MACROMOLECULAR METAMORPHOSIS

By

HAO SUN

A DISSERTATION PRESENTED TO THE GRADUATE SCHOOL
OF THE UNIVERSITY OF FLORIDA IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA

2017
To my parent for their love and support on me
ACKNOWLEDGMENTS

Firstly, I would like to dedicate this dissertation to my parent, who will be very happy and proud to see such a good achievement accomplished by their son. It was a challenging journey for an international student to come to the United States of America, which have a completely different culture in comparison with my home country. This journey would not have been possible without the considerable support and understanding from my parent. In addition, I want to express my sincere gratitude and appreciation to my supervisor Prof. Brent Sumerlin. He provided me the opportunity to experience the most exciting chemistry in polymer science. He is very nice, patient, supportive, and always encouraged me in not only research but also real life. I am very lucky to have learned a great deal of knowledge from him directly.

I also dedicate this dissertation to my friends in Sumerlin research groups, especially Christopher Kabb and Abhijeet Bapat. I want to thank you both for your kind help and for giving me always a positive energy to be able to release my potential.

I am also grateful to my committee members, Prof. Carlos Rinaldi, Prof. Stephen Miller, Prof. Aaron Aponick, and Prof. Khalil Abboud for their valuable time and the great advice to improve my PhD research.

Moreover, I am deeply grateful to the George & Josephine Butler Polymer Research Laboratory in Department of Chemistry at the University of Florida for always providing me a very friendly and comfortable environment during my research journey.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACKNOWLEDGMENTS</td>
<td>4</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>8</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td>9</td>
</tr>
<tr>
<td>LIST OF SCHEMES</td>
<td>13</td>
</tr>
<tr>
<td>LIST OF ABBREVIATIONS</td>
<td>14</td>
</tr>
<tr>
<td>ABSTRACT</td>
<td>18</td>
</tr>
<tr>
<td><strong>CHAPTER</strong></td>
<td></td>
</tr>
<tr>
<td>1 INTRODUCTION</td>
<td>20</td>
</tr>
<tr>
<td>1.1 Synthetic Strategies of Architecture-Transformable Polymers</td>
<td>22</td>
</tr>
<tr>
<td>1.1.1 Dynamic-Covalent Chemistry Approach</td>
<td>25</td>
</tr>
<tr>
<td>1.1.1.1 Thermal-induced topological transformation</td>
<td>25</td>
</tr>
<tr>
<td>1.1.1.2 Light-induced topological transformation</td>
<td>27</td>
</tr>
<tr>
<td>1.1.1.3 Redox-induced topological transformation</td>
<td>30</td>
</tr>
<tr>
<td>1.1.1.4 Mechanically induced topological transformation</td>
<td>33</td>
</tr>
<tr>
<td>1.1.2 Supramolecular Chemistry Approach</td>
<td>33</td>
</tr>
<tr>
<td>1.2 Properties and Applications of Architecture-Transformable Polymers</td>
<td>37</td>
</tr>
<tr>
<td>1.3 Conclusion and Future Prospects</td>
<td>41</td>
</tr>
<tr>
<td>2 RESEARCH OBJECTIVE</td>
<td>44</td>
</tr>
<tr>
<td>3 RADICAL DEPARTURE: THERMALLY-TRIGGERED DEGRADATION OF AZO-CONTAINING POLY(β-THIOESTER)S</td>
<td>47</td>
</tr>
<tr>
<td>3.1 Overview</td>
<td>47</td>
</tr>
<tr>
<td>3.2 Results and Discussion</td>
<td>49</td>
</tr>
<tr>
<td>3.2.1 Synthesis of ACVA Monomer</td>
<td>49</td>
</tr>
<tr>
<td>3.2.2 Step-Growth Copolymerization of ACVA Monomer and HDT</td>
<td>51</td>
</tr>
<tr>
<td>3.2.3 Thermal Degradation Behavior of Polyazo</td>
<td>53</td>
</tr>
<tr>
<td>3.2.4 Preparation and Thermal Degradation of PEG-b-polyazo-b-PEG</td>
<td>57</td>
</tr>
<tr>
<td>3.3 Conclusion</td>
<td>62</td>
</tr>
<tr>
<td>3.4 Experimental Section</td>
<td>63</td>
</tr>
<tr>
<td>3.4.1 Materials and Methods</td>
<td>63</td>
</tr>
<tr>
<td>3.4.2 Synthesis and Experimental Procedures</td>
<td>65</td>
</tr>
<tr>
<td>3.4.2.1 Synthesis of diacrylate monomer (ACVADA)</td>
<td>65</td>
</tr>
</tbody>
</table>
4 THERMALLY-LABILE SEGMENTED HYPERBRANCHED COPOLYMERS: USING REVERSIBLE-COVALENT CHEMISTRY TO INVESTIGATE THE MECHANISM OF SELF-CONDENSING VINYL COPOLYMERIZATION ........................................ 68

4.1 Overview .............................................................................................................................. 68
4.2 Results and Discussion .......................................................................................................... 71
  4.2.1 Preparation of Thermally Reversible Diels-Alder Inimer ............................................. 71
  4.2.2 Synthesis and Characterization of Segmented Hyperbranched PMMA .......... 73
  4.2.3 Polymerization Kinetics of ATRP-SCVP of MMA/Inimer ...................................... 78
  4.2.4 Extension of PEGMA from Hyperbranched PMMA .................................................. 82
  4.2.5 Thermal Degradation of Segmented Hyperbranched PMMA ............................ 85
  4.2.6 Thermal Reformation of Segmented Hyperbranched PMMA ............................ 88
  4.2.7 Mechanism of Degradation and Reconstruction of SHB ....................................... 92
4.3 Conclusions .......................................................................................................................... 96
4.4 Experimental Section .......................................................................................................... 96
  4.4.1 Materials and Measurements ...................................................................................... 96
  4.4.2 Synthesis and Experimental Procedures ................................................................... 98
    4.4.2.1 Synthesis of 2-bromo-2-methyl-propionic acid 2-(1-hydroxymethyl-3, 5-dioxo-10-oxa-4-azatricyclo [5.2.1.02, 6] dec-8-en-4-yl)-ethyl ester .................................................. 98
    4.4.2.2 Synthesis of Diels-Alder inimer 2-bromo-2-methyl-propionic acid 2-(1-methacryloxyethyl-3, 5-dioxo-10-oxa-4-azatricyclo [5.2.1.02, 6] dec-8-en-4-yl)-ethyl ester .................................................. 98
    4.4.2.3 Synthesis of thermally-reversible hyperbranched PMMA ................................... 99
    4.4.2.4 Extension of PEGMA from hyperbranched PMMA ........................................... 100
    4.4.2.5 Thermal degradation of Diels-Alder hyperbranched PMMA ......................... 100
    4.4.2.6 Thermal reconstruction of hyperbranched PMMA ............................................ 100
    4.4.2.7 Radical thiol-ene click reaction between hyperbranched PMMA and 1-thioglycerol .................................................................................................................. 101

5 MACROMOLECULAR METAMORPHOSIS VIA STIMULUS-INDUCED TRANSFORMATIONS OF POLYMER ARCHITECTURE ........................................................................... 102

5.1 Overview .............................................................................................................................. 102
5.2 Results and Discussion ......................................................................................................... 103
  5.2.1. Computational Analysis and Model Reactions ...................................................... 107
5.2.2. Synthesis of P(EG_{44}-b-MA_{19}) Block Copolymer and Study on Its Thermal Reversibility ........................................................................................................... 112
5.2.3. Synthesis of Anthracene-Containing Templates .................................................. 119
5.2.4. Macromolecular Metamorphosis ......................................................................... 124
5.3 Conclusions ........................................................................................................... 139
5.4 Experimental Section ............................................................................................ 140
5.4.1 Materials and Measurements ............................................................................. 140
5.4.2 Synthesis and Experimental Procedures .............................................................. 143
  5.4.2.1 Macromolecular metamorphosis: general procedure ....................................... 143
  5.4.2.2 Model reaction 1: metamorphosis from Fur-MalOH to Anth-MalOH ............... 143
  5.4.2.3 Model reaction 2: metamorphosis from Fur-MalOH to MalOH-Anth-PS .......... 143
  5.4.2.4 Synthesis of PEG_{44}-COOH ....................................................................... 143
  5.4.2.5 Synthesis of PEG_{44} macroinitiator .............................................................. 144
  5.4.2.6 Photoinduced ATRP of methyl acrylate with PEG_{44} macroinitiator ............... 144
  5.4.2.7 Thermal degradation of P(EG-b-MA) block copolymer ................................. 145
  5.4.2.8 Thermal reformation of P(EG-b-MA) block copolymer .................................... 145
  5.4.2.9 Synthesis of anthracene-terminated polystyrene (Anth-PS) ......................... 145
  5.4.2.10 Nitrooxide-mediated copolymerization of styrene and p-chloromethylstyrene (CMS) ........................................................................................................ 145
  5.4.2.11 Functionalization of P(S-co-CMS) with 9-anthracenemethanol ... 146
  5.4.2.12 Synthesis of tris(anthracen-9-ylmethyl)benzene-1,3,5-tricarboxylate (Anth₃) .................................................................................................................. 146
  5.4.2.13 Amphiphilic to hydrophobic metamorphosis: from P(EG-b-MA) to P(S-b-MA) .................................................................................................................. 147
  5.4.2.14 Block to comb metamorphosis: from P(EG-b-MA) to P(S-co-CMS-co-(AnthMS-g-MA)) ................................................................. 147
  5.4.2.15 Block to star metamorphosis: from P(EG-b-MA) to PMA₃ star ................. 147
  5.4.2.16 Synthesis of linear PMA analogue via photoinduced ATRP ....................... 147
  5.4.2.17 Segmented hyperbranched (SHB) to block: metamorphosis from SHB PMMA to P(S-b-MMA) ................................................................. 148
  5.4.2.18 Segmented hyperbranched (SHB) to comb: metamorphosis from SHB PMMA to P(S-b-MMA) ................................................................. 148

LIST OF REFERENCES ........................................................................................................ 149

BIOGRAPHICAL SKETCH .................................................................................................. 162
**LIST OF TABLES**

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-1</td>
<td>Molecular weight information for polyazo and PEG-b-polyazo-b-PEG</td>
<td>53</td>
</tr>
<tr>
<td>4-1</td>
<td>Hyperbranched polymers prepared from via SCVP of inimer and MMA</td>
<td>75</td>
</tr>
<tr>
<td>4-2</td>
<td>Preparation of hyperbranched Inimer/MMA (SHB P3) copolymers and their thermal degradation products (120 °C for 1 h)</td>
<td>77</td>
</tr>
<tr>
<td>4-3</td>
<td>Molecular weight characteristics of segmented hyperbranched polymers and their degradation products (120 °C for 1 h)</td>
<td>86</td>
</tr>
<tr>
<td>4-4</td>
<td>Results from repair of the hyperbranched polymers after heating solutions of the degraded linear polymers at 50 °C for 48 h</td>
<td>87</td>
</tr>
<tr>
<td>5-1</td>
<td>Summary of energy calculations for the reaction between Furan and MalOH. Geometry optimizations were performed at the B3LYP / 6-31 g(d) level and ωB97X-D / 6-31 g(d) was used for energy computations.</td>
<td>109</td>
</tr>
<tr>
<td>5-2</td>
<td>Summary of energy calculations for the reaction between AnthOH and MalOH. Geometry optimizations were performed at the B3LYP / 6-31 g(d) level and ωB97X-D / 6-31 g(d) was used for energy computations.</td>
<td>109</td>
</tr>
<tr>
<td>5-3</td>
<td>Metamorphosis from amphiphilic to hydrophobic: polymer information</td>
<td>125</td>
</tr>
<tr>
<td>5-4</td>
<td>Metamorphosis from block to comb: polymer information</td>
<td>128</td>
</tr>
<tr>
<td>5-5</td>
<td>Metamorphosis from block to star: polymer information</td>
<td>131</td>
</tr>
<tr>
<td>5-6</td>
<td>Metamorphosis from Hyperbranched to Block: Polymer Information</td>
<td>137</td>
</tr>
<tr>
<td>5-7</td>
<td>Metamorphosis from hyperbranched to comb: polymer information</td>
<td>138</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>1-1</td>
<td>Formation and dissociation of core-crosslinked star with thermoreversible furan/maleimide Diels-Alder linkages.</td>
<td>26</td>
</tr>
<tr>
<td>1-2</td>
<td>Schematic illustration of reversible transformations from linear PDMAEMA to chain loops via photochemistry of pendent coumarin functionality.</td>
<td>29</td>
</tr>
<tr>
<td>1-3</td>
<td>Reversible architecture transformation of linear telechelic polymers by irradiation at 365 nm and heating.</td>
<td>30</td>
</tr>
<tr>
<td>1-4</td>
<td>Redox-triggered reversible topological transformation from linear PS to monocyclic (one disulfide linkage) and multiblock PS.</td>
<td>32</td>
</tr>
<tr>
<td>1-5</td>
<td>Architecture transition from star to linear polymer through mechanochemically induced Diels-Alder bond scission.</td>
<td>33</td>
</tr>
<tr>
<td>1-6</td>
<td>Architecture transformation of a 3-arm star polymer to its linear analogue by N-acetylation.</td>
<td>35</td>
</tr>
<tr>
<td>1-7</td>
<td>Synthetic pathways of linear block copolymer and transformation to cyclic block architecture via N-acetylation.</td>
<td>37</td>
</tr>
<tr>
<td>1-8</td>
<td>Light-triggered architecture transformation of hyperbranched graft copolymer.</td>
<td>39</td>
</tr>
<tr>
<td>1-9</td>
<td>Schematic illustrations for the possible gelation of mixed micellar solution.</td>
<td>41</td>
</tr>
<tr>
<td>3-1</td>
<td>$^1$H NMR spectroscopy of polyazo, HDT, and ACVADA.</td>
<td>50</td>
</tr>
<tr>
<td>3-2</td>
<td>$^{13}$C NMR spectrum of ACVADA monomer (CDCl$_3$, 125 MHz).</td>
<td>51</td>
</tr>
<tr>
<td>3-3</td>
<td>GPC characterization of thermal degradation of polyazo.</td>
<td>54</td>
</tr>
<tr>
<td>3-4</td>
<td>$^{15}$N NMR spectroscopy of polyazo degradation.</td>
<td>55</td>
</tr>
<tr>
<td>3-5</td>
<td>GPC characterization of thermal degradation of polyazo in presence of hydroquinone at different temperatures.</td>
<td>56</td>
</tr>
<tr>
<td>3-6</td>
<td>$^1$H NMR spectrum of PEG$_{44}$ acrylate (CDCl$_3$, 500 MHz).</td>
<td>56</td>
</tr>
<tr>
<td>3-7</td>
<td>$^1$H NMR spectrum of triblock copolymer PEG$<em>{44}$-$b$-polyazo$</em>{6}$-$b$-PEG$_{44}$ (CDCl$_3$, 500 MHz).</td>
<td>57</td>
</tr>
<tr>
<td>3-8</td>
<td>Characterization of PEG-$b$-polyazo-$b$-PEG triblock copolymers by GPC, DLS, DOSY and TEM.</td>
<td>58</td>
</tr>
<tr>
<td>3-9</td>
<td>$^1$H NMR spectrum and GPC trace of PEG$<em>{110}$-$b$-polyazo$</em>{5}$-$b$-PEG$_{110}$.</td>
<td>59</td>
</tr>
</tbody>
</table>
DLS and GPC data for degradation of triblock copolymer micelles

GPC traces of samples taken during the thermal degradation of PEG_{44}-b-polyazo_{6}-b-PEG_{44} at 95 °C in water

GPC kinetics of degradation of triblock copolymers in presence and absence of hydroquinone at 80 °C

GPC kinetics of degradation of triblock copolymers in presence and absence of hydroquinone at 95 °C

Synthesis, \(^1\)H NMR spectrum, and \(^{13}\)C NMR spectrum of the Diels-Alder inimer.

\(^1\)H NMR, and \(^{13}\)C NMR of Diels-Alder inimer precursor.

Synthesis of segmented hyperbranched PMMA

Degree of branching as a function of feed ratio at full monomer conversion (blue circles represent DB values obtained from \(^1\)H NMR; dot line represent theoretical values of DB).

GPC kinetic traces of SHBs before and after thermal cleavage of Diels-Alder bonds

\(^1\)H NMR spectrum of hyperbranched PMMA-b-Poly(PEGMA) ("hyper-star").

GPC traces before and after chain extension of SHB P2 with PEGMA

Characterization of "hyper-star" self-assembly in water

GPC traces of "hyper-star" and thermally-cleaved "hyper-star" polymers

\(^1\)H NMR spectroscopy and GPC characterization of thermal degradation of SHB

Kinetics of degradation of SHB PMMA

Reconstruction kinetics of thermally-degraded SHB PMMA by \(^1\)H NMR spectroscopy

DB of original segmented hyperbranched polymers and reconstructed hyperbranched polymers

Reconstruction kinetics of thermally-degraded SHB PMMA by GPC

GPC traces of SHB P4, cleaved L P4 in the presence of anthracene methanol and polymers thermally treated at 50 °C for 48 hours.
<table>
<thead>
<tr>
<th>Page</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-20</td>
<td>$^1$H NMR spectrum of P(S-co-CMS-co-AnthMS) (500 MHz, CDCl$_3$)</td>
</tr>
<tr>
<td>5-21</td>
<td>Gel permeation chromatography of functionalization of P(S-co-CMS) with 9-anthracenemethanol</td>
</tr>
<tr>
<td>5-22</td>
<td>$^1$H NMR spectrum of Anth$_3$ (500 MHz, CDCl$_3$)</td>
</tr>
<tr>
<td>5-23</td>
<td>$^{13}$C NMR spectrum of Anth$_3$ (500 MHz, CDCl$_3$)</td>
</tr>
<tr>
<td>5-24</td>
<td>Gel permeation chromatography of metamorphosis from amphiphilic to hydrophobic</td>
</tr>
<tr>
<td>5-25</td>
<td>Fluorescence spectroscopy of metamorphosis from amphiphilic to hydrophobic</td>
</tr>
<tr>
<td>5-26</td>
<td>$^1$H NMR spectroscopy of metamorphosis from amphiphilic to hydrophobic</td>
</tr>
<tr>
<td>5-27</td>
<td>DOSY NMR of metamorphosis from amphiphilic to hydrophobic</td>
</tr>
<tr>
<td>5-28</td>
<td>Topological transformation from linear amphiphilic block copolymer to comb copolymer</td>
</tr>
<tr>
<td>5-29</td>
<td>Removal of Fur-PEG via precipitation</td>
</tr>
<tr>
<td>5-30</td>
<td>Gel permeation chromatography of metamorphosis from block to star</td>
</tr>
<tr>
<td>5-31</td>
<td>Fluorescence spectroscopy of metamorphosis from block to star</td>
</tr>
<tr>
<td>5-32</td>
<td>$^1$H NMR spectroscopy of metamorphosis from block to star</td>
</tr>
<tr>
<td>5-33</td>
<td>DOSY NMR of metamorphosis from block to star</td>
</tr>
<tr>
<td>5-34</td>
<td>Comparison of gel permeation chromatograms of star and linear poly(methyl acrylate)</td>
</tr>
<tr>
<td>5-35</td>
<td>Comparison of DOSY spectra of star and linear poly(methyl acrylate)</td>
</tr>
<tr>
<td>5-36</td>
<td>Characterizations of metamorphosis from hyperbranched to block</td>
</tr>
<tr>
<td>5-37</td>
<td>DOSY NMR of metamorphosis from hyperbranched to block</td>
</tr>
<tr>
<td>5-38</td>
<td>Characterizations of metamorphosis from hyperbranched to comb</td>
</tr>
<tr>
<td>5-39</td>
<td>DOSY NMR of metamorphosis from hyperbranched to comb</td>
</tr>
<tr>
<td>Scheme</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>1-1</td>
<td>Two approaches to architecture transformation of polymers.</td>
</tr>
<tr>
<td>3-1</td>
<td>Synthetic route to ACVADA monomer and preparation of homopolymer polyazo and triblock copolymer PEG-(b)-polyazo-(b)-PEG by one-pot step-growth polymerization.</td>
</tr>
<tr>
<td>4-1</td>
<td>Chain extension of segmented hyperbranched PMMA (SHB P2) with PEGMA.</td>
</tr>
<tr>
<td>4-2</td>
<td>Reformation of hyperbranched PMMA via Diels-Alder cycloaddition of linear PMMA.</td>
</tr>
<tr>
<td>4-3</td>
<td>In-situ retro-Diels-Alder reaction of furan-maleimide based DA bond and formation of anthracene-maleimide linkage at 120 °C.</td>
</tr>
<tr>
<td>4-4</td>
<td>Thiol-ene reaction between 1-tholglycerol and segmented hyperbranched PMMA.</td>
</tr>
<tr>
<td>5-1</td>
<td>Synthetic route to P(EG(<em>{44})-(b)-MA(</em>{19})).</td>
</tr>
<tr>
<td>5-2</td>
<td>Synthesis of anthracene-containing templates including Anth-PS(<em>{75}) (A), P(S(</em>{58})(-co)-CMS(<em>{14})-(co)-AnthMS(</em>{13})) (B), and Anth(_3) (C).</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>ACVA</td>
<td>4,4’-Azobis(4-cyanovaleric acid)</td>
</tr>
<tr>
<td>ACVADA</td>
<td>4,4’-azobis(4-cyanovaleric acid) derived diacrylate monomer</td>
</tr>
<tr>
<td>AMBIB</td>
<td>9-Anthracenemethyl-2-bromoisoobutyrate</td>
</tr>
<tr>
<td>Anth</td>
<td>anthracene</td>
</tr>
<tr>
<td>Anth₃</td>
<td>tris-anthracene core reagent</td>
</tr>
<tr>
<td>AnthOH</td>
<td>9-anthracenemethanol</td>
</tr>
<tr>
<td>ATRP</td>
<td>Atom-transfer radical polymerization</td>
</tr>
<tr>
<td>CDTPA</td>
<td>4-Cyano-4{(dodecylsulfanylthiocarbonyl)-sulfanyl}-pentanoic acid</td>
</tr>
<tr>
<td>CMA</td>
<td>coumarin methacrylate</td>
</tr>
<tr>
<td>CMS</td>
<td>p-chloromethylstyrene</td>
</tr>
<tr>
<td>CRP</td>
<td>Controlled radical polymerization</td>
</tr>
<tr>
<td>CTA</td>
<td>Chain transfer agent</td>
</tr>
<tr>
<td>CTM</td>
<td>Chain transfer monomer</td>
</tr>
<tr>
<td>DA</td>
<td>Diels-Alder</td>
</tr>
<tr>
<td>DB</td>
<td>Degrees of branching</td>
</tr>
<tr>
<td>DC</td>
<td>Dynamic-covalent</td>
</tr>
<tr>
<td>DCM</td>
<td>Dichloromethane</td>
</tr>
<tr>
<td>DFT</td>
<td>density functional theory</td>
</tr>
<tr>
<td>DLS</td>
<td>Dynamic light scattering</td>
</tr>
<tr>
<td>DMAc</td>
<td>N,N-Dimethylacetamide</td>
</tr>
<tr>
<td>DMAEMA</td>
<td>2-(Dimethylamino)ethyl methacrylate</td>
</tr>
<tr>
<td>DMAP</td>
<td>4-dimethylaminopyridine</td>
</tr>
<tr>
<td>DMPP</td>
<td>dimethylphenylphosphine</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>DMF</td>
<td>Dimethylformamide</td>
</tr>
<tr>
<td>DOSY</td>
<td>diffusion-ordered NMR spectroscopy</td>
</tr>
<tr>
<td>DSC</td>
<td>Differential scanning calorimetry</td>
</tr>
<tr>
<td>EDC•HCl</td>
<td>1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride</td>
</tr>
<tr>
<td>ESI</td>
<td>electrospray ionization</td>
</tr>
<tr>
<td>Fur</td>
<td>furan</td>
</tr>
<tr>
<td>GPC</td>
<td>Gel permeation chromatography</td>
</tr>
<tr>
<td>HDT</td>
<td>1,6-hexanediol</td>
</tr>
<tr>
<td>HL</td>
<td>hexanolactone</td>
</tr>
<tr>
<td>HQ</td>
<td>hydroquinone</td>
</tr>
<tr>
<td>HRMS</td>
<td>High-Resolution Mass Spectrometry</td>
</tr>
<tr>
<td>LCST</td>
<td>Lower critical solution temperature</td>
</tr>
<tr>
<td>MA</td>
<td>Methyl acrylate</td>
</tr>
<tr>
<td>MacroCTA</td>
<td>Macro chain transfer agent</td>
</tr>
<tr>
<td>Mal</td>
<td>Maleimide</td>
</tr>
<tr>
<td>MalOH</td>
<td>N-(2-hydroxyethyl) maleimide</td>
</tr>
<tr>
<td>MALS</td>
<td>Multi-angle light scattering</td>
</tr>
<tr>
<td>MMA</td>
<td>Methyl methacrylate</td>
</tr>
<tr>
<td>$M_n$</td>
<td>Number average molecular weight</td>
</tr>
<tr>
<td>MALS-SEC</td>
<td>multi-angle laser light scattering size exclusion chromatography</td>
</tr>
<tr>
<td>NB</td>
<td>o-nitrobenzyl</td>
</tr>
<tr>
<td>NMP</td>
<td>Nitroxide-mediated polymerization</td>
</tr>
<tr>
<td>NMR</td>
<td>Nuclear magnetic resonance spectroscopy</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>PBA</td>
<td>poly(butyl acrylate)</td>
</tr>
<tr>
<td>PCL</td>
<td>Poly($\varepsilon$-caprolactone)</td>
</tr>
<tr>
<td>PDLA</td>
<td>poly ($D$-lactide)</td>
</tr>
<tr>
<td>PEG</td>
<td>Polyethylene glycol</td>
</tr>
<tr>
<td>P(EG-\text{-b-MA})</td>
<td>poly(ethylene glycol-block-methyl acrylate)</td>
</tr>
<tr>
<td>PEGMA</td>
<td>Poly(ethylene glycol methacrylate)</td>
</tr>
<tr>
<td>PEO</td>
<td>polyethylene oxide</td>
</tr>
<tr>
<td>PLLA</td>
<td>poly($L$-lactide)</td>
</tr>
<tr>
<td>PMA</td>
<td>poly(methyl acrylate)</td>
</tr>
<tr>
<td>PMDETA</td>
<td>$N,N,N',N',N''$-pentamethyldiethylenetriamine</td>
</tr>
<tr>
<td>PMMA</td>
<td>Poly(methyl methacrylate)</td>
</tr>
<tr>
<td>PNIPAM</td>
<td>Poly($N$-isopropylacrylamide)</td>
</tr>
<tr>
<td>PRC</td>
<td>pre-reactive complex</td>
</tr>
<tr>
<td>PRE</td>
<td>persistent radical effect</td>
</tr>
<tr>
<td>PS</td>
<td>Polystyrene</td>
</tr>
<tr>
<td>P(S-co-CMS)</td>
<td>poly(styrene-co-chloromethylstyrene)</td>
</tr>
<tr>
<td>PTHF</td>
<td>poly(tetrahydrofuran)</td>
</tr>
<tr>
<td>PVL</td>
<td>poly($\delta$-valerolactone)</td>
</tr>
<tr>
<td>RAFT</td>
<td>Reversible addition-fragmentation chain transfer</td>
</tr>
<tr>
<td>rDA</td>
<td>retro-Diels-Alder</td>
</tr>
<tr>
<td>ROP</td>
<td>Ring-opening polymerization</td>
</tr>
<tr>
<td>SCVP</td>
<td>Self-condensing vinyl polymerization</td>
</tr>
<tr>
<td>SCVCP</td>
<td>Self-condensing vinyl copolymerization</td>
</tr>
</tbody>
</table>
SEC: Size exclusion chromatography
SHPs: Segmented hyperbranched polymers
SHB PMMA: segmented hyperbranched poly(methyl methacrylate)
TAD: triazolinedione
TEA: Triethylamine
TEM: Transmission electron microscopy
TEMPO: 2,2,6,6-tetramethyl-1-piperidinyloxy
$T_g$: Glass transition temperature
$T_m$: Melting temperature
TREN: tris-(2-aminoethyl)amine
$\delta$-VL: $\delta$-valerolactone
The rapid growth of synthetic polymer chemistry has led to the development of stimuli-responsive polymers that can adapt to surrounding environment by responding to external signals, causing change in their physical and chemical properties. Such “smart” polymers have received considerable attention in the fields of nanomedicine, tissue engineering, optical systems and biosensors, as well as coating, environmental remediation and self-healing materials. Overwhelmingly reports of “smart” polymers relied on the alteration of fundamental parameters of polymers such as composition and size. Nevertheless, architecture, a very basic but important feature of macromolecules, in most cases has been considered constant. Indeed, polymer architecture plays a pivotal role in determining many properties. When designing polymers for specific applications, not only the size of a macromolecule but also its architecture must be considered.

