unique structural features are attractive in generating novel self-assembly behaviors.

A sequential “click” synthetic approach, which takes the advantage of robust, efficient and orthogonal chemical reactions, has been established to facilitate the synthetic work of these GMSAs with precisely-defined structures. The modularity and high efficiency of this approach allow feasible, open, and concise molecular designs for further structural diversifications, and as a result, a systemic investigation of the self-assembly behaviors of GMSAs with various molecular topologies.

Several interesting self-assembled structures with nanometer-scale feature sized have already been observed in the GMSA system, indicating vastly different
behaviors from traditional diblock copolymers. To deepen our understanding, in this thesis, we further enrich the library of GMSAs by adding another two sets of molecules, which are composed of: (1) two functionalized polyhedral silsesquioxane (POSS) cages tethered to one polystyrene (PS) (2DPOSS-PS), and (2) one functionalized POSS cage tethered to the core of oligomeric star-PS with three identical arms (DPOSS-3PS). Their detailed molecular design and synthetic work are presented in the following parts in this thesis.
CHAPTER II
BACKGROUND

During the past decades, extensively studies have been conducted focusing on how molecules would assemble by themselves. However, self-assembly in micro- and meso- scales is still an extremely complicated process involving thermodynamic and kinetic issues, and it remains very challenging to design tailored materials “from scratch”.\textsuperscript{1,2} Luckily, the investigations of several classic self-assembling systems, such as, small-molecule surfactants and block copolymers, have provided a window to look into the depths of self-assembly and offered clues in materials design.

2.1 The self-assembly behaviors of small-molecule surfactants

Surfactants, also referred as amphiphiles, detergents or soaps, have typical molecular structures with hydrophilic polar groups attached with hydrophobic hydrocarbon chains containing 12-18 carbon atoms (see Figure 2.1). Due to these molecular structural characteristics, various ordered-structures can be formed by surfactants in both aqueous and anhydrous states under proper conditions (e.g., concentration and temperature).\textsuperscript{3,4} X-ray diffraction techniques were widely used to
characterize these structures, but the obtained data were too complicated to be properly understood for a long time, which indicated the complexity of structures.\textsuperscript{3,4}

\begin{center}
\includegraphics[width=0.5\textwidth]{surfactant.png}
\end{center}

Figure 2.1. A typical structure of surfactant.

Not until Luzzati \textit{et al.} systemically and carefully analyzed the data of some natural divalent cationic soap structures, was a universal interpretation of the organizations of soap molecules obtained. They found that all the diffraction peaks could be classified into two groups.\textsuperscript{3,4} The first group of peaks which had strong signals located at a small angle region (about several nanometers) and could be assigned to lattices with varied dimensions and symmetries. For example, there were lamellar lattices in one dimension, hexagonal lattices in two dimensions and body-centered cubic lattices, body-centered tetragonal lattices in three dimensions. And the second group of peaks which located at relatively higher angle region (corresponding to below 1 nm sizes) showed almost identical positions and intensities regardless of the positions of the first group peaks, which indicated the existence of a structural element in all these structures.\textsuperscript{3,4}
Due to the fact that all these structures were obtained at high temperatures, the hydrocarbon chains were in disordered states, which could be proved by broad diffraction peaks at the corresponding region.\textsuperscript{3,4} Therefore the structural element mentioned above was composed by the aggregation of metal cations and a finite rod model was proposed based on calculation, which fitted very well with the experimental data.\textsuperscript{3,4}

These rods acted as the elementary components to construct the various lattices at a larger length scale. For example, the formation of the two-dimensional hexagonal lattice was explained as following: the rods aggregated head to tail to form infinite long rods with short gaps in between, and then the infinite rods further self-assembled into the hexagonal lattice.\textsuperscript{3} The hydrocarbon chains would adopt different conformations which might introduce strain to fulfill the space among the lattice constructed by rigid rods.\textsuperscript{3} The lower the temperature, the higher degree of strain would be. To release the stain, other aggregation forms were adopted by the finite rods, for example, they linked three by three or four by four to form two-dimensional grids or three dimensional interwoven networks.\textsuperscript{4,5,6} The relatively positions between the grids or the networks finally determined the detailed lattices.
From the analysis above, we can see that the combination of rigid shapes and flexible components plays an important role in the formation of complex hierarchical structures of surfactants, which is also proved in some rigid-flexible liquid crystal systems.  

2.2 The self-assembly behaviors of block copolymers

The covalently linking of polymers with different components results block copolymers (see Figure 2.2), which was firstly achieved by anionic polymerization techniques. With the developments of several different living polymerization mechanisms and efficient post-polymerization functionalization methods, precise synthesis of block copolymers with homogeneous composition and low dispersity became practical, which greatly enriches the family of block copolymers varied in components, compositions and architectures and facilitates the study of their properties.

Micro-phase separation is the most striking property of block copolymers, which makes them particularly interesting in materials science. The most investigated system of micro-phase separation is the diblock copolymer composed by two immiscible linear polymer chains. Due to the restriction of conjunction points, phase separation at macro-scope cannot be achieved, and ordered segregations at meso-scale of different components are formed to stabilize the whole system.
Micelles with various morphologies in selective solvents of some amphiphile diblock copolymers are also considered as illustrations of micro-phase separation.\textsuperscript{10,11}

![Figure 2.2. A typical structure of block copolymers.](image)

In the bulk state, micro-phase separation phenomena occur to form structures with different symmetries. A phase diagram which is described by two empirical parameters (the production of Flory-Huggins interaction parameter and total degree of polymerization: $\chi^N$ and the volume fraction of one block: $f$) was predicted by theoretical approaches, which qualitatively agreed with the experimental observations.\textsuperscript{9} In this typical phase diagram, there are four kinds of structures: lamellar, hexagonal, double gyroid and body-centered cubic structures, which have been fully characterized by a combination of small angle X-ray scattering (SAXS) and transmission electron microscope (TEM) techniques.\textsuperscript{12,13} Because of their meso-length scales, they are potentially applicable in materials fabrication.\textsuperscript{14}
To achieve more controlled meso-phase structures with tailored sizes and desired symmetries, other symmetry-determining parameters independent of $\chi N$ and the volume fraction should be taken into account.\textsuperscript{15} For example, Milner has theoretically predicted that the molecular architecture should be one of the factors which influence phase diagrams, and that replacing one linear block in traditional diblock copolymers by a star block should be particular useful in tuning the structural symmetry in bulk.\textsuperscript{15} These predictions have been experimentally proved by Hadjichristidis \textit{et al} by synthesizing samples with precise AB, A$_2$B and A$_3$B architectures at the same volume fraction of 50\% for each block, which showed micro-phase separated structures changing from lamella, cylinder to sphere.\textsuperscript{16} The self-assembly behaviors of other architectures, such as comb-linear and hyperbranched-linear block copolymers, have also been investigated.\textsuperscript{17,18}

2.3 General rules of our design

Research in our group aims at rationally designing and synthesizing novel materials that can self-assemble into tailored hierarchical structures at the meso-scale, i.e., 1 to 100 nm.\textsuperscript{19} Achieving this challenging goal is not only scientifically important in understanding the fundamental principles of self-assembly in fields of chemistry and materials science, but also practically relevant in finding potential applications in modern nanotechnology.\textsuperscript{19}
To make these materials in to reality, our approach is to use libraries of nano-sized building blocks to directly construct “giant molecules” with precisely defined structures. One library of these building blocks is featured by the various conformational states, which includes polymers, dendrimers, peptides, proteins and DNA strands. Another library, which is called molecular nano-particle (MNP), is nano-sized molecules with persistent rigid shapes in three dimensions, as represented by [60]fullerene (C$_{60}$) and polyhedral oligomeric silsesquioxane (POSS). These nano-sized building blocks, by incorporating proper functional groups, can have competing interactions as the driving force for self-assembly.

