Novel Polymeric Architectures through Controlled/Living Polymerization, Click Chemistry and Supramolecular Interactions

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Abstract

The properties and functions of polymeric materials are not only dictated by their composition but also their structural arrangement (i.e., architecture or topology). Exploration of polymers with novel molecular architectures has become a practical strategy for developing advanced soft nanomaterials essential to emerging nanotechnologies. Utilizing a combination of modern synthetic chemistries including controlled/living polymerization, click chemistry and supramolecular interactions, this body of research resulted in the development of facile, versatile and highly efficient synthetic pathways for the preparation of a fascinating array of unprecedented macro(supra)molecular architectures.

A scaffold approach that provides access to a library of highly functionalized core cross-linked star (CCS) polymers was developed. Novel functional star macromolecular architectures including fluorescent, saccharide and amphiphilic polyester-based CCS polymers were synthesized by grafting a polyalkyne CCS polymer scaffold with the corresponding azido functional compounds through click chemistry. Factors affecting the grafting efficiency (i.e., click efficiency) of the azido compounds onto the CCS scaffolds were identified. This study not only introduces a versatile and efficient synthetic route towards highly functionalized CCS polymers, but also provides a valuable reference source for the high density functionalization of complex 3-D nanostructures.

The near-quantitative synthesis of polyester-based CCS polymers was demonstrated through organic catalyst-mediated ring opening polymerization. Using this innovative approach, novel benzyl and alkyne end-functional polyester-based CCS polymers were conveniently synthesized in high yields (90 - 96%) at ambient temperatures. Side-reactions that are responsible for trace amounts of low molecular weight impurities in the resulting polymers were identified. The established high-yielding system, which involves no toxic metal catalysts or additives and operates under mild reaction conditions with fast reaction rates, represents a powerful synthetic tool for building new functional star macromolecular architectures.

In addition to CCS polymers, other functional supra(macro)molecular polymers were also explored. Poly(pseudo)rotaxanes with star and bottlebrush supramolecular structures were constructed via self-assembly of the corresponding guest macromolecules.
with α-cyclodextrin (CD) through inclusion complexation. The α-CD inclusion complexation was found to be a useful functionalization strategy for the polyester-based (i.e., poly(ε-caprolactone)) guest macromolecules through non-covalent interactions. Such modification not only alters the inherent chemical and physical properties of the guest polymeric materials but also, surprisingly, affects their molecular size and conformation.

Lastly, the synthesis of a novel stereospecific cyclic polymer was demonstrated through the application of metal-catalysed living radical polymerization and ‘click’ chemistry. With an appropriate ring size, the resultant cyclic polymers are capable of forming an unprecedented ‘polypseudorotaxane-type’ supramolecular structure with the complementary linear stereoregular polymers via stereocomplex helix formation. The ‘polypseudorotaxane-type’ stereocomplex exhibits remarkably different physical properties compared to the conventional triple-helix supramolecules derived from the stereocomplexation of linear stereoregular polymer pairs. These results demonstrate that it is possible to manipulate the microstructures and properties of the supramolecular polymers by changing the shape (or topology) of the assembling components.

The polymeric architectures presented in this thesis possess well-defined hierarchical arrangements of building blocks and functionalities, which imparts them with intriguing characteristics. They may therefore constitute advanced soft nanomaterials with great potential to applications in life sciences and materials technologies. It is anticipated that the established synthetic protocols will aid in the research and development of the next-generation of polymeric materials.
Declaration

This is to certify that

(i) this thesis comprises only my original work towards the PhD except where indicated in the Preface;

(ii) due acknowledgement has been made in the text to all other material used;

(iii) the thesis is less than 100,000 words in length, exclusive of tables, maps, bibliographies and appendices.

Jing Ming Ren

September 2013
Preface

The characterizations of poly(pseudo)rotaxane supramolecular polymers described in Chapters 4 and 5 were performed by Dr. Qiang Fu.

The atomic force microscopy (AFM) analysis described in Chapter 6 was performed by Mr. Yuki Naito and Dr. Motonori Banno (Yashima Group, Nagoya University, Japan).

The modelling study of the cyclic poly(methyl methacrylate) stereocomplex described in Chapter 6 was carried out by Drs. Andrew Joseph Christofferson and George Yiapanis (RMIT University, Australia).
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Publications

Refereed Journal Articles

CHAPTER 2
“Synthesis of a star polymer library of a diverse range of highly functionalized macromolecular architectures”
*Jing Ming Ren*, James Thomas Wiltshire, Anton Blencowe, and Greg Guanghua Qiao

CHAPTER 3
“Organic catalyst-mediated ring-opening polymerization for the highly efficient synthesis of polyester-based star polymers”
*Jing Ming Ren*, Qiang Fu, Anton Blencowe, and Greg Guanghua Qiao

CHAPTER 4
“Synthesis of novel core cross-linked star polymer-based polyrotaxane end-capped via "CuAAC" Click Chemistry”
Qiang Fu, *Jing Ming Ren*, Shereen Tan, Jiangtao Xu, and Greg Guanghua Qiao

CHAPTER 5
“Synthesis of novel cylindrical bottlebrush polypseudorotaxane via inclusion complexation of high density poly(ε-caprolactone) bottlebrush polymer and α-cyclodextrins”
Qiang Fu, *Jing Ming Ren*, and Greg Guanghua Qiao
CHAPTER 6
“Stereospecific cyclic poly(methyl methacrylate) and its topology-guided hierarchically-controlled supramolecular assemblies”
Jing Ming Ren, Kotaro Satoh, Tor Kit Goh, Anton Blencowe, Kanji Nagai, Kenji Ishitake, Masami Kamigaito, Andrew Joseph Christofferson, George Yiapanis, Irene Yarovsky, and Greg Guanghua Qiao

OTHER PUBLICATIONS:
“From transient nanodroplets to permanent nanolenses”
Xuehua Zhang, Jing Ming Ren, Haijun Yang, Yuanhua He, Jingfung Tan, and Greg Guanghua Qiao
Soft Matters 2011, 8, 4314. Featured Cover Article

“Novel drug carriers: from grafted polymers to cross-linked vesicles”
Jiangtao Xu, Qiang Fu, Jing Ming Ren, Gary Bryant, and Greg Guanghua Qiao
Chemical Communications 2013, 49, 33. Featured Cover Article

“Azobenzene-functionalized core cross-linked star polymers and their host-guest interactions”
Shereen Tan, Edgar Hoe Hon Wong, Qiang Fu, Jing Ming Ren, Adrian Sulistio, Katharina Ladewig, Anton Blencowe, and Greg Guanghua Qiao
“Double ‘click’ approach to synthesize nanocages from degradable amphiphilic core cross-linked star polymer”

Jing Ming Ren, James Thomas Wiltshire, and Greg Guanghua Qiao
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“‘Click’ efficiency on high density functionalization of core cross-linked star (CCS) polymers”

Jing Ming Ren, James Thomas Wiltshire, Anton Blencowe, and Greg Guanghua Qiao
32nd Australasian Polymer Symposium Conference (Coffs Harbour, New South Wales, Australia), Feb 13 - 16, 2011 (Poster).

“Synthesis of a core cross-linked star (CCS) polymer library with a diverse range of highly functionalized macromolecular architectures”

Jing Ming Ren, James Thomas Wiltshire, Anton Blencowe, and Greg Guanghua Qiao
32nd Australasian Polymer Symposium Conference (Coffs Harbour, New South Wales, Australia), Feb 13 - 16, 2011 (Oral).

“Fabrication of cylindrical polyrotaxane brush by inclusion complexation of high density poly(caprolactone) brush and α-cyclodextrin”

Qiang Fu, Jing Ming Ren, and Greg Guanghua Qiao
32nd Australasian Polymer Symposium Conference (Coffs Harbour, New South Wales, Australia), Feb 13 - 16, 2011 (Oral).

“Synthesis of cylindrical polyrotaxane brush by inclusion complexation of high density poly(caprolactone) brush and α-cyclodextrin”

Jing Ming Ren, Qiang Fu, and Greg Guanghua Qiao
12th Pacific Polymer Conference, (Jeju Island, South Korea), Nov 13 - 17, 2011 (Oral).
“Organic catalyst-mediated ring opening polymerization towards the near-quantitative synthesis of star polymers”

Jing Ming Ren, Anton Blencowe, Qiang Fu, and Greg Guanghua Qiao

“Novel ‘multiply-controlled’ macrocycles prepared via stereospecific living radical polymerization”

Jing Ming Ren, Kotaro Satoh, Kenji Ishitake, Masami Kamigaito, Anton Blencowe, and Greg Guanghua Qiao

“Stereospecific cyclic poly(methyl methacrylate)s and their supramolecular assemblies”

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“Stereoregular cyclic poly(methyl methacrylate)s: synthesis, characterization and their unique supramolecular assemblies”

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<thead>
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<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>$^{13}$C CP-MAS NMR</td>
<td>Carbon cross-polarization magic angle spinning nuclear magnetic resonance</td>
</tr>
<tr>
<td>2D-ROESY</td>
<td>Two-dimensional rotating frame nuclear Overhauser effect spectroscopy</td>
</tr>
<tr>
<td>AGET</td>
<td>Activator generated by electron transfer</td>
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<tr>
<td>ATRP</td>
<td>Atom transfer radical polymerization</td>
</tr>
<tr>
<td>BnOH</td>
<td>Benzyl alcohol</td>
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<tr>
<td>BOD</td>
<td>4,4′-Bioxepanyl-7,7′-dione</td>
</tr>
<tr>
<td>Bpy</td>
<td>2,2′-Bipyridine</td>
</tr>
<tr>
<td>CCS</td>
<td>Core cross-linked star</td>
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<tr>
<td>CD</td>
<td>Cyclodextrin</td>
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<td>CDCl$_3$</td>
<td>Deuterated chloroform</td>
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<tr>
<td>CL</td>
<td>ε-Caprolactone</td>
</tr>
<tr>
<td>CRP</td>
<td>Controlled radical polymerization</td>
</tr>
<tr>
<td>CuAAC</td>
<td>Copper(I)-catalyzed 1,3-dipolar azide-alkyne cycloaddition</td>
</tr>
<tr>
<td>DBU</td>
<td>1,8-Diazabicyclo[5.4.0]undec-7-ene</td>
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<tr>
<td>DCM</td>
<td>Dichloromethane</td>
</tr>
<tr>
<td>DCTB</td>
<td>$trans$-2-[3-(4-tert-Butylphenyl)-2-methyl-2-propenylidene]-malononitrile</td>
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<td>Diethyl ether</td>
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<td>$D_h$</td>
<td>Hydrodynamic diameter</td>
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<td>DIT</td>
<td>Dithranol (1,8,9-Anthracenetriol)</td>
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<tr>
<td>DLS</td>
<td>Dynamic light scattering</td>
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<td>DMAP</td>
<td>4-(Dimethylamino)pyridine</td>
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<td>DMF</td>
<td>$N,N$-Dimethylformamide</td>
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<td>DMSO</td>
<td>Dimethyl sulfoxide</td>
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<td>DMSO-$d_6$</td>
<td>Deuterated dimethyl sulfoxide</td>
</tr>
<tr>
<td>$dn/dc$</td>
<td>Specific refractive index increment</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Definition</td>
</tr>
<tr>
<td>--------------</td>
<td>------------</td>
</tr>
<tr>
<td>DP</td>
<td>Degree of polymerization</td>
</tr>
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<td>DSC</td>
<td>Differential scanning calorimetry</td>
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<td>EDCI</td>
<td>$N$-(3-Dimethylaminopropyl)-$N'$-ethylcarbodiimide hydrochloride</td>
</tr>
<tr>
<td>FDA</td>
<td>American Food and Drug Administration</td>
</tr>
<tr>
<td>FT-IR</td>
<td>Fourier transform-infrared spectroscopy</td>
</tr>
<tr>
<td>GC-MS</td>
<td>Gas chromatography–mass spectrometry</td>
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<tr>
<td>GPC</td>
<td>Gel permeation chromatography</td>
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<td>GTP</td>
<td>Group transfer polymerization</td>
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<td>$i$-</td>
<td>Isotactic</td>
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<tr>
<td>KTFA</td>
<td>Potassium trifluoroacetate</td>
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<tr>
<td>LP</td>
<td>Linear polymer</td>
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<tr>
<td>MALDI ToF MS</td>
<td>Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry</td>
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<td>MALLS</td>
<td>Multi-angle laser light scattering</td>
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<td>Macrorinitiator</td>
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<td>MM</td>
<td>Macromonomer</td>
</tr>
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<td>MMA</td>
<td>Methyl methacrylate</td>
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<tr>
<td>$M_n,GPC$</td>
<td>Number-average molecular weight determined by GPC</td>
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<td>$M_n,MAL$</td>
<td>Number-average molecular weight determined by MALDI ToF MS</td>
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<tr>
<td>$M_n,NMR$</td>
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<tr>
<td>$M_n,\text{theo}$</td>
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<td>MSA</td>
<td>Methanesulfonic acid</td>
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<tr>
<td>MW</td>
<td>Molecular weight</td>
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<td>MWD</td>
<td>Molecular weight distribution</td>
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<tr>
<td>NaI</td>
<td>Sodium iodide</td>
</tr>
<tr>
<td>$N_{\text{arms}}$</td>
<td>Average-number of arms per star polymer</td>
</tr>
<tr>
<td>NB</td>
<td>Norbornene</td>
</tr>
<tr>
<td>Symbol</td>
<td>Definition</td>
</tr>
<tr>
<td>--------</td>
<td>------------------------------------------------</td>
</tr>
<tr>
<td>$N_{C≡C}$</td>
<td>Number of alkyne repeat units</td>
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<tr>
<td>NHC</td>
<td>N-Heterocyclic carbene</td>
</tr>
<tr>
<td>NMP</td>
<td>Nitroxide-mediated radical polymerization</td>
</tr>
<tr>
<td>NMR</td>
<td>Nuclear magnetic resonance</td>
</tr>
<tr>
<td>PCL</td>
<td>Poly(ε-caprolactone)</td>
</tr>
<tr>
<td>PDI</td>
<td>Polydispersity index</td>
</tr>
<tr>
<td>PEG</td>
<td>Poly(ethylene glycol)</td>
</tr>
<tr>
<td>PgMA</td>
<td>Propargyl methacrylate</td>
</tr>
<tr>
<td>PgOH</td>
<td>Propargyl alcohol</td>
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<tr>
<td>PMDETA</td>
<td>$N,N,N',N'',N''''$-Pentamethyldiethylenetriamine</td>
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<tr>
<td>PMMA</td>
<td>Poly(methyl methacrylate)</td>
</tr>
<tr>
<td>PS</td>
<td>Polystyrene</td>
</tr>
<tr>
<td>PrBA</td>
<td>Poly(tert-butyl acrylate)</td>
</tr>
<tr>
<td>RAFT</td>
<td>Reversible addition-fragmentation chain transfer</td>
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<td>REMP</td>
<td>Ring-expansion metathesis polymerization</td>
</tr>
<tr>
<td>$R_h$</td>
<td>Hydrodynamic radius</td>
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<tr>
<td>RI</td>
<td>Refractive index</td>
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<tr>
<td>ROMP</td>
<td>Ring-opening metathesis polymerization</td>
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<tr>
<td>ROP</td>
<td>Ring-opening polymerization</td>
</tr>
<tr>
<td>SLRP</td>
<td>Stereospecific living radical polymerization</td>
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<tr>
<td>Sn(Oct)$_2$</td>
<td>Stannous octoate</td>
</tr>
<tr>
<td>Sn(OTf)$_2$</td>
<td>Stannous triflate</td>
</tr>
<tr>
<td>SOCl$_2$</td>
<td>Thionyl chloride</td>
</tr>
<tr>
<td>$st$</td>
<td>Syndiotactic</td>
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<tr>
<td>TBAF</td>
<td>Tetra-$n$-butylammonium fluoride</td>
</tr>
<tr>
<td>TBAHS</td>
<td>Tetra-$n$-butylammonium hydrogen sulfate</td>
</tr>
<tr>
<td>TEA</td>
<td>Triethylamine</td>
</tr>
<tr>
<td>TEM</td>
<td>Transmission electron microscopy</td>
</tr>
<tr>
<td>TGA</td>
<td>Thermogravimetric analysis</td>
</tr>
<tr>
<td>THF</td>
<td>Tetrahydrofuran</td>
</tr>
<tr>
<td>TMS</td>
<td>Trimethylsilyl protecting group</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>TMS-PgMA</td>
<td>Trimethylsilyl propargyl methacrylate</td>
</tr>
<tr>
<td>TPMA</td>
<td>Tris(2-pyridylmethyl)amine</td>
</tr>
<tr>
<td>tpy</td>
<td>2,2′:6′:2″-Terpyridine</td>
</tr>
<tr>
<td>UV-vis</td>
<td>UV-Visible spectroscopy</td>
</tr>
<tr>
<td>XRD</td>
<td>X-ray powder diffraction</td>
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Chapter 1

Introduction

Biomacromolecules possess precisely-defined molecular chain length, monomer composition, sequence and stereochemistry (i.e., tacticity). This meticulous structural control not only gives them distinct properties and functions, but also the ability to form intricate and exquisite supramolecular assemblies (e.g., DNA and proteins). These supramolecular entities regulate essential biological processes within all living organisms. In the past, tremendous effort has been devoted by polymer and material scientists to match and emulate nature in synthesizing macromolecules with precisely ‘controlled’ microstructure. The aim of this is to utilize well-defined macromolecules as building blocks to assemble nanostructured materials with regulated domain sizes, and novel functionality, reactivity and solubility characteristics. Those nanostructured materials are central to emerging nanotechnologies, which may provide solutions to current global issues in the areas of resource, health, and energy.

In the past decades, progress in polymer chemistry has undergone a significant revolution. Exciting developments in controlled/living polymerization and highly yielding, simple covalent chemistry (i.e., ‘click’ chemistry) have provided valuable synthetic tools for the preparation of complex polymers with well-defined functional macromolecular architectures, e.g., dendritic, star, bottlebrush and cyclic polymers. The intelligently engineered functional properties and specifically designed structures make these polymeric materials suitable candidates for various nanoscale applications, ranging from membrane technologies and templates, to catalysis and polymer therapeutics.

This thesis focuses on developing synthetic routes towards novel polymeric architectures through the application of controlled/living polymerization, click chemistry and supramolecular chemistry. In this work, detailed studies have been carried out to identify characteristic properties of the prepared macro(supra)molecular architectures for fundamental research interest, as well as the development of materials for commercial applications. Therefore, this chapter introduces the background covering synthetic approaches towards various polymeric architectures including star, brush and cyclic
polymers, and more specifically, different synthetic techniques including controlled/living polymerization techniques and ligation chemistries, and synthetic routes through which hierarchically structured macromolecular architectures can be constructed. The supramolecular chemistry employed in this thesis to assemble high-order polymeric supramolecular structures will also be discussed.

1.1 Synthetic Techniques to Construct Well-defined Macromolecular Architectures
1.1.1 Controlled/Living Polymerization Techniques

The term ‘controlled’ polymerization is defined as a chain growth polymerization reaction that propagates with minimal irreversible chain-transfer or chain-termination reactions, while a ‘living’ polymerization is defined as a chain growth polymerization reaction that propagates without irreversible termination or other side-reactions. These polymerization techniques allow the precise control over the molecular weight (MW) and molecular weight distribution (MWD) of the product polymers (Scheme 1.1).

In controlled/living polymerizations, one initiator generates one living polymer chain via a chain growth mechanism, whereby the MW of the propagating polymer chain increases linearly with monomer conversion. Controlled/living polymerizations proceed until all monomers are consumed and continue growth if additional monomers are added. Thus, block copolymers can be prepared by the sequential addition of monomers. In a controlled/living polymerization, the concentration of active species remains constant, and as a result the polymerization follows 1st order reaction kinetics with respect to the consumption of monomer (i.e., a plot of ln([M]₀/[M]) versus time should be linear). Another notable feature of controlled/living polymerization is that the end-groups of the polymers are retained after polymerization, which allows end-functional polymers to theoretically be prepared in a quantitative yield.
Scheme 1.1 Schematic illustration of living polymerization and well-defined polymers prepared by living polymerization.

Since the living polymerization of styrene was first reported by Swarc in 1956,11 many types of living or controlled polymerization system have been developed e.g., living cationic,12 coordination-insertion,13 group-transfer,14 ring opening,15 and ring opening metathesis polymerization.16 The remarkable progress in the development of living polymerization techniques has led to the preparation of a diverse range of complex macromolecular architectures with well-defined structure and narrow MWDs (Scheme 1.1). The following part of the review will focus on the recent developments in ring opening, ring opening metathesis and living radical polymerizations, and reviews on other living polymerization techniques will not be included.

