SYNTHESIS OF POLYSTYRENE (PS)-POLYHEDRAL OLIGOMERIC SILSESQUIOXANE (POSS)-BASED GIANT MOLECULES WITH SEQUENCE-CONTROLLED POSS HEADS

A Thesis

Presented to

The Graduate Faculty of The University of Akron

In Partial Fulfillment

of the Requirements for the Degree

Master of Science

Siyu Zhang

May, 2016
SYNTHESIS OF POLYSTYRENE (PS)-POLYHEDRAL OLIGOMERIC SILSESQUIOXANE (POSS)-BASED GIANT MOLECULES WITH SEQUENCE-CONTROLLED POSS HEADS

Siyu Zhang

Thesis

Approved: _______________________________
Advisor
Dr. Stephen Z.D. Cheng

Accepted: _______________________________
Dean of the College
Dr. Eric Amis

Faculty Reader
Dr. Yu Zhu

Dean of the Graduate School
Dr. Chand Midha

Department Chair
Dr. Coleen Pugh

Date
ABSTRACT

The design and the synthesis of sequence-controlled linear giant molecules by controlling the sequences and functionalities precisely are great challenges in the field of macromolecular chemistry. In this article, we designed a method to synthesize sequence-controlled linear giant molecules by using two different kinds of polyhedral oligomeric silsesquioxanes (POSSes) based building blocks. Five POSSes heads were attached successively and alternately as a linear chain with a polystyrene tail as a purification tag via azide-alkyne cycloaddition (SPAAC) “click” reactions, oxime ligations, and thiol-ene “click” coupling (TECC). In order to precisely test controlled sequences and functionalities of the POSSes heads, we used many different characterizations, $^1$HNMR spectra, $^{13}$CNMR spectra, FT-IR spectra, UV-vis spectra, and GPC traces, to characterize every precursor of the giant molecules. $^1$HNMR and $^{13}$CNMR also showed the change of the vinyl groups on VPOSSes after TECC reactions. This study pioneers the synthesis for giant molecules with accurately controlled sequences, functionalities, compositions, and topologies. Furthermore, these features defined giant molecules can also be used to test several specific supermolecular self-assembling behaviors.
### TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIST OF FIGURES</td>
<td>v</td>
</tr>
<tr>
<td>LIST OF SCHEMES</td>
<td>vi</td>
</tr>
<tr>
<td><strong>CHAPTER</strong></td>
<td></td>
</tr>
<tr>
<td>I. INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>II. EXPERIMENTAL METHODS</td>
<td>10</td>
</tr>
<tr>
<td>Chemicals and solvents</td>
<td>10</td>
</tr>
<tr>
<td>Materials characterization</td>
<td>11</td>
</tr>
<tr>
<td>Synthetic procedures</td>
<td>11</td>
</tr>
<tr>
<td>Synthesis of CHO-BPOSS-DIBO</td>
<td>12</td>
</tr>
<tr>
<td>Synthesis of Azido Functionalized Polystyrene (PS-N₃)</td>
<td>15</td>
</tr>
<tr>
<td>Synthesis of CHO-VBVBV-PS and CHO-HBHBH-PS</td>
<td>17</td>
</tr>
<tr>
<td>III. RESULTS AND DISCUSSION</td>
<td>20</td>
</tr>
<tr>
<td>Design of Giant Molecules and Synthesis Route</td>
<td>20</td>
</tr>
<tr>
<td>Characterization of Giant Molecules</td>
<td>22</td>
</tr>
<tr>
<td>IV. CONCLUSIONS</td>
<td>29</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>30</td>
</tr>
</tbody>
</table>
## LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Synthesis scheme and catoon of the giant molecule</td>
<td>9</td>
</tr>
<tr>
<td>2.1</td>
<td>$^1$H NMR spectra of the CHO-BPOSS-DIBO building block</td>
<td>14</td>
</tr>
<tr>
<td>2.2</td>
<td>$^1$H NMR spectra of the CHO-VPOSS-DIBO building block</td>
<td>15</td>
</tr>
<tr>
<td>3.1</td>
<td>Chemical structure and catoon of the giant molecule</td>
<td>25</td>
</tr>
<tr>
<td>3.2</td>
<td>UV-Vis spectra of CHO-VPOSS-DIBO, PS-N$_3$, and PS-VPOSS-CHO</td>
<td>26</td>
</tr>
<tr>
<td>3.3</td>
<td>$^1$H NMR spectra of PS-VBVBV-CHO and its precursors</td>
<td>26</td>
</tr>
<tr>
<td>3.4</td>
<td>$^1$H NMR spectra of PS-VBVBV-N$_3$ and its precursors</td>
<td>27</td>
</tr>
<tr>
<td>3.5</td>
<td>GPC traces of PS-VBVBV and its precursors</td>
<td>27</td>
</tr>
<tr>
<td>3.6</td>
<td>FT-IR spectra of PS-VB-CHO and PS-V-N$_3$</td>
<td>28</td>
</tr>
<tr>
<td>3.7</td>
<td>$^1$H NMR spectra of PS-VBVBV-N$_3$ and PS-HBHBH-N$_3$</td>
<td>28</td>
</tr>
</tbody>
</table>
## LIST OF SCHEMES