Taking advantage of dynamic-covalent chemistry, my research aims to expand the scope of stimuli-responsive polymer by exploring novel synthetic approaches to architecture-transformable polymers. My first work lies in the design of a triblock copolymer (PEG-b-polyazo-b-PEG) which contains thermally-labile azo linkages in the central block. Upon heating, degradation of central block occurred, resulting in formation
of small molecular fragments and residual PEG. This conversion dramatically changed the solubility of polymers in water. In my second work, we demonstrated the first example of thermally-reversible segmented hyperbranched polymers (SHPs). These “smart” SHPs were synthesized via self-condensing vinyl copolymerization of methyl methacrylate and an inimer that contained a furan-maleimide linkage between polymerizable group and initiating moiety. At elevated temperature, molecular weights gradually decreased and linear poly(methyl methacrylate) (PMMA) segments were formed due to the cleavage of Diels-Alder based branch points. More importantly, hyperbranched PMMA can be reconstructed from the cleaved linear components via forward Diels-Alder reaction at 50 °C.

Moreover, reversible-covalent chemistry was utilized to prompt the disconnection of chemical bonds and formation of new linkages in situ, giving rise to polymers that can undergo dramatic topological transformations via thermodynamic control. This technique allowed a linear amphiphilic block copolymer or hyperbranched polymer to readily transition into various architecture including comb, star, and hydrophobic linear block. Macromolecular architectural transformations present an entirely novel approach to ‘smart’ polymers.
CHAPTER 1
INTRODUCTION

Since Hermann Staudinger proposed his macromolecular theory in 1920—polymer are made of long chains of small molecules covalently together,\textsuperscript{1} the field of polymer has flourished in nearly every application in our daily life, from industrial use (e.g., cloth, painting, packaging, and building materials) to higher-value-added applications including biomaterials and microelectronics.\textsuperscript{2-5} Indeed, synthetic polymers are now ubiquitous, reaching a remarkable production of 300 million tons in 2015.\textsuperscript{6} Very recently, driven by the advent of synthetic polymer chemistry, polymers have further expanded into novel applications such as molecular-level information storage (supported by DNA-mimic sequence-controlled polymers\textsuperscript{7-9}) and high-efficiency separations of small molecules using single-layer 2D polymeric network.\textsuperscript{10-12}

Thanks to the rapid development of controlled radical polymerization (CRP) techniques (e.g., atom-transfer radical polymerization (ATRP)\textsuperscript{13-15} nitroxide-mediated polymerization,\textsuperscript{16} and reversible addition-fragmentation transfer (RAFT) polymerization\textsuperscript{17-19}) that enables high degree of control, a remarkable array of innovative and more sophisticated polymers with predictable molecular weights, low-polydispersity, and high chain fidelity have been prepared.\textsuperscript{20-23} During CRP process, the excellent tolerance of functional groups facilitates the decoration of polymers with various functionalities that eventually beget the properties and applications of polymeric materials.\textsuperscript{24, 25} Moreover, CRP has been proven to be an elegant approach to synthesizing polymers with various topologies such as hyperbranched,\textsuperscript{26-29} star,\textsuperscript{30-34} and cyclic\textsuperscript{35-39} that were inaccessible by previous polymerization methods. As structure determines properties, design and synthesis of polymers is always guided by
fundamental understanding of structure-property relationships. Indeed, the architecture of a polymer dictates many properties, including the possibility of entanglement with neighboring chains,\textsuperscript{40, 41} the performance on modifying solution viscosity,\textsuperscript{42, 43} and the possibility for self-assembly into complicated nano-objects with various morphology.\textsuperscript{44-47}

The continuous growth of synthetic tools in polymer chemistry also led to the development of a new class of polymers that can adapt to surrounding environment by responding to external signals, inducing change in their physical and/or chemical properties.\textsuperscript{48, 49} These tailor-made polymers, referred to as stimuli-responsive or "smart" polymers, can respond to a broad range of stimuli (for example, pH, temperature, the presence of reducing agents, mechanical force, electric/magnetic field and so on).\textsuperscript{4, 50} Such "smart" polymers are playing an increasingly important role in the fields of triggered drug delivery and release, tissue engineering, optical systems and biosensors, as well as coating, environmental remediation and self-healing materials.\textsuperscript{48} Of the multitude of stimuli-responsive polymers, by far the most examples focus on change in polymer size by deviations of chain conformation (that is, changes in polymer-polymer and/or polymer-solvent interactions).\textsuperscript{51-54} For examples, thermoresponsive poly(N-isopropylacrylamide) (PNIPAM) exhibited a lower critical solution temperature (LCST).\textsuperscript{55-57} Below LCST, PNIPAM is fully extended as random coils (solvated). As the temperature increases above LCST, phase separation occurs as PNIPAM undergoes a transition to a compact globular conformation via entropic control. In addition, the conformation of pH-responsive polymer chain can be tuned by changing environmental pH that governs deprotonation or protonation of ionizable moieties.\textsuperscript{51, 58} Common
examples include polymers prepared by (co)polymerization of acrylic acid or N,N-dimethylaminoethyl methacrylate (DMAEMA).\textsuperscript{59-61}

Despite the overwhelming number of examples in those traditional “smart” polymers (vide supra), recent advances in stimuli-responsive polymers have brought attention to a type of polymers that can undergo topological transformations in response to an external stimulus.\textsuperscript{62-64} The nascent concept of macromolecular topological transformation is garnering more and more interest in the field of stimuli-responsive polymers because these architecture transformations are typically accompanied by dramatic change in physical properties of polymers.\textsuperscript{65, 66} In this review, we mainly discuss the state-of-art synthetic strategy of “smart” polymers that are capable of morphing their entire architecture when a stimulus is applied. A wide range of stimulus that induces topological transformations is analyzed. Various transformable architectures are covered. We then look at how these topological transformations lead to properties change and potential applications. Finally, challenges such as purification of desired architecture after topological transformation and how to conduct topological transformation in bulk polymeric materials will be evaluated.

1.1 Synthetic Strategies of Architecture-Transformable Polymers

Among other parameters such as composition and molecular weight, polymer architectures or topology has been recognized as a critical factor that significantly influences properties of polymers in solution and in bulk.\textsuperscript{26, 67-71} Since the advent of synthetic polymer chemistry, a variety of structurally sophisticated polymers has been achieved, including cyclic, star, branched, comb, network, and so on. In comparison with linear analogues, polymers of sophisticated topologies including star, cyclic, dendritic, and hyperbranched typically possess lower solution viscosity, smaller
hydrodynamic volume, and lower possibility of chain entanglement in the bulk. Therefore, the development of architecture-transformable polymers is particularly interesting from the viewpoint of expanding the scope of stimuli-responsive polymers, understanding the relation of structure and properties, and so on. To endow a polymer with the ability to transform its architecture, the segments of a polymer should be connected by reversible linkages that would allow disassembly and reassembly of polymer segments with high efficiency. Generally, two approaches to architecture-transformable polymers are considered (Scheme 1-1). The first involved incorporation of dynamic-covalent (DC) bonds that link the segments of polymers. These labile covalent bonds should respond to a particular stimulus, causing the cleavage of linkages and leading to transformations in polymer architecture. The second method focuses on utilization of supramolecular interactions such as hydrogen bonding or rotaxane which mechanically “locks” a wheel polymer and an axle polymer. Upon the removal of supramolecular interaction, the wheel polymer would be allowed to move along the axle chain, inducing architecture transition.
Scheme 1-1. Two approaches to architecture transformation of polymers. (a) Various topological transformations through disconnections and reconnections of dynamic covalent bonds; (b) Macromolecular topological transformation using a mechanically-linked system (rotaxane).
1.1.1 Dynamic-Covalent Chemistry Approach

Compared to supramolecular interactions, DC bonds typically have stronger strength, which may lead to enhanced structure stability of polymers. Moreover, most of DC bonds only respond to specific stimuli while remaining stable otherwise. Therefore, it is no surprise a variety of dynamic-covalent chemistry has been applied to the design of “smart” polymers that can change their architecture upon receiving a signal. This section will primarily cover recent examples of architecture-transformable polymers based on stimulus scope. It is also worthy to note that most examples of DC-type topological transformation are in fact degradable structure conversion that not only involves change in topology but also dramatic reductions in molecular weight of original polymers.

1.1.1.1 Thermal-induced topological transformation

The most obvious and well-understood stimulus in smart polymers is temperature. Many thermally-labile functional groups can degrade at elevated temperatures. For example, furan-maleimide based Diels-Alder (DA) linkage can be formed at lower temperatures (that is, R.T. to 60 °C). However, further increasing temperature to above 90 °C would cause cycloreversion of DA adducts, leading to free furan and maleimide moieties. Some pioneering works in thermal-induced topology transformation of polymers have been reported by the Sumerlin group. For example, Sumerlin et al. prepared core-crosslinked star polymers by reacting furan-functional block copolymers with bis-maleimide crosslinker at 50 °C (Figure 1-1). This approach conferred dynamic/reversibility to star polymers since the core of the star is crosslinked by thermally-reversible DA bonds. Both dynamic light scattering (DLS) and gel permeation chromatography (GPC) demonstrated core-crosslinked star was capable
of dissociating back to individual arms on heating at 120 °C, inducing an architecture transformation from star to linear block.\textsuperscript{77} The same group designed and reported the first example of thermally-reversible segmented hyperbranched polymers (SHPs) that contain DA-based branch points.\textsuperscript{26} These SHPs (120 to 515 kg/mol) were synthesized via self-condensing vinyl copolymerization (SCVCP) of methyl methacrylate (MMA) and an inimer consisting of DA linkage between the polymerizable group and initiating moiety. Upon heating, molecular weights rapidly reduced and linear poly(methyl methacrylate) (PMMA) segments (3.5 to 8.7 kg/mol) consisting of terminal maleimide and pendant furan were formed as the DA branch points disintegrated. Moreover, hyperbranched PMMA can be partially reconstructed as these cleaved linear PMMA chains reconnected via forward DA reaction at 50 °C.

![Figure 1-1. Formation and dissociation of core-crosslinked star with thermoreversible furan/maleimide Diels-Alder linkages. Reproduced with permission from ref 77.](image)

DuPrez and co-workers have exploited reversible reactions of indole end-functional polystyrene (PS) and poly(butyl acrylate) (PBA) with a triazolinedione (TAD)
end-group. Due to the robust ligation between indole and TAD, the formation of anticipated block copolymer (PS-b-PBA) was completed within 30 minutes at room temperature. More interestingly, the resulting PS-b-PBA readily transitioned to their homopolymers (PS and PBA) when heating at 120 °C in the presence of excessive 2,4-hexadien-1-ol, which can efficiently react with liberated PBA-TAD and prevent reformation of PS-b-PBA at room temperature.  

Most recently, Sumerlin and coworkers synthesized a novel star polymer containing thermally-labile azo linkages in the core that underwent decomposition during conventional heating. These star polymers exhibited a hydrodynamic diameter of 27 nm in water by DLS. While heating at 90 °C, a gradual reduction in size was observed as a result of azo cleavage. After 12 h, the size was further reduced to 3 nm, in good accordance with the size of linear chains.

1.1.1.2 Light-induced topological transformation

Light has recently attracted tremendous attention because the stimulus can be localized spatiotemporally and it can be also triggered externally. In addition, the irradiation parameters including wavelength, light intensity, and irradiation time can be easily modulated to accommodate the system. Various photo-responsive moieties have been employed in the synthesis of architecture-transformable polymers. In 2015, Mo and Zhao et al. reported the synthesis of a photocleavable hyperbranched graft copolymer by successive RAFT-SCVP and ring-opening polymerization (ROP) using a multi-functional chain transfer monomer. In this approach, hyperbranched poly (polyethylene glycol acrylate) was formed first via SCVP of polyethylene glycol acrylate and a chain transfer monomer containing an o-nitrobenzyl (NB) ester linkage. The resulting polymer still contained hydroxyl groups at each branch point that were further
utilized to initiate ROP of \(\varepsilon\)-caprolactone (CL), creating hyperbranched graft copolymers. Because light-sensitive \(o\)-nitrobenzyl ester moieties were present in branch points, these hyperbranched graft copolymers were capable of transitioning into a mixed set of architecture including linear, star, and graft copolymers under UV irradiation (365 nm).^{85}

Reversible linear to chain loops transformation triggered by light was reported by Zhao and coworkers (Figure 1-2).^{66} In their study, a well-defined random copolymer of DMAEMA and coumarin methacrylate (CMA), namely poly(DMAEMA-co-CMA), was prepared by RAFT polymerization. They showed that chain loops can be introduced onto initially linear polymer structure via the intra-chain photodimerization of coumarin groups upon \(\lambda > 310\) nm UV irradiation in a dilute polymer solution. GPC was used to confirm occurrence of intra-chain cross-linking events by showing a shift of the elution peak to longer times as compared to the original linear polymer. They further investigated reversibility of chain-folding by exposing the aqueous solution of intrachain-folded poly(DMAEMA-co-CMA) to UV light at 254 nm. UV-vis spectra measurements revealed only a partial de-cross-linking occurred with the dimerization degree reduced to 53%. 
In a recent report, Yamamoto and coworkers were able to prepare cyclized poly(l-lactide) (PLLA) and poly (d-lactide) (PDLA) that contain an o-nitrobenzyl group as a photo-cleavable linker. Photoirradiation of cyclic polylactides resulted in cleavage of o-nitrobenzyl linker and concomitant topological transformation to their linear analogue. Despite same molecular weights for cyclic and linear, differential scanning calorimetry (DSC) indicated melting temperature of cyclic stereocomplex (167 °C) is significantly lower than that of cleaved linear analogues (211 °C). The same group further developed an approach to light- and heat- triggered reversible linear-cyclic topological transformation (Figure 1-3). They demonstrated cyclic polyethylene oxide (PEO) or poly(tetrahydrofuran) (PTHF) was efficiently formed in both organic solvent and water by photo-dimerization of linear telechelic PEO or PTHF with anthryl end groups. Moreover, initially linear telechelics can be regenerated by heating the cyclized polymers at 150 °C. Up to 5 cycles of linear-cyclic transformations were achieved.
Figure 1-3. Reversible architecture transformation of linear telechelic polymers by irradiation at 365 nm and heating. Reproduced with permission from ref 64.

### 1.1.1.3 Redox-induced topological transformation

Among biological stimuli (e.g., pH, glucose, enzyme and so on), redox condition is arguably one of the most widely used stimulus in biological systems that rely on the tremendously different redox states between extracellular and intracellular locations.⁸⁶ Various redox-responsive polymers were fabricated by incorporation of redox-sensitive linkages such as diselenide and disulfide into polymers.³¹,⁸⁸-⁹² For example, degradable hyperbranched polymers containing disulfide-based branch points were reported by Tsarevsky and coworkers.⁸⁸ In this report, SCVCP of methyl methacrylate and an inimer bearing disulfide groups created these SHPs that can dissociate and morph their architecture from hyperbranched into linear poly(methyl methacrylate) with low molecular-weight distribution in the presence of reducing agents such as tributylphosphine. Monteiro and Perrier et al. reported the synthesis of cyclic polystyrene by oxidization of α, ω-thiol PS in dilute condition (that is, low polymer
concentration) (Figure 1-4).\textsuperscript{89} The resulting monocyclic PS contained only disulfide linkages and was confirmed by GPC, which showed the molecular weight of cyclic PS was lower than expected due to its lower hydrodynamic volume. More importantly, such disulfide bonds can be readily reduced by zinc and acetic acid, leading to the starting linear telechelic PS with thiol terminal functionalities, which may hold potential for recyclable polymer materials. Bapat and Sumerlin \textit{et al.} demonstrated an example of redox-responsive star polymers that can reversibly transition into linear unimers. In their approach, first, well-defined block copolymers containing a reactive segment poly(styrene-alt-maleic anhydride) was prepared by RAFT polymerization. After that, ring-opening reactions of the anhydride groups in the block copolymers with cystamine led to core-crosslinked stars. The transformation from star to linear unimers bearing pendent thiols can be realized by reductive cleavage of disulfide linkages. Moreover, they demonstrated oxidation of the free thiols of the cleaved unimers resulted in reformation of the stars in the presence of air. Multiple cycles of reversible star-linear transformations were achieved.\textsuperscript{31}
Figure 1-4. Redox-triggered reversible topological transformation from linear PS to monocyclic (one disulfide linkage) and multiblock PS. Adapted from ref 89.

Moreover, polymers containing diselenide bonds have recently attracted increasing interest because of their redox sensitivity and potential application in bio-related area. Zhu et al. provided a novel approach to achieve topological transformation of polymers by incorporating diselenide moieties into the backbone of cyclic PS.\textsuperscript{90} To start with, a well-defined linear PS was synthesized by RAFT polymerization using a bifunctional diselenocarbonate chain transfer agent (CTA). Then aminolysis of the terminal selenocarbonates and in-situ oxidation of selenols allowed the formation of mono-cyclic PS or multi-block cyclic PS dependent on the concentration of $\alpha,\omega$-telechelic PS in solution. Taking the advantage of the reduction responsive performance of diselenide linkers, the shape change from cyclic to linear was accomplished in the presence of sodium borohydride, a reducing agent.
1.1.1.4 Mechanically induced topological transformation

In addition to the above-mentioned stimuli, mechanical force has also been exploited to influence the architecture of polymers via scission in mechanophore linker.\textsuperscript{70,93} Boydston \textit{et al.} reported the synthesis of a three-arm star poly(methyl acrylate) (PMA) containing an anthracene-maleimide DA adduct mechanophore that was located in the core of star (Figure 1-5).\textsuperscript{70} The star polymer was subjected to sonication that led to cycloreversion of DA adduct, resulting in a maleimide terminal linear PMA and an anthracene-centered PMA diblock copolymer. Photoluminescence spectra showed photoluminescence intensity that corresponds to free anthracene increased upon increasing sonication time, confirming the breakage of DA adduct and concomitant formation of anthracene.