Particularly, my research topic focuses on tethering MNPs to polymer blocks to afford various molecular topologies. The marriage of MNPs and polymers leads to the so-called giant molecular shape amphiphiles (GMSAs) and provides a platform to investigate their self-assembly processes. The structures of GMSAs not only possess similarities to both small-molecule surfactants and traditional diblock copolymers in general, but also include the shape effects due to the rigidity of MNPs and the flexibility of polymer tails.
2.4 Polyhedral oligomeric silsesquioxane

2.4.1 Introduction of POSS

Polyhedral oligomeric silsesquioxanes (POSS) are a class of cage molecules which have a common formula of $R_n(SiO_{1.5})_n$, where $R$ represents different substituent groups attached to the silicon atoms.²¹ A precisely-defined POSS framework is composed by Si-O bonds with a silicon atom at each corner and an oxygen atom at the edge (see Figure 2.3). By changing the periphery $R$ groups, the properties of POSS molecules, e.g. the size and the interaction, can be adjusted to satisfy different applications, which provides the potential to construct organic-inorganic hybrid materials with excellent physical properties.²¹ The prevailing POSS derivatives have the value of $n$ to be 8, with a perfectly cubic arrangement of the Si atoms (the $T_8$ POSS). Usually, the diameter of one $T_8$ POSS molecule is 1 to 2 nanometers depending on the $R$ groups.²¹ The nano-scale rigid shape and the tunable properties make POSS molecules be particular interesting building blocks in the construction of GMSAs.
2.4.2 Preparation of POSS derivatives

The simplest method to synthesize a homo-substituted POSS molecule with identical substituent groups is the polycondensation of trifunctional monomer, RSiX$_3$, (see Scheme 2.1).$^{22}$ By this method, homo-substituted POSS molecules (R can be a hydrogen atom, methyl group, phenyl group, other alkyl groups and vinyl groups, etc.) are directly obtained. It should be noted that during this synthesis, T$_8$ POSS for example, other POSS derivatives such as T$_{10}$ or T$_{12}$ POSS side-products are also produced with much lower yields.$^{21,22}$ Repeated recrystallization serves as a good purification technique to remove the minor impurities.$^{21,22}$
To synthesize hetero-substituted POSS molecules with precisely-controlled structures, there are three common methods. The first method is to co-condensate different trifunctional monomers.\textsuperscript{21,22} This method is simple and direct, but can only result in a mixture of products with all possible combinations of monomers and cumbersome purification is required. The second method utilizes a two-step synthesis: an incomplete condensation reaction or a cleavage reaction of the cubic framework, followed by a sequential condensation with a different silane.\textsuperscript{23} POSS molecules with one hetero-substitution can be obtained in such a controlled manner.\textsuperscript{23} Recently, Joseph \textit{et al.} have successfully synthesized fluorinated POSS (FPOSS) with unusual cage structures containing nine silicon atoms (see Scheme 2.2).\textsuperscript{24} The third method is based on mono-functionalization of homo-substituted POSS derivatives without breaking the POSS cages. Feher’s group has reported many examples, among which one useful POSS product bearing a reactive hydroxyl group and seven vinyl groups (VPOSS-OH) (see Scheme 2.3) was synthesized via an addition reaction and the following hydrolysis from an octavinyl POSS precursor (OVPOSS).\textsuperscript{25}
2.4.3 Synthesis of POSS-Polymer Hybrids

POSS molecules bearing at least one reactive functional group can be covalently incorporated into polymers to afford POSS-polymer hybrids. At the beginning, macro-monomers with a pendant POSS group were synthesized and then polymerized by different mechanisms, such as condensation polymerization, (controlled) free radical polymerization, and ring-opening metathesis polymerization (see Scheme
Homo-polymers, random copolymers and block copolymers can all be synthesized via this methodology. The reported POSS-polymer hybrids presented interesting physical properties, like high glass transition temperatures and flame retardant behaviors.\textsuperscript{27}

POSS-polymer hybrids which represent the shape amphiphiles of polymer tethered nanoparticle have also been reported.\textsuperscript{28, 29, 30, 31} In these hybrids, alkyl-substituted POSS molecules were used as the MNPs and various polymer chains (polystyrene, polyethylene oxide, polycaprolactone, etc.) were used as the tethers. Such hybrids can be achieved by either “growing-from” or “grafting-to” methods.

Following the “growing-from” method, polymerizations of various monomers by different types of mechanism, for example, controlled free radical polymerization (see Scheme 2.5) and ring opening polymerization (ROP, see Scheme 2.6), were initiated by the functional group in a hetero-substituted POSS cage with seven alkyl groups remaining intact.\textsuperscript{28,31}
Scheme 2.5. “Growing-from” synthesis of POSS-end-capped PS by ATRP initiated by a POSS derivative.\textsuperscript{28}

Scheme 2.6. “Growing-from” synthesis of POSS-end-capped polycaprolactone by ROP initiated by a hydroxyl-POSS derivative.\textsuperscript{31}

Chemical ligation of POSS moieties onto polymer chains can also happen after the polymerization, i.e., through post-polymerization functionalization strategy. In a typical “grafting-to” method, POSS cages and pre-prepared polymer chains were conjugated together by proper chemical reactions between matching functional groups.
on the POSS cages and polymer blocks.\textsuperscript{29,30} For example, using urethane linkages, a very similar POSS-PS hybrid (see Scheme 2.7) to the product in Scheme 2.5 and a POSS end-capped telechelic polyethylene oxide hybrid (see Scheme 2.8) were synthesized with high yields. It is worth noting that only commercially available alkyl-substituted POSS cages were used to construct these hybrids in the previous studies, which had limited tunability in interaction parameters. It was found, in most cases, alkyl chain substituted POSS cages can hardly microphase separate from the polymer domains, as reflected by the broad diffraction halo in the X-ray scattering results. To achieve strong enough competing interactions, it is desirable that the functional groups are polar groups to bring in amphiphilicity, and that at the same time the selection of functional groups can be readily tuned for feasible structural diversification.

Scheme 2.7. “Grafting-to” synthesis of POSS-end-capped PS by urethane linkage.\textsuperscript{29}
Scheme 2.8. “Grafting-to” synthesis of POSS-end-capped PEO in both chain ends by urethane linkage.\textsuperscript{30}
CHAPTER III

PREVIOUS INVESTIGATIONS OF SYNTHETIC METHODLOGY

A lot of work has been done in our group to establish a synthetic methodology which is efficient and modular to facilitate the construction of complex giant molecular shape amphiphiles of different topologies for systemic research of their self-assembly behaviors (see Figure 3.1).