<table>
<thead>
<tr>
<th>Scheme</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>Synthesis scheme of the CHO-BPOSS-DIBO</td>
<td>14</td>
</tr>
<tr>
<td>2.2</td>
<td>Synthesis scheme of the CHO-VPOSS-DIBO</td>
<td>15</td>
</tr>
<tr>
<td>2.3</td>
<td>Synthesis scheme of PS-VBV-BV-CHO and PS-HBBH-BH-CHO</td>
<td>19</td>
</tr>
</tbody>
</table>
CHAPTER I
INTRODUCTION

Natural biomaterials always have unique features. Compared with the synthetic ones, natural biomaterials are always higher biocompatible, bio-efficient and stable, due to their special and complicated structures. The structures contain not only primary ones, but also secondary, tertiary and quaternary ones. Although the synthetic biomaterials can be synthesis into a unique primary structure, which is familiar with the natural ones, the further hierarchical structures of the synthetic ones are almost totally different with the natural biomaterials. For example, the researches on artificial chromosomes in yeast show the primary structures, the short one and the long one, are familiar with the chromosomes, but the stabilities and bio-efficiency of the artificial ones are much lower than the natural chromosomes.¹ This example shows that slightly differences between primary structures can define apparently differences among secondary, tertiary and quaternary structures. These differences can lead to different features and properties of natural materials. Complicated and precisely defined structure with different compositions and functionalities is related to natural materials’ special and useful properties tightly. So, in order to replicate these unique properties, the structures of synthetic biomaterials should be controlled precisely and specifically
during replicating the natural materials’ structures or researching on the molecules’ behavior of natural biomaterials.

The tight relationship between natural biomaterials’ structures and properties can be demonstrated by structures and properties of deoxyribonucleic acid (DNA) and proteins, which play the most important role in natural biomaterials. DNA consists of nucleotides containing four different nucleobases, which are cytosine, guanine, adenine, and thymine. They connect with each other in linear molecules by covalent bonding. DNA has double helix structure as the secondary structure formed by hydrogen bonding. After further hierarchical self-assembly behavior, DNA forms millions types of chromosomes. As an important bioinformation carrier, chromosomes or DNA plays a significant role in artificial intelligence field, especially in computational molecular biology and bioinformatics. After constantly researching on DNA in these fields recent three decades, the tight relationship between its unique structures and special material properties has been illustrated clearly. Calladine et al. reported when any nucleobase pairs were stacked on top of each other into a long continuous assembly chain, a helix structure will be generated automatically. And if the base pairs stacked uniform, the helix structures were also uniform. So, the sequence of nucleobase pairs directly defines the three-dimensional structure and the properties of double helix of DNA. These work show a tight relationship between primary and the secondary structures of DNA chain by researching on the precisely defined sequence of DNAs’ primary structures. Different sequences in primary structures of DNA always cause helix structures with different pitches after
self-assembly behavior, and different nuleobase pairs cause different hydrogen bonding strength in the secondary structures. Then, the special secondary structures, double helix structures, with different pitches and sequences of nucleobase pairs form further different complicated hierarchical structures and determine a lot of different, significant, and unique biological properties of DNA. As one of the special properties of DNA brought by the secondary structures, two exact copy templates of the genetic information was provided by the DNA’s double helix structures, in order to protect the chemical identity of the genetic information in DNA.\(^5\) Apart from that, different sequences of nucleobase pairs in DNA’s primary structures make DNAs and chromosomes carry different kinds of genetic bioinformation, which can lead to different processing of transcription and translation.

Besides DNA, proteins can also be a good example to explain the tight relationship between various hierarchical structures and material properties. As carriers of storing and transporting different particles ranging from electrons to macromolecules, proteins affect every property of living organisms.\(^6\) From collagens to enzymes in living organism, primary structures of proteins are formed in many different sequences of amino acid according to the different DNA templates through transcription and translation. Compared with four kinds of nucleobases in DNA, the types of amino acids in protein are much more than that of nucleobases. So, at least 20 kinds of amino acids bring protein more kinds of primary structures than DNA has. Sequences, functionalities, compositions, and length of polypeptide chains are all the controlled parameters of the primary structures. Furthermore, in previous works, the
primary structures of proteins, specific sequences of amino acids in polypeptide chains, decide its three-dimensional structures.\(^7\) The secondary structures, three-dimensional structures, are formed by curling and folding of the polypeptide chains with different kinds of primary structures. Various polypeptide chains define various three-dimensional structures of the chains. The three-dimensional folds of proteins not only determine the protein functions but also affect on the abilities of binding other proteins or ligands, stabilities and mechanical behaviors.\(^8\) The polypeptide chains are processed further in order to form some specific and complicated spatial structure after the processors of curling and folding. The tertiary structures of proteins have more precise spatial structures compared with the secondary structures, and the processors of forming tertiary structures are also influenced by the primary structure of proteins. Then the quaternary structures are formed by several polypeptide chains with tertiary structures through self-assembling behavior, and the properties, as well as the functions of the proteins are determined by the unique quaternary structures. So, the sequences, functionalities, compositions, and length of specific primary structures of polypeptide chains can define the secondary structures, and then influence on the tertiary and quaternary structures, as well as the properties and functions of the proteins.