1.1.1.1 Ring Opening Polymerization (ROP)

One particular type of controlled polymerization that is heavily utilized throughout the work presented in this thesis is the ring opening polymerization (ROP) to generate polyesters. ROP is a controlled polymerization technique that proceeds in a chain growth fashion by consecutively ‘opening’ strained cyclic monomers to form a linear polymer. There are three conventional ROP mechanisms depending on the catalytic system used, including anionic, cationic and coordination-insertion mechanism.17 The coordination-insertion mechanism has been thoroughly investigated, and is extensively used for the
preparation of aliphatic polyesters with well-defined structures. One of the most common catalysts utilized in the ROP of cyclic esters via the coordination-insertion mechanism is tin(II) 2-ethylhexanoate, commonly referred as stannous octoate (Sn(Oct)$_2$). Compared to other organometallic catalysts, Sn(Oct)$_2$ is inexpensive and with high initiation efficiency.$^{18}$ More importantly, Sn(Oct)$_2$ has low toxicity and has been approved by the American Food and Drug Administration (FDA) as a food additive, making it an ideal catalyst for the synthesis of polyesters for biomedical as well as other industrial applications. The coordination-insertion mechanism$^{18-19}$ of Sn(Oct)$_2$-mediated ROP involves three key steps as illustrated in Scheme 1.2.

![Scheme 1.2](image)

**Scheme 1.2** Mechanism for Sn(Oct)$_2$-catalyzed ROP of $\varepsilon$-caprolactone.

Metal carboxylates such as Sn(Oct)$_2$ behave as Lewis acids and are very weak nucleophiles compared to metal alkoxides. Therefore, Sn(Oct)$_2$ is unable to initiate ROP and alcoholic co-initiators are required to replace the carboxylate ligands to form the active stannous dialkoxide derivatives 1.1 (Step 1, Scheme 1.2). The addition of a strained cyclic ester monomer (e.g., $\varepsilon$-caprolactone 1.2), results in the coordination, ring-opening and the
insertion of the monomer 1.2 into the stannous alkoxide bond to form the propagating species 1.3. The propagating species 1.3 can either react with another monomer (Step 2) or undergo reversible chain transfer between the stannous alkoxide moiety and a hydroxyl group (Step 3); the hydroxyl group can originate from either an unreacted initiator or another polymer chain terminus. The rapid exchange gives a dynamic equilibrium between the activated and deactivated chains (1.3 and 1.4, respectively), resulting in a controlled polymerization and polymers with narrow MWDs. Elevated reaction temperatures are usually required for the ROP of lactones (e.g., ε-caprolactone) with Sn(Oct)$_2$ and other organometallic initiators in order to obtain appreciable reaction rates. Elevated temperatures are undesirable for industrial scale processes where energy conservation is particularly important from an economical and environmental perspective. In addition, high reaction temperatures and long reaction times may lead to both inter- and intramolecular transesterification (i.e., ‘back-biting’) reactions, which cause the polyester product to have a broad MWD.

Recent developments in organo-catalysis have introduced several robust organic catalysts (e.g., N-heterocyclic carbenes (NHCs), bi-functional thioureas, triazabicyclodecene and sulfonic acid derivatives) that are able to efficiently catalyze ROP of cyclic esters under mild conditions and with fast reaction rates. In particular, the sulfonic acid derivative, methanesulfonic acid (MSA), has recently been reported to be a highly efficient catalyst for the controlled ROP of lactones or dilactones. Compared to other organic catalysts, MSA is a low cost and readily available laboratory reagent. Furthermore, MSA has the added benefit of being environmentally benign, as it is considered to be a natural product that forms as part of the natural sulphur cycle. The excellent catalytic performance and polymerization control provided by MSA is potentially due to its highly efficient ‘bi-functional’ activation capability (Scheme 1.3).
The proposed mechanism of MSA-catalyzed ROP is summarized in Scheme 1.3. The acidic proton and basic oxygen atoms on MSA 1.6 may act as hydrogen-bonding donor and acceptor, respectively. Such unique molecular structure allows 1.6 to work as a ‘proton shuttle’ during the polymerization. In the presence of an alcoholic initiator 1.5 and cyclic monomer (using ε-caprolactone 1.2 as example), 1.6 initiates the nucleophilic attack of 1.5 to the carbonyl carbon on 1.2 by accepting the alcoholic proton from 1.5 whilst transferring the acidic proton to the exo-oxygen of 1.2, resulting in a tetrahedral intermediate 1.7 (Scheme 1.3, Step 1). In the following step, the donation of proton from 1.6 to the endo-oxygen of 1.7 leads to the cleavage of the C-O bond (i.e., the ring-opening of 1.7) generating propagating species 1.8 (Step 2). The concomitant activation of 1.2 and 1.8 by 1.6 repeat during propagation to afford a ‘living’ polyester 1.9.

ROP is not sensitive to radical scavengers such as O₂, so reactions can be easy handled since no degassing is required. The drawback associated with ROP is its sensitivity to water, which may act as an initiating species, although with lower efficiency than common alcoholic initiators. The presence of water in the reaction can also contribute to polymers having ill-defined chain ends as well as broad MWDs.
Polyesters synthesized via ROP are attractive soft nanomaterials for various pharmaceutical and biomedical applications. Poly(ε-caprolactone), in particular, has been given FDA approval and is considered both biocompatible and biodegradable, as its degradation products are capable of being absorbed by the body with minimum tissue reaction.25

1.1.1.2 Ring Opening Metathesis Polymerization (ROMP)

More recently, ring opening metathesis polymerization (ROMP) has emerged as a powerful synthetic technique to construct well-defined polymers with intriguing biological, electronic, and mechanical properties.16 Similar to ROP, ROMP is a chain growth polymerization process involving the ‘ring-opening’ and conversion of strained cyclic olefins into unsaturated polymers. ROMP is based on olefin metathesis, a unique metal-mediated C=C bond exchange process.26 A general mechanism for ROMP is shown in Scheme 1.4. The initiation process begins with the coordination of a transition metal alkylidene complex (i.e., the initiator) with a cyclic olefin. A four-membered metallacyclobutane intermediate is subsequently formed through [2+2]-cycloaddition (Scheme 1.4, Step 1). The coordinated monomer then ring-opens as the ring strain is released through cycloreversion. A new alkylidene complex is then formed and serves as the propagating chain. This alkylidene complex has a similar reactivity towards olefin monomers despite of its increase in size (due to the incorporated monomer). During propagation, analogous ring opening steps repeat to form a long chain polymer (Step 2). Polymerization continues until all of the monomer is consumed, the reaction equilibrium is reached or the reaction is terminated. ROMP is often terminated by reacting the propagating polymer with an electron-rich or symmetrical bifunctional alkene. The purpose of the termination reaction is to 1) selectively remove the transition metal complex and 2) to install a specific end-group functionality in place of the metal catalyst (Step 3).
Similar to most olefin metathesis reactions, ROMP reactions are generally reversible. Depolymerization can take place in the opposite direction as shown in Scheme 1.4. However, ROMP reactions are equilibrium-controlled process and the position of the equilibrium (monomer versus polymer) is governed by the thermodynamics of the polymerization. ROMP, like other ring opening polymerizations is driven from monomer to polymer by the release of ring-strain associated with cyclic olefins balanced by entropic penalties. Therefore, common monomers amenable to ROMP are cyclic olefins having a considerable degree of strain, for example, cyclobutene, cyclopentene, cis-cyclooctene and norbornene. The ROMP mechanistic pathway is complicated by two side-reactions, including intermolecular chain-transfer and intramolecular chain-transfer (‘back-biting’) reactions, which are often observed with other ROP processes (Section 1.1.1.1). These chain-transfer reactions collectively broaden MWD of the product polymers. Due to the metal-mediated and equilibrium-controlled nature, specially designed metathesis catalysts are required to achieve well-controlled ROMP. These catalysts should satisfy the following criteria:

1) exhibit fast initiation (i.e., convert into propagating polymer chain rapidly and quantitatively)
2) mediate the polymerization without significant chain transfer side reactions
3) react with terminating agents to facilitate end-group functionalization
4) demonstrate good solubility in common organic solvents
5) show high functional group tolerance and stability toward H₂O and O₂

Recent advances in catalyst design has led to a series of transition metal complexes based on titanium (Ti),
28 tantalum (Ta),
29 tungsten (W),
30 molybdenum (Mo)
31 and ruthenium (Ru)
32 that mediate controlled ROMP reactions. In particular, Mo and Ru-based catalysts have demonstrated high tolerance towards various functional groups (e.g., esters/amides, ketones, aldehydes etc.) as a result of their low oxophilicity. The successful preparation and isolation of these catalysts has provided a window of opportunity for the synthesis of well-defined functional macromolecular architecture, including block, random, and grafted copolymers, end-functionalized polymers, and star, brush and cyclic polymers.

1.1.1.3 ‘Living’ Radical Polymerization

Radical polymerization has been applied as an efficient technique for both laboratory- and industry-scale polymer syntheses as a result of the many advantages it provides over other polymerization techniques, including mild reaction conditions, high functional group tolerance and a large variety of polymerizable monomers.

Living radical polymerization had been a long-standing synthetic challenge to polymer chemists as the highly reactive radical species undergoes irreversible bimolecular coupling and disproportionation leading to chain terminations.
10, 33 Otsu et al. first demonstrated the possibility of living radical polymerization in 1980s through the proposed ‘iniferter’ systems.
34 In the late 1990s, a number of living radical polymerization systems were developed, including nitroxide-mediated radical polymerization (NMP),
35 atom transfer radical polymer (ATRP)
36 (also known as metal-catalysed living radical polymerization
37) and reversible addition-fragmentation chain transfer (RAFT) polymerization
38 (Scheme 1.5). The common feature of living radical polymerizations is the reversible capping of propagating radical species generating inactive ‘dormant’ species. The fast equilibrium between the ‘active’ (i.e., propagating) and ‘dormant’ species control the chain growth polymerization by providing all polymer chains equal opportunity to grow. In addition, the dynamic equilibrium lowers the instantaneous concentration of radicals within the reaction system, and hence termination or chain transfer events are minimized.
Therefore, with an appropriate capping agent, radical polymerization may proceed in a controlled manner.

![Scheme 1.5](image)

**Scheme 1.5** Various ‘living’ radical polymerizations based on the reversible activation of ‘dormant’ species into ‘active’ radical species.

As a direct result of the high functional group tolerance in ‘living’ radical polymerization, functionalities can be easily introduced into polymers via polymerization of monomers with pendent functional groups. End-group functionalities can also be conveniently installed via the use of functional initiators and end-group modifications. Coupled with highly efficient ligation techniques (e.g., click chemistry), ‘living’ radical polymerization has been exploited as a versatile synthetic tool for the preparation of a diverse range of polymer architectures, including random, block, gradient and alternating copolymers, and star (Section 1.2.1), brush/comb (Section 1.2.2) and cyclic polymers (Section 1.2.3).
1.1.1.4 Stereospecific Living Radical Polymerization

Stereoregularity (or tacticity) is defined as the relative stereochemistry of adjacent chiral centres within a macromolecule. Such order or arrangement within a polymer significantly affects its chemical and physical properties, for instance, glass transition temperature, solubility, crystallinity and mechanical strength.\(^{39}\)

The pioneering work on stereospecific polymerization was conducted by Natta and co-workers, who reported the first synthesis of stereospecific polypropylene using a coordination polymerization technique.\(^{40}\) This study directed tremendous research effort towards the development of stereospecific polymerizations via coordination\(^ {41}\) and anionic\(^ {42}\) mechanisms. In comparison, the control of stereochemistry in radical polymerization was much more difficult to achieve as a result of a lack of electronic interactions, which create a stereochemically selective environment for the polymerization to propagate. In radical polymerization, the sp\(^2\) -planar or planar-like propagating radical species is generally not persistent enough for the stereospecific propagation.\(^ {39}\) Recent development of stereospecific radical polymerization has introduced several methodologies that offer the control of stereoregularity based on bulky substituented monomer structures,\(^ {43}\) and solvent and/or additive effects\(^ {44}\) (Scheme 1.6). However, the stereochemical control provided by these techniques is still less efficient compared to those achieved in the coordination polymerization of \(\alpha\)-olefins and anionic polymerization of methacrylic monomers.
**Scheme 1.6** Schematic illustration for the stereospecific living radical polymerization (SLRP) with dual control over MW and tacticity.

The judicious combination of living radical polymerization and stereospecific radical polymerization allows the simultaneous control of MW and tacticity of polymers (**Scheme 1.6**). These advanced polymerization techniques, termed stereospecific living radical polymerization (SLRP), have been utilized for the synthesis of stereocontrolled polymeric architectures, including stereoblock, stereogradient, and stereospecific star polymers. However, in SLRP systems, both MW and tacticity controlling components should be meticulously designed so that they do not interfere with each other.

Solvent-monomer interactions act as one of the most effective means for stereochemical control in radical polymerization. In order to achieve stereochemical control the solvents need to coordinate with the pendent groups in the monomer and/or the propagating polymer chain during solvation. Hence, the inherent structure will adopt an appropriate configuration to create a stereospecific environment for the addition of monomers to the growing chain terminus. However, low reaction temperatures and a large excess of the solvent are necessary for the stereospecific polymerization as a result of the weak interaction between the solvent and monomer. During the polymerization, stereospecificity can be introduced through the steric repulsion between the bulky group coordinated to the incoming monomer and that of the penultimate unit of a propagating chain (**Scheme 1.7**). Unfortunately, most common solvents are ineffective in changing the
inherent tacticity of polymers through radical polymerization methods. Later on, fluorinated alcohols such as 1,1,1,3,3,3-hexafluoro-2-phenylpropan-2-ol (PhC(CF₃)₂OH) were introduced by Okamoto et al.⁵⁰ as effective solvents for inducing the stereospecific control of radical polymerizations, even for common neutral vinyl monomers. When PhC(CF₃)₂OH is employed as the solvent in SLRP of methyl methacrylates (MMA) at 0 °C the polymerization yields living syndiotactic poly(methyl methacrylate) (PMMA) with diad syndiotacticty (rr) of upto 78%,⁵¹ as opposed to PMMA prepared by conventional radical polymerization, which has rr of approximately 60 %.

![Scheme 1.7 Schematic models for solvent-mediated stereospecific radical polymerization.](image)

1.1.2 Copper(I)-catalyzed 1,3-dipolar azide-alkyne cycloaddition (CuAAC) – Click Chemistry

The concept of click chemistry was first introduced by Sharpless and co-workers in 2001.⁵ In polymer chemistry, the term ‘click chemistry’ refers to a range of highly robust, efficient and orthogonal chemical reactions, including pyridyl disulfide exchange, Michael addition, copper(I)-catalyzed azide-alkyne cycloaddition, Diels-Alder cycloaddition, thiol-ene/yne addition and oxime condensation.⁴ In concert with controlled/living polymerization techniques, click chemistry has been extensively utilized for the preparation of well-defined
functional macromolecular architectures. The common features of click chemistry may include:

1) fast reaction rate
2) mild reaction conditions (insensitive to O₂ and protic solvents)
3) very high yields (≥ 95%)
4) high functional group tolerance (i.e., high selectivity)
5) starting materials and reagents are readily available and inexpensive
6) inoffensive side-reaction products, which can be easily removed via a non-chromatographic method
7) stable products under physiological condition

Copper(I)-catalyzed 1,3-dipolar azide-alkyne cycloaddition (CuAAC) is a classic type of click reaction that has found widespread application in organic synthesis, bioconjugation, polymer chemistry, materials science and nanotechnology. CuAAC is a notable variation of the Huisgen 1,3-dipolar cycloaddition, in which an organic azide reacts with an alkyne to afford a five membered 1,2,3-triazole ring. The copper(I)-catalyzed variant was first reported in 2002 in independent publications by Meldal et al. at the Carlsberg Laboratory and Sharpless et al. at the Scripps Research Institute.

The use of copper(I) as catalyst in the azide-alkyne cycloaddition results in the exclusive formation of the 1,4-disubstituted 1,2,3-triazole, and significantly accelerates the reaction, allowing it to proceed at room temperature. Without catalysts, the reaction only proceeds slowly at elevated temperatures and provides a mixture of 1,4 and 1,5 regioisomers (Scheme 1.8).
The mechanistic cycle of CuAAC based upon density functional theory calculations\(^{56}\) is illustrated in Scheme 1.9. Initially, the copper(I) species coordinates with the triple bond of a terminal alkyne to form the \(\pi\)-complex 1.10 (Scheme 1.9). In the presence of a base, the acidic hydrogen of the terminal alkyne is deprotonated to generate the Cu acetylide intermediate 1.11. Experimental studies have shown that the cycloaddition reaction is second order with respect to Cu, which suggests that the transition state involves two Cu atoms in a bimolecular complex 1.12.\(^{56-57}\) One Cu atom in the complex is bonded to the acetylide whilst the azide displaces a weakly coordinated ligand of the other Cu atom, resulting in the copper-azide-acetylide complex 1.13. The coordinated azide and alkyne then undergo intramolecular cycloaddition to give the cyclic intermediate 1.14. Finally, the Cu complex is released from the triazole product 1.15 via protonation; the proton source is the hydrogen that had been previously abstracted from the terminal acetylene by the base. The regenerated catalyst complex is then free to participate again in the catalytic cycle. Overall, the Cu(I) catalytic process gives a rate enhancement of 10\(^5\) and an absolute regioselectivity of 1,4-triazole formation.

Scheme 1.8 Scheme showing the triazole regioisomers formed via Huisgen 1,3-dipolar cycloaddition and CuAAC.
CuAAC can be carried out in a variety of polar and non-polar organic solvents, aqueous solutions, and mixtures thereof. Common solvents utilized in CuAAC include THF, DMSO, MeOH, acetone, DMF, toluene and water. As a result of the high coordination affinity of nitriles with Cu(I) nitrile-containing solvents (e.g., acetonitrile) are generally avoided as they retard the reaction rate leading to low yields. For organic solvent systems, copper(I) halides (e.g., CuBr and CuI) are often used as the copper source in combination with tertiary or aromatic amine-based ligands (Figure 1.1). Not only do performed Cu(I)-ligand complexes exhibit enhanced solubility in most organic solvents, but the ligands effectively protect Cu(I) species from oxidation into inactive Cu(II) species. Furthermore, amine ligands may act as the base responsible for the deprotonation of the Cu acetylide complex during the CuAAC reaction.
In aqueous systems, Cu(II) salts (e.g., copper(II) sulphate) are often employed as the copper source, along with the addition of a reducing agent (e.g., sodium ascorbate) that is responsible for generating the Cu(I) species in-situ. Such systems eliminate the need for the formation of Cu(I)-ligand complexes, and the reducing agent can be added in excess to make up for oxygen present in the reaction system. The addition of excess reducing agent would convert any oxidized Cu(II) back to Cu(I), to ensure a sufficient supply of Cu(I) to the reaction system.

In polymer chemistry and materials science, CuAAC has been employed as a mechanism for step-growth polymerization, a ligation technique for coupling polymers, functionalization of polymers with small molecules, and bioconjugation between polymers with biomacromolecules. More recently, the exploitation of CuAAC has been extended into the construction of polymeric materials with complex structures (e.g., dendrimers, brush and star architectures) and unique topologies (e.g., cyclic, tadpole, and cyclic brush configurations) for demands in various industrial and research settings.
1.2 Synthetic Approaches to Different Polymeric Architectures

1.2.1 Synthesis of Star Polymers

Star polymers consist of multiple polymers (i.e., arms) radiating from a central core.\textsuperscript{70} Compared to linear polymer counterparts with the same MW, star polymers possess a greater number of end-group functionalities and exhibit lower intrinsic viscosities and higher solubility characteristics.\textsuperscript{70b, 71} Star polymers not only satisfy the curiosity of academic research, but also have been exploited or are under investigation for a number of commercial applications ranging from engine oil\textsuperscript{72} and coating technologies\textsuperscript{73} to drug delivery\textsuperscript{74} and biomedical devices.\textsuperscript{75} In general, there are two main synthetic approaches for the synthesis of star polymers via controlled/living polymerization techniques, namely, the core-first and the arm-first approaches.

1.2.1.1 Core-first Approach

The core-first synthetic approach utilizes a multi-functional initiator to initiate the controlled polymerization of monomers to form star polymers (\textbf{Scheme 1.10}). Controlled polymerization techniques, such as living anionic polymerization,\textsuperscript{76} group transfer polymerization (GTP),\textsuperscript{77} NMP,\textsuperscript{78} ATRP,\textsuperscript{79} and RAFT\textsuperscript{80} polymerization have been utilized to prepare star polymers via the core-first approach.

\begin{equation}
\text{Initiator} \quad \text{+} \quad \text{Monomer (M)} \quad \text{Polymerization} \quad \rightarrow \quad \text{Star Polymer}
\end{equation}

\textbf{Scheme 1.10} Synthesis of star polymers via the core-first approach.