![Figure 1-5. Architecture transition from star to linear polymer through mechanochemically induced Diels-Alder bond scission. Reproduced with permission from ref 70.](image)

\textbf{1.1.2 Supramolecular Chemistry Approach}

In the past two years, several topology-transformable polymers based on rotaxane chemistry have been systematically studied by Takata \textit{et al} (Scheme 1-1).\textsuperscript{62,65,
In comparison with dynamic-covalent chemistry approach, this rotaxane protocol prompted the topological transformation without changes in absolute molecular weight and composition. In 2015, their pioneering work in this concept described the synthesis of a mechanically-linked star polymer and its transition into a linear polymer (Figure 1-6). In their approach, first, a tris-hydroxyl functional pseudo [2] rotaxane initiator was employed to initiate ROP of δ-valerolactone (δ-VL), followed by end-capping with a bulky stopper (3,5-dimethylphenyl isocyanate) after polymerization. The resulting three-arm star poly(δ-valerolactone) (PVL) was composed of an axle PVL chain which center was connected to the wheel PVL segment via ammonium/crown ether based rotaxane. Then the star was treated with an excess amount of acetic anhydride in the presence of trimethylamine, causing N-acetylation of the central ammonium moiety. As a result, center rotaxane linkage was “unlocked” because acetylated moiety has no interaction with the crown wheel. Furthermore, due to the fact that the interaction of the urethane/crown ether is stronger than that of ester (in the PVL backbone)/crown ether, the wheel PVL translated from the “unlocked” center to the urethane terminus of axle PVL, eventually leading to topological transformation from star to linear. GPC was used to analyze the star and linear that is produced by transformation. It clearly showed the apparent number-averaged molecular weight of linear PVL (9.5 kDa) is bigger than that of star counterpart (8.0 kDa), suggesting a relatively larger hydrodynamic volume of linear analogue.

To increase the complexity of architecture-transformable polymers, they further applied the same strategy to realize transformation of an ABC star terpolymer to a linear ABC terpolymer. By using pseudo[2]rotaxane initiator that comprised three different
functionalities (including trithiocarbonate, hydroxyl, and alkyne), the synthesis of ABC star copolymer was achieved by successive ROP, RAFT polymerization, and copper (I)-catalyzed alkyne-azide cycloaddition click chemistry. Similar to their first report on star/linear transformation, ABC star terpolymer can readily transition to ABC linear terpolymer by removing the interaction between ammonium and crown ether via N-acetylation.

Figure 1-6. Architecture transformation of a 3-arm star polymer to its linear analogue by N-acetylation. Reproduced with permission from ref 62.

Rotaxane chemistry was also extended to linear/cyclic transformations. In their first report on this type of transformation demonstrated the synthesis of cyclic PTHF from its linear form. In the process of cyclization, protection of secondary ammonium end group (station A) eliminated the hydrogen bonding between ammonium and crown ether, allowing the crown ether wheel to move along the axle polymer chain from station A to station B, which is the opposite polymer end containing ammonium moiety that was formed by deprotection. From a synthetic point of view, this approach is potentially useful for large-scale cyclic polymer synthesis since it does not require high-
dilute conditions which are typically applied in most approaches involving cyclization of linear polymer precursors.

Due to the ability to self-assemble in both bulk and in solution, the last decade has seen considerable progress in the field of block copolymer materials.\textsuperscript{45, 96, 97} On the other hand, cyclic polymer is intriguing owing to the absence of chain-ends.\textsuperscript{68, 98} The applicability of this rotaxane protocol was then stretched to the synthesis of cyclic block copolymer (CBC) that can potentially merge the unique properties of both linear block and cyclic architecture. In their approach, a stable pseudo[2]rotaxane was used as an initiator for sequential ROP of monomers $\varepsilon$-caprolactone and hexanolactone (HL), creating macromolecular [2]rotaxane with block copolymer poly($\varepsilon$-caprolactone)-block-poly(hexanolactone) as its axle component. Then axle and the wheel were linked via ring-closing metathesis reaction between two olefinic groups, forming a lasso-shaped structure. Finally, $N$-acetylation of ammonium at station A eliminated its interaction with crown ether, prompting the wheel to translate along the axle and reach the other terminus (station B). Since station B contains a urethane moiety that can interact with crown ether, the wheel was thus “locked” again, resulting in the architecture transformation from linear block to cyclic block (Figure 1-7).\textsuperscript{95}

Besides rotaxane chemistry, hydrogen bonding has been utilized in linear/cyclic transition. Barner-Kowollik group demonstrated cyclization of linear polystyrene through orthogonal conjugation based on $\alpha,\omega$-hydrogen-bonding between a Hamilton wedge and a cyanuric acid. \textsuperscript{1}H NMR and DLS analysis showed cyclization mainly occurred below 0.5 mM.\textsuperscript{99}
Figure 1-7. Synthetic pathways of linear block copolymer and transformation to cyclic block architecture via N-acetylation. Adapted from ref 95.

1.2 Properties and Applications of Architecture-Transformable Polymers

Morphing the architecture of a polymer can lead to dramatic change in a variety of chemical/physical properties such as the possibility of chain entanglement, the capability of modifying viscosity/rheology in solution, the ability to self-assembly, LCST, glass transition temperature ($T_g$), and melting point ($T_m$), among others. These dynamic features promise architecture-transformable polymer materials as excellent candidates in many potential applications.

Taking advantage of topological effect, Zhao et al. was able to optically tailor the LCST of the thermosensitive water-soluble PDMAEMA through reversible photo-driven transformation from linear to chain loop. Photodimerization of coumarin resulted in introduction of intra-chain loops and a large increase in LCST because loops can reduce the possibility of entanglement with neighboring chains which leads to repulsive force and retarded chain aggregation. To probe the optical tunability of cloud points, a
series of polymers with various extents of intra-chain dimerization (i.e., different amount of loops per chain) were prepared in exposure to long wavelength UV irradiation at different times. The transmittance measurement revealed cloud points of polymers increased with increasing degree of dimerization.

Mo and Zhao et al. observed a change in self-assembly behavior upon transition from hyperbranched graft polymers to a mixture of linear, star, and comb under UV irradiation, which led to cleavage of o-nitrobenzyl ester based branch points. The original hyperbranched graft polymer formed micellar morphology in water. However, after architecture transformation, vesicles and multi-compartment vesicles were present due to re-assembly of polymers with new topologies (Figure 1-8). To exemplify the utilization of this polymer in smart drug delivery system, Nile red was encapsulated into the micelles and underwent release triggered by light. The on-demand release profile of Nile red was realized.85
Figure 1-8. Light-triggered architecture transformation of hyperbranched graft copolymer. (a) Light-triggered architecture transformation of hyperbranched graft copolymer; (b) TEM images of nano-objects formed by hyperbranched graft copolymer in water before and after UV irradiation for 1min, 5min, and 10 min; (c) Fluorescence emission spectra (excited at 530 nm) of Nile red loaded hyperbranched graft copolymer based nanoparticle under UV irradiation for varying time. The decrease in fluorescence intensity indicated Nile red was released during UV-irradiation. Adapted from ref 85.

The Takata group demonstrated the transformation of the polymer topology (from linear block to cyclic block) clearly led to a macroscopic variation in crystallinity of the block copolymer PCL-b-PHL, despite the similar composition of linear and cyclic polymers. According to DSC thermograms, linear PCL-b-PHL exhibited not only a glass transition peak of PHL but also a melting peak of PCL. However, upon transformation, cyclic PCL-b-PHL showed a much higher melting point that stems from reduced entropy change for cyclic polymer.
Yamamoto and Tezuka et al. provided an approach to photo-triggered hydrogel formation via architecture transformation of cyclic block copolymers (PLLA-b-PEO and PDLA-b-PEO) into linear stereocomplex.\(^{100}\) As shown in Figure 1-9, a mixture of micellar dispersion deriving separately from linear PLLA-b-PEO-b-PLLA and PDLA-b-PEO-b-PDLA created hydrogel as chain ends of micelle-forming polymers protruded out of the micelles and resulted in three-dimensional structure via stereocomplex formation. However, no gelation occurred when using cyclic polymer based micelles because cyclic polymers are free of chain ends, which eliminated the possibility of stereocomplex formation in the investigated conditions. These results elucidated the effect of topology in gelation behavior. Finally, a mixture of micellar solution of light-sensitive NB-containing cyclic PLLA-b-PEO and PDLA-b-PEO formed a gel upon UV irradiation that cleaved NB linkages and promoted topological conversion from cyclic to linear.
Figure 1-9. Schematic illustrations for the possible gelation of mixed micellar solution formed from (a) linear PLLA-b-PEO-b-PLLA and linear PDLA-b-PEO-b-PDLA; (b) cyclic PLLA-b-PEO and cyclic PDLA-b-PEO; (c) photocleavable NB-PLLA-b-PEO and NB-PDLA-b-PEO. Adapted from ref 100.

1.3 Conclusion and Future Prospects

In summary, this review places focus on the stimuli scope and synthetic strategies of architecture-transformable polymers which have recently emerged as a new class of stimuli-responsive polymer. A range of dynamic bonds (covalent or supramolecular) have been exploited to enable architecture-transformable polymers to change their entire shape on exposure to a specific stimulus. These macromolecular architecture transformations typically led to concomitant changes in many solution and/or bulk properties such as self-assembly behavior, chain entanglement, and
thermal properties (e.g., $T_g$ and $T_m$). Although many examples relied on responsiveness to simply one stimulus, we envision one of the future directions is the design and synthesis of multi-stimuli responsive architecture-transformable polymer. It may be interesting to introduce multiple orthogonal dynamic bonds into the same architecture-transformable polymer to allow access to various pathways of shape change that could lead to completely different variations in properties. Another important point could be how to achieve full reversibility of topological transformations, which would allow reversible switching of polymer properties. Additionally, several challenges still remain in the viewpoints of both synthesis and applications. One challenge stems from the efficiency of architecture transformation. In a macromolecular system, it is usually difficult to separate a mixed set of polymers, especially for those with similar molecular weights and solubility in common solvents. Therefore, highly-efficient architecture transformations accompanied by robust reactions (such as “click” and “unclick”) are desired for ease of purification. Furthermore, it is also noteworthy all the examples of macromolecular architecture transformation outlined in this review were performed in solution state that may restrict applications of this process in material science. So there is a significant need to explore these transformations in bulk. However, in a bulk system, polymers of high $T_g$ may suffer from limited mobility and thus reduce availability of reactive groups located on the chains, causing low efficiency of new bond formation which may dictate reassembly of chains. One possible strategy to overcome this hurdle would be applying a processing temperature that is higher than $T_g$ of investigated polymers. In addition, high crystallinity of some polymers can prevent the penetration of light, limiting their potential in photo-responsive architecture-transformable polymeric
materials in bulk. Therefore, more rational design and study needs to be conducted to facilitate the transition of this concept from solution into bulk state. Given the considerable progress of traditional stimuli-responsive polymeric materials in the field of modern manufacturing, biology, and medicine, we believe that the development of architecture-transformable polymers will not only expand the scope of stimuli-responsive polymers but also open the door to an unprecedented class of adaptive materials with unique properties and applications.
CHAPTER 2
RESEARCH OBJECTIVE

The purpose behind this research is to expand the state-of-art scope of stimuli-responsive polymers and bring out a new concept “architecture-transformable polymer” to the community of polymer science. The rapid development of synthetic polymer chemistry has led to the blossoming of stimuli-responsive or “smart” polymers that can adapt to surrounding environment by responding to external signals, inducing change in their physical and/or chemical properties. Such “smart” polymer materials have received more and more attention in the applications of biomaterials (e.g., drug delivery system and tissue engineering), optical systems and biosensors, as well as industry manufacturing including coating, environmental remediation and self-healing materials. A great deal of “smart” polymers has relied on simply change in composition and molecular weight. However, architecture, a very fundamental feature of polymer, is typically inalterable once synthesized. Indeed, polymer architecture plays a pivotal role in determining many properties such as the possibility of chain entanglement, self-assembly behavior in solution and solid state, solution/melt rheology, and thermal properties. Therefore, not only the size of a macromolecule but also its architecture must be considered when designing polymers for specific applications.

Combining the basic concept of dynamic-covalent chemistry and concurrent controlled radical polymerization techniques, my research has focused on preparing adaptive polymer and materials which can morph their entire architecture in response to a stimulus. The first work relied on the design and synthesis of a “smart” triblock copolymer (PEG-b-polyazo-b-PEG) containing multiple thermally-labile azo linkages in the main chain of central block. When heating, azo-containing central block
disintegrated, leading to formation of small molecular fragments and residual PEG. This transformation dramatically changed the solubility of polymers in water. The original PEG-b-polyazo-b-PEG was capable of self-assembling into micelles (23 nm). However, thermal-induced degradation resulted in disassembly of micelles as evidenced by macroscopic aggregation of small molecular fragments and distribution of unimers (2 nm) in DLS.

In my second work, we reported the first example of thermally-reversible segmented hyperbranched polymers (SHPs). These SHPs were synthesized via self-condensing vinyl copolymerization of methyl methacrylate (MMA) and an inimer that is consisting of a furan-maleimide linkage between the polymerizable group and initiating component. At 90 or 120 °C, molecular weights of SHPs gradually decreased as heating time increased. Complete cleavage of furan-maleimide linkages resulted in linear poly(methyl methacrylate) (PMMA) segments with a terminal maleimide and pendent furan functionalities. Moreover, hyperbranched PMMA can be reconstructed via forward Diels-Alder reaction of cleaved linear PMMA at 50 °C. Perhaps most importantly, these thermally-labile SHPs were utilized to confirm the mechanism of self-condensing vinyl copolymerization, which was first established in 1995.

In the final chapter, by using reversible-covalent chemistry to prompt the disconnection of chemical bonds (i.e., furan-maleimide cycloadducts) and formation of new linkages (i.e., anthracene-maleimide bonds) in situ, we reported smart polymers that undergo dramatic topological transformations via thermodynamic control. This technique successfully allowed a linear amphiphilic block copolymer or hyperbranched polymer to readily transform into comb, star and hydrophobic block copolymer
architectures. Given the wide application of traditional stimuli-responsive polymer materials in nanomedicine, biology, and manufacturing, architecture-transformable polymers may present an entirely new approach to ‘smart’ polymers.
CHAPTER 3
RADICAL DEPARTURE: THERMALLY-TRIGGERED DEGRADATION OF AZO-CONTAINING POLY(β-THIOESTER)S

3.1 Overview

Smart macromolecules are capable of responding to the presence of external signals. During the past decade, stimuli-responsive polymers have led to significant successes in a diverse range of applications, such as triggered drug/gene release, disease diagnosis, tissue engineering, coatings, and textiles. Since the advent and evolvement of controlled polymerization techniques and their combination with highly efficient chemical transformations to construct complex polymers, various architectures of stimuli-responsive polymers have been accessed, including main-chain, dendritic, segmented hyperbranched, cyclic, star, and gel (co)polymers. One particularly interesting class of responsive materials involves macromolecules that can be triggered to degrade into small molecular fragments upon exposure to discrete stimuli. Such a transition from high to low molecular weight leads to immense structural changes that are accompanied by significant impacts on physicochemical properties and phase behaviors. Polymers that undergo main-chain degradation in response to a specific chemical or physical trigger have been prepared utilizing monomer units bearing acylals, disulfides, Diels-Alder linkages, o-nitrobenzyl groups, and peroxides, among others. Upon application of the proper stimulus, these polymers fragment into smaller molecules, resulting in disintegration of the macromolecular backbones.

Reprinted from ACS Macro lett., 2016, 5, 688-693, with permission from the American Chemistry Society.
Recently, poly(β-thioester)s have garnered significant attention due to their inherent biodegradability and potential applications in plastics recycling and biomedical research.\textsuperscript{129} The preparation of poly(β-thioester)s has been demonstrated using base-catalyzed thiol-ene step-growth polymerization.\textsuperscript{130} In this straightforward approach, dithiol-functional monomers and di(meth)acrylate monomers are typically copolymerized in the presence of catalytic base under mild conditions. The base-catalyzed thiol-ene reaction is highly efficient and therefore allows for high monomer conversion, giving rise to polymers with high degrees of polymerization.\textsuperscript{131} In addition, the functional group tolerance of base-catalyzed thiol-ene polymerizations has been reported.\textsuperscript{132-135} By inserting functionalities (e.g., ethylene glycol units, o-nitrobenzyl moieties, pendent hydroxyl groups, and amino acid sequences) into dithiol monomers or di(meth)acrylate monomers, “smart” poly(β-thioester)s with intriguing physicochemical properties have been designed and prepared. However, to the best of our knowledge, poly(β-thioester)s that can undergo thermally triggered degradation beyond gradual ester hydrolysis have not been reported.

Herein, we present the first example of thermally-degradable poly(β-thioester)s containing aliphatic azo linkages in the backbone of polymers. A novel azo-based diacrylate monomer was synthesized and copolymerized with excess 1,6-hexanediolthiol (HDT) for the preparation of α,ω-telechelic polymers bearing thiol end groups. These thiol groups were further reacted with 2-hydroxyethyl acrylate or poly(ethylene glycol) (PEG) acrylate to generate end-capped homopolymers or triblock copolymers, respectively (Scheme 3-1). Thermal cleavage of the incorporated azo units led to a radical-based degradation process\textsuperscript{136,137} and afforded a mixture of lower molecular
weight polymers and small molecules. The variables affecting degradation, including
temperature, solvent (i.e., organic and aqueous), and presence or absence of radical
scavengers, were thoroughly investigated. By exploiting homolytic dissociation via azo
bonds, as opposed to many other previous reports of thermally degradable polymers
that rely on, for example, retro-Diels-Alder reactions, this route should provide polymers
that are irreversibly degraded. Moreover, variation of the specific functionality adjacent
to the azo group could allow the degradation kinetics to be tailored to a specific
application.

3.2 Results and Discussion

3.2.1 Synthesis of ACVA Monomer

With the goal of preparing triblock copolymers with thermally-degradable
“polyazo” central blocks, we began our preliminary exploration by designing and
synthesizing a 4,4'-azobis(4-cyanovaleric acid) derived diacrylate monomer (ACVADA)
containing a central azo moiety. 4,4'-Azobis(4-cyanovaleric acid) was coupled with two
equivalents of 2-hydroxylethyl acrylate using a carbodiimide coupling approach at 0 °C
in the absence of light. Successful synthesis of the novel diacrylate compound was
confirmed by $^1$H NMR (Figure 3-1) and $^{13}$C NMR spectroscopy (Figure 3-2). Notably, the
signal attributed to the protons of the methyl groups at ~1.6 ppm exists as two singlet
peaks, which is consistent with the existence of cis and trans isomers in the product of
ACVADA.
Figure 3-1. $^1$H NMR spectroscopy of polyazo, HDT, and ACVADA. (a) 1H NMR spectra of dithiol functional polyazo10 (top blue line), HDT (middle green line), and ACVADA (bottom red line). Disappearance of signals attributed to acrylate (blue dashed line box, 5.8-6.5 ppm) indicated ACVADA monomer was completely consumed; (b) 1H NMR spectrum of hydroxyl functionalized polyazo10 end capped with 2-hydroxyethylacrylate.
3.2.2 Step-Growth Copolymerization of ACVA Monomer and HDT

Next, using dimethylphenylphosphine (DMPP) as the catalyst, step-growth copolymerization of ACVADA and HDT was performed. Thiol-acrylate reactions are highly exothermic, so the polymerization was conducted at 0 °C in the absence of light to minimize potential azo dissociation. To synthesize polymers containing terminal thiols that could be further functionalized or chain extended, an excess of the dithiol comonomer was employed. The molar feed ratios of HDT to ACVADA were 1.16/1, 1.13/1, and 1.08/1, respectively. Monomer conversion of ACVADA was monitored by $^1$H NMR spectroscopy, and the disappearance of acrylate groups (5.8-6.5 ppm) was observed after 1 h of polymerization (Figure 3-1 a). The resulting polyazo polymers
having molecular weights of 3,000, 3,500, or 6,100 g/mol were prepared by varying the comonomer ratio. Thereafter, polyazo\textsubscript{10} (Table 3-1) was further modified with 2-hydroxyethyl acrylate (HEA) via a thiol-ene click reaction (Scheme 3-1). In this process, ten equivalents of HEA relative to the terminal thiol groups were added to ensure complete end-group conversion. \textsuperscript{1}H NMR spectroscopy confirmed successful Michael addition by the appearance of peaks at 3.82 and 4.25 ppm ascribed to the methylene protons \((k\) and \(l)\) adjacent to the terminal hydroxyl groups (Figure 3-1 b). In addition to allowing subsequent installation of PEG blocks (vide infra), transformation of the terminal thiol groups of the polyazo polymers prevented disulfide formation, which might otherwise have led to continued polymerization of the thiol-terminated polymer.

Scheme 3-1. Synthetic route to ACVADA monomer and preparation of homopolymer polyazo and triblock copolymer PEG\textendash{}polyazo\textendash{}PEG by one-pot step-growth polymerization.
Table 3-1. Molecular weight information for polyazo and PEG-b-polyazo-b-PEG.

<table>
<thead>
<tr>
<th>Polymer ID $^a$</th>
<th>Feed ratio $^b$</th>
<th>$M_n$ (g/mol)</th>
<th>$D$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyazo$_5$</td>
<td>1.16</td>
<td>3 000</td>
<td>1.85</td>
</tr>
<tr>
<td>Polyazo$_6$</td>
<td>1.13</td>
<td>3 500</td>
<td>1.62</td>
</tr>
<tr>
<td>Polyazo$_{10}$</td>
<td>1.08</td>
<td>6 100</td>
<td>1.62</td>
</tr>
<tr>
<td>PEG$_{44}$-b-polyazo$<em>6$-b-PEG$</em>{44}$</td>
<td>1.13</td>
<td>6 800</td>
<td>1.21</td>
</tr>
<tr>
<td>PEG$_{110}$-b-polyazo$<em>6$-b-PEG$</em>{110}$</td>
<td>1.16</td>
<td>10 700</td>
<td>1.58</td>
</tr>
</tbody>
</table>

$^a$Number-average degrees of polymerizations were determined by $^1$H NMR spectroscopy; $^b$Feed ratio represents the initial ratio of HDT to ACVADA.

3.2.3 Thermal Degradation Behavior of Polyazo

Because thermally-labile azo bonds were embedded within the backbone of the polyazo polymers, we postulated that degradation into small molecules should be possible upon heating. Therefore, the thermal degradation behavior of polyazo$_{10}$ was examined. It is well known that the radicals generated by scission of azo compounds can be consumed by several reaction pathways, including disproportionation, recombination, transfer (i.e., to solvent, polymer, and low molecular weight fragments), or addition to oxygen.$^{14,106}$ Depending on the fates of these radicals, complex degradation mechanisms may result. Among these events, irreversible radical recombination was considered to be the most detrimental to the potential degradation route of the polymer. To minimize the rate of recombination, we first investigated the effect of adding hydroquinone (HQ), a radical scavenger that can transfer a hydrogen to a carbon-centered radical. In this study, polyazo$_{10}$ ($M_n = 6,100$ g/mol) was heated at 95 °C in the absence and presence of HQ (10 equiv. with respect to azo units, 4 mg/mL). Reduction in molecular weight of polyazo$_{10}$ upon heating was examined by GPC, which displayed longer retention times as the heating time increased (Figure 3-3 a and b). For the degradation without HQ, a relatively slow reduction in molecular weight was
observed, resulting in a molecular weight of 4,400 g/mol after 10 min of heating.

Continuing the heating for 240 min, the molecular weight gradually leveled off at 2,100 g/mol, with no further change in molecular weight at longer reaction times. In the presence of HQ, the molecular weight of polyazo$_{10}$ decreased sharply from 6,100 g/mol to 2,050 g/mol within 10 min of heating (Figure 3-3 c). Subsequently, the degradation proceeded at a slower rate, suggesting most of the degradation had been completed during the first 10 min. These results suggest that addition of HQ effectively suppressed radical recombination, thus resulting in a larger extent of degradation in terms of apparent molecular weight reduction.