In recent years, inspired by the relationship between hierarchical structures and unique properties of natural biomaterials, such as DNA and proteins, much interest is focused on controlling the primary architecture of polymers or macromolecules to form materials with controlling self-assembly behavior and unique properties.
Matyjaszewski concluded recent works about controllable main types of primary polymer architecture and showed different aspects, sequence, composition, topology and functionality. Among these aspects, one popular and active research aspect is sequence controlled polymer synthesis inspired by sequence-controlled natural biomaterials. In this aspect, a lot of types of typical examples have been used to demonstrate the synthesis strategies and properties of those sequence controlled polymers. For example, Zhang et al. used controlled polymerization technique, living radical polymerization (LRP) to synthesis sequence-controlled multi-block glycopolymers successfully, which are used for preventing DC-SIGN and gp120 binding; Chan-Seng et al. researched on functional N-substituted maleimides (MIs) on polystyrene backbone through controlled radical polymerization (CRP); Gutekunst et al. described a method to synthesis sequence-cotrllled polymer with ring opening metathesis polymerization (ROMP) of unstrained macrocyclic structures; Yu et al. asserted a way to produce sequence-controlled polymers with three different building blocks, sequential Michael addition thio-ene and radical-mediated thiol-ene reactions. Among these synthesis strategies are published before, the most relatively evident one is connecting functionalized building blocks successively through the solid phase synthesis strategy. Although synthesis sequence-controlled polymer through this strategy have many advantages, such as simplifying and accelerating the multistep synthesis, avoiding the large losses of final products, and decreasing the aggregation of the by-products, the solid phase synthesis strategy has some backwards. For example, it is hard to synthesis precise sequence-controlled polymer
with limited size of monomers or building blocks,\textsuperscript{12} the definite size of sequence-controlled molecules lead difficulties to characterize its self-assemble behavior and hierarchical structures.\textsuperscript{20} So, in order to solve these problems, by using the solid phase synthesis as the synthesis strategy, “nanoatoms” formed giant molecules\textsuperscript{20} are synthesized to research on the sequence-controlled giant molecules.

According to studies on giant molecules, every material has two different preparation strategies to produce macromolecules or giant molecules.\textsuperscript{21} The first strategy, the traditional one, is to assemble supermolecules built up by molecules through secondary interactions.\textsuperscript{21} The second strategy is to assemble supermolecules made up of giant molecules synthesized precisely by “nanoatoms”.\textsuperscript{21} Fortunately, the second strategy overcome two mentioned backwards successfully. The “nanoatoms”, such as fullerenes, polyhedral oligomeric silsesquioxanes (POSSes), polyoxometalates, and folded globular proteins,\textsuperscript{21} are all larger than the atoms used in the normal solid phase synthesis strategy. The larger building blocks or monomers are more easily to precisely control during the synthesis, and characterize the giant molecules self-assemble behavior, as well as the hierarchical structures. The second strategy gives us brand new and unique ideas to design and synthesize sequence-controlled linear giant molecules by precisely controlling the nanoatoms’ sequences, numbers, and the types of chemical functional groups in order to form further hierarchical structure, even unique materials through giant molecules’ self-assembling behavior.

So, designing a synthesis route by using the second tragedy of “nanoatoms” to synthesize sequence-controlled linear giant molecules through solid phase synthesis is
the key point of our researches. Apart from that, in order to synthesize the giant molecule which can form hierarchical structures through self-assembly behavior, “nanoatoms” with three-dimensional functionalized cage structure and persistent size and volume, such as polyhedral Oligomeric Silsesquioxanes (POSSes)\(^{22-26}\), are designed to be used as building blocks. The POSSes with firm structure and a functionalized cage are the smallest silicon nanoparticle with a diameter around 1 nm.\(^{25,27-31}\) Functionalizing its cage structure will lead to diverse nano particles which can be used to control the functionalities of the giant molecules. Among these diverse nanoparticles, the most common nanoparticles are vinyl functionalized POSSes (VPOSSes) and isobutyl functionalized POSSes (BPOSSes). For the POSSes based giant molecule with a tail-like flexible polymer chain as a purification tag, atom-transfer radical-polymerization (ATRP) is an inefficient reaction and difficult to get single distribution product, so the “grafting-to”\(^{32-34}\) and “grafting-from”\(^{20,35}\) strategies are the best replaced ones to synthesize such giant molecule with polymer purification tag. Apart from the specific synthesis strategies of connecting polymer tails and POSSes building blocks, the giant molecules are designed with functionalized POSSes by controlling their shapes, umbers, and functionalities\(^{25,26,36-40}\). So, by using two mentioned synthesis strategies and controlling the features of POSSes building blocks, different sequences of linear giant molecules were designed and synthesized with polymer tails as a purification tag and POSSes heads.\(^{33,35,41-43}\)

In this article, according to the former design about the giant molecules, two kinds of nano particles, VPOSSes and BPOSSes, were decorated as CHO-VPOSS-DIBO\(^{44}\) and
CHO-BPOSS-DIBO, and then reacted with each other successively and alternately via strain-promoted azide-alkyne cycloaddition (SPAAC) reaction\cite{45-50}. The SPAAC reaction was a metal-free, high efficient and stable “click” approach compared with the normal “click” reactions.\cite{45-50} Before the SPAAC “click” reaction between the giant molecules precursors and the following reacted building blocks, linear “click” adaptors\cite{52} were utilized to change the aldehyde group at the end of the giant molecules precursors into an azido group, in order to get ready for the reaction with the following reacted building blocks. The sequence-controlled linear giant molecules contained three VPOSSes and two BPOSSes building blocks, and were decorated with polystyrene on one end as a purification tag. (Figure 1.1) To show the controlling of POSSes building blocks’ functionalities, thiol-ene “click” coupling (TECC)\cite{43} were used to convert vinyl functionalized POSSes (VPOSSes) into to hexyl-substituted POSSes (HPOSSes). As characterization, UV-vis spectrum, IR spectrum, NMR spectrum, and GPC trace were used after every step of the SPAAC “click” reaction in order to test the designs of the sequence-controlled linear chain-like structures, synthesis routes, as well as characterize the structures of the sequence-controlled linear giant molecules based on POSSes building blocks and polymer tails.
Figure 1.1 Synthesis scheme and cartoon of the giant molecule. The cyclic synthesis method with oxime ligations and SPAAC “click” reactions connected two kinds of POSSes building blocks successively and alternatively to synthesize the sequence-controlled linear giant molecules. It contained three VPOSSes and two BPOSSes building blocks, and were decorated with polystyrene on one end as a purification tag.
CHAPTER II