To ensure star polymers with well-defined structure are formed (i.e., equal number of arms with similar arm lengths) the initiating sites on the core must have equal reactivity, 100\% initiation efficiency, and the initiation rate must be greater than the propagation rate, so the degree of polymerization (DP) achieved by each arm is comparable. The main
advantages of the core-first approach are high star polymer yields and facile separation of the star polymer from the crude reaction mixture. The disadvantages of the core-first approach are that the star polymers often suffer from low arm numbers (usually 3~8) and a relatively small core domain. To overcome this, functionalized hyperbranched and dendritic polymers, functionalized nanoparticles and poly(saccharides) have been used as initiators to prepare star polymers with large core domains and high arm numbers.

1.2.1.2 Arm-first Approach

In the arm-first approach, linear polymers capable of further chain extension (i.e., macroinitiators), or with polymerizable end-group functionality (i.e., macromonomers) are firstly synthesized. Star polymers are then formed either via the polymerization of a di(or higher)-functional monomer (i.e., the cross-linker) initiated by the macroinitiator, or the copolymerization of the cross-linker and the macromonomer initiated by a low molar mass initiator (Scheme 1.11). Star polymers synthesized via this approach have a unique three-dimensional globular architecture consisting of a densely cross-linked core surrounded by a large number of radiating arms (typically 10-100). As such, they are often referred as the core cross-linked star (CCS) polymers, as this term highlights their unique core structure and distinguishes them from other types of star polymers.

Scheme 1.11 Synthesis of star polymers via the arm-first approach.

Compared to the core-first approach, star polymers with different arm compositions (i.e., miktoarm star polymers) are easily accessible via the arm-first approach. After the star-formation step, the initiating sites isolated within the core domain may initiate the
polymerization of other monomers to form a second generation of arms via the ‘in-out’ method\textsuperscript{86} (Scheme 1.11). Alternatively, miktoarm star polymers can be prepared by using a mixture of different types of macroinitiators to initiate the star-formation.\textsuperscript{87} In addition, other more complex architectures, for instance, star polymers with block copolymer,\textsuperscript{88} dendron terminated\textsuperscript{89} or even brush polymer arms,\textsuperscript{90} have also been prepared via the arm-first approach. However, the major weakness inherent to the arm-first approach is incomplete arm-to-star conversions.\textsuperscript{91} Tedious and time-consuming purification processes are often required to isolate the star polymer product from unreacted macroinitiator. The choice of cross-linker, catalyst, and reaction conditions is central to enhancing the ‘livingness’ of the macroinitiators and providing high arm-to-star conversions (> 90\%).\textsuperscript{92} Various controlled/living polymerization techniques (Section 1.1.1) have been exploited for the synthesis of CCS polymers via the arm-first approach. This has allowed the preparation of high MW CCS polymers, in excess of one million in some cases, while the products still maintain narrow MWD (PDI < 1.3). Furthermore, a high degree of functionality can be conveniently introduced either in the core\textsuperscript{93} or at the periphery\textsuperscript{89, 94} of the CCS polymers via these techniques.

1.2.2 Synthesis of Molecular Brush Polymers

Cylindrical molecular brush polymers consist of a linear polymer backbone, to which a number of grafted side-chains are covalently attached.\textsuperscript{95} Different from graft polymers, the conformation of brush polymers is influenced by the grafting density of the side-chains. In addition, the physical properties of molecular brush polymers are often affected by the side-chain grafting density, length, stiffness and composition.\textsuperscript{96} Molecular brush polymers are able to switch conformation in response to changes in the surrounding environment or external stimuli,\textsuperscript{97} and this enhances the significance and practical values of these macromolecules.\textsuperscript{98} Brush polymers have demonstrated potential applications in micro-mechanical applications serving as miniature cushions,\textsuperscript{99} molecular pistons\textsuperscript{100} and artificial muscles.\textsuperscript{97a} Furthermore, the large number of end-group functionalities makes them ideal candidates for molecular sensor\textsuperscript{101} and drug delivery applications.\textsuperscript{102} Owing to the significant molecular size, cylindrical molecular brush polymers can be readily observed by imaging techniques such as atomic force microscopy (AFM)\textsuperscript{103} and
transmission electron microscopy (TEM). Hence, cylindrical molecular brush polymers serve as an informative model system to observe and study physical phenomena such as reptation, spreading, molecular conformational transition, and surface adsorption-induced structural alteration. Cylindrical molecular brush polymers can be prepared via three general strategies as outlined in the proceeding sections.

1.2.2.1 *Grafting-from Approach*

This approach begins with the synthesis of a functional polymer backbone as a multi-functional macroinitiator, which is subsequently used to initiate the polymerization of monomers to form the side chains of the brush polymer (Scheme 1.12). The macroinitiator can be prepared directly via polymerization of monomers carrying initiating functionalities, or indirectly via post-polymerization functionalization to introduce the initiating sites. Controlled polymerization techniques such as living anionic polymerization and ATRP are often employed for brush polymer syntheses via the grafting-from approach, since intramolecular and intermolecular termination events that lead to macrocyclic side chains and/or macroscopic gelation are minimized. Therefore, molecular brush polymers with long molecular backbones and high side-chain densities can be prepared with narrow MWD.

![Scheme 1.12 Synthesis of brush polymers via the grafting-from approach.](image)

However, compared to the grafting-through approach (Section 1.2.2.2), the grafting-from route suffers from a lower control over the grafting density and side-chain length, since both parameters are limited by the backbone macroinitiator initiation efficiency and steric factors. Through controlled/living polymerization techniques, brush polymers with various functional side-chains have been synthesized using acrylic.
methacrylic$^{100b, 110, 113}$, acrylamide$^{55}$ and styrene$^{114}$ monomers. In addition, more advanced molecular brush architectures have been prepared by varying the backbone length, and the side-chain and backbone compositions. These architectures include core-shell molecules with block copolymer side-chains,$^{115}$ AB and ABA block brush,$^{116}$ star-like$^{117}$ and molecular brush polymers with gradient grafting density.$^{112b}$ More recently, hollow polymeric capsules or nanotubes have been synthesized using cylindrical brush polymers with degradable core and cross-linkable shell domains as templates.$^{108a, 118}$

1.2.2.2 Grafting-through Approach

In this approach, linear polymers with a polymerizable functional terminus (i.e., macromonomers (MMs)) are firstly prepared (Scheme 1.13). Subsequent polymerization of the MMs ‘through’ their terminal functionality leads to the formation of molecular brush polymers. Polymerizable chain ends can be installed onto the MMs either via the use of a functional initiator to initiate the polymerization$^{119}$ or post-polymerization modification.$^{120}$ Since the MMs are prepared and characterized separately prior to the grafting-through polymerization, the resultant molecular brush polymers have a well-defined grafting density and side chain length. However, the backbone can suffer from low DPs as a result of steric repulsion between the propagating brush polymer and the incoming MMs. Furthermore, as a result of the steric hindrance and low concentration of polymerizable chain end functionality, prolonged reaction times are often required to achieve a moderate MM conversion.$^{121}$ As a consequence, tedious and time-consuming purification is often needed to separate the unreacted MMs.

![Scheme 1.13 Synthesis of brush polymers via the grafting-through approach.](image-url)
Recent advances in ROMP have led to the introduction of a class of highly active, fast initiating ruthenium (Ru)-based metathesis catalysts with high functional group tolerance. These desirable features make them ideal catalysts for the synthesis of molecular brush polymers via the polymerization of norbonenyl terminated MMs (Scheme 1.14).

![Scheme 1.14 Synthesis of brush polymers via the grafting-through approach and ROMP.](image)

Compared to (meth)acrylic terminated MMs, norbonenyl MMs provide larger spacing between the side chains, providing a kinetically favourable environment for propagation. Furthermore, the ring strain of the norbonenyl functionality is released after polymerization, which provides an additional thermodynamic driving force for the grafting-through polymerization. As a result of the high reactivity of Ru catalysts, polymerization of MMs proceeds at a fast rate, even at low norbonenyl concentrations.\(^{119b}\) Functionalized brush (co)polymers\(^{120a,120b}\) with high MWs, large backbone DPs (up to 600), and controlled backbone and side chain lengths have been successfully synthesized using Ru-based catalysts with ROMP. High density molecular brush polymers prepared via ROMP have demonstrated great application potential in various material science and nanotechnology applications, in particular, polymer therapeutics. Johnson et al. reported the synthesis of water soluble and biocompatible polyethylene glycol (PEG)-branch-azide bivalent bottlebrush polymers via ROMP and the grafting-through approach. Photocleavable anticancer therapeutics were attached to the core domain of the bottlebrush polymer via click chemistry (Section 1.1.2), creating a UV-responsive drug delivery vehicle.\(^{102a,102c}\) Using a similar approach, Zou et al. reported the synthesis of pH-sensitive bottlebrush polymer-drug conjugates as anti-cancer drug delivery devices.\(^{122}\)
1.2.2.3 *Grafting-onto Approach*

This approach is based upon the coupling of end-functionalized polymers with a polymer backbone containing complementary functional groups on the repeat units (Scheme 1.15). One attractive advantage of this method is the brush polymer backbone and side chains can be prepared separately. They can be synthesized independently via mechanisms appropriate to the respective monomer structure and functionality, and characterized before the coupling reaction. However, steric repulsion between bulky side chains is the major concern for the grafting-onto strategy, limiting the grafting density. To drive the grafting reaction to high conversions an excess of side chains is often utilized and therefore, lengthy purification processes are required to isolate the brush polymers from the excess side chains. The most efficient and high yielding chemistries (e.g., click reactions and highly efficient nucleophilic substitutions) are preferred for the coupling reactions in the grafting-onto approach.

![Scheme 1.15 Synthesis of brush polymers via the grafting-onto approach.](image)

In a typical case of the side-chain attachment by nucleophilic substitution, the grafting-onto approach involves the synthesis of well-defined side chains by living anionic polymerization, and the subsequent coupling reaction of the side chains with the backbone repeat units that are susceptible to nucleophilic attack (e.g., alkyl and benzylic halides). For example, Deffieux *et al.* demonstrated the reaction of polystyryllithium anionic polymers with a poly(chloroethyl vinyl ether) backbone to give a high MW molecular brush with high grafting density. In the case of side-chain attachment by click chemistry, Gao *et al.* demonstrated the use of CuAAC (Section 1.1.2) as the coupling chemistry to synthesize a range of molecular brush polymers with different types of side-chain compositions,
including PEG, polystyrene (PS) and poly(tert-butyl acrylate) (PtBA). In this study, a poly(alkyne) backbone was prepared from poly(hydroxyethyl methacrylate) (synthesized via ATRP) modified with 4-pentynoic acid. Azide end-functionalized polymers were then attached onto the polymer backbone via CuAAC. This study elucidated that side-chain graft density is highly dependent on the length and bulkiness of the side chain.

1.2.3 Synthesis of Cyclic Polymers

Cyclic polymers are one of the most interesting classes of polymeric structures. They possess simple molecular structure, but intriguing physical and chemical properties as a result of the topology restriction imposed by the tethering of chain ends. For example, cyclic polymers exhibit smaller hydrodynamic radii, higher glass transition temperatures, higher thermal stability, and larger refractive index values than their linear counterparts. Cyclic macromolecules have attracted significant interest across various scientific disciplines. However, detailed understanding of the physical and chemical properties of cyclic polymers has been limited by their complicated syntheses. Firstly, large-scale synthesis of cyclic polymers is difficult to achieve. Furthermore, most methods yield cyclic products containing linear impurities, which may lead to erroneous results in property measurements of the cyclic materials. Tremendous effort has therefore been directed towards the development of synthetic approaches that afford high-purity cyclic polymers.

As a result of modern advances in synthetic polymerization and modification techniques, several synthetic approaches have been devised and demonstrated very success for the preparation of cyclic polymers with high purities. These approaches can generally be divided into two classes: (1) end-to-end coupling, and (2) ring-expansion.

1.2.3.1 End-to-end coupling approach

The end-to-end coupling approach (also known as ring-closure approach) yields cyclic polymers through the coupling of the chain ends of linear precursors, and can be subdivided into three categories based upon the coupling method, including: (i) bimolecular homodifunctional, (ii) unimolecular homodifunctional, and (iii) unimolecular heterodifunctional approaches (Scheme 1.16). The distinct feature of the end-to-end coupling approach is that it requires high ‘Ruggli-Ziegler’ dilution to favour the
intramolecular coupling and avoid polycondensation reactions.\textsuperscript{125d} For homodifunctional couplings that are bimolecular in nature, it is more difficult to prepare extremely high purity cyclic polymers (Scheme 1.16, i) as two consecutive reactions are involved; the intermolecular coupling between the linear polymer and the linking agent, and then the intramolecular ring-closure. Typically, an optimized condition often favours one but disfavours the other reaction. In contrast, unimolecular homo- and heterodifunctional coupling approaches (Scheme 1.16, ii and iii) may generate high purity cyclic macromolecules under high dilution if a highly efficient coupling chemistry is used.

*Bimolecular homodifunctional approach.* In this approach (Scheme 1.16, i), the use of exact stoichiometric amounts of linear polymers and coupling agents are crucial to prevent linear impurities. However, even with equimolar quantities, linear bi-products cannot be totally eliminated via high dilution. This is due to the complication of secondary couplings, including the coupling between the preformed heterotelechelic polymer (synthesized by coupling of the coupling agent and the bis-functional linear precursor) and another coupling agent or bis-functional linear precursor, which competes with intramolecular cyclization, leading to linear contaminants. As a result, tedious purification process is required to isolate pure cyclic polymers. Living anionic polymerization that allows the formation of living polymers with well-defined MW and narrow MWD has been extensively used to prepare linear precursors for the bimolecular homodifuctional coupling approach. The pioneering studies for the preparation of cyclic polymers via this route were nearly simultaneously reported by three different research groups including those of Hocker,\textsuperscript{126} Rempp,\textsuperscript{127} and Vollmert.\textsuperscript{128} Since then, cyclic homopolymers and copolymers with diverse compositions derived from styrenics, vinylpyridines, ethylene oxides and dienes have been prepared.\textsuperscript{129}
**Scheme 1.16** Schematic representation of common end-to-end coupling techniques for the preparation of cyclic polymers: i) bimolecular homodifunctional, ii) unimolecular homodifunctional, and iii) unimolecular heterodifunctional approaches.

**Unimolecular homodifunctional approach.** This approach overcomes the complication of bimolecular coupling by direct coupling between identical polymer chain end functionalities (Scheme 1.16, ii). In contrast to the bimolecular approach, dilution of the linear polymer precursor will effectively suppress the oligomerization without reducing the rate of intramolecular coupling since the reactive groups are tethered to each other. Given that efficient coupling chemistries, including ring-closing metathesis\(^{130}\) and disulfide bridging\(^{131}\) can be utilized, well-defined cyclic polymers with high purity (> 90%) can be made at high dilution with minimal oligomeric by-products.

**Unimolecular heterodifunctional approach.** Ring-closure of linear polymers bearing complementary chain-ends provides an effective route to cyclic polymers if the end-groups can be efficiently installed and coupled at high dilution (Scheme 1.16, iii). This approach has several advantages over the two previously-described synthetic approaches. One
The significant advantage of this approach over the bimolecular homodifunctional coupling is the complementary functionalities are tethered to each other, eliminating problems associated with inexact stoichiometries. Furthermore, no intermolecular reaction is required, so high dilution can be utilized to prevent intermolecular condensation without slowing the rate of cyclization. Compared to the unimolecular homodifunctional approach, the effective concentration of reactive functional pairs on different chains is reduced by half, and this lowers the possibility of oligomerization. However, the unimolecular heterodifunctional coupling approach is more synthetically involved, as it requires the quantitative instalment of complementary chain ends onto the linear polymer precursors. These functional chain ends are usually installed via the combination of functional initiators and post-polymerization end-group transformations. Incomplete instalment of complementary chain ends will lead to linear impurities and reduction in the cyclization yield.

Compared to living anionic polymerization techniques, controlled radical polymerization (CRP) such as NMP, ATRP, and RAFT polymerization are more attractive for the synthesis of linear polymer precursors for the unimolecular heterodifunctional approach. This is because linear polymers with controlled MW and narrow MWD can be prepared via CRPs under less stringent reaction conditions. More importantly, CRPs have high functional group tolerance, and therefore, there is a large family of complementary functional groups available for the end-group modification to afford heterotelechelic polymers with complementary reactive chain ends.

Laurent and Grayson devised an elegant approach to prepare cyclic polymers with high purity through the unimolecular heterodifunctional coupling approach, using a combination of ATRP and click chemistry. In this study, α-alkyne, ω-azide heterotelechelic polystyrenes (prepared via ATRP and subsequent azidation) were added drop-wise into a solution of Cu(I) catalyst to induce ring-closure. This synthetic approach exploited the robustness and high efficiency of click chemistry, and minimized the instantaneous concentration of the heterotelechelic polymer precursor through continuous feeding, so that the intramolecular cyclization is highly favoured over oligomerization. As a result, high purity cyclic polymers can be isolated with negligible amounts of linear by-products foregoing the need for rigorous purification. The key merit of this approach is that the ring-closure of linear precursors can be efficiently achieved at high concentration (0.09 mM
final concentration) without the need of excessive amounts of solvent. Later, a diverse number of cyclic (co)polymers, including cyclic poly(N-isopropylacrylamide),\textsuperscript{132a} poly(methyl acrylate-\textit{b}-styrene),\textsuperscript{137} poly(\textepsilon-\text{-}caprolactone)\textsuperscript{138} and poly(4-vinylbenzylcarbazole),\textsuperscript{135b} have been prepared in high purity via analogous approaches.

1.2.3.2 Ring-expansion Approach

The ring-expansion approach involves an initiator or catalyst from which a cyclic polymer chain is grown, and the chain ends are attached to the initiator by relatively labile bonds (e.g., organometallic or electrostatic interactions). During propagation, monomers are continuously inserted into the weak bond, and this process is driven by thermodynamic effects, such as ring strain in cyclic monomers (\textbf{Scheme 1.17}). At the end of polymerization, cyclic polymers might still retain the initiating species, or in other cases, the catalyst will be expelled through ‘back-biting’ or ‘intermolecular chain transfer’ reactions. The significant advantage of this approach is that cyclic polymers can be prepared in large scales and high dilution is not required, as compared to the end-to-end coupling approach. Additionally, as the cyclic structure is maintained during polymerization, high MW cyclic polymers can be easily obtained without the entropic penalty associated with the end-to-end coupling approach. Linear contaminants can be eliminated by the rigorous purification of the monomer and initiator before polymerization. However, judicious selection of monomer and initiator pairs is essential to optimize the reaction so that side-reactions, such back-biting and depolymerization, are suppressed. As a consequence, high MW cyclic polymers with narrow MWDs can be prepared.

\textbf{Scheme 1.17} Schematic representation of the ring-expansion approach for the preparation of cyclic polymers.
Kricheldorf and Lee\textsuperscript{139} carried out the initial work on ring-expansion polymerization and prepared a variety of complex cyclic polymer topologies based on lactone or lactide monomers using cyclic tin alkoxide initiators.\textsuperscript{140} However, one major drawback of this technique is that the tin alkoxide bond present in the resultant cyclic polymer is unstable and readily undergoes hydrolysis. Li et al.\textsuperscript{141} reported a refined route to overcome the issue of the liable alkoxide bond by introducing a short block of a photo-cross-linkable lactone with an acrylate side chain into the polyester macrocycles. After UV crosslinking, the initiator can be removed while the integrity of the macrocyclic structure is still maintained.

Bielawski et al. demonstrated an elegant approach to prepare large ring cyclic olefins through the application of ring-expansion metathesis polymerization (REMP) using a cyclic Ru catalyst.\textsuperscript{125a} The polymerization process occurs through the repetitive insertion of monomers into the Ru catalyst to achieve the ‘ring-expansion’ of the cyclic structure. However, the polymerization process is accompanied by two competing mechanisms. Depolymerization occurs as the monomer is consumed. Likewise, at low monomer concentration, the Ru catalyst can undergo intramolecular chain transfer to regenerate the cyclic catalyst and an inactive cyclic poly(olefin). Both competing mechanisms cause broad MWD of the cyclic product with a typical value around 2.0. The rate of REMP is very rapid as high MW macrocycles can be synthesized in the order of minutes. REMP has yielded the highest MW macrocycles to date (upto 1200 kDa). Using the same principal, our research group synthesized a library of functionalized macrocyclic oligo(cyclooctene)s via Hoveyda–Grubbs catalyst mediated REMP in excellent yields.\textsuperscript{142}

Recently, Waymouth and co-workers\textsuperscript{143} reported the use of N-heterocyclic carbene (NHC)-catalyzed zwitterionic ring opening polymerization to prepare cyclic polylactide and polylactones in the absence of alcohol initiators, which are typically used to prepare linear polymers. After initiation, a zwitterionic propagating chain is generated and the chain ends are held in close proximity through electrostatic interaction. The ring expansion occurs when the cyclic lactide or lactone monomer is attacked by the alkoxide anion, leading to ring-opening and integration of the monomer into the propagating polymer chain. Back-biting occurs when the propagating ring size is sufficiently large. This leads to the formation of a stable cyclic polymer while regenerating the NHC catalyst. Through this technique, well-defined cyclic polyesters with narrow MWDs (PDI < 1.3) can be prepared.
with extremely high cyclic purity. Owing to the strong electrostatic interaction, the monomer concentration during polymerization can be as high as 0.6 M while still generating high purity cyclic polymers without linear by-products.