Figure 3.1. Cartoons for various topologies for GMSAs.
3.1 The preparation of mono-substituted POSS blocks

Most of the work in our group has been based on the octavinyl-POSS (OVPOSS), which has a cubic framework with eight vinyl groups at the periphery. Mono-functionalization of the eight vinyl groups on OVPOSS can be feasibly achieved to afford a mono-substituted POSS molecule, which introduces the position to link with the polymer blocks, with the other seven vinyl groups serving as precursors to various functionalities in the following steps (see Scheme 3.1). \(^{32}\)

![Scheme 3.1. Functionalization on POSS surface.](image)

Two methods have been used to synthesize mono-substituted POSS molecules in our group. The first one was reported by Feher et al. in 1999 to obtain mono-hydroxyl-substituted vinyl-POSS (VPOSS-OH) (see Scheme 2.3). \(^{25}\) The second method was proposed by Li et al. to successfully install two hydroxyl groups onto one corner in OVPOSS by thiol-ene reaction (VPOSS-diOH, see Scheme 3.2). \(^{33}\) The hydroxyl groups on these two molecules can be potentially transformed into other
functionalities, which allow different chemistries to conjugate with the polymer blocks. One of a particular interesting functional group introducing onto VPOSS cage is the alkyne group, which affords a building block called VPOSS-alkyne (see Scheme 3.3).\textsuperscript{34}

\begin{center}
\textbf{Scheme 3.2. Synthesis scheme of VPOSS-diOH.}\textsuperscript{33}
\end{center}

\begin{center}
\textbf{Scheme 3.3. Synthesis scheme of VPOSS-alkyne.}\textsuperscript{34}
\end{center}

3.2 The “growing-from” and “grafting-to” strategies

Both the “growing-from” and “grafting-to” strategies were employed to tether polymer blocks with different components and architectures onto the VPOSS containing blocks. In the “growing-from” strategy, VPOSS derivatives are used as macro-initiators to directly initiate the polymerization of monomers such as L-lactide (see Scheme 3.4), polystyrene (see Scheme 3.5) and ε-caprolactone (see Scheme 3.6).\textsuperscript{32,33} However, the “growing-from” strategy has some limitations when
vinyl-group-functionalized POSS derivatives are used as the initiators. To be specific, from example in Scheme 3.5, we can see that the separated molecular parameters of two polymer chains are challenging to be precisely controlled. Another problem of the “growing-from” strategy is the compatibility of polymerization condition and vinyl groups of on the POSS cage, which restricts the diversity of component in the polymer blocks.

Scheme 3.4. “Growing-from” synthesis scheme of VPOSS-PLLA.\(^{32}\)

Scheme 3.5. “Growing-from” synthesis of PS-VPOSS-PS.\(^{33}\)
In the “grafting-to” strategy, polymer blocks bearing functional groups are prepared by living polymerizations, e.g., anionic polymerization and ATRP, and are then tethered onto POSS molecules by effective chemical reactions. Hydrosilylation is the first reaction employed in our group. This tethering reaction was first tested on tethering PS-b-PDMS onto an isobutyl-POSS with one vinyl group at a corner (see Scheme 3.7). Later it was expanded to conjugate OVPOSS and polystyrene (see Scheme 3.8). In one case, two strategies were used together to tether PS and PCL chains to a VPOSS cage (see Scheme 3.9).
Compared to the “growing-from” strategy, the “grafting-to” method has more freedom in polymer chain preparation and allows the easy control of the polymer molecular weights, which makes it a more effective and precise strategy to construct GMSAs. However, the hydrosilylation reaction is not a perfect choice for the “grafting-on” strategy, because of the strict reaction condition and tedious purification by fractional precipitation due to the side reaction of multiple additions. Thus, to expand the “grafting-to” strategy, other high efficient reactions should be employed.

3.3 “Click” chemistry

“Click” chemistry refers to chemical reactions which are selective and high efficient under mild condition with little side reactions. Thus, “click” chemistry has been accepted as a powerful tool to conjugate building blocks with complicated structures with various components. The most well-known “click” chemistry is the
copper-catalyzed azide-alkyne cycloaddition (CuAAC) reaction, which forms a triazole ring between azide and alkyne groups in the presence of copper catalyst (see Scheme 3.10). This reaction shows high tolerance to other functionalities and can be conducted under mild conditions with high efficiency (e.g., room temperature and normal humidity). As a result, since its debut in 2001, this “click” concept has been extensively applied to achieve the ligation between complex building blocks, even biomolecules such as proteins and DNA strands included. One example is shown in Scheme 3.11, illustrating the employment of CuAAC reaction as an effective tool to post-polymerization modify a polymer, which affords a complex molecular structure. The ligation between polymer chains and POSS derivatives has also been preliminary explored (see Scheme 3.12).

![CuAAC Reaction](image)

**Scheme 3.10.** Cu-catalyzed azide-alkyne cycloaddition.
Scheme 3.11. A complex structure synthesized via CuAAC reaction.\textsuperscript{38}
Another kind of well-investigated “click” chemistry is the thiol-ene reaction, which refers to the radical addition reaction between thiols and alkenes in the presence of either a thermo- or a photo- radical initiator (see Scheme 3.13).\textsuperscript{41} Thiol-ene reactions initiated by photo-initiators are high efficient and can be conducted in air at room temperature, which facilitates the synthetic procedure and extends its applications to more systems such as at surfaces and interfaces.\textsuperscript{42} The thiol-ene reaction has been successfully used to polymerize thiols and alkenes by step mechanism, synthesize dendrimers and modify polymers.\textsuperscript{43} Starting from the reported vinyl-substituted POSS derivatives, the thiol-ene reaction can be employed to modify MNPs after its conjugation with polymer chains (the post-polymerization functionalization), which will be covered in the later part.
3.4 Building blocks bearing “click” functional groups and sequential “click” strategy

The ligation between different blocks is realized by the recognition and combination of pair functionalities (e.g., alkyne-azide), like a lock and a key. Thus, to achieve our goals in molecular design, the installation of “click” functional groups onto different blocks is essential. Here, we focus on the functionalization of polymer chains since the introducing of functional groups which are “clickable” or precursors of “clickable” groups onto POSS cages with precisely-defined structure has already been discussed in Scheme 3.3 as an example.

A living polymerization (e.g., anionic polymerization, ATRP, RAFT, ROMP) which is an effective method to tune the length and component of the tethering polymer chain can afford at least one clickable site which can be further linked with nanoparticles by proper chemical transformations.\(^{38}\) For example, it is straightforward to introduce an azide group at the end of a polymer chain which is polymerized by ATRP or a thiol group by RAFT (see Scheme 3.14). Under proper conditions, the ligation between polymers and NMPs will be formed when “click” groups from polymer chains match groups from NMPs.
Summarizing all the factors involved, a sequential “click” strategy was proposed to modularly synthesize a library of GMSAs with various molecular topologies.\textsuperscript{34} There are two “click” reactions involved: (1) the conjugation between VPOSS-alkyne and polymer blocks bearing azide group by CuAAC reaction, and (2) the following thiol-ene reaction to transform all the remaining vinyl groups into diverse functionalities to modified the surface on the POSS cages (see Scheme 3.15).\textsuperscript{34} And a facile design named as molecular “click” adaptor enriched the diversity of GMSAs’ topologies, which allows the conjugation of multiple POSS heads and control over polymer architectures (see Scheme 3.16).\textsuperscript{44}
Scheme 3.15. The sequential “click” approach.\textsuperscript{34}

Benefits from the sequential “click” approach, a series of samples, hydroxyl-functionalized POSS tethered with polystyrene (DPOSS-PS) with different tethering length, have been synthesized, which provides the possibility of systematical
research. The result shows that they behave similarly to traditional diblock copolymers in micro-phase separation to form ordered structures but with feature size around 10 nm, which is still difficult to their traditional block copolymer analogues.\textsuperscript{20}

Other molecular topologies, like three POSS heads tethered by one polystyrene chain (3DPOSS-PS) and gemini surfactant (2DPOSS-2PS) have already been synthesized by sequential “click” method in combination with proper molecular “click” adaptors (see Scheme 3.16).\textsuperscript{44}