EXPERIMENTAL METHODS

Chemicals and Solvents

Methanol (Fisher Scientific, reagent grade); dichloromethane (Certified ACS); hexanes (Certified ACS); tetrahydrofuran (THF, Certified ACS, EM Science); N,N-dimethylformamide (DMF, Sigma-Aldrich, anhydrous 99.8%); chloroform (Certified ACS); ethyl acetate (Fisher Scientific); toluene (Certified ACS); silica gel (VWR, 230–400 mesh); 1-thioglycerol (Sigma, >99%); styrene (Acros Organic, 99.5%) was purified by silica gel column to remove the inhibitor; 2-hydroxy-1-[4-(2-hydroxyethoxy)phenyl]-2-methyl-1-propanone (Sigma, 98%); Octavinyl POSS (VPOSS, Hybrid Plastics, >97%); trisilanollsobutyl POSS (Aldrich, >97%); Ethyl 2-bromo-2-methylpropanoate (Aldrich, 97%); hydrogen chloride solution (Aldrich); 4-formylbenzoic acid (Aldrich, 97%); triethylamine (Et3N, Aldrich, >99%); N,N'-diisopropylcarbodiimide (DIPC, Acros Organics, 99%); succinic anhydride (Aldrich, >99%); 4-formylbenzoic acid (Aldrich, 97%); 4-(dimethylamino) pyridine (DMAP, Aldrich, 99%); copper(I) bromide (Aldrich, 98%); tetraethylammonium hydroxide solution (1.0 M in water); trimethoxy (vinyl) silane (Aldrich, 98%); 2-mercapoethanol (Aldrich, >99%); sodium azid
(Aldrich, >99%); N,N,N’,N”,N’’-pentamethyldiethylene-triamine (PMDETA, Aldrich, 99%); p-toluenesulfonic acid (TsOH, Aldrich, 98.5%).

Materials Characterization

$^1$HNMR and $^{13}$C NMR spectrum were measured by Varian Mercury 300 NMR and 500 NMR spectrometers. Using CDCl$_3$ (Aldrich, 100%) as the solvent, the residual solvent peak as the reference in $^1$HNMR spectra was at δ 7.27 ppm and $^{13}$C NMR was at δ 77.00 ppm. Infrared spectra was tested by Excalibur Series FT-IR spectrometer through spreading sample solution (10 mg/mL) with THF on KBr disk, and waiting the THF to evaporate. Then the Win-IR software analyzed the data and gave out the FT-IR spectra plots. UV-vis absorption spectrum was collected by Ocean Optics, Inc. Chem 2000 UV-Vis spectrometer, and the samples were dissolved in THF or CHCl$_3$ at certain concentration (10$^{-4}$ mol/L). Gel permeation chromatography (GPC) was tested on a Waters 150-C Plus instrument with three HR-Styrigel columns, mixed bed, and a triple detector system. Samples were dissolved in THF with certain concentration according to their molecular weight.

Synthetic Procedures

According to previous works, the synthesis of VPOSS-diOH$^{25}$ (Figure 2.1), CHO-VPOSS-OH$^{51}$ (Figure 2.1), CHO-VPOSS-DIBO$^{51}$ (Scheme 2.2, Figure 2.2), and the linear “click” adaptors$^{52}$ were reported.
Synthesis of CHO-BPOSS-DIBO

Monovinylisobutyl POSS. Trisilanollsobutyl POSS (20g, 1.0 eq), trimethoxy(vinyl)silane (4.115g, 1.1 eq), and tetraethylammonium hydroxide solution (1.0 M in water, 1mL, $2.5 \times 10^{-5}$ eq) were dissolved in THF. The solution was stirred at room temperature for 24 hours. Then the methanol was added in the solution to form precipitate, and the precipitate was filtered. The residue was washed with methanol, and dried in a vacuum environment. After the solvent removal, the product was gained as a white powder (23.7 g, 0.98 eq, 98%). (Scheme 2.1)

BPOSS-diOH. Monovinylisobutyl POSS (5.93g, 1.0 eq), 1-thioglycerol (3.803g, 5.0 eq), and 2-hydroxy-1-[4-(2-hydroxyethoxy)phenyl]-2-methyl-1-propanone (78.9mg, 0.05 eq) were dissolved in THF. The solution was stirred for 40min at room temperature by irradiation under 365 nm UV light. Then the solution was precipitated in methanol/water solvent (MeOH : H$_2$O=1:1), and the precipitate was filtered. The residue was washed with methanol/water solvent (MeOH : H$_2$O=1:1), and dried in a vacuum environment. After the solvent removal, the product was gained as a white powder (6.60 g, 0.90 eq, 90%).  