1.3 Supramolecular Chemistry

Supramolecular chemistry is a domain of chemistry focusing on the assembly of systems from a discrete number of subunits or components. Different from traditional chemical systems based upon covalent bonds, supramolecular structures are held together by weak and reversible non-covalent interactions between the assembling components. These forces include hydrogen bonding, metal coordination, hydrophobic interactions, π-π stacking, and electrostatic effects.

Non-covalent interactions are responsible for the formation of biological supramolecular assemblies such as DNA and proteins, which are essential components for important biological functions, for example, genetic information storage and replication, and O2 transportation in the blood stream. Early studies focused on elucidating the formation mechanism and functional properties of biological supramolecular assemblies trigged the initial interest in supramolecular chemistry. More recently, the field of supramolecular chemistry has advanced significantly to the stage where it is possible to design synthetic building blocks to assemble highly complex materials with unique and exciting functions and properties.

1.3.1 Inclusion Complexation of Poly(ε-caprolactone) and α-Cyclodextrin

Cyclodextrins (CDs) are cyclic oligosaccharides composed of D-glucose units that are joined by α-1,4-glucosidic linkages.144 The most common subtypes of CDs include α-CD, β-CD and γ-CD comprised of 6, 7, and 8 D-glucose units, respectively, although CDs with larger ring sizes exist naturally or can be synthetically prepared.145 The three dimensional structure of CDs can be considered as a truncated cone with hydroxyl groups located at the outer surface (Figure 1.2). The primary hydroxyls at the narrow side and secondary hydroxyls at the wide side of the truncated cone render CDs water soluble. The ether-like carbon frame of CDs creates an inner hydrophobic cavity, which can either partially or entirely accommodate lipophilic molecules with appropriate sizes. The main
driving forces for the formation of these so-called host-guest inclusion complexes are hydrophobic and van der Waals interactions. Other factors such as the release of CD ring strain, changes in solvent-surface tensions and hydrogen bonding also aid in the inclusion complex formation.\(^{146}\)

**Figure 1.2** Structural representation and dimensions of various cyclodextrins.\(^{144}\)

<table>
<thead>
<tr>
<th></th>
<th>Dimensions (nm)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>α-CD</td>
<td>0.45 1.32 0.57 1.37 0.78</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-CD</td>
<td>0.61 1.49 0.78 1.53 0.78</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>γ-CD</td>
<td>0.77 1.61 0.95 1.69 0.78</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Polyrotaxanes and polypseudorotaxanes are supramolecular assemblies that can be prepared by threading CDs onto linear polymer chains with or without end-caps, respectively (Figure 1.3 a and b, respectively). In 1992, Harada and co-workers demonstrated the first successful preparation of polyrotaxanes by threading α-CDs onto a linear PEG chain.\(^{147}\) The threaded α-CDs were trapped by capping the PEG chain with bulky end groups, thereby creating a ‘molecular necklace’ interlocked supramolecular structure. Since this initial demonstration, tremendous research effort has been focused on the development of CD-based polyrotaxanes and polypseudorotaxanes. α-CD, β-CD and γ-CD have been threaded onto a variety of hydrophilic and hydrophobic polymers, to afford polyrotaxanes and polypseudorotaxanes with different structural and characteristic properties.\(^{148}\)
In the past, significant attention has been focused on the development of poly(pseudo)rotaxanes constructed from CDs and linear aliphatic polyesters (e.g., poly(lactide) and poly(ε-caprolactone)). These materials have demonstrated superior mechanical strength, biocompatibility and degradability (originating from the polyester axle), and are suitable for a diverse range of applications in life sciences and nanotechnology. In particular, poly(pseudo)rotaxanes fabricated from α-CD and poly(ε-caprolactone) have proven useful as controlled drug release devices, for networks/gel formation, and as shape memory materials.

1.3.2 Stereocomplexation of Poly(methyl methacrylate) (PMMA)

Nature has mastered supramolecular interactions in assembling a vast array of intricate and exquisite supramolecular assemblies. An elegant example is the DNA double helix, which consists of two separate strands of nucleotides connected through hydrogen bonds. Some synthetic polymers have also been reported to adopt helical structures, including poly(isocyanates), poly(triphenylmethyl methacrylates), and poly(acetylenes). In comparison, multiple-stranded artificial helices such as the PMMA stereocomplex are rare. The PMMA triple-stranded supramolecule consists of an inter-twined double-stranded helix of isotactic (it-)-PMMAAs wrapped by a single strand of syndiotactic (st-)-PMMA in an it-/st- 1:2 stoichiometry (Scheme 1.18). The formation of the PMMA stereocomplex solely relies on van der Waals forces, and no specific interaction such as π-π stacking or hydrogen bonding is involved.
PMMA stereocomplex formation has been exploited as an assembly mode for the fabrication of ultrathin films, nanoparticles, network and gel formations, as well as fibers and dialysis membranes. Moreover, other interesting and remarkable characteristic properties of PMMA stereocomplexes that have been explored, include stereospecific polymerization-templating, molecular recognition capability and helix-sense stereocomplexation.

The PMMA stereocomplex was discovered in 1961 by Watanabe et al. who reported the solvent-specific crystallization behaviour of the st- and it-PMMA mixture, and found that the resultant crystallite has an apparent melting point. Schomaker and Challa proposed that the crystallization of the PMMA stereocomplex undergoes two different mechanistic pathways, including 1) fringe-micellar growth and 2) lamellar growth. However, to date, the formation mechanism of the PMMA triple-helix stereocomplex has not been conclusively elucidated.

A large variety of st-poly(methacrylate)s having primary and secondary ester groups (e.g., poly(ethyl methacrylate) and poly(isopropyl methacrylate)) are able to form stereocomplexes with it-PMMA. However, attempts to prepare stereocomplexes with it-poly(methacrylate)s other than it-PMMA have not yet been successful. This is understandable if one considers the triple-helix structure of the stereocomplex; the modification of the ester groups of the outer st-PMMA chain should have a smaller influence on the feasibility of the stereocomplex formation than that of the ester groups of the inner it-PMMA chains.
So far, limited examples of stereoregular polymethacrylate-based macromolecular architectures (e.g., stereoblock,\textsuperscript{161} comb,\textsuperscript{42b,162} and star\textsuperscript{47,163}) that undergo supramolecular assembly through stereocomplexation have been reported. PMMA stereoblock polymers were successfully prepared by Kitayama \textit{et al.}\textsuperscript{164} and found to exhibit unique solution viscosity behaviour in specific solvents. Compared to the corresponding mixture of \textit{it}- and \textit{st}-PMMA, the stereoblock polymer showed a large Huggins’ constant as a result of intramolecular association resulting from stereocomplexation. Uniform MW three-arm stereoregular PMMA (two \textit{it}-PMMA and one \textit{st}-PMMA arms) star polymers have been synthesized via living anionic polymerization and post-polymerization coupling. GPC analysis of its intramolecular stereocomplex revealed PMMA stereocomplexes could be formed in both \textit{st}/\textit{it}- stoichiometric ratios of 1:1 and 1:2, thus providing a molecular-level understanding of PMMA stereocomplex formation.\textsuperscript{163} More recently, our own research group\textsuperscript{47} reported the synthesis of syndiotactic PMMA CCS polymers via SLRP, and utilized the CCS polymers with complementary linear \textit{it}-PMMA to construct an array of polymeric network structures ranging from the nano- to macro-scales. The study of stereoregular PMMAs with different molecular architectures and a detailed understanding of their supramolecular self-assembly will not only improve the fundamental understanding of PMMA triple-helix stereocomplex formation, but also aid in the development of hierarchically structured advanced nanomaterials.
1.4 **Scope of Thesis**

1.4.1 **Thesis Objective**

The research aim of this thesis is to develop efficient synthetic routes towards novel well-defined macro(supra)molecular architectures through the application of controlled/living polymerization, click chemistry and supramolecular interactions for the development of advanced functional materials (**Scheme 1.19**).

**Scheme 1.19** *Research theme of this thesis: the synthesis of unprecedented well-defined macro(supra)molecular architectures through the application of controlled/living polymerization, click chemistry and/or supramolecular interactions for the development of advanced functional materials.*

In this work, linear polymeric building blocks with control over MW, end-group functionality and/or stereochemistry were synthesized via controlled polymerizations. Through a second controlled polymerization or click chemistry, novel macromolecular architectures, including CCS, bottlebrush and cyclic polymers, with well-defined dimensions were successfully prepared from the corresponding linear polymeric building blocks. The resultant macromolecular architectures then served as precursors for the construction of various unprecedented high-order supramolecular polymers via supramolecular chemistry.
1.4.2 Outline of this thesis

The work presented in this thesis can be divided into three main parts:


Part 2. Synthesis and characterization of novel poly(pseudo)rotaxane supramolecular architectures.


In Part 1, facile and efficient synthetic routes were devised towards a library of CCS polymers with various functional macromolecular architectures. Chapter 2 describes a synthetic method to prepare a large variety of CCS polymers with high peripheral functionality through a scaffold approach via click chemistry (Figure 1.4).
Chapter 2 described the near-quantitative synthesis of CCS polymers via organic catalyst-mediated ROP (Figure 1.5). The generalization of this efficient synthetic technique to prepare other functional star architectures was demonstrated in the synthesis of a novel degradable CCS polymer with high ‘clickable’ end functionality.

Figure 1.4 Chapter 2: Synthesis of a diverse range of functional CCS polymers with high peripheral functionality via click chemistry.
Figure 1.5 Chapter 3: Near-quantitative synthesis of well-defined PCL-based CCS polymers.

In Part 2, the synthetic strategies to prepare novel poly(pseudo)rotaxane supramolecular architectures are presented. In Chapter 4, the first synthesis of CCS-based polyrotaxane is demonstrated. These unique supramolecular structures were prepared via the inclusion complexation of alkyne functional PCL-based CCS polymers and α-cyclodextins, followed by an end-capping reaction via click chemistry (Scheme 1.20). The resultant CCS-based polyrotaxanes were characterized and found to possess unique core-shell morphology in comparison to the PCL CCS polymer precursor.

Scheme 1.20 Chapter 4: Synthesis of CCS polyrotaxane through the inclusion complexation of PCL CCS polymer and α-cyclodextrin, and ‘click’ end-capping.
Chapter 5 describes a synthetic approach to prepare a novel, high density PCL bottlebrush polymer via the ROMP of a norbornenyl PCL macromonomer. α-CDs were then threaded onto the side-chains of the PCL bottlebrush polymers via inclusion complexation, resulting in the formation of an unprecedented bottlebrush polypseudorotaxane supramolecular architecture. The bottlebrush polypseudorotaxane possesses higher hydrodynamic volume than the PCL bottlebrush precursor, and an elongated cylindrical morphology upon inclusion complexation as opposed to the 3D globular morphology of the PCL bottlebrush polymer precursor (Scheme 1.21).

Scheme 1.21 Chapter 5: Synthesis of bottlebrush polypseudorotaxane (BB-IC) through the inclusion complexation of high density PCL bottlebrush polymer (BB) and α-CDs.

In Part 3 (Chapter 6), the synthesis of a novel stereospecific cyclic polymer (i.e., cyclic syndiotactic (c-st-)PMMA) is described. The simultaneous control over MW, MWD, tacticity and topology enable the c-st-PMMA to form a unique ‘polypseudorotaxane-type’ supramolecular assembly with the complementary linear isotactic (l-it-)PMMAs via stereocomplexation. The new stereocomplex is essentially different from the conventional linear PMMA triple-helix stereocomplex, and it demonstrates controlled crystallization mechanism. Such regulation in crystallization mode originates from the topology constraint of the st-PMMA assembly component (Scheme 1.22).
Scheme 1.22 Chapter 6: Preparation of the PMMA ‘polypseudorotaxane-type’ stereocomplex using the l-it-PMMA and c-st-PMMA pair (Route I), and the conventional triple-helix stereocomplex using the l-it-PMMA and l-st-PMMA pair (Route II).

Chapter 7 includes the concluding remarks and some proposed future research directions of the work presented in this thesis.
1.5 Reference


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PART 1

Synthesis and Characterization of Novel Star Macromolecular Architectures
Chapter 2

Synthesis of a Star Polymer Library with a Diverse Range of Highly Functionalized Macromolecular Architectures

2.1 Chapter Perspective

An efficient and versatile synthetic route towards a library of star macromolecular architectures with different functional properties is presented in this chapter. Various highly functionalized core cross-linked star (CCS) polymers were prepared by grafting the corresponding azido functional compounds onto a CCS polymer scaffold with high alkyne functionality via click chemistry. Factors affecting the grafting efficiency were closely examined in terms of the nature of the azido functional compounds and their compatibility with the star scaffold. The effect of macromolecular architecture on the click functionalization was evaluated by comparing the grafting efficiencies of various azido functional compounds onto the CCS with those onto a polyalkyne linear macroinitiator. Hence, a useful macromolecular model, which may be utilized to predict the efficiency of high density functionalization of complex 3-D nanostructures, is established.
2.2 Introduction

CCS polymers represent a unique type of three-dimensional (3D) macromolecular architecture consisting of a cross-linked core surrounded by a number of radiating arms, typically 10 to 100. CCS polymers can often possess very high molecular weights, whilst still maintaining excellent solubility characteristics and low viscosities comparable to linear or branched polymers with lower molecular weights. The distinctive rheological properties and 3D globular structure of CCS polymers has attracted significant interest and resulted in a number of potential applications, including polymer therapeutics and drug delivery, cascade reaction catalysis, microporous films and paint additives. In this thesis, significant amount of research effort is devoted in developing efficient synthetic method to prepare novel functional star polymer architectures for the interest of fundamental research as well as material development. An efficient and versatile synthetic approach to prepare a diverse range of CCS polymer with high coronal functionality is described in this chapter.

Often, the design and synthesis of CCS polymers carrying high desirable functionality and spatial control over their location is required to meet their application needs. Especially in polymer therapeutics, the synthesis of CCS polymers with high coronal functionality would be particularly beneficial for drug loading and conjugation of targeting moieties. Functional groups at the periphery of nanometer-sized drug carriers could facilitate drug encapsulation through either covalent bonding or non-covalent (e.g., electrostatics) interactions with complementary drugs such as peptides, proteins, nucleic acids and other therapeutic agents. Thus, an increased functional group density offers larger drug-loading potential. Moreover, a high number of reactive functional sites increases the chance of success in attachment of targeting moieties and binding agents to the carrier, which ultimately facilitates greater cell adhesion and site-specific drug delivery.

CCS polymers with high functionality, good structural control and narrow molecular weight distributions (MWDs) can be readily synthesized via controlled polymerization techniques, and the arm-first approach. Functional groups can be integrated into the periphery of CCS polymers via two discrete approaches; end-functional star polymers can be prepared from telechelic macroinitiators/macromonomers or block copolymer macroinitiators in which one block consists of a number of pendent
functionalities. The drawback of the former is that the resulting star polymers possess a relatively low number of functionalities at the periphery, since the number of functional units is equal (restricted) to the number of arms. To overcome this, dendritic macroinitiators have been used to prepare CCS polymers,\textsuperscript{19} leading to stars with up to 1100 peripheral functional groups. However, the preparation of dendritic macroinitiators generally involves multiple protection/deprotection steps, which require time and labour intensive synthetic protocols, especially considering that high dendron generation is required to achieve high functionality. In contrast, stepwise polymerization of functional monomers to yield block copolymer macroinitiators suitable for CCS polymer formation\textsuperscript{20} is a more promising and synthetically convenient route to introduce a large number of coronal functionalities. However, this synthetic route requires the preparation of desirable functional monomers before polymerization, which may be synthetically involved.\textsuperscript{21} Furthermore, controlled polymerization of functional monomers can be restricted as a result of steric constraints and coordination/reaction of the monomer with the catalyst, initiator or propagating chains.\textsuperscript{22} To avoid this, protected monomers are often employed and deprotected post-polymerization to afford the desired functional polymers.\textsuperscript{21,23,24} In addition, monomers with bulky pendent groups can suffer from poor conversion as a result of polymerization-depolymerization equilibrium.\textsuperscript{25} Therefore, a facile and efficient route which provides access to a diverse range of highly corona-functionalized CCS polymers from a single scaffold would be immensely invaluable.

More recently, our research group demonstrated the synthesis of a CCS polymer with high loadings of corona-isolated terminal alkyne (click) functionalities.\textsuperscript{26} As a result of the efficient nature and functional group tolerance of CuAAC chemistry,\textsuperscript{27-29} azido substituted compounds with a range of functionalities can be grafted onto the alkyne CCS polymer scaffold to yield a wide variety of corona-functionalized star polymers.

Herein this chapter first described the preparation of a clickable CCS polymer scaffold via an improved synthetic approach, and then the grafting of various azido substituted compounds via CuAAC chemistry to afford highly corona-functionalized star polymers with unique and interesting architectures and properties. The grafting efficiency with different azido compounds and polymers was determined and factors affecting the
click efficiency were investigated. Thus, this work provides a valuable reference for the high density functionalization of 3D nanostructures.

### 2.3 Results and Discussion

#### 2.3.1 Improved Synthesis of ‘Clickable’ CCS Polymer Scaffold

In our previous publication two issues were encountered during the preparation of alkyne CCS polymers, including poor macroinitiator-to-star conversion and star-star coupling. Therefore, a new synthetic strategy was developed to overcome these problems. Initially, the alkyne CCS polymer scaffold was prepared via the arm-first approach to act as a versatile platform for the preparation of a diverse library of highly functionalized stars with tunable structures and properties (Scheme 2.1). In the arm formation step, macroinitiator 2.3 was firstly synthesized via ROP of ε-caprolactone (CL) and subsequent atom transfer radical polymerization (ATRP) of trimethylsilyl propargyl methacrylate (TMS-PgMA) using the asymmetric difunctional initiator 2-hydroxyethyl 2′-methyl-2′-bromopropionate 2.1 (Scheme 2.1(i) and (ii), respectively). In the star formation step (Scheme 2.1(iii)), ROP of 4,4′-bioxepanyl-7,7′-dione (BOD) cross-linker using macroinitiator 2.3 and Sn(OTf)₂ as catalyst yielded star CCS 2.1 with TMS protected alkyne functionalities. The TMS protecting groups on the corona of CCS 2.1 were removed using TBAF (Scheme 2.1(iv)) to afford CCS 2.2 with clickable terminal alkyne groups suitable for the subsequent CuAAC functionalization.