In this thesis, we further fulfill this library of GMSAs by adding two new sets of molecules: (1) two functionalized POSS cages tethered to one polystyrene (PS) chain end (2DPOSS-PS), and (2) one functionalized POSS cage tethered to the core of one star-PS with three identical arms (DPOSS-3PS).
CHAPTER IV
EXPERIMENTAL

4.1 Chemicals and solvents

Toluene (ACS grade, EMD), methanol (reagent grade, Fisher Scientific), dichloromethane (DCM, Fisher Scientific), ethyl acetate (Fisher Scientific), tetrahydrofuran (THF, Fisher Scientific), N,N-dimethylformamide (DMF, anhydrous 99.8%, Sigma-Aldrich), and hexanes (Certified ACS, Fisher Scientific) were used as received. 4-Pentynoic acid (98%, Acros Organics), N,N’-diisopropylcarbodiimide (DIPC, 99%, Acros Organics), copper(I) bromide (98%, Acros Organics), 4-dimethylaminopyridine (DMAP, ≥99%, Sigma-Aldrich), N,N,N’,N’’,N’’-pentamethyldiethylenetriamine (PMDETA, 99%, Sigma-Aldrich), trifluoromethanesulfonic acid (99%, Acros Organics), α-bromoisobutryl bromide (98%, Sigma-Aldrich), 2-hydroxy-4’-(2-hydroxyethoxy)-2-methylpropionophenone (Irgacure 2959, 98%, Sigma-Aldrich), sodium azide (NaN₃, 99%, Sigma-Aldrich), 1-thioglycerol (≥98%, Fluka), 1,3-dibromo-2-propanol (95%, Sigma-Aldrich), 2-(bromomethyl)-2-(hydroxymethyl)-1,3-propanediol (99%, Acros Organics), and OctaVinyl-POSS (OVPOSS, >97%, Hybrid Plastics) were used as received. Silica gel
(Sorbent Technologies Inc., 230-400 mesh) was activated by heating to 140 °C for 12 hours. Mono-hydroxyl heptavinyl substituted POSS (VPOSS-OH), VPOSS-alkyne, azide-end-capped PS-N₃ were synthesized as reported.³⁴

4.2 Molecular characterization

The ¹H and ¹³C NMR spectra were obtained in CDCl₃ (99.8% D, Sigma-Aldrich) or in DMSO-d₆ (99.9% D, Cambridge Isotope Laboratories, Inc) using a Varian NMRS 500 spectrometer. The ¹H NMR spectra were referred to the residual proton in CDCl₃ at δ 7.27 ppm (or in DMSO-d₆ at 2.50 ppm), and ¹³C NMR spectra were referred to ¹³CDCl₃ at δ 77.00 ppm (or ¹³C atoms in DMSO-d₆ at 39.52 ppm).

Infrared spectra of polymer products were recorded on an Excalibur Series FT-IR spectrometer (DIGILAB, Randolph, MA) by drop-casting sample films on a KBr plate from solutions in THF. The data were processed using the Win-IR software.

Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectra were recorded on a Bruker Ultraflex III TOF/TOF mass spectrometer (Bruker Daltonics, Billerica, MA), equipped with a Nd:YAG laser which emits at 355 nm. The matrix compound used in the measurements was \textit{trans}-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenylidene]-malononitrile (DCTB, >99%, Aldrich) and was dissolved in CHCl₃ at a concentration of 20.0 mg/mL. Sodium trifluoroacetate (NaTFA) was used as the cationizing agent and was prepared as a MeOH/CHCl₃ (v/v = 1/3) solution at a concentration of 10.0 mg/mL.
The matrix and cationizing agent solutions were mixed in the ratio of 10/1 (v/v). The sample was prepared by depositing 0.5 μL of matrix and salt mixture on the wells of a 384-well ground-steel plate, allowing the spots to dry, depositing 0.5 μL of each sample on a spot of dry matrix, and adding another 0.5 μL of matrix and salt mixture on top of the dry sample. Mass spectra were measured in the reflection mode. Data analyses were conducted with the Bruker’s flexAnalysis software.

Gel permeation chromatography (GPC) curves were obtained from a Waters 150-C Plus instrument with three HR-Styragel columns [100 Å, mixed bed (50/500/10^3/10^4 Å), mixed bed (10^3, 10^4, 10^6 Å)]. Three detectors were equipped, which were a differential viscometer (Viscotek 100), a differential refractometer (Waters 410), and a laser light scattering detector (Wyatt Technology, DAWN EOS, λ = 670 nm). THF was the eluent at a flow rate of 1.0 mL/min at 35 °C. The sample was desolved in THF with a concentration of ~5 - 10 mg/mL depending on the sample’s molecular weight and then filtered through a 0.45 μm Teflon filter to remove impurities before injection. Molecular weights from GPC curves (M_n,SEC and M_w,GPC) and polydispersity indexes (PDIs) were obtained from the light scattering detector and the refractometer, and the data was processed by the equipped software.
4.3 Synthetic procedures

4.3.1 Synthesis of 1yne-2Br

To a 50 mL round-bottomed flask equipped with magnetic stirring bar were added 1,3-dibromo-2-propanol (218 mg, 1.0 mmol), 4-pentynoic acid (98 mg, 1.0 mmol) and DMAP (25 mg, 0.20 mmol), followed by the addition of 10 mL dried CH₂Cl₂ to fully dissolve the solids. The flask was capped by a rubber septum. DIPC (232 μL, 1.5 mmol) was added dropwise into the flask via syringe. The mixture was stirred for 24 hours. After that, the white precipitate was filtered out, and the filtrate was evaporated by rotary evaporation. The residue was purified by flash column chromatography on silica gel with hexanes/CH₂Cl₂ (v/v = 1:1) as the eluent to afford the product as a clear liquid (238 mg, 0.80 mmol). Yield: 80%. ¹H NMR (CDCl₃, 500 MHz, ppm): δ 5.18 (m, 1H), 3.61 (d, 4H), 2.63 (m, 2H), 2.54 (m, 2H), 2.00 (m, 1H). ¹³C NMR (CDCl₃, 125 MHz, ppm): δ 170.51, 81.92, 71.27, 69.40, 33.23, 31.20, 14.38.

4.3.2 Synthesis of 3yne-1Br

To a 50 mL round-bottomed flask equipped with magnetic stirring bar were added 2-(bromomethyl)-2-(hydroxymethyl)-1,3-propanediol (100 mg, 0.50 mmol), 4-pentynoic acid (160 mg, 1.6 mmol) and DMAP (30 mg, 0.15 mmol), followed by the addition of 10 mL dried CH₂Cl₂ to fully dissolve the solids. The flask was capped by a rubber septum. DIPC (348 μL, 2.25 mmol) was added dropwise into the flask via
syringe. The mixture was stirred for 24 hours. After that, the white precipitate was filtered out, and the filtrate was evaporated by rotary evaporation. The residue was purified by flash column chromatography on silica gel with CH$_2$Cl$_2$ as the eluent to afford the product (180 mg, 0.41 mmol) as a clear viscous liquid. Yield: 82%. $^1$H NMR (CDCl$_3$, 500 MHz, ppm): δ 4.23 (s, 6H), 3.53 (s, 2H), 2.59 (m, 6H), 2.52 (m, 6H), 2.01 (m, 3H). $^{13}$C NMR (CDCl$_3$, 125 MHz, ppm): δ 170.96, 82.12, 69.41, 62.99, 42.27, 33.25, 32.35, 14.38.