$^1$H NMR (CDCl$_3$, 500MHz, ppm, $\delta$): 3.77 (m, 2H, -CH$_2$OH), 3.57 (q, 1H, -CHOH-), 2.60-2.75 (m, 4H, -CH$_2$SCH$_2$-), 1.84-1.89 (m, 7H, -CH$_2$CH(CH$_3$)$_2$), 1.00 (m, 42H, -CH$_2$CH(CH$_3$)$_2$), 0.62 (d, 14H, -CH$_2$CH(CH$_3$)$_2$). $^{13}$C NMR (CDCl$_3$, 125MHz, ppm, $\delta$): 76.75-77.26, 69.49, 65.43, 35.58, 22.48-25.66, 13.60. (Scheme 2.1)

CHO-BPOSS-OH. BPOSS-diOH (3.07g, 1.0 eq), 4-formylbenzoic acid (485mg, 1.0 eq), and 4-(dimethylamino) pyridine (DMAP) (39.5mg, 0.1 eq) were dissolved in
anhydrous dichloromethane. N,N'-diisopropylcarbodiimide (DIPC) (815mg, 2.0 eq) was added into solution dropwise at 0 °C under stir. The solution was stirred at room temperature for 12 hours. Then the precipitate was filtered and washed with dichloromethane for three times, and the filtrate was purified by a silica gel column with dichloromethane/ethyl acetate solvent (V(CH₂Cl₂) : V(EA)=100:1). The product was afforded from eluent as a white powder (1.78g, 0.51 eq, 51%). \(^1\)H NMR (CDCl₃, 500MHz, ppm, δ): 10.10 (s, 1H, -CHO), 8.21 (d, 2H, aromatic), 7.95 (d, 2H, aromatic), 4.40-4.52 (m, 2H, -CH₂OOC-), 4.11 (m, 1H, -CHOH-), 2.68 (m, 4H, -CH₂SCH₂-), 1.83 (m, 7H, -CH₂CH(CH₃)₂), 1.00 (m, 42H, -CH₂CH(CH₃)₂), 0.62 (d, 14H, -CH₂CH(CH₃)₂). \(^1\)C NMR (CDCl₃, 125MHz, ppm, δ): 191.40, 165.46, 139.33, 134.75, 130.29, 129.48, 77.00, 67.76, 35.91, 22.40-26.70, 13.55. (Scheme 2.1)

CHO-BPOSS-DIBO. CHO-BPOSS-OH (707.8mg, 1.0 eq), DIBO-COOH (190.3mg, 1.1 eq), and 4-(dimethylamino) pyridine (DMAP) (7.3mg, 0.1 eq) were dissolved in anhydrous dichloromethane. N,N'-diisopropylcarbodiimide (DIPC) (149.9mg, 2.0 eq) was added into solution dropwise at 0 °C under stir. The solution was stirred at room temperature for 12 hours. Then the precipitate was filtered and washed with dichloromethane/hexane solvent for three times, and the filtrate was purified by a silica gel column with hexane/ethyl acetate solvent (V(Hexane): V(EA)= 15: 1). The product was afforded from eluent as a white powder (732.5mg, 0.89 eq, 89%). \(^1\)HNMR (CDCl₃, 500MHz, ppm, δ): (s, 1H, -CHO), 8.21 (m, 2H, aromatic), 7.95 (m, 2H, aromatic), 7.20-7.31 (m, 8H, aromatic of DIBO), 5.6 (s, 2H, -CH₃CH- of DIBO), 5.40 (s, 1H, -CH₂CH(OOC-CH₂-), 4.68 (s, 2H, -CH₃CH- of DIBO), 4.39-4.68 (m,
2H, -CH₂OOC-), 2.8(m, 4H, -CH₂SCH₂-), 1.83 (m, 7H, -CH₂CH(CH₃)₂), 1.00 (m, 
42H, -CH₂CH(CH₃)₂), 0.62 (d, 14H, -CH₂CH(CH₃)₂). ¹³C NMR (CDCl₃, 125MHz, 
ppm, δ): 191.46, 170.45, 171.43, 165.07, 150.85, 139.29, 134.44, 121.38-130.29, 
112.97, 109.87, 77.00, 70.68, 65.01, 46.34, 21.99, 13.50. (Scheme 2.1, Figure 2.1)
Bromo Functionalized Polystyrene (PS-Br). Copper(I) bromide (120mg, 1.0 eq),
2-hydroxy-1-[4-(2-hydroxyethoxy)phenyl]-2-methyl-1-propanone (163mg, 1.0 eq),
and styrene (17.5g, 200 eq) were dissolved into 20 mL of toluene in a flask with
magnetic stirrer. The solution was degassed for three cycles (one degas cycle included freezing, pumping, and thawing). \( \text{N,N,N',N'''-pentamethyldiethylene-triamine (PMDETA)} \) (145mg, 1.0 eq) was added into the solution with nitrogen protection. After two extra degas cycles, the flask was immersed in 110 °C oil bath for 180 min. Then the flask was quenched by immersion in iced water. The solution was purified by a short silica column with toluene (for styrene) and THF (for PS-Br). The eluent was dried for a while and precipitated in methanol. The precipitate was filtered, and the residue was washed with methanol for three times. Then the residue was dried in a vacuum environment. After the solvent removal, the product was gained as a white powder.