In the arm formation step, ROP and ATRP were repeated several times with various monomer initiator ratios to afford macroinitiators 2.2 and 2.3 with various degrees of polymerization; the theoretical and determined molecular weight characteristics and monomer unit ratios indicated good control of the polymerization was observed in all cases (Table 2.1).
Scheme 2.1 Synthetic route for the preparation of highly corona-functionalized CCS polymers via sequential ROP, ATRP and CuAAC chemistry: (i) formation of poly(ε-caprolactone) macroinitiator (HO-PCL-Br) 2.2 through ROP of CL using initiator 2.1, (ii) synthesis of poly(ε-caprolactone-\textit{b}-trimethylsilyl propargyl methacrylate) macroinitiator (HO-P(CL-\textit{b}-TMS-PgMA)-Br) 2.3 through ATRP of TMS-PgMA using macroinitiator 2.2, (iii) preparation of alkyne functionalized star CCS 2.1 via the arm-first approach and ROP of BOD cross-linker with macroinitiator 2.3, (iv) deprotection of TMS-protected CCS 2.1 using TBAF in acetic acid to afford terminal alkyne functionalized star CCS 2.2, and (v) corona functionalization of CCS 2.2 via CuAAC chemistry using CuBr/PMDETA as the catalyst.
Table 2.1 Characterization of PCL (HO-PCL-Br) 2.2, and poly(ε-caprolactone-block-trimethylsilyl propargyl methacrylate)-Br (HO-P(CL-b-TMS-PgMA)-Br) 2.3.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Samples</th>
<th>PCL</th>
<th>(\text{P(TMS-PgMA)})</th>
<th>PCL</th>
<th>(\text{P(TMS-PgMA)})</th>
<th>(M_n) (kDa)</th>
<th>PDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HO-PCL-Br</td>
<td>28.5</td>
<td>-</td>
<td>29</td>
<td>-</td>
<td>3.5</td>
<td>1.2</td>
</tr>
<tr>
<td>2</td>
<td>HO-PCL-Br</td>
<td>38</td>
<td>-</td>
<td>43</td>
<td>-</td>
<td>4.1</td>
<td>1.30</td>
</tr>
<tr>
<td>3</td>
<td>HO-PCL-Br</td>
<td>45</td>
<td>-</td>
<td>48</td>
<td>-</td>
<td>5.1</td>
<td>1.20</td>
</tr>
<tr>
<td>4</td>
<td>HO-P(CL-b-TMS-PgMA)-Br</td>
<td>38</td>
<td>18</td>
<td>43</td>
<td>18</td>
<td>8.7</td>
<td>1.2</td>
</tr>
<tr>
<td>5</td>
<td>HO-P(CL-b-TMS-PgMA)-Br</td>
<td>38</td>
<td>50</td>
<td>43</td>
<td>64</td>
<td>16.0</td>
<td>1.4</td>
</tr>
<tr>
<td>6</td>
<td>HO-P(CL-b-TMS-PgMA)-Br</td>
<td>38</td>
<td>24</td>
<td>43</td>
<td>27</td>
<td>11.3</td>
<td>1.2</td>
</tr>
<tr>
<td>7</td>
<td>HO-P(CL-b-TMS-PgMA)-Br</td>
<td>45</td>
<td>28</td>
<td>48</td>
<td>31</td>
<td>12.0</td>
<td>1.2</td>
</tr>
</tbody>
</table>

\(^{i}\) Degree of polymerization (DP) calculated from monomer conversion as determined by GC-MS. \(^{ii}\) Degree of polymerization (DP) determined from \(^1\)H NMR spectroscopic analysis. \(^{iii}\) Number average molecular weight (\(M_n\)) and polydispersity (PDI) determined from GPC using THF as eluent based upon the assumption of 100% mass recovery.

A TMS protected PgMA monomer was employed to minimize potential side reactions, including propagating radical addition to terminal alkyne moieties (leading to branched or cross-linked products at high monomer conversions)\(^{23,32}\) and strong coordination of terminal alkynes to Cu(I) complexes (such as those commonly used as ATRP catalysts)\(^{40,41}\). Polymers prepared from each synthetic step were characterized via GPC (Figure 2.1) and \(^1\)H NMR spectroscopic analysis. The GPC results show a decrease in elution times corresponding to MW increases across each synthetic stage. Low polydispersities (PDI < 1.30) were observed for all polymers prepared indicating narrow MWDs and controlled polymeric architectures were generated in all cases.
Figure 2.1 GPC (THF) refractive index (RI) chromatograms of (i) HO-PCL-Br macroinitiator 2.2 ([2.1]:[Sn(Oct)2]:[CL] = 2:1:80, 110 °C in toluene) (Table 2.1, Entry 2), (ii) HO-P(CL-b-TMS-PgMA)-Br macroinitiator 2.3 ([2.2]:[CuBr]:[PMDETA]:[TMS-PgMA] = 1:1:2:35, 80 °C in anisole) (Table 2.1, Entry 4), (iii) crude CCS 2.1 ([2.3]:[Sn(OTf)2]:[BOD] = 10:1:100, 65 °C in 1:4 THF:Toluene, (iv) fractionated CCS 2.1, and (v) deprotected CCS 2.2 polymer consisting of 70% CCS polymer and 30% unincorporated polymer as determined by deconvolution of the RI chromatograms using Gaussian functions.

In the star-formation step, stannous triflate (Sn(OTf)2) was used as the catalyst for ROP of the BOD cross-linker, allowing the alkyne star CCS 2.1 to be prepared under milder reaction conditions at a temperature of 65 °C. In comparison to the previously reported synthesis using stannous 2-ethylhexanoate (Sn(Oct)2) as the catalyst at 100 °C,26 Sn(OTf)2 provides significantly improved macroinitiator-to-star conversions from 40% to 60%, and reduced the amount of the star-star coupling from approximately 15% to < 1%
(Figure 2.1(iii)). Overall, the new Sn(OTf)₂ catalytic system utilized increased the yield of the CCS polymers from 31% to 60% due to the elimination of high molecular weight star-star coupled products.²⁶ These results indicate that Sn(OTf)₂ and the lower reaction temperature suppresses transesterification during ROP,⁴²,⁴³ minimizing intramolecular backbiting of terminal hydroxyl groups and intermolecular transesterification. Intramolecular backbiting leads to cyclization of the arm macroinitiators resulting in loss of their active hydroxyl terminus, thus preventing them from participating in ROP and integration into the CCS polymers. Intermolecular transesterification at high BOD conversions would result in active hydroxyl initiating sites in the core of preformed CCS polymers attacking ester moieties of adjacent CCS polymers, which is believed to be the major cause of star-star coupling. Lowering the reaction temperature would suppress both types of transesterification and allow high macroinitiator-to-star conversions with minimal star-star coupling. Sn(OTf)₂ has been reported⁴²,⁴³ to be capable of catalyzing ROP of lactones at low temperatures and fast reaction rates. The results obtained in this study suggest Sn(OTf)₂ is a superior catalyst for the synthesis of alkyne functionalized CCS polymers. The crude CCS polymer was purified via fractional precipitation to afford the fractionated star CCS₂.₁ with a $M_n$ of 300 kDa and low PDI of 1.25 (Figure 2.1(iv)). From the MW and conversion data the average number of arms ($N_{arms}$) incorporated into each CCS polymer was calculated to be 25 with each arm containing ~18 pendent TMS protected alkyne groups; thus, each star possess ~450 alkyne groups (see Appendix 2). Even after multiple fractional precipitations, clean separation of CCS₂.₁ could not be achieved as evidenced from a shoulder at high retention time (Figure 2.1(iv)), which corresponds to unincorporated polymer. Following the isolation of CCS₂.₁, the alkyne groups on the corona were deprotected to afford alkyne star CCS₂.₂ (Scheme 2.1(iv)) with a $M_n$ of 267 kDa, which correlates well with the theoretical value of 265 kDa (Figure 2.1(v)), based upon the $M_n$ of CCS₂.₁ and number of alkyne groups per star. GPC and $^1$H NMR spectroscopic analysis (Figure 2.2) indicate that no degradation of the PCL components occurs under the acidic deprotection conditions. Deconvolution of the GPC RI chromatogram of CCS₂.₂ (Figure 2.1(v)) provided an estimate of 70% deprotected CCS polymer and 30% unincorporated polymer.
Figure 2.2 $^1$H NMR spectra (CDCl$_3$, 400 MHz) of TMS-protected alkyne functionalized star CCS 2.1 and alkyne functionalized star CCS 2.2. Note: no degradation of PCL components was detected since area ratio of resonance 1 over resonance 2a remains the same after the removal of TMS protecting groups.

The 30% unincorporated polymer is likely to originate from ‘arm’ macroinitiator 2.3 that has been chain extended$^1$ with BOD but not incorporated into CCS polymers (i.e. P(BOD-b-CL-b-TMS-PgMA)). There are two possible causes for the presence of unconverted P(BOD-b-CL-b-TMS-PgMA): (i) during the ROP mediated CCS formation some of the BOD chain extended macroinitiators P(BOD-b-CL-b-TMS-PgMA) are terminally inactive,$^{44,45}$ due to insufficient Sn(II) catalyst being available to complex with the hydroxyl group of the macroinitiator and initiate cross-linking, as the Sn(II) catalysts are mostly trapped in the core of the preformed CCS polymers, and (ii) the inactive macroinitiators with pendent cross-linkable functionality cannot diffuse effortlessly into the preformed CCS polymers and are therefore not incorporated due to steric restrictions.$^{1,44}$
thus prolonged polymerization times would be required to convert all the unreacted macroinitiators. The unincorporated P(BOD-\(b\)-CL-\(b\)-TMS-PgMA) present in the crude CCS cannot be completely isolated via fractional precipitation (Figure 2.1(iv)) and this most likely results in the 30% unincorporated polymer in the final alkyne CCS polymer product (Figure 2.1(v)).

2.3.2 Synthesis of Azido Substituted Compounds

Following the improved synthesis of the alkyne CCS polymer scaffold CCS 2.2, a range of azido substituted derivatives (Figure 2.3) were prepared to demonstrate the versatility of the click approach towards the preparation of a library of highly corona-functionalized stars and to assess factors affecting the ‘click’ efficiency.

![Figure 2.3 Structures of azido substituted compounds C1-7 and terminal azido functionalized polymers P1-4 employed for click functionalization of alkyne star CCS 2.2.](image)

The azido substituted compounds prepared in this study can be divided into four main classes: (i) polycyclic aromatic hydrocarbons, including 1-(azidomethyl)-naphthalene C1, 3-azidopropyl anthracene-9-carboxylate C2 and 3-azidopropyl 4-oxo-4-(pyren-4-yl) butanoate C3; (ii) saccharides, including \(\beta\)-galactopyranosyl azide C5 and mono-6-deoxy-
6-azido-β-cyclodextrin C6; (iii) small hydrophobic molecules with linear structures, including 3-azidopropyl furan-2-ylmethylcarbamate C4 and 1-azidodecane C7, and; (iv) macromolecules, including PEG with various molecular weights (P1-3) and poly(tert-butylacrylate) (PtBA) P4. The successful synthesis of C1-7 was confirmed by NMR spectroscopic analysis, GC-MS and MALDI ToF MS (C6 only). Azido terminated PEG with various molecular weights ($M_n = 440, 1070$ and $1800$ kDa) were prepared by mesylation of poly(ethylene glycol) monomethyl ether followed by azide substitution and characterized via GPC, $^1$H NMR spectroscopic analysis and MALDI ToF MS. Quantification of the degree of azide substitution was achieved using $^1$H NMR spectroscopic analysis and MALDI ToF MS (see Appendix 2, Figure A2.1 - 2.3), which revealed a high degree of azide functionalization ($> 85\%$) for all PEG samples. Terminal azido PtBA P4 was prepared first via ATRP of tert-butyl acrylate using methyl 2-bromopropionate as the initiator followed by substitution of the ω-bromo group with azide. The polymer P4 was analyzed via GPC, $^1$H NMR spectroscopic analysis and MALDI ToF MS, with the latter revealing quantitative azide substitution (see Appendix 2, Figure A2.4) in agreement with the literature.46

2.3.3 Functionalization of Alkyne CCS Polymer Scaffold via CuAAC

Functionalization of the alkyne CCS polymer scaffold CCS 2.2 was achieved by grafting the azido substituted compounds C1-7 and P1-4 via CuAAC chemistry using Cu(I)/PMDETA as the catalyst (Scheme 2.1(v)) to afford CCS C1-7 and CCS P1-4, respectively (Table 2.2). The reactions were performed by adding an excess of the azido substituted compounds to a 0.037 mM (16.8 mM pendent alkyne groups) solution of CCS 2.2. This solution was subjected to several freeze-pump-thaw cycles prior to the addition of a degassed Cu(I)/PMDETA catalyst stock solution (20 mol% relative to alkyne) to prevent oxidation of the catalyst and possible side reactions. All reactions were conducted under argon at room temperature for 48 h. Low reaction temperatures and catalyst loadings were employed to suppress potential side reactions, and long reaction times were used to compensate for the retarded rate of CuAAC chemistry resulting from steric congestion of the pendent alkyne groups. At the end of the reactions, the Cu/PMDETA catalyst was
isolated via the addition of excess dodecanthiol\textsuperscript{,47} which forms an insoluble copper complex that can be removed by filtration. Incomplete removal of copper complex was found to lead to gel formation as the result of star-star coupling upon isolation of the functionalized stars. All click-functionalized CCS polymers (except CCS P4) were isolated from the crude reaction solution via precipitation and characterized by GPC, $^1$H NMR spectroscopic analysis and dynamic light scattering (DLS) (Table 2.2).

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Mass\textsuperscript{a} (g mol\textsuperscript{-1})</th>
<th>CE\textsuperscript{b} (%)</th>
<th>Error\textsuperscript{c} (%)</th>
<th>Functional Units No.\textsuperscript{d}</th>
<th>$M_n^{\text{theo}}$ (kDa)</th>
<th>$M_n^{\text{NMR}}$ (kDa)\textsuperscript{b}</th>
<th>$M_n^{\text{GPC}}$ (kDa)\textsuperscript{f}</th>
<th>PDI</th>
<th>$D_n$\textsuperscript{g} (nm)</th>
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<tr>
<td>CCS 2.1\textsuperscript{h}</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>300</td>
<td>1.25</td>
<td>29.6</td>
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<tr>
<td>CCS 2.2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>265</td>
<td>267/(257)\textsuperscript{j}</td>
<td>1.30</td>
<td>18.0(25.5)\textsuperscript{i}</td>
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<tr>
<td>CCS C1</td>
<td>183.2</td>
<td>99\textsuperscript{+}</td>
<td>10</td>
<td>450</td>
<td>358</td>
<td>358</td>
<td>330</td>
<td>1.35</td>
<td>18.6</td>
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<td>76</td>
<td>8</td>
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<td>45</td>
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\textsuperscript{a}Molecular weight for corresponding azido substituted compound. \textsuperscript{b}Click efficiency determined by $^1$H NMR spectroscopic analysis. \textsuperscript{c}Error of click efficiency calculation based upon $^1$H NMR spectroscopic analysis resonance integrations. \textsuperscript{d}Number of azido substituted compounds attached per star. \textsuperscript{e}Number average molecular weight of functionalized stars determined by $^1$H NMR spectroscopic analysis. \textsuperscript{f}Number average molecular weight of functionalized stars determined by GPC (THF) and based upon the assumption of 100% mass recovery. \textsuperscript{g}Hydrodynamic diameter of functionalized stars determined by DLS at 25 ± 0.1 °C. \textsuperscript{h}Protected alkyne star polymer prepared using macroinitiator 2.3 (Table 2.1, Entry 4). \textsuperscript{i}Molecular weight measurement determined by GPC (DMF) and based upon the assumption of 100% mass recovery. \textsuperscript{j}DLS measurement using DMF as solvent at 25 ± 0.1 °C. \textsuperscript{k}Number average molecular weight calculated using MALDI ToF MS. \textsuperscript{l}Number average molecular weight measured by GPC (THF) based upon the assumption of 100% mass recovery.
As a result of the unique architecture of the click-functionalized stars, GPC systems (using THF or DMF as the mobile phase) equipped with MALLS detectors were employed to calculate the MW characteristics of the CCS polymers based upon the assumption of 100 \% mass recovery\textsuperscript{48}, since this allows the absolute MWs to be determined independent of the polymers’ architectures. \textsuperscript{1}H NMR spectroscopic analysis was predominately used to quantify the grafting efficiency of azido substituted compounds, since GPC might give erroneous results due to possible intermolecular coupling of star polymers. Furthermore, DLS was employed to investigate the variation in hydrodynamic volume of the CCS polymers upon click-functionalization. The $M_n$ of the functionalized CCS polymers calculated via GPC (Table 2.2) revealed an increase from 267 (CCS 2.2) to 320-885 kDa depending on the ‘clicked’ compound. DLS results revealed an increase of the hydrodynamic volumes of the functionalized stars after click modification, with hydrodynamic diameters ($D_h$) increasing from 18 to 18.6-145.8 nm. From \textsuperscript{1}H NMR spectroscopic analysis the number of functional compounds attached to each CCS polymer ranged from 45 to 450 and was highly dependent on their structure and functionality. Interestingly, it was noted that some of the functionalized CCS polymers suffer from increased polydispersities ($> 1.30$) and $M_n$ values calculated via GPC are generally higher than those determined by \textsuperscript{1}H NMR spectroscopic analysis, which indicates possible star-star coupling as a result of side reactions. Three possible side reactions that might lead to star-star coupling are illustrated in Scheme 2.2.
Scheme 2.2 Side reactions that could potentially cause star-star coupling during CuAAC reactions including: (a) Sonogashira-type coupling, (b) radical dimerization, and (c) Glaser coupling.

(i) Sonogashira-type coupling of terminal α-carbon on CCS polymer arms with pendent alkyne groups along the arms of the other CCS polymer (after elimination of the terminal bromide groups) can be catalyzed by Cu(I) and tertiary bases (e.g., PMDETA) leading to the formation of star-star coupled products (Scheme 2.2a). (ii) In absence of oxygen (or other radical scavengers) Cu(I)/PMDETA abstracts bromine atoms from the CCS polymers to form terminal radical sites that can undergo intermolecular dimerization, resulting in star-star coupling (Scheme 2.2b). (iii) In the presence of oxygen or a base (e.g., PMDETA), Cu(I) can catalyze the Glaser coupling of terminal alkynes (Scheme 2.2c). Thus, intermolecular coupling of pendent terminal alkynes on CCS polymers could lead to star-star coupling. Intermolecular couplings cannot be detected using characterization techniques such as $^1$H NMR spectroscopic analysis since characteristic resonances resulting from side-reactions are insignificant compared to resonances from the polymer. It is evident that even small proportions of coupling reactions can lead to detrimental effects on the MW.
characteristics of the functionalized star polymers, and given the high functional density of the corona the chance of coupling reactions is amplified.

2.3.4 Synthesis of Fluorescent CCS Polymers

Fluorescent stars CCS C1-3 carrying a high number of polycyclic aromatic hydrocarbons were prepared through grafting of azido substituted naphthalene, anthracene and pyrene (C1-3, respectively) derivatives onto CCS 2.2 via CuAAC chemistry.

![Figure 2.4 GPC (THF) RI chromatograms for (a) naphthalene, (b) anthracene, and (c) pyrene corona-functionalized stars CCS C1-3, respectively, and (d) alkyne CCS polymer scaffold CCS 2.2.](image)

$^1$H NMR spectroscopic analysis (vide infra) revealed that the grafting was successful in all cases with the click efficiency decreasing as the number of aromatic units increased. For
stars CCS C1-3 GPC-MALLS provided increases in MW (Table 2.2), although interestingly the RI chromatograms (Figure 2.4) revealed slight shifts to higher elution time. This unexpected shift may originate from an increase in structure rigidity of the functionalized stars causing delayed elution similar to that reported in linear polymer cyclization.\textsuperscript{50} Furthermore, the high density of aromatic groups on the stars corona may interact with the column material (cross-linked polystyrene) through π-π stacking, thus causing a delay in their elution.

Closer examination of the GPC RI chromatogram for the anthracene corona-functionalized star CCS C2 revealed a bimodal distribution (Figure 2.4b) with broad polydispersity and higher than theoretically predicted $M_n$. These results indicate the occurrence of star-star coupling, which might result from the previously described click side-reactions, but more likely, anthracene dimerization in the presence of light.\textsuperscript{51-53} As a result of the chromophoric nature of the polycyclic aromatic hydrocarbon derivatives used it was possible to quantify their loading via UV-Vis spectroscopic analysis, as demonstrated for the pyrene corona-functionalized star CCS C3 (Figure 2.5).

![Figure 2.5](image)

Figure 2.5 (a) UV-vis spectra (THF) for pyrene corona-functionalized star CCS C3 and azido pyrene C3, and (b) calibration curve for C3 and determination of CCS C3 pyrene loading. Inset: THF solution of CCS C3 under (i) white light and (ii) UV irradiation ($\lambda = 254$ nm).
UV-vis spectra of pyrene derivative C3 were recorded at known concentrations and the absorption measured at 354 nm was utilized to generate a calibration curve, from which the excitation coefficient was determined to be 60000 M\(^{-1}\)cm\(^{-1}\) (Figure 2.5). Utilizing this excitation coefficient the loading of pyrene molecules at the corona of star CCS C3 was calculated to be 370, which is similar to that determined via \(^1\)H NMR spectroscopic analysis (Table 2.2). Furthermore, the fluorescent nature of CCS C3 was demonstrated upon UV irradiation (\(\lambda = 254\) nm) (Figure 2.5), which provides additional evidence for the successful incorporation of pyrene.

2.3.5 Synthesis of Amphiphilic CCS Polymers

Amphiphilic CCS polymers with hydrophobic polyester-based cores and inner shells, and hydrophilic coronas were prepared through grafting CCS C2 with hydrophilic azido substituted saccharides C5 and C6, and PEGs P1-3; GPC RI chromatograms for the resulting amphiphilic stars, CCS C5-6 and CCS P1-3, respectively, are provided in Figure 2.6. Saccharide-based amphiphilic star polymers CCS C5 and CCS C6 were prepared through ‘click’ attachment of mono-azide functionalized \(\beta\)-galactose and \(\beta\)-cyclodextrin onto CCS 2.2, with GPC-MALLS (DMF) revealing increases in \(M_n\) from 267 kDa to 320 and 520 kDa, respectively. GPC RI chromatograms once again revealed peak shifts towards lower elution times (Figure 2.6a and b), possibly indicating an increase in the structural rigidity as previously discussed. The successful click-functionalization of CCS 2.2 with saccharide-based compounds C5 and C6 was also confirmed by \(^1\)H NMR spectroscopic analysis (Appendix 2, Figure A2.5) and DLS (Table 2.2).
Figure 2.6 GPC (DMF) RI chromatograms of (a) $\beta$-galactose corona-functionalized star CCS C5, (b) $\beta$-CD corona-functionalized star CCS C6, (c) PEG$_{400}$, (d) PEG$_{1000}$ and (e) PEG$_{2000}$ corona-functionalized stars CCS P1-3, respectively, and (f) alkyne CCS polymer scaffold CCS 2.2.