4.3.3 General procedures for the CuAAC “click” reaction between PS-N$_3$ and molecular click adaptor

To a 100 mL Schlenk flask equipped with a magnetic stirring bar were added polystyrene-azide, molecular “adaptor”, CuBr (0.05 equivalent per azide group) and 20 mL toluene. The solution was degassed by three times freeze-pump-thaw cycles before PMDETA (1 equivalent per azide group) was added under the protection of nitrogen gas. The mixture was degassed one more time by freeze-pump-thaw cycle and then stirred at room temperature for 12 hours. After the reaction was complete, the solution was directly transformed onto a silica gel column, and toluene was used to remove the unreacted molecules. Then, CH$_2$Cl$_2$ was used to flash the product out of the column. After the removal of solvent, the crude product was dissolved in THF, and then the resulting solution was precipitated in cold methanol. The product was collected by vacuum filtration once as a white powder.
4.3.4 General procedures for the azide substitution reaction

To a 25 mL round-bottomed flask equipped with magnetic stirring bar were added polymer-bromo and NaN₃ (10 equivalent per bromo group) and 3 mL DMF. The mixture was heated up to 85 °C and stirred for 48 hours before cooling down to room temperature. Then the mixture was diluted by CH₂Cl₂, washed by water and brine, dried over Na₂SO₄ and evaporated by vacuum. The crude product was dissolved in THF and the resulting solution was precipitated into cold methanol for three times. The final product was collected by vacuum filtration as a white powder.

4.3.5 General procedures for the CuAAC “click” reaction between modified polymer-azide and VPOSS-alkyne

To a 100 mL Schlenk flask equipped with a magnetic stirring bar were added polystyrene-azide, VPOSS-alkyne (1.1 equivalent per azide group), CuBr (0.05 equivalent per azide group) and 20 mL toluene. The solution was degassed by three times freeze-pump-thaw cycles before PMDETA (1 equivalent per azide group) was added under the protection of nitrogen gas. The mixture was degassed one more time by freeze-pump-thaw cycle and then stirred at room temperature for 12 hours. After the reaction was complete, the solution was directly transformed onto a silica gel column, and CH₂Cl₂ was used to remove the unreacted VPOSS-alkyne. Then, mixture of CH₂Cl₂ and ethyl acetate (v/v = 1/1) was used to flash the product out of the column. After the removal of solvent, the crude product was dissolved in THF, and
then the resulting solution was precipitated in cold methanol. The product was collected by vacuum filtration once as a white powder.

4.3.6 General procedures for the thiol-ene reaction

To an open vial without stirring bar were added the product of VPOSS-PS conjugation, 1-thioglycerol (10.0 equivalent per VPOSS), the photo-initiator Irgacure 2959 (0.10 equivalent per VPOSS, or 0.014 equivalent per vinyl group), and minimum amount of THF to fully dissolve the solids. The reaction is complete after irradiation by 365 nm UV light for 30 min. The mixture was then purified by repeated precipitation from concentrated THF solutions of the crude products into cold MeOH/water mixture (v/v = 1/1 to 1/5) and collected by centrifugation.

4.3.7 Synthesis of PS-2Br

Following the general procedure in 4.3.3, 1yne-2Br (72 mg, 0.24 mmol), PS-N₃ (Mₙ = 4.0 kg/mol, PDI = 1.03, 800 mg), CuBr (1.4 mg, 0.01 mmol), and PMDETA (35 mg, 0.2 mmol, 1.0 equivalent) were used. PS-2Br was obtained as a white powder (688 mg, 0.16 mmol). Yield: 80%. ¹H NMR (CDCl₃, 500 MHz, ppm): δ 7.40-6.35 (m, 190H), 5.12 (m, 1H), 5.01 (m, 1H), 3.70 (m, 2H), 3.66 (m, 4H), 2.99 (m, 2H), 2.73 (m, 2H), 2.40-1.40 (m, 114H), 1.03 (m, 6H), 0.91 (m, 3H). ¹³C NMR (CDCl₃, 125 MHz, ppm): δ 171.15, 145.00, 127.67, 125.35, 70.78, 59.62, 45.54, 43.94, 43.59, 40.12, 30.95, 13.64. GPC: Mₙ,GPC = 4.0kg/mol, Mₘ,GPC = 4.0kg/mol, PDI = 1.02. FT-IR (KBr)
\(\nu\) (cm\(^{-1}\)): 3082.2, 3060.6, 3026.7, 2974.5, 2925.3, 2851.9, 1945.2, 1601.6, 1492.9, 1452.4, 1181.1, 1152.5, 1068.6, 1029.1, 908.3, 758.9, 699.2, 540.9.

4.3.8 PS-2N\(_3\)

Following the general procedure in 4.3.4, NaN\(_3\) (130 mg, 2.0 mmol) and PS-2Br (\(M_n = 4.0\) kg/mol, PDI = 1.02, 430 mg, 0.10 mmol) were used. PS-2N\(_3\) was obtained as a white powder (387 mg, 0.09 mmol). Yield: 90%. \(^1\)H NMR (CDCl\(_3\), 500 MHz, ppm): \(\delta\) 7.40-6.35 (m, 190H), 5.06 (m, 1H), 5.00 (m, 1H), 3.69 (m, 2H), 3.43 (m, 2H), 2.98 (m, 2H), 2.75 (m, 2H), 2.40-1.40 (m, 114H), 1.03 (m, 6H), 0.90 (m, 3H). \(^{13}\)C NMR (CDCl\(_3\), 125 MHz, ppm): \(\delta\) 177.16, 171.40, 145.41, 126.71, 125.36, 120.18, 70.65, 59.61, 50.55, 45.70, 43.76, 41.72.40.29, 33.19, 25.56, 20.51, 13.63. GPC: \(M_{n,GPC} = 4.1\) kg/mol, \(M_{w,GPC} = 4.3\) kg/mol, PDI = 1.05. FT-IR (KBr) \(\nu\) (cm\(^{-1}\)): 3082.7, 3060.0, 3025.9, 2925.2, 2850.9, 2101.9, 1601.10, 1493.3, 1181.2, 1068.3, 1028.8, 907.9, 758.3, 699.0, 541.0.

4.3.9 2VPOSS-PS

Following the general procedure in 4.3.5, VPOSS-alkyne (73.1 mg, 0.10 mmol), PS-2N\(_3\) (\(M_n = 4.1\) kg/mol, PDI = 1.05, 200 mg, 0.047 mmol), CuBr (0.5 mg, 0.005 mmol), and PMDETA (16.3 mg, 0.094 mmol) were used. 2VPOSS-PS was obtained as a white powder (218 mg, 0.038 mmol). Yield: 80%. \(^1\)H NMR (CDCl\(_3\), 500 MHz, ppm): \(\delta\) 7.53 (m, 2H), 7.40-6.35 (m, 190H), 6.20-5.85 (m, 42H), 5.50 (m, 1H), 5.08
(m, 1H), 4.43 (m, 2H), 4.36 (m, 2H), 4.27 (m, 4H), 3.69 (m, 2H), 3.04 (m, 6H), 2.74 (m, 6H), 2.40-1.40 (m, 114H), 1.24 (m, 4H), 1.03 (m, 6H), 0.90 (m, 3H). $^{13}$C NMR (CDCl$_3$, 125 MHz, ppm): $\delta$ 172.17, 144.93, 136.85, 128.24, 127.66, 127.37, 125.35, 60.51, 59.60, 40.03, 33.17, 29.41, 20.61, 13.63, 12.89. GPC: $M_{n,GPC}$ = 4.5 kg/mol, $M_{w,GPC}$ = 4.7 kg/mol, PDI = 1.03. FT-IR (KBr) $\nu$ (cm$^{-1}$): 3082.2, 3061.5, 3026.3, 2973.3, 2924.4, 2852.9, 1945.1, 1872.4, 1804.6, 1733.6, 1602.4, 1493.7, 1452.4, 1408.6, 1275.4, 1124.0, 1067.8, 1029.0, 1008.3, 971.2, 908.7, 757.1, 731.5, 698.3, 583.4, 541.0, 456.7.