![Figure 3-3. GPC characterization of thermal degradation of polyazo. (a) GPC traces of samples taken during thermal degradation of polyazo$_{10}$ at 95 °C without HQ; (b) GPC traces of samples taken during thermal degradation of polyazo$_{10}$ at 95 °C in the presence of HQ; (c) Decrease in $M_n$ determined by GPC in the absence and presence of HQ at 95 °C; (d) Decrease in $M_n$ determined by GPC at three different temperatures in the presence of HQ (60, 80 and 95 °C).](image)
Additionally, degradation of the polymer backbone results in the emission of nitrogen gas. Thus, $^{15}$N NMR spectroscopy was utilized to confirm the consumption of azo units during degradation. As shown in Figure 3-4, the characteristic resonance of the azo group at -171 ppm was not visible in the spectrum of the degradation products.

To discern the influence of temperature on degradation kinetics, polyazo$_{10}$ was heated at 95, 80 and 60 °C in the presence of HQ. GPC was used to monitor the decrease in molecular weight as a function of time at each temperature (Figure 3-5). As expected, degradation was most rapid at 95 °C, leading to a final molecular weight of 1,400 g/mol after 4 h (Figure 3-3 d). Conversely, a slower decrease in molecular weight was observed at 80 °C, resulting in a final degraded product with a molecular weight of 2,000 g/mol. Finally, only a slight shift in the GPC trace occurred when the polymer was heated at 60 °C, indicating the polymers was relatively stable at this temperature throughout the investigated heating time.

Figure 3-4. $^{15}$N NMR spectroscopy of polyazo degradation. (a) Demonstration of thermal degradation of polyazo and resulting emission of N$_2$; (b) $^{15}$N NMR spectrum of polyazo before and after thermal treatment at 95 °C in the presence of hydroquinone (CDCl$_3$, 300 MHz).
Figure 3-5. GPC characterization of thermal degradation of polyazo in presence of hydroquinone at different temperatures. (a) GPC traces of samples taken during the thermal degradation of polyazo at 80 °C in the presence of HQ; (b) GPC traces of samples taken during thermal degradation of polyazo at 60 °C in the presence of HQ.

Figure 3-6. $^1$H NMR spectrum of PEG$_{44}$ acrylate (CDCl$_3$, 500 MHz).
Figure 3-7. $^1$H NMR spectrum of triblock copolymer PEG$_{44}$-b-polyazo$_{6}$-b-PEG$_{44}$ (CDCl$_3$, 500 MHz).

3.2.4 Preparation and Thermal Degradation of PEG-b-polyazo-b-PEG

To prepare amphiphilic polyazo-containing triblock copolymers, PEG$_{44}$-acrylate ($M_n = 2,000$ g/mol) was synthesized (Figure 3-6) and subsequently conjugated to the thiol end groups of polyazo$_6$ ($M_n = 3,500$ g/mol) (Scheme 3-1). The coupling reaction was monitored by $^1$H NMR spectroscopy, with the disappearance of the acrylate signals at 5.8-6.5 ppm indicating PEG$_{44}$-acrylate was near quantitatively consumed (Figure 3-7). As shown in Figure 3-8 a, the GPC trace displayed a shift to higher molecular weight, consistent with attachment of the PEG segments to the end groups of the central polyazo block. To further verify the topology and purity of the triblock copolymer, diffusion-ordered NMR spectroscopy (DOSY) was utilized (Figure 3-8 b). After
conjugation, the polyazo and PEG segments shared the same diffusion coefficient (2.35×10⁻⁶ cm²/s), which was smaller than that of PEG₄₄-acrylate (5.72×10⁻⁶ cm²/s), confirming that PEG₄₄ was chemically bound to polyazo₆ rather than being physically mixed. To demonstrate the versatility of this approach, PEG₁₁₀-acrylate was conjugated to polyazo₅ (Mₐ = 3,000 g/mol). Clean and efficient coupling was confirmed by ¹H NMR spectroscopy and GPC (Figure 3-9). These results demonstrate the highly efficient nature of thiol-acrylate reactions for the synthesis of triblock copolymers.

Figure 3-8. Characterization of PEG-b-polyazo-b-PEG triblock copolymers by GPC, DLS, DOSY and TEM. (a) GPC traces of polyazo₆, PEG₄₄-acrylate, and PEG₄₄-b-polyazo₆-b-PEG₄₄; (b) DOSY NMR spectra of PEG₄₄-b-polyazo₆-b-PEG₄₄ (dark blue line) and PEG₄₄-acrylate (red line); (c) DLS size distribution of PEG₄₄-b-polyazo₆-b-PEG₄₄ triblock copolymer-based micelles in water; (d) TEM image of triblock copolymer-based micelles cast from aqueous solution
Figure 3-9. $^1$H NMR spectrum and GPC trace of PEG$_{110}$-b-polyazo$_5$-b-PEG$_{110}$. (a) $^1$H NMR spectrum of PEG$_{110}$-b-polyazo$_5$-b-PEG$_{110}$ (CDCl$_3$, 500 MHz). The disappearance of acrylate-based signals at 5.8-6.5 ppm suggested PEG$_{110}$ acrylate was completely consumed; (b) GPC traces of PEG$_{110}$-acrylate, polyazo$_5$ and PEG$_{110}$-b-polyazo$_5$-b-PEG$_{110}$. A shift to higher molecular weight indicated the successful coupling reaction between PEG$_{110}$ and polyazo$_5$.

Figure 3-10. DLS and GPC data for degradation of triblock copolymer micelles. (a) DLS size distribution of PEG$_{44}$-b-polyazo$_6$-b-PEG$_{44}$-based micelles before and after thermal treatment at 95 °C; (b) Decrease in $M_n$ determined by GPC of PEG$_{44}$-b-polyazo$_6$-b-PEG$_{44}$ heated in water or DMAc.

Unlike the original polyazo polymer, the resulting triblock copolymer could be dispersed in deionized water due to the hydrophilic nature of the PEG blocks. Aggregates of PEG$_{44}$-b-polyazo$_6$-b-PEG$_{44}$ in water were further examined by dynamic light scattering (DLS) and transmission electron microscopy (TEM) (Figures 3-8 c and d).
TEM provided evidence of self-assembled micelles with a diameter of 18 nm, which was in relatively good agreement with the DLS results ($D_h = 23$ nm). Furthermore, upon heating at 95 °C for 1 h, the solution turned opaque due to aggregation of the degradation products. After removing the insoluble aggregates by filtration (Nylon membrane with 0.20 μm pore size), the particle sizes decreased to 2 nm, as determined by DLS, which was consistent with degradation of the azo moieties and dissociation of the micelles (Figure 3-10 a).

Figure 3-11. GPC traces of samples taken during the thermal degradation of PEG$_{44}$-b-polyazo$_6$-b-PEG$_{44}$ at 95 °C in water.
Figure 3-12. GPC kinetics of degradation of triblock copolymers in presence and absence of hydroquinone at 80 °C. (a) GPC traces of samples taken during the thermal degradation of PEG₄₄-b-polyazo₆-b-PEG₄₄ at 95 °C in the absence of HQ; (b) GPC traces of samples taken during the thermal degradation of PEG₄₄-b-polyazo₆-b-PEG₄₄ at 80 °C in the absence of HQ.

Figure 3-13. GPC kinetics of degradation of triblock copolymers in presence and absence of hydroquinone at 95 °C. (a) GPC traces of samples taken during the thermal degradation of PEG₁₁₀-b-polyazo₅-b-PEG₁₁₀ at 95 °C in the absence of HQ; (b) GPC traces of samples taken during the thermal degradation of PEG₁₁₀-b-polyazo₅-b-PEG₁₁₀ at 80 °C in the absence of HQ.

To investigate the effect of solvent, thermal degradation behaviors of PEG₄₄-b-polyazo₆-b-PEG₄₄ were compared in DMAc (i.e., a non-selective solvent) and water (i.e., a selective solvent). In the case of degradation in DMAc, the final product showed a molecular weight of 2,200 g/mol, which was noticeably smaller than that of the final
product in water ($M_n = 3,600$ g/mol; Figure 3-10 b and Figure 3-11). Moreover, the degradation of the triblock copolymer in water was significantly slower than that in DMAc. This can be ascribed to the self-assembled and compact environment of the azo moieties within the micelle cores, which results in limited diffusion and increased possibility of radical recombination after dissociation. Finally, thermal degradation of $\text{PEG}_{44}-b$-$\text{polyazo}_{6}-b$-$\text{PEG}_{44}$ and $\text{PEG}_{110}-b$-$\text{polyazo}_{5}-b$-$\text{PEG}_{110}$ at 95 and 80 °C in DMAc was monitored by GPC (Figures 3-12 and Figure 3-13). As expected, the triblock copolymers exhibited rapid decomposition kinetics at 95 °C.

**3.3 Conclusion**

In summary, we have designed a robust approach to thermally-labile, main-chain poly($\beta$-thioester)s. Through the utilization of base-catalyzed thiol-ene chemistry, homopolymers and triblock copolymers of azo-containing monomers were prepared in one pot under mild conditions. GPC and $^{15}$N NMR spectroscopy results revealed that polyazo can gradually degrade into small molecular fragments upon heating. The degradation kinetics were dependent on temperature, with significantly enhanced dissociation rates at higher temperatures. Furthermore, the addition of a radical scavenger improved the extent of degradation by limiting radical recombination. Water-soluble $\text{PEG}-b$-$\text{polyazo}-b$-$\text{PEG}$ was prepared and characterized by $^1$H and DOSY NMR spectroscopy and GPC. DLS and TEM results demonstrated the self-assembly of these triblock copolymers in water. Interestingly, for the triblock copolymers, the degradation in DMAc was faster than in water at the same temperature, which is likely due to the congested environment of the polyazo segments in the micellar cores present in the aqueous solution, which served to confine the diffusion of radicals. Given the broad application of stimuli-responsive polymers in modern-day biology, medicine, and
manufacturing, we believe these novel stimuli-responsive polymers will give rise to a new class of poly(β-thioester)-based materials. Current investigation is underway to further explore the possibility of preparing polyazo polymers with enhanced responses at lower temperature.

3.4 Experimental Section

3.4.1 Materials and Methods

All chemicals were used as received unless otherwise noted. Poly(ethylene glycol) monomethyl ether ($M_n = 2$ kg/mol and 5 kg/mol), 2-hydroxyethyl acrylate (>96%), 4,4′-azobis(4-cynovaleric acid) (ACVA, >98%), sodium sulfate (>99%), sodium bicarbonate (>99%), sodium chloride (>99%), 1,6-hexanethiol (HDT, >97%), dimethylphenylphosphine (DMPP, 99%), and $N,N$-dimethylacetamide (99.8%) were purchased from Sigma-Aldrich. 4-Dimethylaminopyridine (4-DMAP, 98%) was purchased from Acros Organics. Triethylamine (TEA) (>99%), acryloyl chloride (>96%), and hydroquinone (HQ) (99%) were purchased from Alfa Aesar. 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC•HCl, >98%), methanol (99.8%), diethyl ether (99.5%), anhydrous dichloromethane (>99%), and anhydrous tetrahydrofuran (>99.5%) were purchased from TCI. $^1$H and $^{13}$C NMR spectra were recorded in CDCl$_3$ using an Inova 500 MHz spectrometer at 25 °C. $^{15}$N NMR spectra were recorded in CDCl$_3$ using a Mercury 300BB MHz spectrometer at 25 °C. DOSY experiments were performed on a Varian Inova spectrometer operating at 500 MHz for $^1$H and equipped with a 5 mm indirect detection probe with z-axis gradients. The samples were run in CDCl$_3$ without temperature regulation to avoid convection. The temperature was 22 °C. The pulse sequence used was bipolar pulse pair stimulated echo. The gradient strength was arrayed as equally spaced squares over 15 values in
the interval 2-60 Gauss/cm. The gradient duration ($\delta$) was 2 ms and the diffusion delay ($\Delta$) was 200 ms. The spectra were collected with a spectral window from -0.5 to 9.5 ppm in 4 transients and with 8 dummy transients in the beginning, with an acquisition time of 2 s and a relaxation delay of 3 s. The total experiment time was ca. 5 minutes. The data were processed with a line broadening of 2 Hz and baseline correction. Integrals were used for fitting the intensity decay equation and the precision was ca. 1%. Molecular weights and molecular weight distributions were determined via multi-angle laser light scattering size exclusion chromatography (MALS-SEC) in $N,N$-dimethylacetamide (DMAc) with 50 mM LiCl at 50 °C and a flow rate of 1.0 mL/min (Agilent isocratic pump, degasser, and autosampler; ViscoGel I-series 10 $\mu$m guard column and two ViscoGel I-series G3078 mixed bed columns, with molecular weight ranges 0−20×10$^3$ and 0−10×10$^6$ g/mol, respectively). Detection consisted of a Wyatt Optilab T-rEX refractive index detector operating at 658 nm and a Wyatt miniDAWN Treos light scattering detector operating at 659 nm. The system was calibrated using poly(methyl methacrylate) (PMMA) standards with molecular weights ranging from 2.2×10$^3$ to 9.88×10$^5$ g/mol. HRMS was carried out using an Agilent 6220 TOF-MS mass spectrometer in the electrospray ionization (ESI) mode. Transmission Electron Microscopy (TEM): Five microliters of the sample was applied onto a Formvar coated 200-mesh Cu grid that was freshly glow discharged (Pelco easiGlow™, Ted Pella, Inc.). The grid was stained with 2% aqueous uranyl acetate. The grids were observed on a Hitachi H7000 microscope operating at 100 kV. The images were recorded with a slow-scan CCD camera (Veleta 2k × 2k). Dynamic light scattering (DLS) analysis was
conducted at room temperature on a Zetasizer Nano-ZS (Malvern) operating at a wavelength of 633 nm.

3.4.2 Synthesis and Experimental Procedures

3.4.2.1 Synthesis of diacrylate monomer (ACVADA)

4,4′-Azobis(4-cyanovaleric acid) (1.0 g, 3.6 mmol) was suspended in dry dichloromethane (50 mL). 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (2.1 g, 11 mmol) and 4-DMAP (0.13 g, 1.1 mmol) were added to the solution at 0 °C. The mixture was stirred for 0.5 h, followed by slow addition of 2-hydroxyethyl acrylate (0.91 mL, 7.9 mmol) at 0 °C. The reaction was left to stir in an ice bath overnight. After the reaction, the solution was diluted to 100 mL with DCM and sequentially washed with HCl solution (1M), saturated sodium bicarbonate solution (1 M), and brine. Following the wash process, the organic layer was dried over sodium sulfate and concentrated by rotary evaporator. The crude product was further purified by flash chromatography on silica gel with ethyl acetate/ hexane (9:1) to yield the product as colorless viscous oil (0.92 g, 54.1%). $^1$H NMR (500 MHz, CDCl$_3$): δ (ppm) 6.40 (m, 2H), 6.09 (m, 2H), 5.82 (m, 2H), 4.31 (s, 8H), 2.23-2.58 (m, 8H), 1.65 (d, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$): δ (ppm) 171.1, 165.8, 131.5, 127.9, 117.4, 71.9, 62.8, 62.0, 33.1, 29.0, 23.9, 23.7. ESI-HRMS: Calcd for [M+Na]$^+$: 499.1799. Found: 499.1779.

3.4.2.2 Synthesis of thermally-degradable polyazo bearing terminal hydroxyl groups

In a typical polymerization procedure ([HDT]$_0$:[ACVADA]$_0$ feed ratio of 1.16:1), 1,6-hexanedithiol (0.26 mL, 1.7 mmol), and DMPP (1µL) were dissolved in DMAc (2 mL). The solution was placed into an ice bath and purged with N$_2$ for 10 min. Thereafter, ACVADA (0.705 g, 1.48 mmol) in DMAc (0.5 mL) was added dropwise into the solution
while purging with N\textsubscript{2} for another 10 min. The reaction mixture was further stirred at 25 °C for 1 h. After the polymerization, 2-hydroxyethyl acrylate (0.19 mL, 1.7 mmol) and TEA (5 µL) were added to the solution. The reaction was left at 25 °C for 4 h. Polyazo was isolated by precipitating into a large volume of cold methanol. The precipitate was dried under vacuum at room temperature for 24 h.

3.4.2.3 Synthesis of PEG-acrylate

PEG-acrylate of two molecular weights (2000 and 5000 g/mol) was synthesized. In a typical procedure for preparing PEG\textsubscript{44}-acrylate, PEG\textsubscript{44} monomethyl ether (5.0 g, 2.5 mmol) and TEA (1.74 mL, 12.5 mmol) were dissolved in dry THF (100 mL). The solution was then placed into an ice bath and acryloyl chloride (1.02 mL, 12.5 mmol) was added dropwise into the solution. Following the addition, the reaction mixture was left to stir at 25 °C overnight. When the reaction was completed, salt was removed by filtration and THF was removed under vacuum. Then the concentrated residue was dissolved into DCM (50 mL) and washed sequentially with HCl solution (1 M), saturated sodium bicarbonate solution (1 M), and brine. The organic phase was dried over sodium sulfate and then concentrated under vacuum. PEG\textsubscript{44}-acrylate was obtained by precipitating into a large volume of cold diethyl ether. The polymer was dried under vacuum at room temperature for 24 h.

3.4.2.4 Synthesis of triblock copolymers PEG-\textit{b}-polyazo-\textit{b}-PEG

In a typical procedure for the preparation of PEG\textsubscript{44}-\textit{b}-polyazo\textsubscript{6-}\textit{b}-PEG\textsubscript{44}, 1,6-hexanedithiol (0.26 mL, 1.7 mmol) and DMPP (1µL) were dissolved in DMAc (2 mL). The solution was placed into ice bath and purged with N\textsubscript{2} for 10 min. Then ACVADA (0.717 g, 1.50 mmol) in DMAc (0.5 mL) was added dropwise while purging with N\textsubscript{2} for another 10 min. The reaction mixture was further stirred at 25 °C for 1 h. After the
polymerization, PEG$_{44}$-acrylate (1.2 g, 0.61 mmol) and TEA (2 µL) were dissolved into DMAc (1 mL) and then added dropwise to the solution. The reaction was left at 25 °C for 17 h. PEG$_{44}$-b-polyazo-b-PEG$_{44}$ was isolated by precipitating into a large volume of cold diethyl ether. The precipitate was dried under vacuum at room temperature for 24 h.

3.4.2.5 Thermal degradation of polyazo in DMAc
In a typical procedure (degradation in the presence of hydroquinone), polyazo (100 mg) and hydroquinone (21 mg, 0.19 mmol) were dissolved in DMAc (5 mL), and the reaction mixture was heated in an oil bath at predetermined temperatures (60, 80, and 95 °C). Samples were taken periodically, quenched in liquid nitrogen, and immediately analyzed by GPC at predetermined time points.

3.4.2.6 Thermal degradation of PEG$_{44}$-b-polyazo$_{6}$-b-PEG$_{44}$ based micelles in DMAc
PEG$_{44}$-b-polyazo$_{6}$-b-PEG$_{44}$ (20 mg) was dissolved in DMAc (1.6 mL), and the reaction mixture was heated in an oil bath at 95 °C. Samples were taken periodically, quenched in liquid nitrogen, and immediately analyzed by GPC at predetermined time points.

3.4.2.7 Thermal degradation of PEG$_{44}$-b-polyazo$_{6}$-b-PEG$_{44}$ based micelles in water
PEG$_{44}$-b-polyazo$_{6}$-b-PEG$_{44}$ (20 mg) was dissolved in H$_2$O (1.6 mL), and the reaction mixture was heated in an oil bath at 95 °C. Samples were taken periodically, quenched in liquid nitrogen, lyophilized, and analyzed by GPC at predetermined time points.
CHAPTER 4
THERMALLY-LABILE SEGMENTED HYPERBRANCHED COPOLYMERs: USING REVERSIBLE-COVALENT CHEMISTRY TO INVESTIGATE THE MECHANISM OF SELF-CONDENSING VINYL COPOLYMERIZATION

4.1 Overview

Segmented hyperbranched polymers (SHPs),\textsuperscript{138-143} a unique class of polymers with long linear chains between branch points, have received significant interest in polymer science. As compared to highly compact conventional hyperbranched polymers synthesized via $AB_2$ or $A_2 + B_3$ condensation polymerization,\textsuperscript{71, 144-147} the minimized steric hindrance between sparsely-branched backbones offers unique functionalization opportunities not available in densely branched structures. In the last decade, self-condensing vinyl polymerization (SCVP)\textsuperscript{27, 88, 138, 148-155} has emerged as a robust method to prepare hyperbranched vinyl polymers. SCVP relies on the presence of a specific $AB^*$ monomer-initiator combination (\textit{i.e.,} “inimer”). Inimers contain a polymerizable moiety capable of undergoing chain growth polymerization and an initiating moiety that can either initiate new chains or condense with polymerizable groups present on other branched chains it encounters. Therefore, SCVP resembles both chain and step-growth polymerizations. Typically polymers prepared by this method have broad molecular weight distributions and molecular weights that increase dramatically at high monomer conversion. The degree of branching achieved during SCVP can be tuned by also including a conventional comonomer that is only capable of propagation. The resulting segmented hyperbranched polymers demonstrate interesting solution and melt

---

properties and contain a high density of functional groups at their periphery that can be used for subsequent addition of linear chains or functionalization with small molecules.

SCVP has been accomplished by a variety of controlled polymerization methods, including living ionic,\textsuperscript{156} group transfer,\textsuperscript{157,160} and controlled radical polymerization (CRP). Of particular interest are the well-established CRP methods: atom transfer radical polymerization (ATRP),\textsuperscript{161,163} reversible addition-fragmentation chain transfer polymerization (RAFT),\textsuperscript{164,168} and nitroxide-mediated polymerization (NMP).\textsuperscript{169-171} For ATRP-based SCVP, the requisite inimer is a compound that contains a vinyl group for propagation and an activated halogen-containing group for initiation. Because of its well-known controlled polymerization characteristics, ATRP has been suggested to offer exceptional control over the architecture of segmented hyperbranched polymers prepared by SCVP and allows for some degree of control over the linear chain length between branch points through careful modification of the ratio of inimer to comonomer in the feed.\textsuperscript{172}

Assuming that each inimer incorporated into a growing chain during SCVP successfully undergoes initiation, the number and location of branch points in the chain is determined directly by the extent of inimer incorporation. In this case, each branch point would occur along the chain at the site at which the inimer is present. Therefore, incorporating a degradable linkage between the propagating and initiating groups of the inimer should lead to segmented hyperbranched polymers that can degrade into linear polymers upon cleavage of the labile linkage.

The field of dynamic-covalent chemistry has been utilized to prepare a variety of self-repairing polymers containing reversible covalent bonds.\textsuperscript{72,173,174} Compared to
supramolecular interactions, the enhanced strength of reversible covalent bonds offers the opportunity to achieve more stable structures while retaining the advantages of reversibility. To date, dynamic-covalent architectures such as block copolymers,\textsuperscript{112} dendrimers,\textsuperscript{115, 175} stars,\textsuperscript{45-47 30, 31, 118, 176} polymeric networks,\textsuperscript{119, 177-183} and cyclic polymers\textsuperscript{117, 184, 185} have been extensively investigated. Diels-Alder cycloadducts, imines, alkoxyamines, boronic esters, and disulfide linkages are among the moieties commonly exploited in the design of these versatile, functional architectures.