Amphiphilic stars CCS P1-3 were prepared by grafting various MW azido substituted PEGs P1-3, respectively, allowing the effect of PEG degree of polymerization to be studied. In contrast to the saccharide functionalized stars, GPC RI analysis revealed a decrease in elution time for the PEG functionalized stars as a result of a large increase in molecular size, which was confirmed by DLS (Table 2.2). It is proposed that the long and flexible grafted PEG chains are capable of extending past the stars original alkyne corona, resulting in an increased molecular size without significantly increasing the overall
structural rigidity. This would also be aided by any incompatibility between the inner shell PCL chains and grafted PEG.

2.3.6 Synthesis of Quantitatively Grafted CCS Polymers

Out of all the CCS polymers functionalized via CuAAC chemistry, three displayed quantitative grafting efficiency, CCS C1, CCS C4 and CCS C7. Whereas GPC RI chromatograms for these stars (Figure 2.7) revealed very slight peak shifts towards lower elution times, the $M_n$s closely resemble the theoretical molecular weights (100% grafting efficiency) (Table 2.2) within the determined margin of error. $^1$H NMR spectroscopic analysis (Table 2.2 and Appendix 2, Figure A2.6) also implied quantitative click efficiency was achieved in agreement with GPC results.

Figure 2.7 GPC (THF) RI chromatograms for quantitatively grafted CCS polymers: (a) naphthalene corona-functionalized star CCS C1, (b) furan corona-functionalized star CCS C4, (c) decane corona-functionalized star CCS C7, and (d) alkyne CCS polymer scaffold CCS 2.2.
The high grafting efficiency can be accounted for by the small molecular size of compounds C1, C4 and C7, which minimizes steric hindrance and improves their ability to penetrate readily into the corona of the star and access complementary reactive sites. GPC RI chromatograms of CCS C4 and CCS C7 (Figure 2.7b) displayed small shoulder peaks at low elution time (t = 15-17 min), which are attributed to intermolecular coupling (i.e., star-star coupling) resulting from the previously discussed click side-reactions.

2.3.7 Click Efficiency of High Density Functionalization of CCS Polymers

Upon isolation, the click efficiency of the grafted CCS polymer was determined by 1H NMR spectroscopic analysis, using the integration of characteristic resonances (Figure 2.8, signals 1 & 2b). For example, resonance 1 (δH = 4.05 ppm) corresponds to methylene protons adjacent to ester groups present along the backbone of the PCL arms, whereas resonance 2b (δH = 5.05 ppm) results from methylene protons adjacent to triazoles formed through click reactions. For all click efficiency calculations resonance 1 was normalized to a value of 43, which corresponds to the average number of CL repeat units per arm. As such, the click efficiency can be calculated using the ratio of the area under resonance 2b (A2b) over the calculated alkyne repeated units (N_{C≡C}) per arm using Equation 2.1, where 

\[ CE = \frac{A_{2b}}{N_{C≡C}} \quad (2.1) \]

In contrast, the low click functionalization and difficulties in the separation of unreacted PrBA-N3, precluded the use of 1H NMR spectroscopic analysis for determination of the click efficiency in the case of the PrBA functionalized star CCS P4. However, even without a good separation, the extent of click functionalization could be calculated from GPC, via integration and comparison of RI peak areas of the star and the unreacted PrBA-N3 before and after reaction (see Appendix 2, Figure A2.7).
Figure 2.8 $^1$H NMR spectra of (a) naphthalene, (b) anthracene, and (c) pyrene functionalized stars CCS C1, CCS C2 and CCS C3, respectively. * Denotes solvent resonances.

The results obtained from click functionalization of the alkyne star CCS 2.2 imply that the molecular size of the azido substituted compounds is a major factor affecting the click efficiency; the larger the molecular size of the azido substituted compounds, the lower the click efficiency. For example, NMR spectroscopic analysis of stars functionalized with C1, C2 and C3, revealed a decrease from 15.9 to 12.7 in the integrated area of the characteristic methylene resonance ($\delta_H = 5.05$ ppm, 2b, Figure 2.8), which indicates a decrease in the number of triazoles formed across these three reactions. This decrease in click efficiency can be explained by the increasing number of aromatic rings in going from C1 to C3, which hinders the ability for the azido compounds to penetrate the stars’ corona and reach the complementary alkyne functionalities. Therefore, the resultant CCS polymers are less functionalized when larger azido substituted compounds are employed. This is also
supported by the series of PEG functionalized stars CCS P1-3, with the click efficiency decreasing as the degree of polymerization of the PEG-N3 P1-3 increased (Appendix 2, Figure A2.8).

**Figure 2.9** ‘Click’ functionalization efficiency of azido substituted compounds onto the alkyne star CCS 2.2 versus the estimated molecular size of those compounds.62

In order to gain a better understanding on the molecular size effect on the click efficiency of various azido compounds, the click efficiency versus estimated molecular size was plotted (Figure 2.9). This graph clearly indicates there is a relationship between the click efficiency and the estimated size of the azido substituted compounds; a linear trend line with negative slope is included to illustrate this relationship. Evidently, terminal azido polymers with higher degrees of polymerization and larger molecular sizes (P2-4) displayed lower grafting efficiencies than azido substituted compounds (C1-4, C6 and C7) as a result of steric effects and entropic penalties.54-57 Amongst the terminal azido polymers, PtBA-N3 possessed the lowest click efficiency due to its bulky pendent tertiary butyl groups along the polymer chain and secondary azide, resulting in a high degree of steric hindrance. Interestingly, the β-galactopyranosyl azide C5 revealed a large deviation from the proposed trend line. With an estimated molecular size of less than 1 nm, the low click efficiency (18%) of C5 indicates that other factors in addition to the proposed size-
efficiency relationship are responsible for its low click efficiency. For example, the hydrophilic nature of C5 could lead to incompatibility issues with the hydrophobic alkyne CCS polymer, making it difficult for C5 to approach and diffuse through the hydrophobic corona and react with the pendent alkynes, as has been reported for compounds with similar structures.\textsuperscript{58} In addition, the secondary azide of C5 attached directly to the sugar without any alkyl spacer between the azide group and the sugar ring would experience more steric restrictions than its primary azide counterparts resulting in decreased click efficiencies.

Contradictory to the proposed theory is the relatively high click efficiency of the mono-azido $\beta$-CD C6, which is also comprised of hydrophilic sugars like C5 and has a significantly larger molecular size. This unexpected result is believed to result from the hydrophobic internal cavity of C6 and slightly lower hydrophilicity than C5, which allows C6 to penetrate the corona of the hydrophobic star more readily. In addition, $\beta$-CDs can form unstable inclusion complexes\textsuperscript{59-61} with hydrophobic moieties, such as the poly(propargyl methacrylate) repeat units of star CCS 2.2. This potential unstable inclusion complex formation would provide an additional synergistic driving force for C6 to pass through and interact with the corona of the star to access the alkyne functionalities. Furthermore, the primary azide of C6 makes it more reactive towards CuAAC chemistry, as opposed to the secondary azide of C5. So it is reasonable for C6 to possess higher click efficiency than C5. On the other hand, comparing C6 to the similarly sized azido pyrene C3 reveals that the click efficiency of C6 is still lower owing to its hydrophilicity-related incompatibility with the hydrophobic alkyne CCS polymer.

For CCS polymers, the arms are constrained within a compact sphere and assume a semi-dilute and random coil conformation at the inner and outer corona, respectively.\textsuperscript{63} Limited space between adjacent arm polymers would hinder the diffusion of azido substituted compounds into the alkyne corona of the CCS polymer during click functionalization. In addition, surrounding arms polymers could shield the pendent alkyne groups away from the approaching azido compounds. Therefore, the click functionalization efficiency on the uncross-linked linear macroinitiator (arm precursor) would be expected to be higher than for the alkyne CCS polymer.
Figure 2.10 Bar chart comparing click functionalization efficiency of azido substituted compounds onto the alkyne star CCS 2.2 and the linear macroinitiator LP.

To demonstrate the effect of CCS architecture on click efficiency, the linear HO-P(CL-b-TMS-PgMA)-Br (Table 2.1, Entry 6) was deprotected and subsequently grafted with selected azide substituted compounds C2, C6 and P2. The click efficiency on the deprotected macroinitiator LP was calculated via $^1$H NMR spectroscopic analysis (see Appendix 2, Figure A2.9 - 2.10) and compared with the click efficiency on CCS 2.2 (Figure 2.10). The linear macroinitiator LP click efficiency was found to be ~13, 13 and 34% higher than for the alkyne star CCS 2.2 for compounds C2, C6 and P2, respectively. It is noteworthy that the click efficiency difference is less significant for polycyclic aromatic hydrocarbon C2 and cyclic saccharide C6 compared to the PEG-N₃ P2. The results reveal that the steric congestion generated by the arm conformation in the CCS polymer has less impact on the diffusion of small sized molecules (e.g., C2 and C6) than macromolecules (e.g., P2).
2.4 Conclusion

In this chapter, an improved synthetic approach towards a clickable alkyne CCS polymer scaffold was reported utilizing the robust stannous triflate (Sn(OTf)$_2$) catalyst for the CCS-formation via ring opening polymerization. The reported approach provides high macroinitiator-to-star conversions and negligible star-star coupling, therefore results in an increased yield of the alkyne CCS polymer. It has been demonstrated that a library of highly corona-functionalized CCS polymers, including fluorescently tagged, saccharide-based and amphiphilic stars, can be prepared by grafting the alkyne CCS polymer scaffold with various azido substituted functional compounds and polymers via CuAAC chemistry. Unfortunately, some of the functional CCS polymers suffer from broad MWDs due to star-star coupling caused by possible side-reactions of CuAAC chemistry. Through NMR spectroscopic analysis the number of the grafted compounds was quantified and ranged from 45 to 450 depending on their molecular size and functionality. The grafting efficiency (i.e., click efficiency) was then studied and in general, it was found that small molecules with primary azide groups can be quantitatively grafted onto the alkyne CCS polymer via CuAAC chemistry. As the molecular size of the azide substituted compounds increase the click efficiency drops. Terminal azido functionalized polymers can also be grafted onto the alkyne CCS polymer scaffold to afford stars with brush-like arms, although lower grafting efficiencies were observed due to steric hindrance and entropic penalties. Based upon the study, an inversely related molecular size to click efficiency relationship was established, even though deviations from this proposed relationship still exist for some azido substituted compounds. These deviations can be explained by the hydrophilicity-related compatibility of functional compounds with the alkyne CCS scaffold, steric hindrance around the azide and other synergic effects, such as the formation of potential inclusion complexes. Moreover, the steric congestion generated by the arm conformation within the CCS polymer results in lower click efficiency as compared to uncross-linked linear polymer (arm precursor). Therefore, this investigation has demonstrated that the high density functionalization of 3D nanostructures via grafting-to approach is dependent on a number of factors and not just the molecular size of the attaching functional compounds.
2.5 Experimental Section

2.5.1 Materials

Anisole (anhydrous, 99.7%), 1-(chloromethyl)-naphthalene (90%), copper(I) bromide (CuBr, 98%), chlorotrimethylsilane (98%), methacryloyl chloride (97%), 2-propyn-1-ol (99%), γ-oxo-1-pyrene butyric acid (tech.), 1,8-diazaacyclo[5.4.0]undec-7-ene (DBU, 98%), tetra-n-butyl ammonium fluoride (TBAF, 1 M solution in THF), stannous 2-ethylhexanoate (Sn(Oct)₂, 95%), stannous triflate (Sn(OTf)₂, 97%), β-cyclodextrin (98%), furfuryl isocyanate (97%), 1-bromodecane (98%), N,N,N',N''-pentamethyldiethylenetriamine (PMDETA, 99%), poly(ethylene glycol) monomethyl ether (Mₙ ~1000 Da), poly(ethylene glycol) monomethyl ether (Mₙ ~2000 Da), tetra-n-butylammonium hydrogen sulfate (TBAHS) (99+%), acetyl bromo-α-D-galactose (> 93%), 4-(dimethylamino)pyridine (DMAP) (99%), sodium iodide (NaI, 99.999%) and potassium iodide (KI, ≥ 99.99%) were all purchased from Aldrich and used as received. Acetic acid (99.8%, Merck), N-(3-dimethylaminopropyl)-N''-ethylcarbodiimide hydrochloride (EDCI) (98+%, Fluka), N,N-dimethylformamide (99.8%, Merck), n-hexane (AR, Chem-Supply), ethyl acetate (AR, Chem-Supply), methanol (MeOH, AR, Chem-Supply), thionyl chloride (Merck), sodium azide (NaN₃, 99%, Chem-Supply), silver chloride (AgCl, 99.5%, Fluka), poly(ethylene glycol) monomethyl ether (Mₙ ~350 Da) (Fluka), 9-anthracenecarboxylic acid (purum, Fluka), 1,8,9-anthracenetriol (DIT, puriss, Fluka) and trans-2-[3-(4-tert.-butylphenyl)-2-methyl-2-propenylidene]-malononitrile (DCTB, puriss, Fluka) were also used as received. Tetrahydrofuran (RCI Labscan, HPLC) (THF) was distilled from sodium benzophenone ketyl. Toluene (Scharlau, HPLC), ε-Caprolactone (CL, 99+%, Aldrich), dichloromethane (99.8%, Merck), triethylamine (99%, Ajax) and tert-butyl acrylate (98%, Aldrich) were distilled from calcium hydride (95%, Sigma-Aldrich). 2-Hydroxylethyl-2'-methyl-2'-bromopropionate 2.1 and 4,4'-bioxepanyl-7,7'-dione (BOD) were synthesized according to literature procedures.³⁰,³¹
2.5.2 **Instrumentation**

Gel permeation chromatography (GPC) (THF as eluent) was performed on a Shimadzu liquid chromatography system fitted with a Wyatt DAWN EOS multi-angle laser light scattering (MALLS) detector (690 nm, 30 mW) and a Wyatt OPTILAB DSP interferometric refractometer (690 nm), using three Phenomenex Phenogel columns (500, $10^4$ and $10^6$ Å porosity; 5 μm bead size) operated at 1 mL/min with column temperature set at 30 °C. GPC (DMF as eluent) was performed on a Shimadzu liquid chromatography system fitted with a Wyatt DAWN-HELEOS LS detector ($\lambda = 658$ nm), Shimadzu RID-10 refractometer ($\lambda = 633$ nm) and Shimadzu SPD-20A UV-Vis detector, using three identical Polymer Laboratories PLgel columns (5 μm, MIXED-C) and HPLC grade DMF with 0.05 M LiBr (70 °C, 1 mL/min) as mobile phase. Astra software (Wyatt Technology Corp.) was used to process the data to determine the MWs either using known $dn/dc$ values or based on the assumption of 100% mass recovery of the polymer where the $dn/dc$ value was unknown. $^1$H NMR spectroscopic analysis was performed on a Varian Unity Plus 400 MHz spectrometer using the deuterated solvent as reference. Gas chromatography was performed on a Shimadzu GC 17-A gas chromatograph equipped with an Agilent J+W DB-5 capillary column (30 m, 5% phenyl siloxane) and coupled to a GCMS-QP50000 mass spectrometer (injector temperature = 250 °C; initial column initial temperature = 40 °C; heat ramp = 10 °C/min; final column temperature = 320 °C). Dynamic light scattering (DLS) measurements were performed using a Malvern high performance particle sizer (HPPS) with a 3.0 mW He-Ne laser operated at 633 nm. Analysis was performed at an angle of 173° and a constant temperature of 25 ± 0.1 °C. MALDI ToF MS was performed on a Bruker Autoflex III Mass Spectrometer operating in positive linear mode; the analyte, matrix (DIT or DCTB) and cationisation agent (NaI or KI) were dissolved in THF at concentrations of 10, 10 and 1 mg/mL, respectively, and then mixed in a ratio of 10:1:1. 0.3 μL of this solution was then spotted onto a ground steel target plate and the solvent was allowed to evaporate prior to analysis. FlexAnalysis (Bruker) was used to analyse the data. UV-Vis spectrophotometry was performed on a Shimadzu UV-2101PC spectrometer using quartz cuvettes with a 1 cm path length.
Synthesis of (trimethylsilyl)propargyl methacrylate (TMS-PgMA). This compound was prepared according to the literature procedures;\textsuperscript{31-33} \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \( \delta \text{H} 0.18 \) (s, 9H, Si(CH\textsubscript{3})\textsubscript{3}), 1.96 (\( m \), 3H, CH\textsubscript{3}), 4.75 (\( d \), 2H, OCH\textsubscript{2}), 5.61 (\( m \), 1H, CCH\textsubscript{2}) cis, 6.17 (\( m \), 1H, CCH\textsubscript{2}) trans ppm; \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \( \delta \text{C} -0.3 \) (Si(CH\textsubscript{3})\textsubscript{3}), 18.3 (CH\textsubscript{3}), 52.9 (OCH\textsubscript{2}), 94.7 (CH\textsubscript{2}C=), 99.1 (CH\textsubscript{2}C=), 126.4 (CCH\textsubscript{2}), 135.7 (CCH\textsubscript{2}), 166.5 (C=O) ppm; LRMS [M\textsuperscript{+}]: C\textsubscript{10}H\textsubscript{16}O\textsubscript{2}Si requires 196.09; found 196.10.

Synthesis of HO-PCL-Br macroinitiator 2.2. A round bottom flask charged with Sn(Oct)\textsubscript{2} (0.79 g, 1.95 mmol, 1 equiv.) was evacuated and back-filled with argon. Subsequently, CL (20.0 g, 200 mmol, 100 equiv.), 2-hydroxylethyl 2′-methyl-2′-bromopropionate 2.1 (0.823 g, 3.90 mmol, 2 equiv.) and toluene (180 mL) were added via syringe. The reaction solution was stirred at 100 °C under argon for 19 h, cooled to room temperature and then precipitated into cold MeOH (800 mL). The precipitate was collected by vacuum filtration and dried in \textit{vacuo} to yield macroinitiator 2.2 as a white powder, 19.0 g (91.2 %); GPC-MALLS (THF): \( M_n = 5.14 \) kDa, PDI = 1.20; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \( \delta \text{H} 1.34-1.46 \) (\( m \), −CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{2}−), 1.61-1.72 (\( m \), −CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{2}−), 1.95 (\( s \), −CH\textsubscript{3}, end group), 2.32 (\( t \), −CH\textsubscript{2}CH\textsubscript{2}CO−), 3.66 (\( t \), −CH\textsubscript{2}CH\textsubscript{2}OH, end group), 4.07 (\( t \), −CH\textsubscript{2}CH\textsubscript{2}O−) ppm. Different MW macroinitiators were prepared by variation of the monomer to initiator ratio (Table 2.1).

Synthesis of HO-P(CL-\textit{b}-TMS-PgMA)-Br macroinitiator 2.3. HO-PCL-Br macroinitiator 2.2 (3.00 g, 0.58 mmol, \( M_n = 5.14 \) kDa, 1 equiv.), TMS-PgMA (4.00 g, 20.4 mmol, 35 equiv.) and PMDETA (0.20 g, 1.20 mmol, 2 equiv.) were added to a Schlenk flask and dissolved in anisole (19 mL). The mixture was subsequently degassed via one freeze-pump-thaw cycle, backfilled with argon and CuBr (85 mg, 0.58 mmol, 1 equiv.) was added under argon. The mixture was then degassed via another two freeze-pump-thaw cycles, backfilled with argon and heated at 85 °C for 5 h. The reaction was stopped (TMS-PgMA conversion = 50%) by dipping the reaction solution into liquid nitrogen. After warming to room temperature, the reaction solution was diluted with THF (100 mL) and passed through an alumina column to remove the copper complex. The solution was then
concentrated to ~15 mL in volume and precipitated into cold methanol (200 mL). The precipitate was collected by vacuum filtration and dried in vacuo to afford macroinitiator 2.3 as a white solid, 3.2 g (64 %); GPC-MALLS (THF): $M_n = 8.66$ kDa, PDI = 1.19; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$H 0.17 (s, −Si(CH$_3$)$_3$), 0.80-1.15 (m, −CH$_3$), 1.34-1.46 (m, −CH$_2$CH$_2$CH$_2$−), 1.61-1.72 (m, −CH$_2$CH$_2$CH$_2$−), 1.75-2.10 (m, −CH$_2$C− and s, −CH$_3$ end group), 2.32 (t, −CH$_2$CH$_2$CO−), 3.66 (t, −CH$_2$CH$_2$OH end group), 4.07 (t, −CH$_2$CH$_2$O−), 4.32-4.42 (m, −CH$_2$CH$_2$O− end group), 4.57 (s, −COOCH$_2$−) ppm. Different MW macroinitiators were prepared by variation of the monomer to macroinitiator ratio (Table 2.1).