4.3.10 2DPOSS-PS

Following the general procedure in 4.3.6, 1-thioglycerol (37 mg, 0.34 mmol), 2VPOSS-PS ($M_n = 5.8$ kg/mol, PDI = 1.03, 100 mg, 0.017 mmol) and Irgacure 2959 (0.9 mg, 0.0034 mmol) were used. 2DPOSS-PS was obtained as a white powder (100 mg, 0.014 mmol). Yield: 80%. $^1$H NMR (DMSO-$d_6$, 500 MHz, ppm): $\delta$ 7.74 (m, 2H), 7.40-6.35 (m, 190H), 5.37 (m, 1H), 5.04 (m, 1H), 4.54 (m, 2H), 4.36 (m, 2H), 4.15 (m, 28H), 4.00 (m, 4H), 3.76 (m, 2H), 3.45 (m, 42H), 2.74 (m, 6H), 2.37 (m, 56H), 2.40-1.40 (m, 114H), 0.88 (m, 28), 0.62 (m, 3H). $^{13}$C NMR (DMSO-$d_6$, 125 MHz, ppm): $\delta$ 145.12, 128.01, 71.41, 64.59, 34.93, 30.46, 26.02, 12.63. GPC: $M_{n,GPC} = 7.0$ kg/mol, $M_{w,GPC} = 7.6$ kg/mol, PDI = 1.09. FT-IR (KBr) $\nu$ (cm$^{-1}$): 3392.1, 3060.8, 3026.4, 2925.8, 1944.4, 1725.9, 1602.0, 1493.1, 1452.4, 1416.7, 1284.8, 1250.0, 1180.4, 1101.2, 1031.9, 920.6, 870.9, 758.0, 698.9, 541.0, 475.5.
4.3.11 3PS-Br

Following the general procedure in 4.3.3, 3yne-Br (48 mg, 0.11 mmol), PS-N\textsubscript{3} (\(M_n = 2.2\) kg/mol, PDI = 1.03, 800 mg, 0.36 mmol), CuBr (2.4 mg, 0.016 mmol), and PMDETA (57 mg, 0.33 mmol) were used. 3PS-Br was obtained as a white powder (620 mg, 0.29 mmol). Yield: 80%. \(^1\)H NMR (CDCl\(_3\), 500 MHz, ppm): \(\delta 7.40-6.35\) (m, 310H), 5.07 (m, 3H), 4.01 (m, 6H), 3.68 (m, 6H), 3.26 (m, 2H), 2.89 (m, 6H), 2.62 (m, 6H), 2.40-1.40 (m, 186H), 1.02 (m, 18H), 0.89 (m, 9H). \(^{13}\)C NMR (CDCl\(_3\), 125 MHz, ppm): \(\delta 177.42, 171.80, 145.34, 128.73, 127.64, 126.51, 125.63, 62.48, 59.87, 40.30, 33.26, 30.33, 26.82, 26.06, 24.92, 20.80, 13.89\). GPC: \(M_{n,GPC} = 6.6\) kg/mol, \(M_{w,GPC} = 6.8\) kg/mol, PDI = 1.03. FT-IR (KBr) \(\nu\) (cm\(^{-1}\)): 3060.5, 3026.5, 2925.7, 2851.6, 1945.4, 1727.0, 1601.6, 1492.9, 1452.4, 1181.1, 1068.3, 1029.2, 908.1, 758.7, 699.0, 540.3.

4.3.12 3PS-N\textsubscript{3}

Following the general procedure in 4.3.4, NaN\textsubscript{3} (26 mg, 0.4 mmol) and 3PS-Br (\(M_n = 6.6\)kg/mol, PDI = 1.03, 300 mg, 0.04 mmol) were used. 3PS-N\textsubscript{3} was obtained as a white powder (270 mg, 0.036 mmol). Yield: 90%. \(^1\)H NMR (CDCl\(_3\), 500 MHz, ppm): \(\delta 7.40-6.35\) (m, 310H), 5.05 (m, 3H), 3.93 (m, 6H), 3.66 (m, 6H), 3.22 (m, 2H), 2.87 (m, 6H), 2.61 (m, 6H), 2.40-1.40 (m, 186H), 1.02 (m, 18H), 0.87 (m, 9H). \(^{13}\)C NMR (CDCl\(_3\), 125 MHz, ppm): \(\delta 177.41, 171.88, 145.18, 128.73, 127.85, 125.68, 119.98, 63.36, 62.16, 59.87, 40.41, 26.80, 25.81, 24.92, 20.78, 13.88\). GPC: \(M_{n,GPC} = 7.2\) kg/mol, \(M_{w,GPC} = 8.2\) kg/mol, PDI = 1.14. FT-IR (KBr) \(\nu\) (cm\(^{-1}\)): 3082.6, 3060.4,
4.3.13 VPOSS-3PS

Following the general procedure in 4.3.5, VPOSS-alkyne (22 mg, 0.030 mmol), 3PS-N\(_3\) (\(M_n = 7.2\) kg/mol, PDI = 1.14, 200 mg, 0.028 mmol), CuBr (0.2 mg, 0.0014 mmol), and PMDETA (5 mg, 0.028 mmol) were used. 3PS-VPOSS was obtained as a white powder (177 mg, 0.022 mmol). Yield: 80%. \(^1\)H NMR (CDCl\(_3\), 500 MHz, ppm): \(\delta 7.40\) - 6.35 (m, 310H), 6.20 - 5.85 (m, 21H), 5.06 (m, 3H), 4.19 (m, 2H), 3.87 (m, 6H), 3.76 (m, 2H), 3.69 (m, 6H), 2.88 (m, 8H), 2.63 (m, 8H), 2.40 - 1.40 (m, 186H), 1.19 (m, 2H), 1.01 (m, 18H), 0.87 (m, 9H). \(^1\)C NMR (CDCl\(_3\), 125 MHz, ppm): \(\delta 177.42, 171.66, 145.64, 136.94, 127.92, 125.62, 67.95, 63.16, 59.87, 48.21, 40.30, 33.51, 30.32, 29.68, 25.60, 20.76, 13.89\). GPC: \(M_{n,GPC} = 7.0\) kg/mol, \(M_{w,GPC} = 7.4\) kg/mol, PDI = 1.07. FT-IR (KBr) \(v (\text{cm}^{-1})\): 3083.2, 3061.4, 3027.3, 2926.4, 2852.1, 1875.4, 1805.8, 1728.8, 1601.9, 1553.0, 1492.9, 1452.4, 1408.6, 1266.5, 1127.4, 1029.4, 970.9, 908.6, 759.2, 739.7, 699.5, 582.9, 541.3, 466.0.