Azido Functionalized Polystyrene (PS-N\(_3\)). Bromo functionalized polystyrene (PS-Br) (5.932g, 1.0 eq), and sodium azide (386mg, 10 eq) were dissolved in DMF solvent. The solution was stirred at room temperature for 5 hours. The solution with excess dichloromethane was washed with water and brine. The organic phase was separated from the system, and dried by anhydrous \( \text{Na}_2\text{SO}_4 \) for two times. The solution was concentrated and precipitated in methanol. The precipitate was filtered, and the residue was washed with methanol for three times. Then the residue was dried in a vacuum environment. After the solvent removal, the product was gained as a white powder.
Synthesis of CHO-VBVBV-PS and CHO-HBHBH-PS

PS-VPOSS-CHO. CHO-VPOSS-DIBO (150mg, 1.0 eq) and azido functionalized polymerstyrene (PS-N₃) (1.68g, 1.3 eq) were dissolved in THF in a vial. The solution was stirred at room temperature until the peak at 306 nm wavelength in UV-Vis spectra completely disappeared, and then purified by a silica column with toluene (for azido functionalized polystyrene (PS-N₃)) and dichloromethane/ethyl acetate solvent (V(CH₂Cl₂): V(EA)=1:1) (for PS-VPOSS-CHO). The eluent was precipitated in methanol. The precipitate was filtered, and the residue was washed with methanol for three times. Then the residue was dried in a vacuum environment. After the solvent removal, the product was gained as a white powder. (Scheme 2.3)

PS-VPOSS- N₃ (Oxime Ligation). The linear “click” adaptor³³ (44.7mg, 1.5 eq), PS-VPOSS-CHO (1.0g, 1.0 eq), and triethylamine (Et₃N) (13.6mg, 1.5 eq) were dissolved in THF in a vial. After stir for 5 min, p-toluenesulfonic acid (TsOH) (27.9mg, 1.5 eq) was added in the solution, and stirred at room temperature until the peak at 10.1 ppm in the 1H NMR spectra disappeared completely. The solution was precipitated in methanol. The precipitate was filtered, and the residue was washed with methanol for three times. After the residue was dried in a vacuum environment, the processor, from the precipitation to the evaporation in a vacuum environment, was repeated for three times. After the solvent removal, the product was gained as a white powder. (Scheme 2.3)

PS-VB-CHO (SPAAC “Click” Reaction). PS-VPOSS-N₃ (610.0mg, 1.0 eq) and CHO-BPOSS-DIBO (77.4mg, 1.05 eq) were dissolved in THF. The solution was
stirred at room temperature until the peak at 2100 cm$^{-1}$ in FT-IR spectra disappeared completely. The solution was precipitated in methanol. The precipitate was filtered, and the residue was washed with methanol for three times. After the residue was dried in a vacuum environment, the processor, from the precipitation to the evaporation in a vacuum environment, was repeated for three times. After the solvent removal, the product was gained as a white powder. (Scheme 2.3)

PS-VBVBV-CHO. Azido functionalized polystyrene (PS-N$_3$), three CHO-VPOSS-DIBO and two CHO-BPOSS-DIBO were reacted into linear giant molecules successively and alternatively by the oxime ligations and the SPAAC “click” reactions mentioned before. The product was afforded as a white powder. (Scheme 2.3)

PS-HBHBH-CHO. PS-VBVBV-CHO (100mg, 1.0 eq), 2-Mercaptoethanol (18.9mg, 42 eq), and 2-hydroxy-1-[4-(2-hydroxyethoxy)phenyl]-2-methyl-1-propanone (0.04mg, 0.03 eq) were dissolved in THF. The solution was stirred for 10min at room temperature by irradiation under 365 nm UV light. Then the solution was precipitated into methanol/water solvent (MeOH : H$_2$O=1:5), and the precipitate was filtered. The residue was washed with methanol/water solvent (MeOH : H$_2$O=1:5) for three times, and dried in a vacuum environment. After the solvent removal, the product was gained as a white powder. (Scheme 2.3)
(ix) Linear “click adaptor”, TsOH, THF, R.T.; (x) DIBO-PPOSS-CHO, THF, R.T.;
(xi) 2-Mercaptoethanol, 2-Hydroxy-4’-(2-hydroxyethoxy)-2-methylpropiophenone, 365 nm UV, THF, R.T..

Scheme 2.3 Synthesis scheme of PS-VBVBV-N$_3$ and PS-HBHBH-N$_3$.  