**Synthesis of alkyne functional stars CCS 2.1 and CCS 2.2.** Macroinitiator 2.3 (2.00 g, 0.289 mmol; $M_{n,GPC} = 8.66$ kDa), BOD (0.65 g, 2.89 mmol) and stannous triflate (Sn(OTf)$_2$) (24.6 mg, 0.61 mmol) were added to a flask, and purged with argon. 1:4 THF/toluene (20 mL) was added and the reaction mixture was heated at 65 °C under argon for 99 h (cross-linker conversion via GC = 99%). The reaction mixture was filtered, concentrated and then fractionally precipitated (see Appendix 2) with MeOH to isolate star CCS 2.1, 1.44 g; $M_{n,GPC} = 300$ kDa, PDI = 1.25. The fractionated star CCS 2.1 (1.44 g, 2.16 mmol of alkyne-TMS groups) and acetic acid (0.15 mL, 2.70 mmol) were dissolved in THF (24 mL) under argon at 0 °C and a 0.2 M TBAF solution in THF (10.8 mL) was added dropwise. The reaction solution was stirred at 0 °C for another 30 min and then at room temperature for a further 12 h. The reaction mixture was then concentrated to ~5 mL in volume and precipitated into MeOH (50 mL). The precipitate was dried in vacuo to afford the terminal alkyne star CCS 2.2, 1.11 g (49 %); GPC-MALLS (THF) $M_n = 267$ kDa, PDI = 1.30; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$H 0.80-1.20 (m, 3H, −CH$_3$), 1.35-1.47 (m, −CH$_2$CH$_2$CO−), 1.61-1.72 (m, −CH$_2$CH$_2$CH$_2$−), 1.80-2.10 (m, −CH$_2$C−), 2.32 (t, −CH$_2$CH$_2$CO−), 2.53 (s, C =CHH), 4.08 (t, −CH$_2$CH$_2$O−), 4.57 (s, −COOCH$_2$−) ppm (Figure 2.2).

**Synthesis of deprotected arm initiator HO-P(CL-b-PgMA)-Br (LP 1).** HO-P(CL-b-TMS-PgMA)-Br macroinitiator (Table 2.1, Entry 6) (0.50 g, 1.19 mmol of alkyne-TMS groups, $M_n = 11.3$ kDa) and acetic acid (0.10 mL, 1.79 mmol) were dissolved in THF (12.8
mL) under argon at 0 °C and a 0.2 M TBAF solution in THF (5.8 mL) was added dropwise. The reaction solution was stirred at 0 °C for another 30 min and then at room temperature for a further 12 h. The reaction mixture was then concentrated to ~5 mL in volume and precipitated into MeOH (20 mL). The precipitate was dried in vacuo to afford LP 1, 0.38 g (92 %); GPC-MALLS (THF) \( M_n = 9.2 \text{ kDa}, \ PDI = 1.20; ^1\text{H NMR (400 MHz, CDCl}_3\): \( \delta \text{H} 0.80-1.20 (m, 3H, \text{−CH}_3), 1.35-1.47 (m, \text{−CH}_2\text{CH}_2\text{CO}−), 1.61-1.72 (m, \text{−CH}_2\text{CH}_2\text{CH}_2−), 1.80-2.10 (m, \text{−CH}_2\text{C}−), 2.32 (t, \text{−CH}_2\text{CH}_2\text{CO}−), 2.53 (s, \text{C}≡\text{CH}), 3.64 (t, \text{−CH}_2\text{CH}_2\text{OH end group}), 4.08 (t, \text{−CH}_2\text{CH}_2\text{O}−), 4.57 (s, \text{−COOCH}_2−) \text{ppm.}

**Synthesis of 3-azidopropanol.** NaN\(_3\) (2.80 g, 43.1 mmol) and TBAHS (85.0 mg, 0.25 mmol) were dissolved in MilliQ water (50 mL). 3-Chloropropanol (2.04 g, 21.6 mmol) was then added and the mixture was stirred at 80 °C for 24 hours. The mixture was extracted with diethyl ether (75 mL × 3) and the organic extracts were combined, dried (MgSO\(_4\)), filtered and concentrated in vacuo to yield a clear liquid, 1.80 g (82 %); \(^1\text{H NMR (400 MHz, CDCl}_3\): \( \delta \text{H} 1.82 (\text{quin}, 2H, \text{J} = 6.6 \text{ Hz}, \text{CH}_2), 1.91 (\text{br s}, 1H, \text{CH}_2\text{OH}), 3.44 (t, 2H, \text{J} = 6.6 \text{ Hz}, \text{CH}_2\text{N}_3), 3.74 (t, 2H, \text{J} = 6.6 \text{ Hz}, \text{CH}_2\text{O}) \text{ppm}; ^{13}\text{C NMR (100 MHz, CDCl}_3\): \( \delta \text{C} 31.4 (\text{CH}_2), 48.4 (\text{CH}_2\text{N}_3), 59.6 (\text{OCH}_2)) \text{ppm; LRMS [M−H]^+]: C}_3\text{H}_7\text{N}_3\text{O requires 100.11; found 100.30.}

**Synthesis of 1-(azidomethyl)-naphthalene C1.** 1-(Chloromethyl)-naphthalene (2.00 g, 11.3 mmol), NaN\(_3\) (1.47 g, 22.6 mmol) and DMF (50 mL) were heated at 65 °C for 24 h. The reaction mixture was centrifuged to remove excess NaN\(_3\) and then the solvent was removed in vacuo. The residue was dissolved in dichloromethane (50 mL) and then washed with distilled water (50 mL × 3). The organic extract was dried (MgSO\(_4\)), filtered and concentrated in vacuo to afford C1 as a brown powder, 1.90 g (86 %); \(^1\text{H NMR (400 MHz, CDCl}_3\): \( \delta \text{H} 4.78 (s, 2H, \text{CH}_2\text{N}_3), 7.42-7.61 (m, 4H, 4\text{ArH}), 7.86-7.92 (m, 2H, 2\text{ArH}), 8.02-8.05 (m, 1H, 1\text{ArH}) \text{ppm; ^{13}\text{C NMR (100 MHz, CDCl}_3\): \( \delta \text{C} 52.9 (\text{CH}_2\text{N}_3), 123.5 (\text{ArCH}), 125.2 (\text{ArCH}), 125.2 (\text{ArCH}), 126.7 (\text{ArCH}), 127.2 (\text{ArCH}), 128.8 (\text{ArCH}), 129.4 (\text{ArCH}), 131.0 (\text{ArCC}), 131.3 (\text{ArCC}), 133.9 (\text{ArCC}) \text{ppm; LRMS [M+]': C}_11\text{H}_9\text{N}_3 \text{requires 183.08; found 183.30.}
Synthesis of 3-azidopropyl anthracene-9-carboxylate C2. Anthracene carboxylic acid (2.22 g, 10.0 mmol) and thionyl chloride (SOCl₂) (30 mL) were added to a dried flask under argon. The reaction mixture was refluxed under argon for 90 min and the excess SOCl₂ was removed in vacuo. The resulting residue was azeotroped with benzene (10 mL × 3), redissolved in anhydrous THF (40 mL) and cooled to 0 °C. Triethylamine (2.4 mL, 32.7 mmol) was added, followed by 3-azidopropanol (0.97 g, 9.0 mmol) in anhydrous THF (30 mL) dropwise. The reaction solution was stirred at 0 °C for 30 min, warmed to room temperature and stirred for 48 h, and then filtered and concentrated. The crude product was redissolved in dichloromethane (50 mL), washed with 2 M HCl (50 mL × 2) and distilled water (50 mL), dried (MgSO₄), filtered and concentrated in vacuo to afford C2 as a light brown solid, 2.5 g (90 %); ¹H NMR (400 MHz, CDCl₃): δH 2.09 (quin, 2H, J = 6.4 Hz, CH₂), 3.45 (t, 2H, J = 5.2 Hz, OCH₂), 4.67 (t, 2H, J = 5.2 Hz, CH₂N₃), 7.44–7.54 (m, 4H, 4ArH), 7.99–8.01 (m, 4H, 4ArH), 8.48 (s, 1H, ArH) ppm; ¹³C NMR (100 MHz, CDCl₃): δC 8.3 (CH₂), 48.2 (CH₂N₃), 62.5 (OCH₂), 124.7 (2ArCH), 125.6 (2ArCH), 127.2 (2ArCH), 127.7 (ArCH), 128.5 (ArCC), 128.7 (2ArCH), 129.5 (2ArCH), 131.0 (ArCH), 169.6 (C=O) ppm.

Synthesis of 3-azidopropyl 4-oxo-4-(pyrene-4-yl) butanoate C3. γ-Oxo-1-pyrenebutyric acid (1.20 g, 3.97 mmol), EDCI (0.840 g, 4.37 mmol) and DMAP (97.0 mg, 0.79 mmol) were dissolved in anhydrous dichloromethane (24 mL) under argon. 3-Azidopropanol (0.39 mL, 3.90 mmol) was then added and the mixture was stirred at 30 °C for 40 h. The reaction mixture was then washed with 0.05 M HCl (100 mL × 3), dried (MgSO₄), filtered and the filtrate concentrated in vacuo. The crude product was purified via column chromatography on silica using 2:8 hexane:dichloromethane. The desired compound (Rf = 0.06) was collected, dried (MgSO₄), filtered and concentrated in vacuo (0.1 mbar, 50 °C) to give C3 as a dark brown solid, 0.90 g (64 %); ¹H NMR (400 MHz, CDCl₃): δH 1.92 (quin, 2H, J = 6.4 Hz, CH₂), 2.90 (t, 2H, J = 6.4 Hz, CH₂CO₂), 3.39 (t, 2H, J = 6.4 Hz, CH₂N₃), 3.53 (t, 2H, J = 6.4 Hz, COCH₂), 4.23 (t, 2H, J = 6.4 Hz, CO₂CH₂), 8.00–8.05 (m, 2H, 2ArH), 8.13–8.23 (m, 5H, 5ArH), 8.38 (d, 1H, J = 8.0 Hz, ArH), 8.91 (d, 1H, J = 9.6 Hz, ArH) ppm; ¹³C NMR (100 MHz, CDCl₃): δC 28.3 (CH₂CO₂), 28.9 (CH₂), 37.0 (OCH₂), 48.3
(CH₂N₃), 61.7 (CO₂CH₂), 124.1 (ArCH), 124.3 (ArCC), 124.8 (ArCC), 125.0 (ArCH),
126.1 (ArCC), 126.3 (ArCH), 126.3 (ArCH), 126.4 (ArCH), 127.1 (ArCH), 129.5 (ArCH),
129.6 (ArCC), 129.7 (ArCH), 130.5 (ArCH), 131.1 (ArCC), 131.7 (ArCC), 133.9 (ArCC)
ppm.

**Synthesis of 3-azidopropyl furan-2-ylmethylcarbamate C4.** Furfuryl isocyanate (370 mg,
3.00 mmol) was dissolved in anhydrous THF (5 mL) in a dried Schlenk tube under argon,
and 3-azidopropanol (300 mg, 2.97 mmol) and triethylamine (21 µL, 0.14 mmol) were
added. After 24 h at 50 °C, the reaction mixture was concentrated in vacuo, and purified via
column chromatography on silica (R₁ = 0.73, 1:99 methanol:dichloromethane) to afford C4
as a pale yellow oil, 420 mg (62 %); ¹H NMR (400 MHz, CDCl₃): δH 1.88 (quin, 2H, J =
8.0 Hz, CH₂), 2.29 (t, 2H, J = 8.0 Hz, CH₂N₃), 4.16 (t, 2H, J = 8.0 Hz, OCH₂), 4.34 (d, 2H,
CH₂N), 5.05 (br s, NH), 6.21 (d, 1H, ArH), 6.30 (m, 1H, ArH), 7.34 (m, 1H, ArH) ppm; ¹³C
NMR (100 MHz, CDCl₃): δC 28.5 (CH₂), 38.9 (CH₂N), 48.2 (CH₂N₃), 62.0 (OCH₂), 107.2
(ArCH), 110.4 (ArCH), 142.2 (ArCH), 151.5 (ArCC), 156.0 (C=O) ppm; LRMS [M+]:
C₉H₁₂N₄O₃ requires 224.09; found 224.00.

**Synthesis of β-galactopyranosyl azide C5.** β-galactopyranosyl azide was prepared
according to literature³⁴ with slight modification. To acetobromo-α-D-galactose (5.0 g, 12.2
mmol) in dichloromethane (50 mL) was added NaN₃ (4.40 g, 67.7 mmol), TBAHS (4.10 g,
12.2 mmol) and saturated NaHCO₃ (50 mL) in sequence. The reaction mixture was stirred
vigorously at room temperature for 3 h and then diluted with ethyl acetate (500 mL). The
organic layer was washed with saturated NaHCO₃ (200 mL) and concentrated in vacuo.
The residue was dissolved in MeOH (35 ml) and a solution of 10 M KOH (9.0 mL) was
added and stirred at room temperature for 3 h. The mixture was concentrated in vacuo and
purified via column chromatography on silica using 3:7 MeOH/dichloromethane to afford
C5 as a white powder, 2.00 g (80 %); ¹H NMR (400 MHz, d₆-DMSO): δH 3.26-3.36 (m,
3H, 2CHOH, H-2,4, CH₂CH, H-5), 3.42-3.52 (m, 2H, CH₂OH, H-6), 3.63 (d, 1H, CHOH,
H-3), 4.31 (d, 1H, CHN₃, H-1), 4.50-5.50 (m, 4H, 4OH, OH-2,3,4,6) ppm; ¹³C NMR (400
MHz, d₆-DMSO): δC 60.8 (CH₂, C-6), 68.5 (CH, C-2), 70.7 (CH, C-4), 73.7 (CH, C-3),

85
78.0 (CH, C-1), 91.1 (CH, C-5) ppm.

**Synthesis of mono-6-deoxy-6-azido-β-cyclodextrin C6.** β-CD derivative C6 was prepared according to a literature procedure.\(^{35-38}\) β-Cyclodextrin (6.0 g, 5.29 mmol) was suspended in water (50 mL) and 8.25 M NaOH (2 mL) was added dropwise over 10 min. p-Toluenesulfonyl chloride (1.1 g, 5.67 mmol) in acetonitrile (30 mL) was added dropwise, causing immediate formation of a white precipitate. After 2 h at room temperature the precipitate was filtered off, redissolved in anhydrous DMF (20 mL) and NaN\(_3\) (0.80 g, 12.3 mmol) was added. After 24 h at 65 °C the reaction solution was concentrated in vacuo and the unwanted salts were removed via dialysis (Thermoscientific, MWCO 1000) against water for 48 h. The resultant aqueous suspension was collected and freeze-dried to afford a white solid, 0.6 g (10 %); \(^1\)H NMR (400 MHz, \(d_6\)-DMSO): \(\delta_H\) 3.26-3.80 (br s, 42H, 28CHO and 7CHO, 4.44-4.55 (m, 6H, 6OH), 4.80-4.90 (m, 7H, 7CHO), 5.60-5.80 (m, 14H, 14OH) ppm; \(^13\)C NMR (100 MHz, \(d_6\)-DMSO): \(\delta_C\) 51.0 (CH\(_2\)N\(_3\)), 59.7-60.0 (m, CH\(_2\)O), 70.0-72.9 (m, CHO), 81.4-82.8 (m, CHO), 101.4-102.1 (m, CHO) ppm; MALDI ToF MS [M+Na\(^+\)]: C\(_{42}\)H\(_{60}\)N\(_3\)NaO\(_{34}\) requires 1182.37; found 1182.20.

**Synthesis of 1-azidodecane C7.** 1-Bromodecane (5.03 g, 22.6 mmol) and NaN\(_3\) (3.00 g, 46.1 mmol) were dissolved in DMF (50 mL) and heated at 65 °C for 24 h. After cooling to room temperature the reaction mixture was centrifuged to remove excess NaN\(_3\) and washed with hexane (50 mL x 3). The hexane extracts were collected, dried (MgSO\(_4\)), filtered and concentrated in vacuo to afford C7 as a pale yellow oil, 4.0 g (97 %); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta_H\) 0.87 (t, 3H, \(J = 6.8\) Hz, CH\(_3\)), 1.25 (m, CH\(_2\)), 1.58 (quin, 2H, \(J = 6.8\) Hz, CH\(_2\)CH\(_2\)N\(_3\)), 3.23 (t, 2H, \(J = 6.8\) Hz, CH\(_2\)N\(_3\)) ppm; \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta_C\) 14.2 (CH\(_3\)), 22.8 (CH\(_2\)), 22.9 (CH\(_2\)), 26.9 (CH\(_2\)), 29.0 (CH\(_2\)), 29.3 (CH\(_2\)), 29.5 (CH\(_2\)), 29.7 (CH\(_2\)), 51.6 (CH\(_2\)N\(_3\)) ppm; LRMS [M+]: C\(_{10}\)H\(_{21}\)N\(_3\) requires 183.17; found 182.50.

**Synthesis of terminal azido functionalized PEGs P1-3.** The general procedure employed for the preparation of terminal azido functionalized PEG was as follows: PEG monomethyl ether (20 mmol, 1 equiv.) was initially dried via azeotropic distillation with toluene (100
mL × 3). Subsequently, triethylamine (24 mmol, 1.2 equiv.) and dichloromethane (80 mL) were added and the mixture was cooled to 0 °C before methanesulfonyl chloride (30 mmol, 1.5 equiv.) was added dropwise. The reaction was kept at 0 °C for 30 min and then at room temperature for 12 h. The reaction was filtered and the filtrate was concentrated in vacuo. The residue was dissolved in DMF (50 mL), and NaN₃ (200 mmol, 10 equiv.) was added. The reaction mixture was heated to 65 °C for 12 h, cooled to room temperature and concentrated in vacuo. The residue was dissolved in water (200 mL) and then washed with dichloromethane (100 mL × 2). The organic extracts were collected, washed with water (200 mL) and saturated NaCl (200 mL × 2), dried (MgSO₄), filtered and concentrated in vacuo to afford the desired mono-azido PEGs; ¹H NMR (400 MHz, CDCl₃): δ (s, 3H, OCH₃ end group, and t, 2H, CH₂N₃ end group), 3.45–3.85 (m, –CH₂O–) ppm; MALDI ToF MS: P₁ Mₙ = 440, PDI = 1.01; P₂ Mₙ = 1070, PDI = 1.02; P₃ Mₙ = 1800, PDI = 1.02 (see Appendix 2, Figure A2.1–2.3).

**Synthesis of terminal azido-functionalized PtBA P₄.** The procedure to synthesize PtBA-N₃ was adopted from the literature with slight modification. Deoxygenated acetone (4.2 mL) and tBA (15 g, 117 mmol) were added to a Schlenk tube. The solution was degassed by three freeze-pump-thaw cycles and then CuBr (170 mg, 1.17 mmol), CuBr₂ (14 mg, 0.63 mmol) and PMDETA (250 μL, 1.18 mmol) were added. The reaction solution was stirred at room temperature for 30 min and then methyl 2-bromopropionate (270 μL, 2.34 mmol) was added under argon. The reaction mixture was heated at 65 °C for 13 h (monomer conversion via GC = 50 %), cooled to room temperature and precipitated into cold methanol (-15 °C, 600 mL). The precipitate was collected and redissolved in DMF (50 mL). NaN₃ (1.52 g, 23.4 mmol) was added and the reaction mixture was then stirred at room temperature for 24 h. The solvent was removed in vacuo and the residue was redissolved in dichloromethane (50 mL) and washed with saturated NaCl (50 mL × 2) and distilled water (50 mL × 2). The organic extract was collected, dried (MgSO₄), filtered and concentrated in vacuo to afford PtBA-N₃ P₄, 6.00 g (77 %); GPC-MALLS: Mₙ = 5.85 kDa, PDI = 1.12; ¹H NMR (400 MHz, CDCl₃): δ (s, 3H, –C(CH₃)–), 1.20–2.00 (m, –C(CH₃)₃, and –CH₂CH–), 2.00–2.50 (m, –CH₂CH–), 2.90–3.00 (d, –CH₂N₃ end group), 3.66 (s, –OCH₃,
Synthesis of highly functionalized CCS polymers via CuAAC chemistry. The general procedure for synthesizing corona-functionalized stars CCS C1-5, CCS C7 and CCS P4 was as follows: initially a 0.085 mM catalyst stock solution was prepared by dissolving CuBr (0.085 mmol, 1 equiv.), and PMDETA (0.085 mmol, 1 equiv.) in degassed DMF. In a Schlenk tube, alkyne star CCS 2.2 (0.187 µmol, 0.084 mmol alkyne groups, 1 equiv.) and the azido compound (0.42 mmol, 5 equiv. or 0.17 mmol, 2 equiv. P4 only) were dissolved in DMF (5 mL). The mixture was degassed via two freeze-pump-thaw cycles, backfilled with argon and then the catalyst stock solution (0.1 mL) was added. The reaction solution was subjected to one additional freeze-pump-thaw cycle, backfilled with argon and stirred at room temperature for 48 h. The Cu(I) catalyst was removed via addition of 1-dodecanethiol (0.088 mmol, 1 equiv.) to form an insoluble copper complex (the solution immediately became cloudy and the characteristic colour of the CuBr/PMDETA complex completely disappeared). After a further 24 h at room temperature the reaction mixture was centrifuged to remove the insoluble copper salts and the supernatant was concentrated in vacuo to ~1-2 mL in volume and then precipitated in methanol (25 mL) twice. The precipitate was collected via centrifugation and dried in vacuo to give the click-functionalized stars.