Degradable SHPs synthesized by SCVP have been prepared utilizing degradable inimers bearing disulfide,\textsuperscript{88} ester\textsuperscript{88} or acylal\textsuperscript{186} groups. In response to changing pH or heat, these “smart” segmented hyperbranched polymers could be quantitatively cleaved to linear polymer chains. However, to the best of our knowledge, the reconstruction of degradable SHPs has not been studied. This is likely due to the lack of suitable kinetics for esterification and acylal formation and the lack of selectivity during disulfide formation, the latter of which may lead to undesired gelation rather than the reconstruction of segmented hyperbranched architectures. In our study, we present the synthesis of a novel, thermally reversible ATRP inimer that contains a Diels-Alder linkage between its polymerizable and initiating groups. This inimer was copolymerized with methyl methacrylate (MMA) for the facile preparation of hyperbranched PMMA with predetermined linear segment lengths. Cleavage of the incorporated inimer units upon heating afforded linear PMMA copolymer fragments with narrow dispersity. The reconstruction of hyperbranched PMMA from cleaved linear PMMA was then examined. Additionally, the retained halogen atoms on the chain termini of the hyperbranched PMMA were used to initiate the polymerization of a water-soluble monomer to yield
amphiphilic core-shell hyperbranched-linear copolymers (i.e., “hyper-stars”) through a grafting-from method.

Perhaps most significantly, the labile nature of the Diels-Alder inimer was exploited to “reverse engineer” the segmented hyperbranched polymers to determine the extent to which individual branches grew in the controlled manner expected for ATRP. While SCVP is expected to cause non-linear evolutions of molecular weight with conversion and to generate branched polymers with broad molecular weight distributions, the control afforded by ATRP is assumed to mediate the growth of individual branches. In this study, we triggered the degradation of these segmented hyperbranched copolymers to allow the detailed analysis of their individual linear components. Therefore, the reversibility of the Diels-Alder inimer yielded adaptive/responsive materials while also providing fundamental insight into the mechanism of a widely utilized method of branched polymer synthesis.

### 4.2 Results and Discussions

#### 4.2.1 Preparation of Thermally Reversible Diels-Alder Inimer

Our goal was to prepare segmented hyperbranched polymers capable of dissociating into their individual linear components and undergoing repair during a subsequent reconstruction process. To accomplish this, we synthesized a novel inimer that contained a Diels-Alder adduct between its polymerizable and initiating fragments with the expectation that heating to a temperature which favored the retro-Diels-Alder reaction would lead to cleavage of the branched structure to yield linear polymers. Successful synthesis of the precursor and Diels-Alder inimer were confirmed by $^1$H NMR and $^{13}$C NMR spectroscopy (Figure 4-1 and Figure 4-2). The combination of
extended reaction times (48 h) and relatively high temperatures (75 °C) during the synthesis of the inimer precursor favored the near-quantitative formation of the more thermodynamically stable exo cycloadduct.

Figure 4-1. Synthesis, $^1$H NMR spectrum, and $^{13}$C NMR spectrum of the Diels-Alder inimer.
Figure 4-2. $^1$H NMR, and $^{13}$C NMR of Diels-Alder inimer precursor.

4.2.2 Synthesis and Characterization of Segmented Hyperbranched PMMA

Copolymerization of the Diels-Alder inimer with MMA afforded branched PMMA with degrees of branching (DB) that should depend on the [MMA]:[inimer] ratio. To
determine the temperature at which the polymerizations could be conducted, the thermal stability of the inimer was investigated. No change in the NMR spectra of the inimer was observed after 24 h at 45 °C, suggesting that the retro-Diels-Alder reaction did not occur to an appreciable extent under these conditions. Therefore, 45 °C was chosen as the polymerization temperature for the SCVP of MMA and the newly designed inimer.

To discern the influence of the [monomer] : [CuBr] ratio, two different ratios (40:1 and 100:1) were applied to the copolymerization of MMA and inimer, keeping the initial monomer concentration at a constant value of 5 M in toluene. Table 1 presents the results of these experiments. The overall conversions of vinyl groups rapidly approached 99% within 4 hours at a lower monomer to catalyst ratio (40:1). However, at 100:1 ratio of monomer to catalyst, the monomer conversion only reaches 80% after 20 hours, indicating a slower polymerization process than those at a higher catalyst loading condition. Furthermore, the molecular weight and PDI of the resulting polymers at monomer to catalyst ratio (40:1) were also significantly larger than those at a higher monomer to catalyst ratio (100:1). Those results suggest condensation between low molecular weight macromolecules occurred at higher monomer conversions, resulting in sizable increase in polymer molecular weight and broader distribution of molecular weight. This phenomenon is in accordance with the inherent nature of SCVP.
Table 4-1. Hyperbranched polymers prepared from via SCVP of inimer and MMA.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Feed ratio&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Conversion (%)</th>
<th>Time (h)</th>
<th>(M_n, RI) (g/mol)</th>
<th>(M_W, MALLS) (g/mol)</th>
<th>(D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHB P1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>15</td>
<td>99</td>
<td>4</td>
<td>11 000</td>
<td>120 000</td>
<td>3.62</td>
</tr>
<tr>
<td>SHB P2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>30</td>
<td>99</td>
<td>3</td>
<td>17 000</td>
<td>260 000</td>
<td>4.95</td>
</tr>
<tr>
<td>SHB P3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>60</td>
<td>99</td>
<td>4</td>
<td>36 300</td>
<td>515 000</td>
<td>5.37</td>
</tr>
<tr>
<td>SHB P4&lt;sup&gt;b&lt;/sup&gt;</td>
<td>30</td>
<td>75</td>
<td>20</td>
<td>8 800</td>
<td>23 400</td>
<td>2.33</td>
</tr>
<tr>
<td>SHB P5&lt;sup&gt;b&lt;/sup&gt;</td>
<td>60</td>
<td>80</td>
<td>20</td>
<td>10 700</td>
<td>33 100</td>
<td>1.83</td>
</tr>
</tbody>
</table>

<sup>a</sup> ([MMA]<sub>0</sub> + [inimer]<sub>0</sub>):[CuBr]:[bpy]<sub>0</sub> = 40:1:2, [MMA]<sub>0</sub> = 5 M.  
<sup>b</sup> ([MMA]<sub>0</sub> + [inimer]<sub>0</sub>):[CuBr]:[bpy]<sub>0</sub> = 100:1:2, [MMA]<sub>0</sub> = 5 M.  
<sup>c</sup> Feed ratio represents initial molar ratio of MMA to inimer.

Figure 4-3. Synthesis of segmented hyperbranched PMMA. (a) General protocol for the preparation of segmented hyperbranched PMMA by SCVP; (b) \(^1\)H NMR of SHB P2 (see Table 4-1); (c) Representation of segmented hyperbranched PMMA.

Notably, at monomer to catalyst ratio of 100:1, the conversion only reached 80% after extended reaction times and did not increase significantly after 20 h. This result suggests the catalyst efficiency was diminished, potentially due to the persistent radical
The high ATRP equilibrium constant of 2-haloisobutyrate results in irreversible conversion of activating Cu(I)X to deactivating Cu(II)X. The accumulating Cu(II)X shifts the equilibrium towards the dormant species, reducing the concentration of propagating radicals. Therefore, in the application of SCVP of MMA, a sufficient catalyst loading or addition of a reducing agent (e.g., Cu(0)) is necessary to overcome the PRE and to reach high conversion.

Given that 40:1 was determined as a satisfactory value of monomer to catalyst ratio, three segmented hyperbranched PMMA (SHB P1, SHB P2, and SHB P3) with linear segments between branches of varying lengths were synthesized under these conditions (Table 4-1). Their structures were confirmed by 1H NMR spectroscopy (Figure 4-3). As shown in Table 4-1, molecular weights determined by GPC at 99% conversion increased with the initial feed ratio of monomer to inimer, in accordance with previous reports. The values of the absolute $M_w$ determined for each branched polymer from GPC–MALLS were significantly higher than the corresponding apparent molecular weights determined by conventional calibration with PMMA standards. This well-known phenomenon stems from the compact, globular structure of the hyperbranched polymers as compared to the linear calibration standards.

Degrees of branching of SHB P1-P3 were estimated by 1H NMR based on an equation assuming number of terminal bromide is equal to number of branch point (Equation 4-1), where $A_b$ and $A_g$ are the integrations of bridge-head group on Diels-Alder bond (labeled b in Figure 2) and methoxyl groups on monomer units (labeled g in Figure 4-3).

$$DB = \frac{2A_b}{2A_b + \frac{A_g}{3}}$$  \hspace{1cm} (Equation 4 – 1)
A graph of calculated DB versus feed ratio of monomer to inimer (Figure 4-4) was excellently consistent with theoretical equation proposed by Müller.\textsuperscript{187} It was found higher content of inimer resulted in higher DB values at full monomer conversion (> 99%).

![Graph showing degree of branching versus feed ratio](image)

Figure 4-4. Degree of branching as a function of feed ratio at full monomer conversion (blue circles represent DB values obtained from \textsuperscript{1}H NMR; dot line represent theoretical values of DB).

Table 4-2. Preparation of hyperbranched Inimer/MMA (SHB P3) copolymers and their thermal degradation products (120 °C for 1 h).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Time (h)</th>
<th>Conv. (%)</th>
<th>Before thermal degradation</th>
<th>After thermal degradation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>$M_n$ (g/mol)</td>
<td>$M_w/M_n$</td>
</tr>
<tr>
<td>1</td>
<td>0.5</td>
<td>40</td>
<td>6300</td>
<td>2.13</td>
</tr>
<tr>
<td>2</td>
<td>1.0</td>
<td>56</td>
<td>7100</td>
<td>2.24</td>
</tr>
<tr>
<td>3</td>
<td>2.0</td>
<td>92</td>
<td>11 900</td>
<td>3.71</td>
</tr>
<tr>
<td>4</td>
<td>4.0</td>
<td>99</td>
<td>36 300</td>
<td>5.37</td>
</tr>
</tbody>
</table>

\textsuperscript{a}([MMA]\textsubscript{o} + [inimer]\textsubscript{o}):[CuBr]:[bpy]\textsubscript{o} = 40:1:2, [MMA]\textsubscript{o} = 5 M, [MMA]\textsubscript{o}:[inimer] = 60: 1.

\textsuperscript{b}$M_n$ theo = 60×conversion×$M_{monomer}+M_{inimer}$.
4.2.3 Polymerization Kinetics of ATRP-SCVP of MMA/Inimer

As the discussion above indicates, the commonly accepted mechanism of SCVP would predict that the length of linear PMMA between branches can be controlled by the feed ratio (and relatively reactivities) of MMA and inimer. While the evolution of molecular weight with conversion is expected to be non-linear as a result of the combined step/chain-growth polymerization mechanisms, it reasons that each individual arm of the branched polymer should grow in a manner predicted by the general ATRP process. The presence of degradable linkages at each branched point allowed us to cleave the branched polymers to yield their linear components. We reasoned that analysis of the resulting linear polymers would provide insight into the control achieved during the growth of each individual arm.

To further understand the SCVP mechanism and to investigate the regularity of the linear segments that result, kinetic studies were conducted with an initial monomer to inimer ratio of 60:1 under the aforementioned optimized reaction conditions. At predetermined time points, aliquots were taken from the SCVP reaction solution. The aliquots were divided with one portion being immediately used for \(^1\)H NMR spectroscopy and GPC analysis to obtain information on the intact hyperbranched PMMA. The remaining solution was precipitated into cold methanol to remove residual monomer, dried, redissolved in toluene, and subjected to heating at 120 °C to completely cleave the polymer at its branch points by a retro-Diels-Alder reaction. After 1 h, the reactions were quenched by immersion in liquid nitrogen, and the degraded linear PMMA samples were characterized by GPC.
Figure 4-5. GPC kinetic traces of SHBs before and after thermal cleavage of Diels-Alder bonds. (a) GPC traces as a function of conversion during the SCVP of MMA (top) and the corresponding cleaved linear PMMA after the retro-Diels-Alder reaction at 120 °C (bottom); (b) $M_n$ and PDI of hyperbranched PMMA as a function of monomer conversion during the SCVP of MMA; (c) $M_n$ and PDI of the corresponding cleaved linear PMMA as a function of monomer conversion (dotted line represents theoretical $M_n$).

The results of this kinetic study are summarized in Table 4-2. As shown in Figure 4-5 a and b, the molecular weight and PDI of the intact hyperbranched PMMA grew as a function of time and conversion as expected. At high conversion, a substantial increase in molecular weight of hyperbranched polymers was observed from 11,900 (92%) to 36,300 (99%). Broad molecular weight distributions were observed, with significant multimodality developing as the polymerization proceeds. These observations are consistent with the expected behavior of SCVP. This is likely due to condensation between macromolecules becoming more prominent as the viscosity of the medium increases. However, analysis of the samples that resulted after cleavage of
the hyperbranched polymers yielded results that were indicative of linear polymers with narrow molecular weight distributions. Additionally, across most of the conversion range, the increase in $M_n$ followed the theoretical prediction calculated from [MMA] : [inimer] ratios and conversion. Furthermore, the polydispersity indices of segments remain relatively low (<1.4) up to high monomer conversion (Table 4-2 and Figure 4-5 c). These results suggest the individual branches of polymers made by SCVP grow in a controlled manner, similar to that expected for ATRP with more conventional (i.e., non-inimer) alkyl halide initiators. At very high conversions (>99%), a small high molecular shoulder on the GPC traces of the linear polymer was observed, and there was deviation from the theoretical molecular weight. This observation could result from the highly congested environment of the propagating chain ends late in the polymerization. Just as an increased contribution from termination reactions can be observed at high conversion during conventional ATRP, the same can occur in this case, especially given the high local concentration of chain ends in hyperbranched systems. At high catalyst loadings (40:1), more extensive activation and faster propagation compromised the amount of control normally afforded by ATRP. It is expected that better precision could be achieved by employing lower catalyst concentrations, however, in the case of SCVP, this would lead to a dramatic reduction in monomer conversion and degree of branching. It should be noted that the similar reactivities of monomer and inimer vinyl group in this particular system enhances the regulation of chain growth during SCVP.145
Scheme 4-1. Chain extension of segmented hyperbranched PMMA (SHB P2) with PEGMA.

Figure 4-6. $^1$H NMR spectrum of hyperbranched PMMA-b-Poly(PEGMA) ("hyper-star").
4.2.4 Extension of PEGMA from Hyperbranched PMMA

The ability for chain extension from hyperbranched polymers is intriguing in regards to the preparation of more complex architectures. To confirm the retention of terminal bromide (Br) atoms on the hyperbranched polymers, SHB P2 was used as a multifunctional macroinitiator and was chain extended with PEGMA (60:1 PEGMA : Br; Scheme 4-1) to yield core-shell copolymers with branched PMMA cores and linear poly(PEGMA) shells. After 7 h (34% conversion), the reaction was stopped, and the structure of the “hyper-star” copolymer was verified by $^1$H NMR spectroscopy (Figure 4-6), which indicated peaks characteristic of both PMMA and poly(PEGMA), and GPC, which revealed a reduction in the retention time that was indicative of an increase in molecular weight (Figure 4-7). Unlike the original PMMA-based starting material, the amphiphilic hyper-star could be dispersed in water (a selective solvent). Aqueous solutions of these materials were further characterized by dynamic light scattering (DLS).
and transmission electron microscopy (TEM) (Figure 4-8). DLS offered evidence of self-assembled particles with a hydrodynamic diameter ($D_h$) of 23 nm in neutral water, which was in good agreement with TEM results (21 nm in diameter). Notably, the hydrodynamic radius of the hyper-star in toluene (a non-selective solvent for PMMA and poly(PEGMA)) was only 7 nm, which is a size consistent with that of molecularly dissolved unimers (Figure 4-8 c). Therefore, it seems reasonable that dissolution in water leads to assembly of individual hyper-stars into micellar structures in which an aggregated hydrophobic PMMA core is stabilized by a water-soluble poly(PEGMA) corona. The formation of larger nanostructures indicates that the core of SHB P2 must be sparsely branched to the degree that intermolecular interactions between hyper-star macromolecules are possible (Figure 4-8 a).

Figure 4-8. Characterization of “hyper-star” self-assembly in water. (a) Proposed self-assembly of hyper-stars in water; (b) TEM of hyper-star based micelles cast from aqueous solution; (c) DLS of solutions of the hyper-stars in water (selective solvent) and toluene (non-selective solvent).
Furthermore, the hyper-star was thermally treated at 120 °C in toluene for one hour. A shift to longer retention time was observed by GPC analysis, indicative of degradation and reduced molecular weight (Figure 4-9 a). The results suggest the formation of linear block copolymer PMMA$_{30}$-b-Poly(PEGMA$_{20}$), with a higher molecular weight than the corresponding cleaved PMMA$_{30}$ homopolymer (Figure 4-9 b). The polydispersity of the resultant block copolymers remains as low as 1.42, suggesting relatively controlled chain extension from the SHB P2 core. The lack of a low molecular weight shoulder in the chromatogram reinforces this point, along with providing evidence of high initiation efficiency from the macroinitiator. Therefore, even at high monomer conversion, a significant number of bromide groups are retained during the preparation of hyperbranched PMMA.

![Figure 4-9. GPC traces of “hyper-star” and thermally-cleaved “hyper-star” polymers. (a) GPC traces of hyperbranched PMMA-b-Poly(PEGMA) and thermally cleaved PMMA-b-Poly(PEGMA); (b) GPC traces of linear PMMA-b-Poly(PEGMA) and PMMA cleaved from segmented hyperbranched polymers.](image-url)
4.2.5 Thermal Degradation of Segmented Hyperbranched PMMA

Degradation of the hyperbranched PMMA was studied in more detail to gain insight into the efficiency and kinetics of the thermally driven retro-Diels-Alder reaction (Figure 4-10 a). The degradation of SHB P1-P5 was carried out under heating at 90 or 120 °C. The results were summarized in Table 4-3. $^1$H NMR spectroscopy was employed to observe the degradation process (Figure 4-10 b). After 1 h at 120 °C, complete disappearance of the signals associated with the Diels-Alder adduct was observed, while the signals from the pendant furan and terminal maleimide groups became apparent. This observation is consistent with quantitative cleavage of branching points to result in only linear segments. Accordingly, a shift of the GPC chromatograms to longer retention times occurred within 1 h, with no further differences being observed after extended thermal treatment (Figure 4-10 c). These results suggest the retro-Diels-Alder degradation process is rapid and highly efficient at 120 °C. At the lower temperature of 90 °C, the reversion reaction was significantly slower, which facilitated the monitoring of the degradation process (Figure 4-11 a). The degradation of SHB P1 into its linear segments under 90 °C was monitored by $^1$H NMR and GPC (Figure 4-11 b and 7c).
Figure 4-10. $^1$H NMR spectroscopy and GPC characterization of thermal degradation of SHB. (a) Retro Diels-Alder reaction of SHB P1; (b) 1H NMR before and after thermal treatment of SHB P1; (c) GPC traces before and after thermal treatment of SHB P1 as a function of time.

Table 4-3. Molecular weight characteristics of segmented hyperbranched polymers and their degradation products (120 °C for 1 h).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Before thermo-degradation</th>
<th>After thermo-degradation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GPC</td>
<td>GPC-MALLS</td>
</tr>
<tr>
<td></td>
<td>$M_n$ (g/mol)</td>
<td>$M_w/M_n$</td>
</tr>
<tr>
<td>SHB P1</td>
<td>11 000</td>
<td>3.62</td>
</tr>
<tr>
<td>SHB P2</td>
<td>17 000</td>
<td>4.95</td>
</tr>
<tr>
<td>SHB P3</td>
<td>36 300</td>
<td>5.37</td>
</tr>
<tr>
<td>SHB P4</td>
<td>8 800</td>
<td>2.33</td>
</tr>
<tr>
<td>SHB P5</td>
<td>10 700</td>
<td>1.83</td>
</tr>
</tbody>
</table>
Figure 4-11. Kinetics of degradation of SHB PMMA. (a) Degradation of segmented hyperbranched polymers at 90 °C; (b) GPC traces of samples taken during thermal degradation of SHB P1 at 90 °C; (c) Evolution of absolute $M_w$ and retro-Diels-Alder conversion as a function of reaction time.

Table 4-4. Results from repair of the hyperbranched polymers after heating solutions of the degraded linear polymers at 50 °C for 48 h.

<table>
<thead>
<tr>
<th>Entry</th>
<th>$M_n$ (g/mol)</th>
<th>$M_w/M_n$</th>
<th>$M_n$ (g/mol)</th>
<th>$M_w/M_n$</th>
<th>$M_w$ (g/mol)</th>
<th>Healing efficiency</th>
<th>$\gamma^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>LP1$^a$</td>
<td>3500</td>
<td>1.65</td>
<td>6400</td>
<td>3.03</td>
<td>37300</td>
<td>73%</td>
<td>82%</td>
</tr>
<tr>
<td>LP2$^a$</td>
<td>5600</td>
<td>1.78</td>
<td>9200</td>
<td>3.13</td>
<td>52100</td>
<td>65%</td>
<td>66%</td>
</tr>
<tr>
<td>LP3$^a$</td>
<td>8700</td>
<td>1.73</td>
<td>12000</td>
<td>2.36</td>
<td>39600</td>
<td>48%</td>
<td>35%</td>
</tr>
</tbody>
</table>

$^a$ $\gamma$ represents recovery ratio of degree of branching.
Scheme 4-2. Reformation of hyperbranched PMMA via Diels-Alder cycloaddition of linear PMMA.

GPC traces for samples taken at various extents of reaction during the degradation of SHB P1 at 90 °C offered evidence of degradation, as the molecular weight distributions became more narrow and unimodal and the average molecular weight decreased with time (Figure 4-11 b). Moreover, it was particularly interesting that the progress of the retro-Diels-Alder reaction, as determined by $^1$H NMR spectroscopy, was directly coupled to the reduction in molecular weight determined by GPC (Figure 4-11 c).

The degradation reaction reached a maximum conversion of ~80% after 15 h, after which the equilibrium between cycloaddition and cycloreversion was established with no further reaction being observed.

4.2.6 Thermal Reformation of Segmented Hyperbranched PMMA

Diels-Alder chemistry has been widely employed in the area of self-healing materials due to its frequent classification as a “click” reaction$^{103}$ and its facile reversibility. Taking advantage of these properties, our novel inimer-based hyperbranched polymers were expected to exhibit self-repairing behavior on the molecular scale similar to other Diels-Alder-based bulk polymeric materials.$^{76}$
Thermal reassembly of SHB P1-P3 was investigated by $^1$H NMR spectroscopy using the corresponding cleaved linear polymers (L P1, L P2 and L P3, Table 4-3). The linear polymers were allowed to recombine at 50 °C in toluene (Scheme 4-2). At the onset of the reaction of L P1, no Diels-Alder cycloadduct peaks were observed. As the polymer solution was heated, the Diels-Alder reaction between furan and maleimide proceeded, as evidenced by the gradual growth of peaks at 5.2-5.3 ppm, coinciding with the decrease of maleimide peaks at 6.7 ppm (Figure 4-12 b). After 24 h of heating, 70% of maleimide groups were consumed as determined by $^1$H NMR spectroscopy. However, an additional 24 h of heating only resulted in a 3% increase in conversion, suggesting that equilibrium had been established. Notably, the pattern of cycloadduct signal at 5.2-5.3 ppm slowly shifts from 5.25 ppm to 5.20 ppm, indicating the formation of the favored exo isomer over a long period of heating. Furthermore, the Diels-Alder cycloaddition efficiency was also tested for L P2 and L P3 (Figure 4-12 a). Interestingly, the efficiency of repair was decreased with an increase in linear polymer length, which is likely due to the increased steric hindrance that limits the ability of terminal maleimide and pendant furan groups on long chains to recombine. Concurrently, the concentration of functionality on the polymers decreases as the length of linear segments increases, resulting in lower Diels-Alder reaction rates. Degree of branching of reconstructed SHB P1-P3 (Figure 4-13) was also calculated according to equation 4-1. It was clearly observed that bigger size of segments (i.e. higher feed ratio of monomer to inimer) led to decreased recovery ratio of DB which was defined by the ratio of recovered DB to original DB (Table 4-4).
Figure 4-12. Reconstruction kinetics of thermally-degraded SHB PMMA by $^1$H NMR spectroscopy. (a) Reconstruction kinetics of SHB P1-P3 quantified by $^1$H NMR spectroscopy; (b) $^1$H NMR spectra of SHB P1 during repair at 50 °C. Peak assignments correspond to the proton labels in Scheme 4-2.