4.3.14 DPOSS-3PS

Following the general procedure in 4.3.6, 1-thioglycerol (15 mg, 0.14 mmol), VPOSS-3PS (\(M_n = 7.4\) kg/mol, PDI = 1.07, 100 mg, 0.014 mmol) and Irgacure 2959 (0.35 mg, 0.0014 mmol) were used. DPOSS-3PS was obtained as a white powder (85
mg, 0.010 mmol). Yield: 74%. $^1$H NMR (CDCl$_3$, 500 MHz, ppm): $\delta$ 7.49 (m, 1H), 7.40-6.35 (m, 310H), 5.04 (m, 3H), 4.21 (m, 2H), 3.82 (m, 6H), 3.68 (m, 7H), 3.57 (m, 14H), 3.27 (m, 14H), 2.90 (m, 8H), 2.66 (m, 36H), 2.40-1.40 (m, 186H), 1.01 (m, 32H), 0.86 (m, 9H). $^{13}$C NMR (CDCl$_3$, 125 MHz, ppm): $\delta$ 177.09, 171.76, 145.34, 127.93, 125.62, 72.65, 71.02, 65.40, 64.88, 59.88, 40.31, 35.40, 27.97, 26.69, 25.78, 20.63, 13.88, 12.71. GPC: $M_n$,$_{GPC}$ = 8.6 kg/mol, $M_w$,$_{GPC}$ = 11.0 kg/mol, PDI = 1.3. FT-IR (KBr) $\nu$ (cm$^{-1}$): 3367.6, 3061.0, 3026.9, 2926.4, 2567.9, 1873.2, 1727.9, 1601.7, 1493.6, 1452.4, 1283.5, 1131.6, 1069.5, 1030.4, 909.4, 759.1, 699.3, 541.6, 472.4.
CHAPTER V
RESULTS AND DISCUSSIONS

In our current design of GMSAs based on fourteen hydroxyl groups modified POSS (DPOSS) and polystyrene, there are two aspects to enlarge the molecular asymmetry. The first approach focuses on the DPOSS blocks: if the DPOSS head is treated as a basic unit with certain interaction parameter, how can we enlarge this unit to realize one-dimensional, two-dimensional and even three dimensional shapes which possess the possibility to adopt different packing symmetries in self-assembly processes? The second approach aims to control the architecture over the polystyrene blocks to introduce more variations in this system.

Therefore, in this thesis, two molecules reflecting these two aspects are designed, and their synthetic methods and molecular characterizations are presented, which enriches our library of GMSAs.

5.1 The molecular design, synthesis and characterization of 2DPOSS-PS

In the molecular design of 2DPOSS-PS, two DPOSS cages are linked together at one polystyrene chain end, which enlarges the aspect ratio of the DPOSS block and
affords a one-dimensional rod-like shape at nanometer scale. At least two changes can be introduced by such design: the first one is obvious that the volume fraction of the DPOSS block is increased compared to DPOSS-PS, when the tethering polystyrene chains are the same, which will tune the boundary condition of micro-phase separation. The second change is caused by the asymmetry, the double of aspect ratio, introduced on the DPOSS block. By its alignment, hierarchical structures with different phases within the DPOSS domain are potentially to be formed under proper conditions. The detailed molecular design and synthetic scheme are presented in Scheme 5.1.

Scheme 5.1. Molecular design and synthesis scheme of 2DPOSS-PS.
The synthesis of this molecule followed a previous established scheme which combined sequential “click” method and molecular click adaptor together. This synthetic scheme has been used to synthesize three hydroxyl-functionalized-POSS cages tethered to one PS chain end (3DPOSS-PS) and giant gemini surfactant with two POSS head and two PS tails (2DPOSS-2PS) successfully in an efficient and modular manner. The molecular click adaptor designed for 2DPOSS-PS has the particular structure which one alkyne group and two bromo groups link at one carbon atom center (1yne-2Br). This molecular click adaptor is synthesized by Steglich esterification reaction promoted by DIPC at the presence of DMAP as catalyst (see Scheme 5.2). The molecular structure and purity of the product is confirmed by the combination of $^1$H NMR and $^{13}$C NMR spectra. All the peaks in the $^1$H MNR has be assigned to the protons in the product as labeled in Figure 5.1 and the integration value ratio agrees with the value ratio of protons in product. The number of peaks in the $^{13}$C NMR is identical with the number of different carbons in the final product.

Scheme 5.2. Synthesis scheme of molecular “click” adaptor 1yne-2Br.
Figure 5.1. $^1$H NMR and $^{13}$C NMR spectra of 1yne-2Br.

The alkyne group on the molecular “click” adaptor is consumed after the first CuAAC “click” reaction to react with one polystyrene chain bearing an azide group at the chain end, which results a polystyrene chain with two bromo groups (PS-2Br). The complete of this reaction is proved by the disappearance of a peak at 2094 cm$^{-1}$ in FT-IR spectra (see Figure 5.2), which corresponds to the signal from azide groups. A shift of GPC curve (see Figure 5.3) to lower retention volume, which corresponds to a
larger molecular weight after the click reaction, is another proof of the successful reaction. The excess amount of molecular click adaptor can be easily removed by flash silica gel chromatography and precipitation, since a higher molecular polarity caused by the triazole ring from the product and the smaller molecular weight of the adaptor molecule compared to the product. The chemical structure of the product is also characterized by $^1$H NMR and $^{13}$C NMR spectra: all the peaks in the spectrum are assigned to the product as shown in figure (see Figure 5.4 and 5.5).

Figure 5.2. FT-IR spectra of the products in the synthesis of 2DPOSS-PS.
The next step is to transform these two bromo groups into azide groups which are latently “clickable” to conjugate two POSS cages. Due to the low reactivity of these two bromo groups, this reaction has to be conducted at an elevated temperature and a longer reaction time is required. Impurities were possible to be produced under such reaction conditions. Therefore, to guarantee the smooth application of sequential “click” reactions, three times precipitation to remove all the byproducts are necessary. The complete substitution of azide groups is proved by the reappearance of the peak at 2094 cm$^{-1}$ with a double intensity compared to the original PS-N$_3$ in FT-IR.

Figure 5.3. GPC curves of the products in the synthesis of 2DPOSS-PS.
spectra. The GPC curve shows a symmetric mono-distribution with a little bit left shift compared to PS-2Br, which can be attributed to the slight molecular weight change. The product in this step is fully characterized by $^1$H NMR and $^{13}$C NMR spectra and all the peaks in $^1$H NMR have been properly assigned, as shown in Figure 5.5.
Figure 5.4. $^1$H NMR spectra of synthesis 2DPOSS-PS.
Figure 5.5. $^{13}$C NMR spectra of synthesis 2DPOSS-PS.
After this reaction, following the sequential “click” procedures, the final product 2DPOSS-PS is successfully obtained. The conjugation between two POSS cages and polystyrene chain is achieved by CuAAC “click” reaction and a little excess amount of VPOSS-alkyne was required to make sure the total conversion of azide groups in polystyrene chain. The appearance of a peak from silicon-oxygen stretching at 1100 cm$^{-1}$ and the disappearance of the peak comes from azide groups in the product are regarded as a real-time proof of the successful reaction. The GPC curve shows a further left shift to higher molecular weight side, which corresponds to a higher hydrodynamic volume of the product in THF after the “click” reaction. The most convincing evidence comes from the MALDI-TOF result (see Figure 5.6) which shows a narrow mono-distribution with m/z interval of one repeat unit (104.1 Da). Take the mono-isotopic mass peak of 31 mer as the example, the theoretical m/z value of 2VPOSS-PS-31mer-Na$^+$ can be calculated as 730.0×2 (2VPOSS-alkyne) + 222.1 (lyne-2Br) + 3383.0 (PS-31mer) +23.0 (Na$^+$) = 5088.6 Da, whereas the observed value is 5088.5 Da. The little difference between the calculated value and the observed one indicates a precisely defined molecular structure exactly as our expectation. Due to the fact that molecules with low molecular weights are easy to be ionized, the average molecular weight observed in MALDI-TOF result (the peak value) is lower than the results from other characterization methods.
The last step is to transform all the 14 vinyl groups on two POSS cages into functionalities by thiol-ene reaction. A broad peak corresponding to the hydrogen bonding in the final product in FT-IR spectra is an evidence of this reaction. The most powerful proof of the total conversion of these vinyl groups is the disappearance of the peaks corresponded to vinyl groups, which are at about 6 ppm in $^1$H NMR and at about 140 ppm in $^{13}$C NMR, respectively. The two products in the sequential “click” steps are fully characterized by NMR techniques and all the peaks in $^1$H NMR have been assigned to protons in molecules. The overlap of GPC curves confirms the successful synthesis by shifting to a higher molecular weight side.