19
CHAPTER III

RESULTS AND DISCUSSION

Design of Giant Molecules and Synthesis Route

Solid phase synthesis strategies with suitable “nanoatoms” were used to synthesize the main chain of the giant molecules with five POSSes. As well as the “grafting-to”\textsuperscript{32-34} and “grafting-from”\textsuperscript{20, 35} synthesis strategies were used to react the polystyrene tails as purification tag on to the giant molecules. By using these two strategies, we designed sequence-controlled linear giant molecule chemical structures with well designed building blocks, proper linkers between building blocks and polymer tails, and efficient synthesis routes. As with the designs, the products contained one polystyrene tail as a purification tag, as well as three VPOSSes and two BPOSSes building blocks, and the synthesis routes were cyclic methods with SPAAC “click” reactions\textsuperscript{45-50} and oxime ligations\textsuperscript{44, 52, 55}. (Figure 3.1) Selecting a suitable building block was one of the important parts of the structure design. CHO-VPOSS-DIBO\textsuperscript{45} as a building block had three different functional groups, an aldehyde group (for oxime ligations), a vinyl group (for thiol-ene “click” reactions), and a alkyne group (for SPAAC “click” reactions). These properties allowed us to control the sequences, numbers, and functionalities of the giant molecules easily by “click” approaches and oxime ligations. For the same reason, CHO-BPOSS-DIBO
was also selected as another building block with isobutyl groups. Apart from the aldehyde groups and alkyne groups, the isobutyl groups in BPOSSes building blocks increased the length of hydrophobic part in the sequence-controlled linear giant molecules, which could bring the giant molecules more changes of self-assembly behaviors and properties. According to the designs of the linkers in the sequence-controlled linear giant molecules, linear “click” adaptors\textsuperscript{44, 55} with amino groups and azido groups, as well as a proper molecule length were used to connect building blocks on to the precursors of the giant molecules through oxime ligations, which were the reactions between amino groups and aldehyde groups, and SPAAC “click” approaches, which were the reactions between alkyne groups and azido groups. Apart from that, because of the good perceptibility in the methanol, polystyrene with proper molecular weight was used as purification tag in the structure of the giant molecules. In the design of the synthesis route, cyclic synthesis methods with oxime ligations and SPAAC “click” reactions were used to synthesize the sequence-controlled linear giant molecules. In order to change the functional groups, aldehyde groups, into “clickable” functional groups, azido groups, oxime ligations were used to connect the linear “click” adaptors with the giant molecule precursors with aldehyde groups. As the previous work reported, “click” approach\textsuperscript{43, 45-50} was the best synthesis approach to react the selected building blocks with the precursors of the sequence-controlled linear giant molecules containing the linear “click” adaptors\textsuperscript{44, 55}, because the approach had high efficiency, and produced less byproducts than other kinds of reactions\textsuperscript{44, 53-55}. Among many kinds of “click” reactions, SPAAC “click”
reaction had many outstanding advantages, such as mild reaction conditions, metal-free reaction, and high efficiency. So, by using the SPAAC “click” reactions, the building blocks reacted with the precursors of the giant molecules containing linear “click” adaptors. After the design of the building blocks, linkers and polymer tails, as well as the synthesis route, the synthesis of sequence-controlled linear giant molecules was rational and predictable. In order to control the functionalities of the giant molecules, the thiol-ene “click” coupling (TECC) was used to change the VPOSSes in the PS-VBV-BV-N₃ giant molecules into hexyl-substituted POSSes (HPOSSes). Increasing content of HPOSSes in the sequence-controlled linear giant molecules increased the length of hydrophilic part, which could bring the giant molecules more changes of self-assembly behaviors and properties.

Characterization of Giant Molecules

During the synthesis of sequence-controlled linear giant molecules, the extent of the oxime ligation and SPAAC “click” reactions were the important factors to test by different kinds of characterizations. The measurement of these reactions extent affected the purification and yield of the giant molecules and its precursors. In order to test the extent of the reactions between azido functionalized polystyrene (PS-N₃) and VPOSS building block (CHO-VPOSS-DIBO), UV-Vis spectra was used to characterize the disappearance of the VPOSS building blocks’ alkyne groups in the solution. Due to the excess azido functionalized polystyrene, and the complete reaction of VPOSSes building blocks, the peak at 306 nm wavelength, the peak of
alkyne groups, in UV-Vis spectra disappeared completely after the reaction extent arrived at 100%. (Figure 3.2) Apart from this, the extent of the oxime ligation, between linear “click” adaptors and the giant molecule precursors with aldehyde groups, could be tested by $^1$H NMR spectra. According to the slightly excess linear “click” adaptors, and the complete reactions of the giant molecule precursors with aldehyde groups, the peak at δ 10.1 ppm, the peak of aldehyde groups, in $^1$H NMR spectra disappeared completely after the oxime ligations extent arrived at 100%. (Figure 3.3, 3.4) To test the extent of the SPAAC “click” reactions, between the building blocks with alkyne groups and the giant molecule precursors with azido groups, FT-IR spectra was used to test the disappearance of the giant molecule precursors’ azido groups in the solution. Because of the slightly excess building blocks, and the complete reaction of the giant molecule precursors with azido groups, the peak at 2100 cm$^{-1}$ wavenumber, the peak of azido groups, in FT-IR spectra disappeared completely after the SPAAC “click” reaction extent arrived at 100%. (Figure 3.6) Compared with the normal characterization of chemical structures, such as $^1$H NMR and $^{13}$C NMR, these special characterizations containing UV-Vis spectra (for alkyne groups), $^1$H NMR spectra (for aldehyde groups), and FT-IR spectra (for azido groups) were more convenient and rapid to define the extent of the reactions. Those efficient characterizations simplified the purifications of every precursor and enhanced the yield of every reaction. Apart from the convenient and rapid characterizations, $^1$H NMR spectra, $^{13}$C NMR spectra, and GPC trace were also used to characterize the structures, molecular weight, and polydispersity of every precursor
and the sequence-controlled linear giant molecules. Comparing the $^1$H NMR spectra of every precursor and the giant molecules with the azido groups or the aldehyde groups, the raising peaks at $\delta$ 6.06 ppm depicted increasing numbers of vinyl groups, as well as the VPOSSes, in the precursors; and raising peaks at $\delta$ 1.00 and 0.65 ppm depicted increasing numbers of isobutyl groups, as well as the BPOSSes, in the precursors. (Figure 3.3, 3.4) In the $^{13}$C NMR spectra of those molecules, the raising peaks at $\delta$ 137.12 ppm depicted increasing numbers of the VPOSSes in the precursors, and at $\delta$ 22.49-30.35 ppm depicted increasing numbers of the BPOSSes in the precursors. The $^1$H NMR spectra and $^{13}$C NMR spectra depicted every POSS building block reacted with precursors of the giant molecules successfully. In GPC traces of precursors and the giant molecules, as the increasing numbers of POSSes was reacted with the precursors, the single peak moved towards the higher retention volume. The traces showed every POSS building block reacted with the precursors of the giant molecules successfully, and every giant molecule precursor with different molecular weight had good polydispersity, which were less than 1.10. (Figure 3.5) After the thiol-ene “click” coupling (TECC), changing the VPOSSes in the PS-VBVBV-N$_3$ giant molecules into hexyl-substituted POSSes (HPOSSes), $^1$H NMR spectra, $^{13}$C NMR spectra, and GPC traces were used to characterize the chemical structures, molecular weight, and the polydispersity of the PS-HBHBH-N$_3$ giant molecules. Comparing the $^1$H NMR spectra of the PS-HBHBH-N$_3$ giant molecules and the PS-VBVBV-N$_3$ giant molecules, the peaks of vinyle groups at $\delta$ 6.06 ppm in $^1$H NMR spectra disappeared completely after the thiol-ene “click” coupling (TECC). (Figure
3.7) In the $^{13}$C NMR spectra of those giant molecules, the peaks of vinyle groups at $\delta$ 137.12 ppm disappeared completely after the TECC reactions. The $^1$H NMR and $^{13}$C NMR spectra depicted VPOSSes were changed into HPOSSes completely in the sequence-controlled linear giant molecules. In GPC traces of the PS-HBHBH-N$_3$ giant molecules, the single peak showed the giant molecules’ molecular weight and good polydispersity, which were less than 1.10. The normal characterizations, $^1$H NMR spectra, $^{13}$C NMR spectra and GPC traces, provided a lot of evidences to verify the designed chemical structures, molecular weight and polydispersity during the synthesis.