Figure 4-13. DB of original segmented hyperbranched polymers and reconstructed hyperbranched polymers.
Figure 4-14. Reconstruction kinetics of thermally-degraded SHB PMMA by GPC. (a) Reconstruction of segmented hyperbranched PMMA at 50 °C; (b) GPC traces of reformed SHB P1 as a function of time during thermal treatment at 50 °C; (c) Evolution of $M_w$, $M_{w,\text{MALLS}}$ and PDI of repaired SHB P1 as a function of time.

In addition, the evolution of molecular weight during the healing reaction was determined by GPC. As the duration of thermal treatment increases, both absolute $M_w$ and PDI of SHB P1 become larger, indicating successful repair of the hyperbranched polymers (Figure 4-14). Although the conversion of the repair reaction reached 73% after 48 h, the ultimate absolute $M_w$ of the reconstructed hyperbranched polymer was significantly lower (37,300 vs. 120,000 g/mol) than that of the original SHB P1 (Table 4-1 and Table 4-4). This result suggests the efficiency of reconstruction process is limited due to the steric hindrance associated with the condensation of linear polymers to reform the crowded, hyperbranched polymer. In some ways, this phenomenon is similar to the reduced efficiency observed during “grafting-to” type reactions of other polymer systems. Low functional group concentration and steric hindrance limits the efficiency of
the polymer-polymer reactions, while the original hyperbranched polymer was formed under SCVP conditions that more closely approximated those of a "grafting-from" process in which low molecular monomers were reacting with growing chains under less sterically demanding conditions.

4.2.7 Mechanism of Degradation and Reconstruction of SHB

To unequivocally demonstrate degradation and reconstruction occurred via Diels-Alder cycloreversion and cycloaddition, respectively, two model reactions were conducted. The first reaction involved quenching the reactive maleimides that should be produced during the retro-Diels-Alder degradation process such that subsequent repair would become impossible (Scheme 4-3).

The repair of hyperbranched PMMA was attempted in the presence of a large excess of a thermally stable dienophile trapping agent. SHB P4 was cleaved at 120 °C in the presence of 9-anthracenemethanol. While this temperature favors cycloreversion for furan-maleimide Diels-Alder adducts, it favors cycloaddition for anthracenes and maleimides. Therefore, the maleimide groups that result from thermal degradation of the hyperbranches should be scavenged by the excess functional anthracene. The resulting “quenched” linear polymers were then thermally held at 50 °C and characterized by GPC as a function of time. As expected, the traces of the “repaired” SHB P4 did not shift to higher molecular weight (Figure 4-15). The absence of reformation under these conditions confirms that the healing mechanism is centered on the furan-maleimide based Diels-Alder reaction.
Scheme 4-3. In-situ retro-Diels-Alder reaction of furan-maleimide based DA bond and formation of anthracene-maleimide linkage at 120 °C.

The second model reaction involved “locking” of the inimer units within the hyperbranched polymers by the addition of a small molecule thiol to the double bond of the substituted cyclohexene Diels-Alder adduct (scheme 4-4). This reaction was expected to consume the double bond required for cycloreversion.\textsuperscript{190, 191} The oxy-norbornene functional group is susceptible to transformation via thiol-ene chemistry, in which thiols add irreversibly across alkenes under UV irradiation. Consumption of the vinyl groups in Diels-Alder linked segmented hyperbranched polymers by 1-thioglycerol prohibits cycloreversion reactions, eliminating degradation of the polymers. After irradiation (365 nm, 100 W, 100 min), \textsuperscript{1}H NMR reveals quantitative consumption of oxy-norbornene protons (a, 6.5 ppm) and –CHO bridge-head protons (b, 5.23 ppm), while new signals corresponding to –CHO protons (d, 4.8 ppm) and saturated methylene protons (c, 2.1 ppm) were also observed (Figure 4-16). The thiol-“locked” SHB P2 was subjected to heating at 120 °C in toluene and the reaction was monitored by GPC (Figure 4-17). As expected, the “locked” branch points were not altered, confirming that the degradation mechanism is centered on the furan-maleimide based retro-DA reaction.
Additionally, thiol-ene based click chemistry may be utilized to attach desired functionalities at branch points within segmented hyperbranched polymers in a modular manner, further extending their versatility and potential applications.

Not only does this reaction help support the proposed Diels-Alder cycloversion process, it also provides a means by which otherwise thermally-labile hyperbranches can be rendered stable.

Scheme 4-4. Thiol-ene reaction between 1-tholglycerol and segmented hyperbranched PMMA.

Figure 4-15. GPC traces of SHB P4, cleaved L P4 in the presence of anthracene methanol and polymers thermally treated at 50 °C for 48 hours.
Figure 4-16. $^1$H NMR of SHB P2 before (bottom) and after (top) radical thiol-ene reaction with 1-thioglycerol.

Figure 4-17. GPC traces of samples taken during thermal treatment of “locked” SHB P2 at 120 °C.
4.3 Conclusions

In summary, novel hydrophobic and amphiphilic dynamic-covalent macromolecular assemblies have been successfully prepared by ATRP-SCVP. Hyperbranched copolymers with thermally-labile furan-maleimide Diels-Alder adduct branch points were readily cleaved at high temperatures and repaired at lower temperatures. This method extends the concept of self-repair from the materials level to the macromolecular scale. Perhaps most importantly, the ease with which the hyperbranched polymers could be efficiently degraded allowed us to examine the resulting linear polymer products to gain insight into the control achieved during the growth of individual branches by SCVP.

4.4 Experimental Section

4.4.1 Materials and Measurements

2-Bromo-2-methyl-propionic acid 2-(2,5-dioxo-2,5-dihydro-pyrrol-1-yl)-ethyl ester was synthesized in a manner derived from previous publications. Methyl methacrylate (MMA, 99%), methacryloyl chloride (97%), furfuryl alcohol (98%), diethyl ether (99.9%), methanol (99.8%), triethylamine (99.5%) and ethanolamine (99.5%) were purchased from VWR. 9-Anthracenemethanol (97%), benzene (98%), furan (>99%), poly(ethylene glycol) methyl ether methacrylate (PEGMA, \( M_n = 500, 99% \)), copper(I) bromide (99%), 2,2'-bipyridine (bpy, 99%), 2-bromoisobutyryl bromide (98%), 1-thioglycerol (98%), 2,2-Dimethoxy-2-phenylacetophenone (DMPA, 97%), 1,4-dioxane and maleic anhydride (99%) were purchased from Sigma-Aldrich and were used as received. Toluene (99.8%, Sigma) was dried over molecular sieves. Tetrahydrofuran (THF, 99.8%, Sigma) was dried over calcium hydride and freshly distilled under reduced pressure. Monomers were passed through basic alumina columns to remove inhibitors.
and acidic impurities prior to polymerization. All other materials were used as received unless otherwise noted. Transmission Electron Microscopy (TEM) Analysis: Five microliters of the sample was applied onto a formvar coated 200-mesh Cu grid that was freshly glow discharged (Pelco easiGlow™, Ted Pella, Inc.). The grids were observed on a Hitachi H7000 microscope operating at 100 kV. The images were recorded with a slow-scan CCD camera (Veleta 2k × 2k). Gel Permeation Chromatography Analysis: Molecular weight and polydispersity were determined by size exclusion chromatography in dimethylacetamide (DMAc) with 50 mM LiCl at 50 °C and a flow rate of 1.0 mL min⁻¹ (Agilent isocratic pump, degasser, and autosampler, columns: PLgel 5 μm guard + two ViscoGel I-series G3078 mixed bed columns: molecular weight range 0–20 × 10³ and 0–100 × 10⁴ g mol⁻¹). Detection consisted of a Wyatt Optilab T-rEX refractive index detector operating at 658 nm and a Wyatt miniDAWN Treos light scattering detector operating at 659 nm. Relative molecular weights were obtained through calibration with poly(methyl methacrylate) (PMMA) standards of molecular weights ranging from 9.88 × 10⁵ to 602 g/mol. Absolute molecular weights and polydispersities were calculated using the Wyatt ASTRA software. DLS: Dynamic light scattering (DLS) analysis was conducted at room temperature on a Zetasizer Nano-ZS (Malvern) operating at a wavelength of 633 nm. NMR Analysis: ¹H NMR and ¹³C NMR spectra were recorded in CDCl₃ or DMSO-d₆ using an Inova 500 MHz spectrometer. High-Resolution Mass Spectrometry (HRMS): HRMS was carried out using a Agilent 6220 TOF-MS mass spectrometer in the direct analysis in real time (DART) mode with the IonSense DART source unless otherwise specified.
4.4.2 Synthesis and Experimental Procedures

4.4.2.1 Synthesis of 2-bromo-2-methyl-propionic acid 2-(1-hydroxymethyl-3, 5-dioxo-10-oxa-4-azatricyclo[5.2.1.02, 6] dec-8-en-4-yl)-ethyl ester

Maleimide initiator 2-bromo-2-methyl-propionic acid 2-(2,5-dioxo-2,5-dihydro-pyrrol-1-yl)-ethyl ester (10.0 g, 34.5 mmol) was suspended in dry benzene (50 mL). Furfuryl alcohol (7.50 mL, 86.3 mmol) was slowly added over 10 min. Following the addition, the reaction mixture was stirred at 75 °C. The reaction was monitored by $^1$H NMR spectroscopy and quenched when the reaction was completed. The solvent was removed by rotary evaporator, and the crude product was purified by flash chromatography on silica gel with ethyl acetate/hexane (8:2) to yield the desired product as a colorless viscous oil (yield: 92%). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ (ppm) 6.50 (m, 2H), 5.20 (s, 1H), 4.29 (m, 2H), 4.03 (s, 2H), 3.78 (m, 2H), 2.94 (dd, 2H), 1.87 (s, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ (ppm) 175.6, 175.5, 171.4, 138.3, 137.0, 91.5, 80.8, 62.1, 60.6, 55.7, 50.1, 48.1, 37.8, 30.6. ESI-HRMS: Calcd for [M+H]$^+$: 388.0390. Found: 388.0396.

4.4.2.2 Synthesis of Diels-Alder inimer 2-bromo-2-methyl-propionic acid 2-(1-methacryloxymethyl-3, 5-dioxo-10-oxa-4-azatricyclo[5.2.1.02, 6] dec-8-en-4-yl)-ethyl ester

Diels-Alder initiator 2-bromo-2-methyl-propionic acid 2-(1-hydroxymethyl-3,5-dioxo-10-oxa-4-azatricyclo[5.2.1.02,6]dec-8-en-4-yl)-ethyl ester (3.35 g, 8.63 mmol) and triethylamine (1.44 mL, 10.4 mmol) were mixed with anhydrous THF (50 mL). Methacryloyl chloride (1.02 mL, 10.4 mmol) was added dropwise to the solution at 0 °C via addition funnel, and the reaction mixture was left to stir overnight. The solution was filtered, and the filtrate was concentrated by rotary evaporator and purified by flash.
chromatography on silica gel with ethyl acetate/hexane (6:4) to yield the desired product as a colorless viscous oil (yield: 42%) \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) (ppm) 6.56 (d, 1H), 6.44(d, 1H), 6.13(s, 1H), 5.60(s, 1H), 5.27 (s, 1H), 4.96(d, 1H), 4.57(d, 1H), 4.31 (m, 2H), 3.75 (m, 2H), 2.98 (dd, 2H), 1.95(s, 3H), 1.90 (s, 6H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) (ppm) 175.3, 173.9, 171.4, 166.7, 137.4, 137.2, 135.7, 126.3, 89.7, 81.0, 62.1, 61.4, 55.7, 50.0, 48.4, 37.8, 30.6, 18.3. ESI-HRMS: Calcd for [M+H]\(^+\): 456.0652. Found: 456.0657.

4.4.2.3 Synthesis of thermally-reversible hyperbranched PMMA

A series of polymerizations at varying initial feed ratios ([MMA]\(_0\):[inimer]\(_0\)) and ([MMA]\(_0\)+[inimer]\(_0\)):[Catalyst] were performed at 45 °C as denoted in Table 1. The initial monomer concentration and inimer mass were kept constant at 5 M and 0.1 g, respectively. In a typical polymerization procedure, inimer (0.10 g, 0.22 mmol), MMA (0.35 mL, 3.3 mmol), toluene (0.21 mL), and 2,2'-bipyridine (26.3 mg, 0.165 mmol) were charged to a 10 mL Schlenk flask equipped with magnetic stir bar. The reaction mixture was degassed by three freeze-pump-thaw cycles, and then copper (I) bromide (12 mg, 0.083 mmol) was quickly added to the mixture followed by two additional freeze-pump-thaw cycles. Subsequently, the Schlenk tube was placed in a preheated oil bath at 45 °C for 4 h, after which time the monomer conversion had reached 99%. The polymer was isolated by exposing the polymerization solution to air, passing it through a short neutral aluminum column to remove residual copper, and then precipitating in cold methanol. The precipitate (HB P1, Table 1) was dried under vacuum at room temperature for 24 h.
4.4.2.4 Extension of PEGMA from hyperbranched PMMA

HB P2 (Table 4-1) was used as macroinitiator for the polymerization of PEGMA at 45 °C ([PEGMA]₀:[macroinitiator]₀ feed ratio of 60:1). In a typical procedure, HB P2 (100 mg, 0.03 mmol Br), PEGMA (0.83 mL, 1.8 mmol), toluene (0.1 mL), and 2, 2’-bipyridine (14 mg, 0.090 mmol) were charged to a 10 mL Schlenk flask equipped with magnetic stir bar. The reaction mixture was degassed by three freeze-pump-thaw cycles, and then copper (I) bromide (6.5 mg, 0.045 mmol) was quickly added to the mixture followed by two additional freeze-pump-thaw cycles. Subsequently, the Schlenk tube was placed in a preheated oil bath at 45 °C for 7 h, after which time the monomer conversion had reached 34%. The polymer was isolated by exposing the polymerization solution to air, passing it through a short neutral aluminum column to remove residual copper, and then precipitating in a large amount of cold diethyl ether. The precipitate was dried under vacuum at room temperature for 24 h.

4.4.2.5 Thermal degradation of Diels-Alder hyperbranched PMMA

In a typical procedure, HB P1 (100 mg) was dissolved in dry toluene (10 mL), and the reaction mixture was subjected to an oil bath at predetermined temperatures of either 90 or 120 °C. Samples were taken periodically, quenched in liquid nitrogen, and immediately analyzed by ¹H NMR spectroscopy and GPC at predetermined time points. The retro-Diels-Alder reaction conversion was determined by comparing the peak areas of the signals at 5.2-5.3 ppm (furfuryl bridgehead) and 6.7 ppm (maleimide vinyl protons).

4.4.2.6 Thermal reconstruction of hyperbranched PMMA

In a typical procedure, L P1 (Table 4-4, 100 mg) was mixed with dry toluene (0.1 mL) in a 1 mL vial. The vial with viscous mixture was placed in a 50 °C oil bath.
Samples were taken, quenched in liquid nitrogen and analyzed by $^1$H NMR and GPC at predetermined time points.

4.4.2.7 Radical thiol-ene click reaction between hyperbranched PMMA and 1-thioglycerol

A Schlenk flask equipped with magnetic stirrer was charged with HB P2 (100 mg, 0.03 mmol DA linkage), 1-thioglycerol (318 mg, 3.0 mmol), DMPA (37 mg, 0.15 mmol) and 1,4-dioxane (2 mL). The reaction mixture was degassed by three successive freeze-pump-thaw cycles, filled with nitrogen and irradiated by a UV lamp at 365 nm at room temperature. After 100 min, the polymer solution was precipitated three times into cold methanol. The final precipitate was dried under vacuum at room temperature for 24 hours.
CHAPTER 5
MACROMOLECULAR METAMORPHOSIS VIA STIMULUS-INDUCED
TRANSFORMATIONS OF POLYMER ARCHITECTURE

5.1 Overview

All lives transform in nature. On an extended timescale this may be referred to as
growth and differentiation or evolution and diversity; however, an abrupt and
conspicuous transformation in physical structure arises via the well-known biological
process of metamorphosis. As structure begets function, these physical transformations elicit behavioral and habitual changes, often driven by specific
environmental conditions. At the molecular level, the concept of structure and function
has been a fundamental tenant driving the development of new synthetic polymers with
controlled architectures over the last 75 years.

Staudinger’s macromolecular hypothesis clearly describes the relationship
between molecular size and properties for synthetic polymers. However, as synthetic
chemists continually seek to prepare new polymers with increased function and
utility, it has become clear that it is not just the size of a polymer that must be
considered, but also its shape. The role of three-dimensional structure is known to
be important for small molecules; the effect of molecular architecture on
macromolecules can be even more significant. The shape of a polymer determines
many of its properties, such as the possibility of entanglement with neighboring
chains, the ability to modify solution rheology/viscosity, or the possibility for self-
assembly into complex nanosized objects.

In most cases, macromolecular topology has been considered a constant, static feature.\textsuperscript{40,201} A polymer is typically synthesized to be linear, branched, hyperbranched, star-like, cyclic, networked, etc. according to its intended application. However, the field of “smart” or stimuli-responsive polymers has brought attention to the benefits of dynamic properties, giving rise to new materials with the ability to adapt their structure, constitution, and reactivity.\textsuperscript{48,202} Currently, most examples of stimuli-responsive polymers rely on simple deviations in polymer size through alterations of chain conformation or changes in polymer-solvent or polymer-polymer interactions. However, the fundamental characteristic of molecular architecture has not been considered a variable because a macromolecule’s topology is typically “locked” by its covalent primary structure. Thus, we asked a few simple questions: what if a responsive polymer was smart enough to change its covalently-dictated shape when triggered by a specific chemical stimulus? Could this lead to a new generation of smart materials where dramatic transformations in properties could be effected by topological conversions? We refer to this type of transformation in covalent polymer architecture from one distinct topology to another as \textit{macromolecular metamorphosis}.

5.2 Results and Discussions

To explore the concept of macromolecular metamorphosis, we first considered several macromolecular topologies that we could envision being interconverted (Figure. 5-1). Of equal importance was the identification of suitable reversible chemistry, as any transformation in covalent architecture would rely on the ability to break and form covalent bonds with specificity. We reasoned that the incorporation of reversible-covalent bonds would allow segments of a polymer to be disconnected and reconnected
to transform its structure and give rise to new functionality with high efficiency.\textsuperscript{72, 79} Du Prez \textit{et al}. have exploited reversible reactions of polymers via an elegant “trans-click” approach that relied on the reversible ligation of individual triazolinedione- and indole-terminated polymers.\textsuperscript{19} The resulting block copolymers were readily cleaved to their homopolymer components at elevated temperatures in the presence of excess 2,4-hexadien-1-ol, which scavenged the triazolinedione-terminated polymer that was liberated. Although this demonstrates the utility of highly efficient, complementary reactions for altering polymer identity, topological transformations of polymer architectures triggered by competitive “unclick” and “click” reactions remain unexplored.
Figure 5-1. Transformation of an amphiphilic block copolymer and segmented hyperbranched polymer into various macromolecular architectures (i.e., hydrophobic block copolymer, comb polymer, and star polymer) via diene displacement reactions. Thermally-induced retro-Diels-Alder (rDA) reaction of amphiphilic block copolymer leads to a furan-terminal polymer and a maleimide-terminal polymer. In the case of segmented hyperbranched polymers, a rDA reaction generates a degraded linear polymer with maleimide end-functionality and furan pendent groups. Incorporation of an anthracene-containing template (i.e., polymer or low molecular weight compound) in the reaction mixture results in formation of the more thermally stable anthracene-maleimide cycloadduct in situ, inducing macromolecular metamorphosis.