In summary, 2DPOSS-PS, a new type of GMSAs, has been designed and synthesized by the combination of sequential “click” method and a special “click” adaptor molecule with one alkyne and two bromo groups. All the characterization results proved the successful synthesis of this GMSA.
5.2 The molecular design, synthesis and characterization of DPOSS-3PS

To further expand the complexity of GMSAs based on DPOSS and polystyrene, the architecture of the polystyrene blocks should be taken into consideration in the molecular design. As it has been predicted, the employment of a star block to replace a linear block in diblock copolymers should be of particular interests, since by adding one more arm the curvature at the interface changes dramatically.

The effects of polymer architecture in self-assembly have also been proved in another GMSA system based on hydrophilic [60]fullerenes tethered with polystyrene tails. In this work, it has been proved that, at the same molecular weight of tethering polystyrene, the GMSA with two tethers was prone to form vesicle morphology, while the GMSA with one tether formed sphere or cylinder structure in solution.  

Therefore, in our system based on POSS and PS, one more arm is added in the PS block, affording a new topology, which is to replace the linear PS by a star-PS with three identical arms in the giant surfactant. In the synthesis of DPOSS-3PS (see Scheme 5.3), an “arm-first” strategy is employed to synthesis a star architecture with three identical arms of precisely defined structure. The core used to linking three polystyrene chains together is a molecular “click” adaptor with three alkyne groups and one bromo group (3yne-Br), which is to be transformed into an azide group to conjugate with a POSS cage in the following steps. Similarly, this molecular “click” adaptor is synthesized by Steglich esterification reaction promoted by DIPC at the presence of DMAP as catalyst (see Scheme 5.4). After purification by silica gel
column, the structure of product is characterized by the combination of \(^1\)H NMR and \(^{13}\)C NMR spectra (see Figure 5.7). All the peaks in \(^1\)H NMR spectrum have been assigned to the protons in the molecule according to their chemical shift, splitting shape and integration value. The number of peaks in \(^{13}\)C NMR spectrum is the same with the number of different carbon atoms in this molecule.

Scheme 5.3. Molecular design and synthesis of DPOSS-3PS.
Scheme 5.4. Synthesis of 3yne-Br.

Figure 5.7. $^1$H NMR and $^{13}$C NMR spectra of 3yne-Br
The following synthesis work is almost the same with the previous one. In the first CuAAC “click” reaction, all the three alkyne groups are consumed to react with three polystyrene chain bearing azide groups to afford a star architecture with one bromo group in the core (3PS-Br). A little excess amount of PS-N₃ is required to assure the architectural precision of the star polymer, which is proved by FT-IR spectra (see Figure 5.8) and GPC curves (see Figure 5.9). The excess amount of PS-N₃ is easily separated from the product by silica gel column. Due to the quantitative conversion of CuAAC “click” reaction, the disappearance of the azide peak which was there in the crude product at 2094 cm⁻¹ after purification is a proof of completed reaction of all the alkyne groups in the click adaptor molecule. The shape of the GPC curve and the calculated molecular weight from GPC also prove this successful ligation.
Figure 5.8. FT-IR spectra of the products in synthesis of DPOSS-3PS.
The next step is to transform the remaining bromo group into azide group to introduce a “click” reaction site within the star architecture. Similarly, this reaction is conducted at an elevated temperature for a longer reaction time. After three times of precipitation, the complete substitution by azide groups is proved by the reappearance of the peak at 2094 cm⁻¹ with a lower intensity compared to the original PS-N₃ in FT-IR spectra.
Figure 5.10. $^1$H NMR spectra of synthesis DPOSS-3PS.
After this reaction, following the sequential “click” procedures, the final product DPOSS-3PS is successfully synthesized by conjugation 3PS-N$_3$ and VPOSS-alkyne.
followed by thiol-ene to modify the POSS cage. The successful conjugation between star polymer and POSS cage is confirmed by a series characterization, including NMR (see Figure 5.10 and 5.11), FT-IR, GPC and MALDI-TOF (see Figure 5.12). A peak at 1100 cm$^{-1}$ corresponded to the silicon-oxygen stretching in FT-IR, a signal at about 6 ppm in $^1$H NMR corresponded to vinyl groups in POSS cage and a left shift of the mono-distributed GPC curve are evidences of the successful conjugation. The most powerful evidence is the MALDI-TOF result in which the observed result agreed very well with the calculated value. Take the mono-isotopic mass peak of 50 mer as the example, the theoretical m/z value of VPOSS-3PS-50mer-Na$^+$ can be calculated as 730.0 (VPOSS-alkyne) + 401.2 (3yne-Br) + 5674.4 (PS-49mer) + 23.0 (Na$^+$) = 6724.4 Da. Da, whereas the observed value is 6726.0 Da.

![MALDI-TOF MS spectra of VPOSS-3PS.](image)

The last step in this set of synthesis is to convert all the seven vinyl groups into functional groups by thiol-ene reaction. The disappearance of the signals
corresponded to vinyl groups in $^1$H NMR spectrum (peaks at about 6 ppm) and $^{13}$C NMR spectrum (peaks at about 140 ppm) confirm the complete addition reaction. And all the peaks in $^1$H NMR have been assigned to the protons in the chemical structure. The GPC curve again shows a left shift to the high molecular weight.

In summary, the molecular design of a new type GMSA, DPOSS-3PS, which conjugates a functionalized POSS and polystyrene of star architecture with three identical arms, has been successfully synthesized and characterized. All the characterization results are consistent with the chemical structures of the designed molecules.
CHAPTER VI

CONCLUSIONS

Previous research of self-assembly processes based on small-molecule surfactant and block copolymers has suggested that the asymmetry between different blocks play an important role in the formation of complex hierarchical structures. Following previous design based on functionalized POSS and PS in our group, which are asymmetric blocks in many aspects, e.g., rigidity and interaction parameter, two new giant molecular shape amphiphiles have been designed by enlarging the asymmetry, which are desired to possess interesting micro-phase separation structures.

The first one tethers two functionalized polyhedral oligomeric silsesquioxane (POSS) cages at one polystyrene (PS) chain end (2DPOSS-PS), which enlarges the aspect ratio of the POSS block compared to previous studied PS-DPOSS system. And the second one is to conjugate one functionalized POSS cage and polystyrene of a star architecture with three identical arms, which introduces the architecture effects of polymer block in self-assembly.

The detailed synthesis work of these two molecules has been done based on a previous established route which combined sequential “click” and molecular click adaptor together. These two molecules have been synthesized with the overall yield...
about 50% with structural precision to molecular level. $^1$H NMR, $^{13}$C NMR, FT-IR, GPC and MALDI-TOF MS spectra have been used as the characterization methods to fully analyze the chemical structures of all products. The results of these characterizations have proved the successful synthesis. Two new giant molecular shape amphiphiles have been added to our library to systemically study the self-assembly processes in the future.
REFERENCES


14 Park, M.; Harrison, C.; Chaikin, P. M.; Register, R. A.; Adamson, D. H. *Science*
1997, 276 (5317), 1401-1404.