![Chemical structure and catoon of the giant molecule](image)

Figure 3.1 Chemical structure and catoon of the giant molecule. The sequence-controlled linear giant molecules contained one polystyrene tail as a purification tag, as well as three VPOSSes and two BPOSSes building blocks.
Figure 3.2 UV-Vis spectra of CHO-VPOSS-DIBO, PS-N$_3$, and PS-VPOSS-CHO. In the UV-Vis spectra, the peak of VPOSSes building blocks’ alkyne groups at 306 nm wavelength disappeared completely after the SPAAC “click” reaction extent arrived at 100%.

Figure 3.3 $^1$H NMR spectra of PS-VBVBV-CHO and its precursors. The raising peaks at δ 6.06 ppm depicted increasing numbers of vinyl groups, as well as the VPOSSes, in the precursors; and raising peaks at δ 1.00 and 0.65 ppm depicted increasing numbers of isobutyl groups, as well as the BPOSSes, in the precursors. The peak at δ 10.1 ppm related to the aldehyde groups.
Figure 3.4 $^1$H NMR spectra of PS-VBVBV-N$_3$ and its precursors. The raising peaks at $\delta$ 6.06 ppm depicted increasing numbers of vinyl groups, as well as the VPOSSes, in the precursors; and raising peaks at $\delta$ 1.00 and 0.65 ppm depicted increasing numbers of isobutyl groups, as well as the BPOSSes, in the precursors. Disappearance of the peak of aldehyde groups at $\delta$ 10.1 ppm depicted the oxime ligations extent arrived at 100%.

Figure 3.5 GPC traces of PS-VBVBV and its precursors. In GPC traces of precursors and the giant molecules, as the single peak moved towards the higher retention volume, the traces showed every POSS building block reacted with the precursors of the giant molecules successfully, and every giant molecule precursor with different molecular weight had good polydispersity, which were less than 1.10.
Figure 3.6 FT-IR spectra of PS-VB-CHO and PS-V-N₃. In the FT-IR spectra, the peak of giant molecule precursors’ azido groups at 2100 cm⁻¹ wavenumber disappeared completely after the SPAAC “click” reaction extent arrived at 100%.

Figure 3.7 ¹H NMR spectra of PS-VBVBV-N₃ and PS-HBHBH-N₃. The peaks of PS-VBVBV-N₃ giant molecules’ vinyle groups at δ 6.06 ppm in ¹H NMR spectra disappeared completely after the thiol-ene “click” coupling
CHAPTER IV

CONCLUSIONS

In summary, we designed and synthesized a sequence-controlled linear giant molecule with five different successive and alternate POSSes heads and one polystyrene tail as purification tag. We synthesized these linear giant molecules by controlling two different building blocks’ functionalities, sequences, and numbers using thiol-ene “click” coupling (TECC), SPAAC “click” reactions, and oxime ligations. Researching on the geometry and topology of the giant molecules will be next steps in our researches in the future. Apart from that, study on the giant molecules’ self-assembling behavior and physical properties will also be necessary in order to study the relationship between materials physical properties, as well as hierachical structure and the controlled primary structures’ features of the giant molecules, such as sequences, numbers, functionalities, geometry, and topology. Synthesizing by using the building blocks and high efficiency methods to form sequence-controlled linear POSSes based giant molecules will give future research more inspiration and references.
REFERENCES