The strategy we decided to exploit for transformation of covalent architecture relied on two collaborative reactions in which the reactant from a first, reversible reaction could, upon liberation from the first reaction product, react with a second
compound to give rise to the final desired structure. Diels-Alder (DA) chemistry, involving a [4+2] cycloaddition between a diene and a dienophile, is one of the most commonly employed families of “click” reactions due to its versatile substrate scope, high yields, and atom economy. Moreover, the conditions necessary to induce rDA reactions are in many cases relatively mild, allowing facile access to reversibility across a range of temperatures. In the last decade, DA reactions have been extensively explored in constructing recyclable networks, self-healing materials, and complex polymer architectures. Among the numerous available diene/dienophile combinations, the furan-maleimide (Fur-Mal) DA linkage was appealing for our purposes due to its efficient thermal reversibility. Most Fur-Mal functionalities are effectively joined at ambient to moderate temperatures, while the reverse reaction is favored at higher temperatures. On the other hand, the cycloaddition between Mal and an alternative diene, such as anthracene (Anth), is typically near-quantitative at these elevated temperatures. Thermodynamic selectivity between the formation of a Fur-Mal cycloadduct or its Anth-Mal counterpart suggests that the Anth-Mal formation will be significantly favored. Therefore, we envision that a Fur-Mal adduct could transform under thermodynamic control to the more stable Anth-Mal variant upon the addition of an anthracene-containing molecule. While in principle formation of this adduct can be reversed at very high temperatures or under mechanochemical stress, under most non-extreme conditions this reaction should be considered irreversible. We refer to the combination of competitive in situ retro-DA (rDA)/DA reactions as diene displacement reactions.
5.2.1. Computational Analysis and Model Reactions

Computational analysis (Table 5-1 and 5-2) of the forward and reverse Diels-Alder reactions of N-(2-hydroxyethyl) maleimide (MalOH) with furan (Fur) and 9-anthracenemethanol (AnthOH) reveals the reactions’ energy barriers. Using density functional theory (DFT), it was found that the activation energy (ΔG‡) of the Fur-MalOH cycloreversion reaction (123.1 kJ/mol) was comparable to that of the Anth-MalOH cycloaddition (132.4 kJ/mol). The similar activation energies suggest that in situ formation of Anth-MalOH is possible following cleavage of the Fur-MalOH adduct. Notably, ΔG‡ for the rDA reaction of AnthOH and MalOH exceeds 300 kJ/mol, rendering it thermally stable and essentially irreversible at the elevated temperatures considered (Figure. 5-2 A). In light of the above promising theoretical results, experimental models were tested using two low molecular weight derivatives (Fur-MalOH and AnthOH), as well as a system combining a small molecule (Fur-MalOH) and a functional homopolymer polystyrene (Anth-PS) for diene displacement at 120 °C in toluene. Both diene displacement reactions proceeded smoothly, resulting in the expected Anth-Mal adducts (Figure. 5-2 B and Figures 5-3 to 5-9). The combination of these results with our theoretical rationale supports the use of thermodynamically controlled rDA/DA reaction sequences for effective exchange of polymeric components and concomitant transformations in macromolecular architecture.
Figure 5-2. Theoretical rationalization of \( N \)-(2-hydroxyethyl) maleimide (MalOH) based Diels-Alder reactions and model reactions for diene displacement approach. (A) Gibbs free energy profiles for the Diels-Alder cycloadditions and cycloreversions of MalOH with furan and 9-anthracenemethanol (AnthOH) in toluene (\( \mu \)B97X-D/6-31 g(d); TS: transition state); (B) Diene displacement reactions between the Diels-Alder adduct of furan and MalOH (Fur-MalOH) and Anth-containing compounds (AnthOH and anthracene-terminated polystyrene (Anth-PS)) at 120 ºC. Under the investigated conditions, the retro-Diels-Alder reaction occurs first to yield free MalOH which further reacts with Anth-containing compounds via a second Diels-Alder reaction, resulting in thermally stable products (Anth-MalOH and MalOH-Anth-PS) and the original diene (i.e., furan).
Table 5-1. Summary of energy calculations for the reaction between Furan and MalOH. Geometry optimizations were performed at the B3LYP / 6-31 g(d) level and $\omega$B97X-D / 6-31 g(d) was used for energy computations.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Energy (Hartrees)</th>
<th>$G_{\text{rel}}$ (KJ/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furan</td>
<td>-229.9425648</td>
<td>-</td>
</tr>
<tr>
<td>MalOH</td>
<td>-513.1033930</td>
<td>-</td>
</tr>
<tr>
<td>PRC$^a$ (Furan+MalOH)</td>
<td>-743.0459578</td>
<td>0.0</td>
</tr>
<tr>
<td>TS-Furan-MalOH</td>
<td>-743.0364349</td>
<td>25.0</td>
</tr>
<tr>
<td>Furan-MalOH</td>
<td>-743.0833340</td>
<td>-98.1</td>
</tr>
</tbody>
</table>

$^a$PRC: pre-reactive complex

Table 5-2. Summary of energy calculations for the reaction between AnthOH and MalOH. Geometry optimizations were performed at the B3LYP / 6-31 g(d) level and $\omega$B97X-D / 6-31 g(d) was used for energy computations.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Energy (Hartrees)</th>
<th>$G_{\text{rel}}$ (KJ/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AnthOH</td>
<td>-653.8221496</td>
<td>-</td>
</tr>
<tr>
<td>MalOH</td>
<td>-513.1033930</td>
<td>-</td>
</tr>
<tr>
<td>PRC (AnthOH+MalOH)</td>
<td>-1166.9255426</td>
<td>0.0</td>
</tr>
<tr>
<td>TS-Anth-MalOH</td>
<td>-1166.8750951</td>
<td>132.4</td>
</tr>
<tr>
<td>Anth-MalOH</td>
<td>-1166.9990470</td>
<td>-193.0</td>
</tr>
</tbody>
</table>

Figure 5-3. $^1$H NMR spectroscopy of Anth-MalOH (500 MHz, DMSO-$d_6$).
Figure 5-4. $^{13}$C NMR spectroscopy of Anth-MalOH (125 MHz, DMSO-$d_6$).

Figure 5-5. Fluorescence spectroscopy of model reaction 1. The diminishment of fluorescence intensity of product Anth-MalOH (green) relative to 9-anthracenemethanol (orange) is indicative of full consumption of 9-anthracenemethanol, as anthracene cycloadducts are not fluorescent.
Figure 5-6. High-resolution mass spectrum of Anth-MalOH.

Figure 5-7. Gel permeation chromatography of model reaction 2. A slight shift in the chromatogram of MalOH-Anth-PS (orange) relative to Anth-PS (blue) indicates successful formation of the new cycloadduct. Furthermore, a lack of a high molecular weight shoulder reveals polystyrene dimers are not formed via [4+4] cycloaddition of two anthracene moieties.
Figure 5-8. $^1$H NMR spectrum of MalOH-Anth-PS (500 MHz, CDCl$_3$).

Figure 5-9. Fluorescence spectroscopy of model reaction 2. A lack of fluorescence in the *diene displacement* product MalOH-Anth-PS (green) indicates full formation of the cycloadduct.

5.2.2. Synthesis of P(EG$_{44}$-b-MA$_{19}$) Block Copolymer and Study on Its Thermal Reversibility

Our preliminary explorations of *macromolecular metamorphosis* involved synthesizing a poly(ethylene glycol-*block*-methyl acrylate) (P(EG$_{44}$-b-MA$_{19}$)) amphiphilic
block copolymer containing a central Fur-Mal moiety (Scheme 5-1). First, ring opening of succinic anhydride by PEG_{44} monomethyl ether gave rise to carboxylic acid terminal functional PEG_{44}-COOH, which was confirmed by $^1$H NMR spectroscopy (Figure 5-10). Furthermore, PEG_{44}-COOH was conjugated with Diels-Alder initiator via carbodiimide chemistry. $^1$H NMR spectrum confirmed the structure of PEG Macroinitiator by showing both the signals for PEG_{44}-COOH and Diels-Alder initiator (Figure 5-11). GPC displays a shift to a lower elution time for the PEG Macroinitiator (orange) compared to the PEG_{44} monomethyl ether (blue), indicating successful coupling of the Diels-Alder initiator to the starting polymer (Figure 5-12). Chain extension of PEG Macroinitiator with methyl acrylate then led to the block copolymer via photo-induced ATRP. As shown in Figure 5-13, a shift to lower retention time in GPC indicates a successful chain-extension and the formation of the amphiphilic block copolymer P(EG-b-MA).

Scheme 5-1. Synthetic route to P(EG_{44}-b-MA_{19}).
Figure 5.10. $^1$H NMR spectrum of PEG$_{44}$-COOH (500 MHz, CDCl$_3$).

Figure 5.11. $^1$H NMR spectrum of PEG$_{44}$-Macroinitiator (500 MHz, CDCl$_3$).
To ensure the efficiency of the rDA reaction, degradation of the block copolymer was investigated (Figure 5-14). As the Fur-Mal cycloadduct is located between the two
blocks of this polymer, it was expected that cycloreversion would lead to the formation of Fur-PEG$_{44}$ and Mal-PMA$_{19}$ homopolymers. Complete thermal degradation of P(EG$_{44}$-b-MA$_{19}$) at 120 °C by cycloreversion of the Fur-Mal linkage was confirmed by $^1$H NMR spectroscopy. Upon heating at 120 °C for 48 h, a shift of the -CH=O (b) proton from 5.25 ppm to ~6.5 ppm coincides with a shift from the maleimido bridgehead proton (d, 3.0 ppm) to its sp$^2$ maleimide counterpart (d’, 6.7 ppm), indicating formation of the maleimide and furan based cycloreversion products (Figure 5-15). Moreover, degradation of the thermally-labile P(EG-b-MA) block copolymer (blue) led to the appearance of a bimodal chromatogram in GPC, indicative of the formation of the two homopolymers, Fur-PEG and Mal-PMA (orange) (Figure 5-16). The chromatogram of the PEG-Macroinitiator (green) is overlaid for clarity.

Figure 5-14. Various reaction pathways of thermally-reversible amphiphilic block copolymer. Amphiphilic block copolymer (i) degradation via cycloreversion of P(EG$_{44}$-b-MA$_{19}$) to corresponding Fur-PEG$_{44}$ and Mal-PMA$_{19}$ homopolymers, (ii) partial reformation of P(EG$_{44}$-b-MA$_{19}$), and (iii) metamorphosis into hydrophobic block copolymer upon template exchange via diene displacement reaction.
Figure 5-15. $^1$H NMR spectra of P(EG-b-MA) (blue) and its degradation products (orange).

Figure 5-16. Gel permeation chromatograms of P(EG-b-MA) and its degradation products.

Additionally, thermal reformation of the degraded block copolymer was examined by heating the degraded components to 60 °C, which resulted in a mixture of the
reformed block copolymer $\text{P(EG}_{44}\text{-}b\text{-MA}_{19})$ and the residual Fur-PEG$_{44}$ and Mal-PMA$_{19}$ homopolymers. Following heating of a solution of the two functional homopolymers, a mixture of products is observed according to $^1$H NMR spectra (Figure 5-17).

Cycloaddition of maleimide ($d'$) and furan ($a'$-$c'$) yields the original block copolymer ($a$-$d$). Under these conditions, both the *endo* and *exo* adducts are formed, leading to extra resonances in the NMR spectrum. The extent of reformation efficiency reaches 50% after 24 h, in agreement with previously reported data.$^{112}$

Figure 5-17. $^1$H NMR spectrum of reformed P(EG-$b$-MA) block copolymer.
Scheme 5-2. Synthesis of anthracene-containing templates including Anth-PS$_{75}$ (A), P(S$_{58}$-co-CMS$_{14}$-co-AnthMS$_{13}$) (B), and Anth$_3$ (C).

5.2.3. Synthesis of Anthracene-Containing Templates

Following the scission of amphiphilic P(EG$_{44}$-b-MA$_{19}$) (vide supra), we postulated that the resulting dienophile-containing polymer (i.e., Mal-PMA$_{19}$) was able to efficiently conjugate in situ with a template containing anthracene functionality (Figure 5-14). Therefore, relying on the versatility of controlled radical polymerization techniques, we prepared three anthracene-based templates that would dictate the final dienophile-containing polymer architectures (Scheme 5-2).

A chain-end functional homopolymer polystyrene (Anth-PS$_{75}$) was prepared by ATRP of styrene using an anthracene functional initiator (AMBIB). The structure of AMBIB was confirmed by $^1$H and $^{13}$C NMR spectroscopy (Figures 5-18 and 5-19).
Figure 5-18. $^1$H NMR spectrum of AMBIB (500 MHz, CDCl$_3$).
Figure 5-19. $^{13}$C NMR spectrum of AMBIG (125 MHz, CDCl$_3$).

A styrenic polymer containing pendent anthracene moieties was prepared by nitrooxide-mediated polymerization of styrene and $p$-chloromethylstyrene (CMS), followed by post-polymerization modification with 9-anthracenemethanol. The resulting Anth-containing copolymer (P(S$_{58}$-co-CMS$_{14}$-co-AnthMS$_{13}$)) was analyzed by $^1$H NMR spectroscopy. As shown in Figure 5-20, following etherification of the CMS units with 9-anthracenemethanol, new resonances corresponding to the anthracenyl (7.5-8.5 ppm) and methylene (5.4 ppm) protons are present in the $^1$H NMR spectrum. GPC further proved successful post-polymerization functionalization. A comparison of the chromatograms of poly(styrene-co-chloromethylstyrene) (P(S-co-CMS)) (blue) and P(S-co-CMS-co-AnthMS) (orange) displays a clear shift to lower retention times in the functionalized product, indicative of the formation of a higher molecular weight polymer (Figure 5-21).
Figure 5-20. $^1$H NMR spectrum of P(S-co-CMS-co-AnthMS) (500 MHz, CDCl$_3$).

Figure 5-21. Gel permeation chromatography of functionalization of P(S-co-CMS) with 9-anthracenemethanol.
A symmetric tris-anthracene core reagent (Anth\(_3\)) was generated by esterification of 9-anthracenemethanol with 1,3,5-benzenetricarbonyl trichloride. The structure of Anth\(_3\) was confirmed by \(^1\)H and \(^{13}\)C NMR spectra (Figures 5-22 and 5-23).

![\(^1\)H NMR spectrum of Anth\(_3\) (500 MHz, CDCl\(_3\)).](image1)

![\(^{13}\)C NMR spectrum of Anth\(_3\) (500 MHz, CDCl\(_3\)).](image2)
5.2.4. Macromolecular Metamorphosis

In each example, stoichiometric equality of Fur-Mal DA linkages and Anth functionalities was employed. The substrates were mixed in toluene and refluxed for 48 h in the dark. Under these conditions, the thermally-labile Fur-Mal linkage was cleaved to liberate maleimide end groups that formed the thermodynamically preferred Diels-Alder linkages with the Anth template. The resulting macromolecular architectures contain a central Anth-Mal cycloadduct that is thermally stable at 120 °C. Characterization of the polymers before and after transformation using NMR spectroscopy, fluorescence spectroscopy, and GPC depicts clean and efficient transformations from the Fur-template (i.e., amphiphilic block copolymer) to the Anth-templates (i.e., hydrophobic block copolymer, comb copolymer or star polymer).

Exchange of the original Fur-template with the Anth-PS should then elicit “amphiphilic block copolymer to hydrophobic block copolymer” metamorphosis (Figure 5-14 and Figures 5-24 to 5-27 and Table 5-3). Following the diene displacement reaction of P(EG-b-MA) (blue) with Anth-PS (orange), a clean shift in the gel permeation chromatogram to shorter elution times is indicative of efficient formation of the hydrophobic block copolymer P(S-b-MA) (green) (Figure 5-24). Furthermore, the fluorescence intensity attributed to anthracene disappears, indicating the complete cycloaddition between anthracene and maleimide (Figure 5-25). $^1$H NMR spectroscopy displays a disappearance of the resonances corresponding to the Fur-Mal adduct in P(EG-b-MA) (blue) as well as the aromatic protons of Anth-PS (orange). Furthermore, the presence of the Anth-Mal bridgehead protons as well as PS and PMA repeat units in the purified product (green) indicates the formation of the P(S-b-MA) block copolymer (Figure 5-26).
Table 5-3. Metamorphosis from amphiphilic to hydrophobic: polymer information.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Topology</th>
<th>$M_n,_{\text{NMR}}$ (g/mol)</th>
<th>$M_n,_{\text{MALLS}}$ (g/mol)</th>
<th>$D$</th>
<th>$D \times 10^{-6}$ cm$^2$/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEG$_{44}$</td>
<td>Linear homopolymer</td>
<td>2 200</td>
<td>2 500</td>
<td>1.05</td>
<td>N/A</td>
</tr>
<tr>
<td>P(EG$<em>{44}$-b-MA$</em>{19}$)</td>
<td>Linear block</td>
<td>4 390</td>
<td>4 100</td>
<td>1.26</td>
<td>2.81</td>
</tr>
<tr>
<td>Anth-PS$_{75}$</td>
<td>Linear homopolymer</td>
<td>8 150</td>
<td>7 990</td>
<td>1.08</td>
<td>2.57</td>
</tr>
<tr>
<td>P(S$<em>{75}$-b-MA$</em>{19}$)</td>
<td>Linear block</td>
<td>9 900</td>
<td>9 820</td>
<td>1.19</td>
<td>1.80</td>
</tr>
</tbody>
</table>

Figure 5-24. Gel permeation chromatography of metamorphosis from amphiphilic to hydrophobic.
Figure 5-25. Fluorescence spectroscopy of metamorphosis from amphiphilic to hydrophobic.

Figure 5-26. $^1$H NMR spectroscopy of metamorphosis from amphiphilic to hydrophobic.

The diffusion ordered NMR spectroscopy (DOSY) spectra clearly display a slower diffusion coefficient for the final product, P(S-b-MA) (green), than for either of the starting polymers (P(EG-b-MA), blue and Anth-PS, orange). Moreover, the signals
corresponding to the PS and PMA regions in the product maintain the same diffusion coefficient, evident of their covalent attachment following metamorphosis (Figure 5-27).

Figure 5-27. DOSY NMR of metamorphosis from amphiphilic to hydrophobic.

Next, “amphiphilic block copolymer to comb copolymer” metamorphosis was performed (Figure 5-28 and 5-29 and Table 5-4). ^1H NMR spectra of the transformation from block copolymer P(EG_{44}-b-MA_{19}) to comb polymer (P(S_{58}-co-CMS_{14}-co-(AnthMS-g-MA)_{13})) (Figure 5-28 A) show complete disappearance of anthracene signals (orange, 7.3-8.5 ppm) and Fur-Mal resonances (blue, 5.2-5.3 ppm). The appearance of Anth-Mal bridgehead protons in the spectrum of the final polymer (green, 3.25 and 4.75 ppm) further supports a successful transformation. To verify the topology and purity of the comb polymer, diffusion ordered NMR spectroscopy was utilized (Figure 5-28 B). Polystyrene and PMA regions share the same diffusion coefficient, demonstrating PMA side chains are chemically bound to the polystyrene backbone rather than being
physically mixed. Moreover, the diffusion coefficient of the comb polymer is lower than those of the starting polymers (i.e., P(EG\textsubscript{44}-b-MA\textsubscript{19}) and P(S\textsubscript{58}-co-CMS\textsubscript{14}-co-AnthMS\textsubscript{13})), indicative of a larger hydrodynamic radius for the comb polymer. Those diffusion coefficients are in good agreement with the ordering of molecular weights (Table 5-4).

Additionally, GPC displays a shift to a higher molecular weight, corresponding to grafting of Mal-PMA\textsubscript{19} chains to each anthracene unit (Figure 5-28 C), and full disappearance of the fluorescence associated with free anthracene moieties is observed (Figure 5-28 D). Residual Fur-PEG\textsubscript{44} was readily removed by precipitation into methanol, and confirmed by its disappearance in the GPC trace as well as its signals in the \textsuperscript{1}H NMR spectrum (Figure 5-28 A and 5-29). These results demonstrate the robust and efficient nature of \textit{diene displacement}, even under sterically congested conditions.

Table 5-4. Metamorphosis from block to comb: polymer information.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Topology</th>
<th>(M_n), NMR (g/mol)</th>
<th>(M_n), MALLS (g/mol)</th>
<th>(D)</th>
<th>(D \times 10^6) cm(^2)/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>P(EG\textsubscript{44}-b-MA\textsubscript{19})</td>
<td>Linear homopolymer</td>
<td>4 390</td>
<td>4 100</td>
<td>1.26</td>
<td>2.81</td>
</tr>
<tr>
<td>P(S\textsubscript{58}-co-CMS\textsubscript{27})</td>
<td>Linear copolymer</td>
<td>10 420</td>
<td>12 700</td>
<td>1.10</td>
<td>N/A</td>
</tr>
<tr>
<td>P(S\textsubscript{58}-co-CMS\textsubscript{14}-co-AnthMS\textsubscript{13})</td>
<td>Linear copolymer</td>
<td>12 660</td>
<td>15 200</td>
<td>1.18</td>
<td>1.49</td>
</tr>
<tr>
<td>P(S\textsubscript{58}-co-CMS\textsubscript{14}-co-AnthMS\textsubscript{13}-g-MA\textsubscript{19})</td>
<td>Comb</td>
<td>28 640</td>
<td>31 100</td>
<td>1.36</td>
<td>1.05</td>
</tr>
</tbody>
</table>
Figure 5-28. Topological transformation from linear amphiphilic block copolymer to comb copolymer. (A) $^1$H NMR spectrum shows anthracene signals (7.3-8.5 ppm, orange) and Fur-Mal peaks (5.2-5.3 ppm, blue) were no longer present in the product (green). New resonances attributed to the bridgehead protons of the Anth-Mal adduct are visible at 3.25 ppm and 4.75 ppm; (B) DOSY NMR spectra; (C) GPC displays a shift in molecular weight correlating to grafting of Mal-PMA$_{19}$ chains to each anthracene unit; (D) Lack of fluorescence emission of the resulting polymer (green) further supports consumption of Anth by efficient conjugation via formation of Anth-Mal linkages.
We further explored the topological transformation from amphiphilic block copolymer to star polymer (Figures 5-30 to 5-35 and Table 5-5). Upon the transformation, a shift in the gel permeation chromatogram to lower retention time from P(EG-b-MA) (blue) to the PMA star polymer (green) indicates the formation of a higher molecular weight polymer. Furthermore, the molecular weight of the star polymer ($M_{n,GPC-MALLS} = 5.6$ kg/mol) is approximately three times that of the PMA block ($M_{n,GPC-MALLS} = 1.9$ kg/mol), corresponding to the attachment of three PMA arms to the trifunctional aromatic core. The small peak at 14 minutes in the star polymer chromatogram may be attributed to a low degree of anthracene-anthracene dimer formation.
formation between Anth₃ core reagents, leading to polymers with higher-than-expected molecular weights (Figure 5-30).

Figure 5-30. Gel permeation chromatography of metamorphosis from block to star.

Table 5-5. Metamorphosis from block to star: polymer information.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Topology</th>
<th>(M_n, \text{NMR} ) (g/mol)</th>
<th>(M_n, \text{MALLS} ) (g/mol)</th>
<th>(D )</th>
<th>(D \times 10^6 \text{ cm}^2/\text{s} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>P(EG₄₄-b-MA₁₉)</td>
<td>Linear block</td>
<td>4 390</td>
<td>4 100</td>
<td>1.26</td>
<td>2.81</td>
</tr>
<tr>
<td>Anth₃</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>9.24</td>
</tr>
<tr>
<td>(PMA₁₉)₃</td>
<td>Star</td>
<td>6 450</td>
<td>5 630</td>
<td>1.30</td>
<td>2.64</td>
</tr>
<tr>
<td>PMA₆₂</td>
<td>Linear homopolymer</td>
<td>N/A</td>
<td>5 350</td>
<td>1.06</td>
<td>2.29</td>
</tr>
</tbody>
</table>

In addition, following metamorphosis from linear to star, the fluorescence intensity attributed to anthracene disappears, indicating the complete cycloaddition between anthracene and maleimide (Figure 5-31). In \(^1\text{H} \) NMR spectra, a lack of signals corresponding to anthracenyl protons (7.3-8.5 ppm, f-j) is observed. Furthermore, resonances attributed to cycloadducts of Anth₃ and Mal-PMA₁₉ are visible, indicating complete conjugation of PMA arms to the Anth₃ core (Figure 5-32).
Figure 5-31. Fluorescence spectroscopy of metamorphosis from block to star.

Figure 5-32. $^1$H NMR spectroscopy of metamorphosis from block to star.

The measured diffusion coefficient for the PMA$_3$ star (green) is lower than that of both starting materials (P(EG-b-MA), blue and Anth$_3$, orange), indicative of a higher
molecular weight species. Moreover, the signals for the aromatic core align with the polymeric signals, indicative of covalent attachment (Figure 5-33).

Figure 5-33. DOSY NMR of metamorphosis from block to star.

A comparison of linear PMA (green, $M_n$,GPC-MALLS=5.35 kg/mol) and PMA$_3$ star (blue, $M_n$,GPC-MALLS=5.63 kg/mol) shows a clear difference in the elution times (Figure 5-34). If both PMA polymers were of the same architecture, it would be expected that the larger molecular weight polymer would elute first; however, as star polymers have a smaller hydrodynamic volume than their linear counterparts, it elutes later in the gel permeation chromatogram. The small peak at 14 minutes in the star polymer chromatogram may be attributed to a low degree of anthracene-anthracene dimer formation between Anth$_3$ core reagents, leading to polymers with higher-than-expected molecular weights. The diffusion coefficient for the PMA$_3$ star polymer (green, $M_n$,GPC-.
$M_{\text{ALLS}}=5.63 \text{ kg/mol}$ is higher than that of the linear PMA analogue (orange, $M_{n,\text{GPC-MALLS}}=5.35 \text{ kg/mol}$), indicating a smaller hydrodynamic volume of the star polymer relative to its linear counterpart (Figure 5-35).

Figure 5-34. Comparison of gel permeation chromatograms of star and linear poly(methyl acrylate).
Figure 5-35. Comparison of DOSY spectra of star and linear poly(methyl acrylate).

As a second example of *macromolecular metamorphosis*, a segmented hyperbranched poly(methyl methacrylate) (SHB PMMA\textsubscript{15}) with Fur-Mal branch points served as the initial Fur-template. The hyperbranched PMMA was synthesized by self-condensing vinyl polymerization, according to our reported procedure.\textsuperscript{26} In our previous work, we demonstrated that Fur-Mal based SHB PMMA polymers are capable of degrading into linear PMMA segments with terminal maleimide and pendent furan functionalities. Therefore, we envisioned that cleaved maleimide terminated PMMA\textsubscript{15} could further react with polymers containing anthracene moieties. To accomplish topological transformations of hyperbranched polymers, SHB PMMA\textsubscript{15} was treated under *diene displacement* conditions with either the aforementioned Anth-PS\textsubscript{75} or P(S\textsubscript{58}-co-CMS\textsubscript{14}-co-AnMS\textsubscript{13}). The resulting block and comb copolymers were then examined.
in detail using $^1$H and DOSY NMR spectroscopy, fluorescence spectroscopy, and GPC. According to criteria discussed for the previous example, the results revealed successful *macromolecular metamorphosis* from “hyperbranched to block” (Figures 5-36 and 5-37 and Table 5-6) and “hyperbranched to comb” (Figures 5-38 and 5-39 and Table 5-7).

![Characterizations of metamorphosis from hyperbranched to block.](Image)

**Figure 5-36.** Characterizations of metamorphosis from hyperbranched to block. (A) Gel permeation chromatography of metamorphosis from hyperbranched to block; (B) Fluorescence spectroscopy of metamorphosis from hyperbranched to block; (C) $^1$H NMR spectroscopy of metamorphosis from hyperbranched to block.
Figure 5-37. DOSY NMR of metamorphosis from hyperbranched to block. The block copolymer P(S-b-MMA) (green) diffuses slower than either of the starting materials. Furthermore, the signals attributed to PS and PMMA, as well as the bridgehead protons share a common diffusion coefficient, indicating covalent attachment.

Table 5-6. Metamorphosis from Hyperbranched to Block: Polymer Information.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Topology</th>
<th>$M_{n, \text{NMR}}$ (g/mol)</th>
<th>$M_{n, \text{MALLS}}$ (g/mol)</th>
<th>$D$ (cm$^2$/s)</th>
<th>$D$ ($\times 10^{-6}$ cm$^2$/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHB PMMA$_{15}$</td>
<td>Hyperbranched</td>
<td>N/A</td>
<td>16 400</td>
<td>2.10</td>
<td>2.62</td>
</tr>
<tr>
<td>Mal-PMMA$_{15}$</td>
<td>Linear homopolymer</td>
<td>1 790</td>
<td>1 480</td>
<td>1.07</td>
<td>N/A</td>
</tr>
<tr>
<td>Anth-PS$_{75}$</td>
<td>Linear homopolymer</td>
<td>8 150</td>
<td>7 990</td>
<td>1.08</td>
<td>2.57</td>
</tr>
<tr>
<td>P(S$<em>{75}$-b-MMA$</em>{15}$)</td>
<td>Linear block</td>
<td>9 120</td>
<td>9 700</td>
<td>1.09</td>
<td>2.12</td>
</tr>
</tbody>
</table>
Figure 5-38. Characterizations of metamorphosis from hyperbranched to comb. (A) Gel permeation chromatography of metamorphosis from hyperbranched to comb; (B) Fluorescence spectroscopy of metamorphosis from hyperbranched to comb; (C) $^1$H NMR spectroscopy of metamorphosis from hyperbranched to comb.

Table 5-7. Metamorphosis from hyperbranched to comb: polymer information.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Topology</th>
<th>$M_n$, NMR (g/mol)</th>
<th>$M_n$, MALLS (g/mol)</th>
<th>$D$ ($\times 10^6$ cm$^2$/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHB PMMA$_{15}$</td>
<td>Segmented Hyperbranched</td>
<td>N/A</td>
<td>16 400</td>
<td>2.10</td>
</tr>
<tr>
<td>Mal-PMMA$_{15}$</td>
<td>Linear homopolymer</td>
<td>1 790</td>
<td>1 480</td>
<td>1.07</td>
</tr>
<tr>
<td>P(S$<em>{58}$-co-CMS$</em>{14}$-co-AnthMS$_{13}$)</td>
<td>Linear copolymer</td>
<td>12 660</td>
<td>15 200</td>
<td>1.18</td>
</tr>
<tr>
<td>P(S$<em>{58}$-co-CMS$</em>{14}$-co-(AnthMS$<em>{13}$-g-MMA$</em>{15}$))</td>
<td>Comb</td>
<td>26 400</td>
<td>24 300</td>
<td>1.27</td>
</tr>
</tbody>
</table>
5.3 Conclusions

In summary, we have presented several examples of *macromolecular metamorphosis*, a robust method of rendering macromolecular architecture (a polymer property that is typically considered constant) dynamic and transformable through the application of a proper stimulus. Through the combination of simple reactions that are competitively under kinetic and thermodynamic control, macromolecular architecture can be preordained to transform when triggered and to potentially be accompanied by dramatic transformations in materials properties. The specific combination of rDA
“unclick” and DA “click” reactions have been exploited here to effect these architectural transitions, but a wide variety of other reactions can be envisioned to bring about similar phenomena. These transformations may be carried out using any cooperative functionalities in which a compound generated by the first reaction efficiently proceeds via a second reaction pathway to provide the desired product. Given the widespread application of traditional stimuli-responsive materials in current medicine, biology, and manufacturing, we believe that the ability of a macromolecule to morph its entire structure and shape will give rise to an unprecedented class of materials with unique properties and applications. Many physical and morphological properties are governed by topology (e.g., crystallinity, mechanical strength, etc.), thus, macromolecular metamorphosis can lead to dramatic changes in polymer properties without alteration of the chemical composition.

5.4 Experimental Section

5.4.1 Materials and Measurements

9-Anthracenemethyl-2-bromoisobutyrate\(^2\)\(^{12}\) (AMBIB), 1-(2-hydroxyethyl)-1H-pyrrole-2,5-dione\(^1\)\(^{12}\) (Fur-MalOH), 2,3-dihydroxypropyl 2-bromoisobutyrate\(^2\)\(^{13}\), and tris[2-dimethylamino)ethyl]amine\(^2\)\(^{14}\) (Me\(_6\)TREN) were synthesized according to literature methods. All chemicals were used as received unless otherwise noted. Monomers were passed through a column of basic alumina to remove inhibitors and acidic impurities prior to polymerization. CuBr (98%, Sigma) was stirred with glacial acetic acid, rinsed with methanol, and dried prior to use. Poly(ethylene glycol) monomethyl ether (\(M_n = 2\) kg/mol), succinic anhydride (>99%), \textit{tris}-(2-aminoethyl)amine (TREN, 96%), formic acid (>95%), formaldehyde (37 wt% in water), 9-anthracenemethanol (97%), \(\alpha\)-bromoiso\-butyryl bromide (98%), 2,2,6,6-tetramethyl-1-piperidinoxy (TEMPO, 98%), \(p\)-
chloromethylstyrene (90%), benzoyl peroxide (>98%), sodium hydride (60% dispersion in mineral oil), and 1,3,5-benzenetricarbonyl trichloride (98%) were purchased from Sigma-Aldrich. Styrene (99%), N,N,N′,N′,N′′-pentamethyldiethylenetriamine (PMDETA, 99%), 9-(chloromethyl)anthracene (>98%), methyl methacrylate (99%), tetrabutylammonium chloride (95%), and 4-dimethylaminopyridine (98%) were purchased from Acros Organics. Triethylamine (>99%), methyl acrylate (99%), furan (99%), and CuBr₂ (99%) were purchased from Alfa Aesar. Sodium hydroxide was purchased from Fisher Scientific. 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC•HCl, >98%) was purchased from TCI. ¹H and ¹³C NMR spectra were recorded in CDCl₃ and DMSO-d₆ using an Inova 500 MHz spectrometer at 25 °C. DOSY experiments were run on a Varian Inova spectrometer operating at 500 MHz for ¹H and equipped with a 5 mm indirect detection probe with z-axis gradients. The samples were run in CDCl₃ without temperature regulation to avoid convection. The temperature was 22 °C. The pulse sequence used was bipolar pulse pair stimulated echo. The gradient strength was arrayed as equally spaced squares over 15 values in the interval 2-60 Gauss/cm. The gradient duration (δ) was 2 ms and the diffusion delay (Δ) was 200 ms. The spectra were collected with a spectral window from -0.5 to 9.5 ppm in 4 transients and with 8 dummy transients in the beginning, with an acquisition time of 2 s and a relaxation delay of 3 s. The total experiment time was ca. 5 minutes. The data were processed with a line broadening of 2 Hz and baseline correction. Integrals were used for fitting the intensity decay equation and the precision was ca. 1%. Molecular weight and polydispersity were determined by gel permeation chromatography in N,N-dimethylacetamide (DMAc) with 50 mM LiCl at 50 °C and a flow
rate of 1.0 mL min\(^{-1}\) (Agilent isocratic pump, degasser, and autosampler, columns: Viscogel I-series 10 μm guard + two ViscoGel I-series G3078 mixed bed columns: molecular weight range \(0 \sim 20 \times 10^3\) and \(0 \sim 100 \times 10^4\) g mol\(^{-1}\)). Detection consisted of a Wyatt Optilab T-rEX refractive index detector operating at 658 nm and a Wyatt miniDAWN Treos light scattering detector operating at 659 nm. The system was calibrated using 10 poly(methyl methacrylate) (PMMA) standards from \(9.88 \times 10^5\) to 602 g/mol. Absolute molecular weights and polydispersities were calculated using the Wyatt ASTRA software with \(dn/dc\) values determined by assuming 100% mass recovery during GPC analysis. 

**Fluorescence Spectroscopy:** All measurements were taken using a Molecular Devices SpectraMax M2 Multimode Microplate Reader at 25 °C. 

Fluorescence measurements were conducted with 150 μL of sample on black 96-well polypropylene microplates (Greiner Bio-One) with an excitation wavelength of 360 nm. HRMS was carried out using an Agilent 6220 TOF-MS mass spectrometer in the electrospray ionization (ESI) mode.

Density functional theory (DFT) calculations were performed using Spartan '14.\(^{215}\) Geometry optimizations of reactants, products, and transition states were performed at the B3LYP/6-31 g(d) level of theory.\(^{216, 217}\) The conventional B3LYP functional has been proven to generate adequate geometries but performs poorly in energy calculations.\(^{79, 218}\) Therefore, the energies were refined with \(\omega\) B97X-D functional including dispersion corrections\(^{219}\) and a 6-31 g(d) basis set. The activation energies of Diels-Alder reactions have been estimated as the energy difference between the total energy of the transition state and the energy of the isolated reactants. The energies of all compounds and transition states are summarized in Table 5-1 and 5-2.
5.4.2 Synthesis and Experimental Procedures

5.4.2.1 Macromolecular metamorphosis: general procedure

Furan-maleimide containing polymer (1 eq. maleimide) and anthracene containing polymer/small molecule (1 eq. anthracene) were dissolved in toluene (5 mL) and heated at 120 °C for 48 h. The reaction mixture was precipitated into an excess of cold methanol (×3).

5.4.2.2 Model reaction 1: metamorphosis from Fur-MalOH to Anth-MalOH

Fur-MalOH (0.10 g, 0.48 mmol) and 9-anthracenemethanol (99 mg, 0.48 mmol) were mixed in toluene (5 mL) and heated at 120 °C for 24 h. Upon cooling, the product was collected as a white precipitate and dried. $^1$H NMR (500 MHz, DMSO-$d_6$): δ (ppm) 7.68 (d, 1H); 7.44 (d, 1H); 7.17 (m, 6H); 5.33 (t, 1H); 4.85 (m, 2H); 4.70 (s, 1H); 4.60 (t, 1H); 3.26 (s, 2H); 3.01 (t, 2H); 2.57 (m, 2H); $^{13}$C NMR (125 MHz, DMSO-$d_6$): δ (ppm) 176.44, 175.73, 142.55, 142.50, 139.93, 139.45, 126.25, 126.09, 125.84, 125.80, 124.72, 124.40, 123.64, 122.41, 58.18, 56.40, 49.24, 47.47, 45.39, 44.97, 39.33; ESI-HRMS: Calcd. for [M+H]$^+$: 350.1387. Found: 350.1375.

5.4.2.3 Model reaction 2: metamorphosis from Fur-MalOH to MalOH-Anth-PS

Fur-MalOH (2.6 mg, 13 μmol) and Anth-PS (0.10 g, 13 μmol) were mixed in toluene (5 mL) and heated at 120 °C for 24 h. The reaction mixture was concentrated and precipitated into cold methanol (×2).

5.4.2.4 Synthesis of PEG$_{44}$-COOH

Poly(ethylene glycol) monomethyl ether ($M_n = 2.0$ kg/mol, 2.0 g, 1.0 mmol), triethylamine (0.27 ml, 2.0 mmol), and 4-dimethylaminopyridine (0.24 g, 2.0 mmol) were added to 1,4-dioxane (30 mL) in a round bottom flask equipped with magnetic stirrer.
Succinic anhydride (0.20 g, 2.0 mmol) was added and the mixture was stirred at room temperature. After 24 hours, the solvent was removed under vacuum. The residue was taken up in 50 mL of 1 M HCl and washed with diethyl ether (3 × 50 mL). The aqueous solution was extracted with dichloromethane (3 × 50 mL). The organic portions were combined and dried \textit{in vacuo} to afford the product as a white powder.

\textbf{5.4.2.5 Synthesis of PEG\textsubscript{44} macroinitiator}

The Diels-Alder based initiator, 2-bromo-2-methyl-propionic acid 2-(1-hydroxymethyl-3, 5-dioxo-10-oxa-4-azatricyclo[5.2.1.0\textsubscript{2, 6} dec-8-en-4-yl)-ethyl ester, was synthesized according to our previous report. To a round bottom flask equipped with magnetic stirrer, PEG\textsubscript{44}-COOH (1.0 g, 0.50 mmol), EDC•HCl (0.25 g, 1.25 mmol), 4-dimethylaminopyridine (15.3 mg, 0.125 mmol) and anhydrous dichloromethane (20 mL) were added. Diels-Alder initiator (0.40 g, 1.0 mmol) was added and the mixture was stirred at room temperature for 48 h. The solvent was removed under vacuum and the residue was taken up in 20 mL deionized water. The desired product was extracted with dichloromethane (3 × 20 mL). The organic layers were combined and concentrated, followed by precipitation into an excess of cold diethyl ether. The resulting polymer was collected and dried \textit{in vacuo} to afford the product as a white powder.

\textbf{5.4.2.6 Photoinduced ATRP of methyl acrylate with PEG\textsubscript{44}-macroinitiator}

PEG\textsubscript{44} macroinitiator (0.25 g, 0.10 mmol), methyl acrylate (0.27 mL, 3.0 mmol), CuBr\textsubscript{2} (0.45 mg, 2.0 μmol) and Me\textsubscript{6}TREN (3.2 μL, 0.010 mmol) were dissolved in DMSO (0.27 mL) in a Schlenk flask equipped with magnetic stirrer. The solution was degassed via three successive freeze-pump-thaw cycles, and irradiated with a 365 nm lamp. After 3 h, the polymer was precipitated three times into an excess of cold diethyl ether to yield the amphiphilic block copolymer.
5.4.2.7 Thermal degradation of P(EG-b-MA) block copolymer

P(EG-b-MA) (24 mg, 5.9 μmol) was dissolved in toluene (3 mL) and heated to 120 °C in an oil bath. After 24 h, the reaction was quenched in an ice-water bath and the solvent was removed rapidly \textit{in vacuo}.

5.4.2.8 Thermal reformation of P(EG-b-MA) block copolymer

Degraded Mal-PMA (24 mg, 5.9 μmol) and Fur-PEG (24 mg, 5.9 μmol) mixture was dissolved in toluene (0.5 mL) and heated to 60 °C. After 48 h, the reaction was quenched in an ice-water bath and the solvent was removed \textit{in vacuo}.

5.4.2.9 Synthesis of anthracene-terminated polystyrene (Anth-PS)

AMBIB (0.33 g, 0.96 mmol), styrene (10 g, 96 mmol), and PMDETA (0.10 mL, 0.48 mmol) were charged to a Schlenk flask equipped with magnetic stirrer. The solution was degassed \textit{via} three successive freeze-pump-thaw cycles. CuBr (70 mg, 0.48 mmol) was added to the top of the frozen solution under nitrogen atmosphere. With the solution frozen, the headspace was degassed through repeated pump-purge cycles. The mixture was thawed, and placed into a thermostatted oil bath at 100 °C. After 7 h, the polymerization was quenched through cooling in a water bath and exposure to air. The mixture was precipitated three times into an excess of cold methanol, and the resulting polymer was dried \textit{in vacuo}.

5.4.2.10 Nitroxide-mediated copolymerization of styrene and \textit{p}-chloromethylstyrene (CMS)

TEMPO (0.11 g, 0.69 mmol), styrene (5.0 g, 48 mmol), \textit{p}-chloromethylstyrene (3.1 g, 21 mmol), and benzoyl peroxide (0.11 g, 0.46 mmol) were dissolved in anisole (7 mL) in a Schlenk flask equipped with magnetic stirrer. The reaction mixture was degassed \textit{via} three successive freeze-pump-thaw cycles and subjected to a
thermostatted oil bath at 95 °C. After 3 h, the temperature was raised to 130 °C and heating was continued for another 15 h. The reaction was cooled and exposed to air to terminate the polymerization. The solution was concentrated and precipitated three times into an excess of cold methanol to yield the copolymer.

5.4.2.11 Functionalization of P(S-co-CMS) with 9-anthracenemethanol

The functionalized polymer was prepared according to a previous report.28 9-Anthracenemethanol (0.35 g, 1.7 mmol) was dissolved in anhydrous THF (3 mL) and added to a vial containing 60% sodium hydride dispersion (41 mg, 1.7 mmol). The reaction mixture was stirred under nitrogen atmosphere for 30 min, at which time a 2 mL solution of P(S-co-CMS) (0.60 g polymer, 1.5 mmol CMS) in anhydrous THF was added. The solution was refluxed in the absence of light for 12 h. The reaction was quenched and precipitated three times into an excess of cold methanol.

5.4.2.12 Synthesis of tris(anthracen-9-ylmethyl)benzene-1,3,5-tricarboxylate (Anth₃)

1,3,5-Benzene-1,3,5-tricarbonyl trichloride (0.39 g, 1.5 mmol) was dissolved in anhydrous DCM (50 mL) in a round bottom flask equipped with magnetic stirrer, and cooled to 0 °C. 9-anthracenemethanol (1.0 g, 4.8 mmol) and triethylamine (0.67 mL, 4.8 mmol) were dissolved in anhydrous DCM (30 mL). This solution was added dropwise over the course of 1 h via addition funnel, and the reaction was allowed to warm to room temperature and stirred for 16 h. The reaction mixture was diluted with dichloromethane and washed with saturated NaHCO₃ (2 × 50 mL), deionized water (2 × 50 mL), and brine (2 × 50 mL). The organic layer was collected and dried under vacuum. The crude product was recrystallized from hexane/ethyl acetate (50/50) to yield the product as a yellow powder. ¹H NMR (500 MHz, CDCl₃): δ (ppm) 8.69 (s, 3H), 8.52 (s, 3H), 8.30 (d,
6H), 8.03 (d, 6H), 7.42 (m, 12H), 6.33 (s, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$): δ (ppm) 165.12, 135.04, 131.49, 131.29, 131.21, 129.60, 129.22, 126.91, 125.70, 125.27, 123.91, 60.17.

5.4.2.13 **Amphiphilic to hydrophobic metamorphosis: from P(EG-b-MA) to P(S-b-MA)**

P(EG-b-MA) (50 mg, 11 μmol) and Anth-PS (94 mg, 11 μmol) were dissolved in toluene (5 mL). The solution was heated at 120 °C for 48 h, then precipitated into a large excess of cold methanol to yield the hydrophobic block copolymer P(S-b-MA).

5.4.2.14 **Block to comb metamorphosis: from P(EG-b-MA) to P(S-co-CMS-co-AnthMS-g-MA))**

P(EG-b-MA) (0.10 g, 23 μmol) and P(S-co-CMS-co-AnthMS) (22 mg, 23 μmol) were dissolved in toluene (5 mL). The solution was heated at 120 °C for 48 h, then precipitated into an excess of cold methanol to yield the comb polymer P(S-co-CMS-co-AnthMS-g-MA)).

5.4.2.15 **Block to star metamorphosis: from P(EG-b-MA) to PMA$_3$ star**

P(EG-b-MA) (0.10 g, 23 μmol) and Anth$_3$ (5.9 mg, 23 μmol Anth) were dissolved in toluene (5 mL). The solution was heated at 120 °C for 48 h, then precipitated into an excess of cold methanol to yield the hydrophobic star polymer PMA$_3$.

5.4.2.16 **Synthesis of linear PMA analogue via photoinduced ATRP**

2,3-Dihydroxypropyl 2-bromoisobutyrate (100 mg, 0.415 mmol), methyl acrylate (2.32 g, 26.9 mmol), CuBr$_2$ (1.9 mg, 8.3 μmol), and Me$_6$TREN (11.5 mg, 49.8 μmol) were dissolved in DMSO (2.44 mL). The solution was purged with nitrogen and irradiated with a 365 nm lamp for 3 h, at which time the mixture was precipitated into an excess of cold methanol (x3). The polymer was dried *in vacuo* to yield a transparent viscous liquid.
5.4.2.17 Segmented hyperbranched (SHB) to block: metamorphosis from SHB PMMA to P(S-b-MMA)

SHB PMMA was synthesized according to our previous report.\textsuperscript{31} SHB PMMA (100 mg, 0.0670 mmol Mal) and Anth-PS (550 mg, 0.0670 mmol) were dissolved in toluene (5 mL). The solution was heated at 120 °C for 48 h, then precipitated into an excess of cold methanol to yield the block copolymer P(S-b-MMA).

5.4.2.18 Segmented hyperbranched (SHB) to comb: metamorphosis from SHB PMMA to P(S-b-MMA)

SHB PMMA (100 mg, 67 μmol Mal) and P(S-co-CMS-co-AnthMS) (65 mg, 67 μmol Anth) were dissolved in toluene (5 mL). The solution was heated at 120 °C for 48 h, then precipitated into an excess of cold methanol to yield the comb polymer P(S-co-CMS-co-(AnthMS-g-MMA)).
LIST OF REFERENCES


82. C. Fu, J. Xu and C. Boyer, Chemical Communications, 2016, 52, 7126-7129.


BIOGRAPHICAL SKETCH

Hao Sun was born in Honghu, People’s republic of China. He received his bachelor degree in applied chemistry from Wuhan University in China in 2009. He then pursued a master degree in polymer chemistry and physics from Sun Yat-sen University under the supervision of Prof. Daping Quan. During his master research, he aimed to explore organocatalyzed ring-opening polymerization of various functional cyclic carbonate monomers to prepare biocompatible functional polymer materials.

After graduation with a master degree in 2011, Hao was admitted to PhD program in chemistry at Southern Methodist University. He joined the Sumerlin group and transferred to University of Florida with Dr. Sumerlin in 2012.

During his PhD journey he was able to work on controlled radical polymerization techniques, especially atom-transfer radical polymerization. By using these polymerization techniques, he prepared a variety of architecture-transformable polymers that may potentially open a door to a new class of stimuli-responsive polymers. As the first author, he has published three papers in premier chemistry journals such as Nature Chemistry, Chemical Science, and ACS Macro Letters. Due to his outstanding achievement, he won two awards including Eastman Chemical Company fellowship in 2015.

He enjoys sports and spending his free time in outdoor recreation. He received his PhD degree in chemistry in the summer of 2017.