The general procedure for synthesizing corona-functionalized stars CCS P1-3 and CCS C6 was as follows: initially a 0.085 mM catalyst stock solution was prepared by dissolving CuBr (0.085 mmol, 1 equiv.), and PMDETA (0.085 mmol, 1 equiv.) in degassed DMF. In a Schlenk tube, alkyne star CCS 2.2 (0.187 µmol, 0.084 mmol of alkyne groups, 1 equiv.) and the azido compound (0.17 mmol, 2 equiv.) were dissolved in DMF (5 mL). The mixture was degassed via two freeze-pump-thaw cycles, backfilled with argon and then the catalyst stock solution (0.1 mL) was added under argon. The reaction solution was subjected to one additional freeze-pump-thaw cycle, backfilled with argon and stirred at room temperature for 48 h. The Cu(I) catalyst was removed via addition of 1-dodecanethiol (0.088 mmol, 1 equiv.) to form an insoluble copper complex. After a further 24 h at room
temperature the reaction mixture was centrifuged to remove the insoluble copper salts. The supernatant was dialyzed (Thermoscientific, MWCO = 3500) against water for 4 days and freeze-dried to afford the click-functionalized stars.

**Synthesis of highly functionalized linear polymers via CuAAC chemistry.** The general procedure for synthesizing linear polymers (LP C2, LP C6 and LP P2) with high pendent functionality was as follows: initially a 150 mM catalyst stock solution was prepared by dissolving CuBr (150 mmol, 1 equiv.), and PMDETA (150 mmol, 1 equiv.) in degassed DMF. In a Schlenk tube, deprotected macroinitiator LP 1 (5.43 µmol, 0.147 mmol alkyne groups, 1 equiv.) and the azido compound (0.29 mmol, 2 equiv. or 0.74 mmol, 5 equiv. P2 only) were dissolved in DMF (4 mL). The mixture was degassed via two freeze-pump-thaw cycles, backfilled with argon and then the catalyst stock solution (0.1 mL) was added. The reaction solution was subjected to one additional freeze-pump-thaw cycle, backfilled with argon and stirred at room temperature for 48 h. The Cu(I) catalyst was removed via addition of 1-dodecanethiol (0.150 mmol, 1 equiv.) to form an insoluble copper complex. After a further 24 h at room temperature the reaction mixture was centrifuged to remove the insoluble copper salts. For the synthesis of LP C6 and LP P2, the supernatant was dialyzed (Thermoscientific, MWCO = 3500) against water for 4 days and freeze-dried to afford the grafted linear polymer. For LP C2, the supernatant was concentrated *in vacuo* to ~1-2 mL in volume and then precipitated in methanol (25 mL) twice. The precipitate was collected via centrifugation and dried *in vacuo* to give the grafted linear polymer. GPC-MALLS (THF): LP C2 $M_n = 43.4$ kDa, PDI = 1.52; GPC-MALLS (DMF): LP C6 $M_n = 26.7$ kDa, PDI = 1.15; LP P2 $M_n = 39.7$ kDa, PDI = 1.27.
2.6 Reference and Notes


(27) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B., *Angew. Chem.* **2002**, *114*, 2708.


Polymer standards were tested with the GPC systems using the known \(dn/dc\) values or the known injected mass of polymer sample based on the assumption of 100% mass recovery from the GPC RI chromatogram. The determined MW results of the polymer standards determined by both methods were in good agreement with slight difference within error margin. See following references for similar methods used: (a) Kim, Y. S.; Kadla, J. F., Biomacromolecules 2010, 11, 981; (b) Wiltshire, J. T.; Qiao, G. G., J. Polym. Sci., Part A: Polym. Chem. 2009, 47, 1485; (c) Li, W.; Matyjaszewski, K., J. Am. Chem. Soc. 2009, 131, 10378.


Madison, P. H.; Long, T. E., Biomacromolecules 2000, 1, 615.


Molecular modelling and size estimation were implemented using ChemDraw Ultra (version 12.0). All structures were optimized with MM2 to minimize steric energy. For polymers, random coil conformations were adopted.

Chapter 3

Organic Catalyst-mediated Ring Opening Polymerization for the Highly Efficient Synthesis of Polyester-based Star Polymers

3.1 Chapter Perspective

In chapter 3, a facile, highly efficient, and metal-free synthetic route towards well-defined polyester-based CCS polymers through methanesulfonic acid-mediated ROP is described. Highly ‘living’ PCL macroinitiators were linked together with bis-cyclic ester (BOD) to afford the PCL-based CCS polymers via either a two-pot or a one-pot, two-step strategy. The fast and near-quantitative CCS polymer formation at ambient temperature was observed. Generalization of this efficient synthetic technique to prepare other functional star architectures was demonstrated by the successful synthesis of a novel degradable CCS polymer with high ‘clickable’ end functionality. Side-reactions that prevent the arm-to-star conversion to reach 100% were identified and their mechanisms were explained in the context of the CCS formation.
3.2 Introduction

Functional polyester-based star polymers have attracted great attention due to their potential application to the research fields of nano-fillers, degradable materials and polymer therapeutics.\(^1\) Polyester-based CCS polymers are considered interesting candidates for *in-vivo* drug delivery devices due to their biocompatibility, biodegradability and large core size, which provides drug loading capacity.\(^2\) However, the previously established synthetic protocols (see also Chapter 2) for the preparation of functional polyester-based star polymers via ROP suffer from moderate yields, owing to the inefficient arm-to-star conversion (< 60 %) and undesirable high molecular weight (MW) star-star coupled products leading to broad molecular weight distributions (MWD)s.\(^3\) Tedious and time-consuming purification processes are often required to isolate the pure star polymers from low and high MW impurities, and this results in poor yields and reduces the wide spread use and commercialisation of these materials.\(^4\)

Recently, very high yielding CCS polymer synthesis has been achieved using various controlled polymerization techniques. For controlled radical polymerization, Matyjaszewski and co-workers have reported the synthesis of CCS polymers in > 98 % yields via Activator Generated by Electron Transfer (AGET)-ATRP,\(^5\) and our own research group have reported the > 99 % yield synthesis of CCS via ruthenium-catalyzed living radical polymerization.\(^6\) Recently, Boyer and co-workers have optimized the synthesis of star polymers via RAFT polymerization to achieve much improved yields of > 90 %.\(^7\) Similarly, Aoshima *et al.* reported the > 99 % yield of poly(vinyl ether) CCS polymers via living cationic polymerization.\(^8\) CCS polymers prepared via these aforementioned methods have high star purity and therefore, further purification is generally not required. Nevertheless, these synthetic approaches have their own inherent weaknesses. Controlled radical polymerization techniques suffer from termination reactions (i.e., radical dimerization and disproportionation) and are sensitive to the radical scavengers (e.g., oxygen) or require the addition of excess reducing agents (e.g., AGET-ATRP).\(^9\)
comparison, living cationic polymerization requires even more stringent reaction conditions, being susceptible to both oxygen and protic impurities (e.g. water). In contrast, ROP of lactones and lactams requires far less stringent reaction condition since it is inert to oxygen and reasonably tolerant of water, although under certain conditions water can act as a polymer chain initiator during polymerization.\textsuperscript{10} However, for the synthesis of CCS polymers via ROP, water impurities may not be detrimental since the initiation of the bislactone-based cross-linkers would lead to the formation of reactive cross-linked nanonetworks that would be expected to facilitate cross-linking of macroinitiators (MI)s to yield star polymers. Unlike radical polymerization, side-reactions such as bimolecular termination and disproportion that lead to ‘dead’ chain polymers, which cannot participate in the star-formation, are absent in ROP. Therefore, ROP may be considered a valuable approach for both laboratory- and industrial-scale syntheses of star polymers, especially if the arm-to-star conversion can be maximized eliminating the need for purification.

ROP mediated by the tin(II) organometallic complexes Sn(Oct)\textsubscript{2} and Sn(OTf)\textsubscript{2} follows a coordination-insertion mechanism,\textsuperscript{11} which often requires elevated reaction temperatures to achieve a fast reaction rate. Thus, the synthesis of CCS polymers via ROP using tin(II) complexes requires reaction temperatures of 65–110 °C to achieve a satisfactory star formation rate.\textsuperscript{1a, 1c} However, elevated reaction temperatures are disfavoured, especially for industrial scale processes where energy conservation is particularly important from a cost and environmental perspective. Furthermore, tin(II) based organometallic complexes are strong transesterification agents.\textsuperscript{11,12} Therefore, ROP mediated by tin(II) complexes might suffer from intramolecular transesterification reactions, leading to the formation of cyclic impurities and broad polymer MWDs, and these transesterification reactions would be more prominent at elevated reaction temperatures. This is particularly important during star synthesis as cyclization of the polyester MIs (arms) leads to the formation of non-cross-linkable (‘dead’) cyclic polymer chains without ‘active’ terminal groups, which cannot take part in star formation.\textsuperscript{13} It is also speculated that bulky
tin(II) complexes cannot diffuse effortlessly out of the cross-linked core of the performed star polymers, to catalyze further cross-linking of the unbounded MIs or low MW star precursors. As a result of insufficient catalysis, the star formation process often requires lengthy reaction times to achieve moderate arm-to-star conversions. Evidently, given the aforementioned issues associated with the previously reported CCS polymer synthesis via ROP, more robust catalysts with small molecular size, higher catalytic activity and lower transesterification rates are required to allow the formation of well-defined star at low reaction temperatures and fast reaction rates.

Recent advances in organo-catalysis have introduced several robust catalysts (e.g., N-heterocyclic carbenes (NHCs), bi-functional thioureas, triazabicyclodecene and sulfonic acid derivatives) that can efficiently catalyze the controlled ROP of cyclic esters under mild reaction conditions and offer comparable reaction rates to organometallic catalytic systems operating at elevated temperatures. More importantly, previous studies have shown that organic catalysts have low transesterification rates even at high monomer conversions.

The work in this chapter describes the highly efficient synthesis of PCL-based CCS polymers via ROP using the organic catalyst methanesulfonic acid (CH$_3$SO$_3$H). The robust nature of methanesulfonic acid was exploited to catalyze the ROP of lactones to form CCS polymers at ambient temperature. The ambient reaction temperature along with low transesterification rate of the catalytic system would significantly suppress the transesterification side-reactions. In the absence of other chain termination reactions, it is anticipated that the CH$_3$SO$_3$H-mediated ROP system will be capable of giving very high yields of functional CCS polymers.
3.3 Results and Discussion

The synthesis of PCL CCS polymers was achieved in two steps, involving (i) ring opening polymerization (ROP) of ε-caprolactone (CL) using benzyl alcohol (BnOH) or propargyl alcohol (PgOH) as the initiator to afford living poly(ε-caprolactone) ‘arm’ MIs (PCL-OH) (Scheme 3.1(i)), followed by (ii) ROP of the bislactone cross-linker, 4,4’-bioxepanyl-7,7’-dione (BOD), using the PCL-OH as the MI and CH₃SO₃H as the catalyst (Scheme 3.1(ii)).

![Scheme 3.1 Synthesis of PCL CCS polymers via ROP and the ‘arm-first’ approach.](image-url)
3.3.1 Kinetics of Poly(ε-caprolactone)-based Star Polymers Synthesis

Table 3.1 Characterization of PCL<sub>arm</sub>PBOD<sub>core</sub> CCS polymers via ROP and arm-first approach.

<table>
<thead>
<tr>
<th>Polymer&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Catalyst&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Macroinitiator (MI)</th>
<th>Expt. condition</th>
<th>MI&lt;sub&gt;Mn&lt;/sub&gt;&lt;sup&gt;c&lt;/sup&gt;, GPC</th>
<th>MI&lt;sub&gt;conv.&lt;/sub&gt;&lt;sup&gt;d&lt;/sup&gt;</th>
<th>CCS&lt;sub&gt;Mn&lt;/sub&gt;, GPC</th>
<th>CCS&lt;sub&gt;Mw&lt;/sub&gt;/&lt;sub&gt;Mn&lt;/sub&gt;</th>
<th>&lt;i&gt;N&lt;sub&gt;arm&lt;/sub&gt;&lt;/i&gt;&lt;sup&gt;f&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCS 3.1a</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;SO&lt;sub&gt;3&lt;/sub&gt;H</td>
<td>Bn-PCL-OH 1a</td>
<td>1/30/3</td>
<td>9.9</td>
<td>0.95</td>
<td>326</td>
<td>1.25</td>
<td>19</td>
</tr>
<tr>
<td>CCS 3.1b</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;SO&lt;sub&gt;3&lt;/sub&gt;H</td>
<td>Bn-PCL-OH 1b</td>
<td>1/55/3</td>
<td>15.6</td>
<td>0.92</td>
<td>488</td>
<td>1.32</td>
<td>17</td>
</tr>
<tr>
<td>CCS 3.1c</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;SO&lt;sub&gt;3&lt;/sub&gt;H</td>
<td>Bn-PCL-OH 1c</td>
<td>1/90/3</td>
<td>24.8</td>
<td>0.96</td>
<td>680</td>
<td>1.28</td>
<td>15</td>
</tr>
<tr>
<td>CCS 3.1d</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;SO&lt;sub&gt;3&lt;/sub&gt;H</td>
<td>Bn-PCL-OH 1d</td>
<td>1/128/3</td>
<td>36.2</td>
<td>0.90</td>
<td>550</td>
<td>1.18</td>
<td>8</td>
</tr>
<tr>
<td>CCS 3.2&lt;sup&gt;g&lt;/sup&gt;</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;SO&lt;sub&gt;3&lt;/sub&gt;H</td>
<td>Bn-PCL-OH 2</td>
<td>-</td>
<td>12.2</td>
<td>0.95</td>
<td>295</td>
<td>1.23</td>
<td>15</td>
</tr>
<tr>
<td>CCS 3.3</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;SO&lt;sub&gt;3&lt;/sub&gt;H</td>
<td>HC≡C-PCL-OH 3</td>
<td>1/30/3</td>
<td>11.8</td>
<td>0.94</td>
<td>286</td>
<td>1.30</td>
<td>15</td>
</tr>
<tr>
<td>CCS 3.4</td>
<td>Sn(Oct)&lt;sub&gt;2&lt;/sub&gt;</td>
<td>Bn-PCL-OH 1a</td>
<td>1/30/0.5</td>
<td>9.9</td>
<td>0.85</td>
<td>364</td>
<td>1.20</td>
<td>21</td>
</tr>
</tbody>
</table>

<sup>a</sup>Experimental conditions: For CCS 3.1a-d, 3.2 and 3.3, [MI]<sub>0</sub> = 50 mg/mL, room temperature, dichloromethane; For CCS 3.4, [MI]<sub>0</sub> = 50 mg/mL, 110 ºC, toluene. MI and cross-linker (BOD) conversion were monitored via GPC and GC-MS, respectively. <sup>b</sup>Catalyst utilized in the star formation reaction. <sup>c</sup>MI<sub>Mn</sub> of MI determined by GPC MALLS using dn/dc = 0.078 mL/g. <sup>d</sup>Macroinitiator conversion based upon the area fraction ratio of star polymers, determined by deconvolution of the GPC RI chromatograms using Gaussian function. <sup>e</sup>MI<sub>Mn</sub> of functionalized stars determined by GPC MALLS and based upon the assumption of 100 % mass recovery. <sup>f</sup>Number-average value of arms per star polymer calculated from Equation A3.1 (Appendix 3). <sup>g</sup>Experimental conditions for one-pot synthesis: [PhCH<sub>2</sub>OH]<sub>0</sub>/[CL]<sub>0</sub>/[BOD]<sub>0</sub>/[CH<sub>3</sub>SO<sub>3</sub>H]<sub>tot</sub>= 1/100/30/3, where [CH<sub>3</sub>SO<sub>3</sub>H]<sub>tot</sub> is the total methanesulfonic acid concentration in the star formation reaction.

Initially, four PCL MIs with different molecular weights (MWs) (Bn-PCL-OH 3.1a-d, Table 3.1) were prepared via ROP, using BnOH as the initiator and Sn(Oct)<sub>2</sub> as the catalyst at 110 ºC in toluene. All reactions were terminated at monomer conversions of < 80 % to avoid undesirable transesterifications, which might arise at high conversion (>
Gel permeation chromatography (GPC) revealed that Bn-PCL-OH 3.1a-d have number average molecular weight ($M_{n,\text{GPC}}$) values ranging from 9.9 to 36.2 kDa. The $M_{n,\text{GPC}}$ values of Bn-PCL-OH 3.1a-d, their number average MWs calculated based upon $^1$H NMR spectroscopic analysis ($M_{n,\text{NMR}}$) and theoretical number average MWs ($M_{n,\text{theo}}$) based upon monomer conversion (via GC-MS analysis) were all in good agreement (see Appendix 3, Table A3.1). The GPC RI chromatograms of Bn-PCL-OH 3.1a-d revealed monomodal distributions with narrow polydispersities (PDI < 1.2) (Figure 3.1A-D, $t = 0$ hr). These results suggest that the occurrence of inter- or intra-molecular transesterifications during MI synthesis is negligible,\(^{13, 19}\) and that all the MIs are living with ‘active’ hydroxy termini suitable to initiate ROP of the cross-linker (BOD) in the subsequent star formation step. Subsequently, star formation using MIs Bn-PCL-OH 3.1a-d was conducted at room temperature in dichloromethane using methanesulfonic acid as the catalyst to afford CCS 3.1a-d, respectively. In all cases the reactions were followed over time by GPC (Figure 3.1A-D). Very high final arm-to-star conversions, ranging from 90–96 %, were obtained for all stars CCS 3.1a-d (Table 3.1) as determined by deconvolution of the GPC RI chromatograms (see Appendix 3, Figure A3.1). It was observed that as the MW of the MIs Bn-PCL-OH 3.1a-d increased from 9.9 to 36.2 kDa so did the reaction time (18 to 69 h) required to obtain high arm-to-star conversion (Figure 3.1E), and the number-average value of arms per star ($N_{\text{arm}}$) decreased from ca. 19 to 8. These are common observations for the synthesis of star polymers via the arm-first approach; high MW MIs generally require long reaction times, and the resulting stars have lower arm-to-star conversions and lower $N_{\text{arm}}$ due to steric limitations.\(^{8, 20}\)
Figure 3.1 GPC RI chromatograms over time for the synthesis of CCS polymers: (A) CCS 3.1a, MI, Bn-PCL-OH 3.1a, $M_n,_{GPC} = 9.9$ kDa, PDI = 1.08 (Table 3.1, Entry 1), (B) CCS 3.1b, MI; Bn-PCL-OH 3.1b, $M_n,_{GPC} = 15.6$ kDa, PDI = 1.04 (Table 3.1, Entry 2), (C) CCS 3.1c, MI; Bn-PCL-OH 3.1c, $M_n,_{GPC} = 24.8$ kDa, PDI = 1.06 (Table 3.1, Entry 3), (D) CCS 3.1d, MI; Bn-PCL-OH 3.1d, $M_n,_{GPC} = 24.8$ kDa, PDI = 1.08 (Table 3.1, Entry 4), (E) summary of GPC-RI chromatograms of MI 3.1a-d and CCS 3.1a-d at reaction end point (Table 3.1, Entry 1-4), and (F) one-pot synthesis of CCS 3.2: MI; Bn-PCL-OH 3.2, $t = 8$ h; CL monomer conversion (GC) = 93%; $M_n,_{GPC} = 12.2$ kDa, PDI = 1.12 (Table 3.1, Entry 5).
The preparation of PCL CCS polymers could also be conducted in a one-pot, two-step strategy without isolation of the intermediate MIs. Initially, the PCL MI was prepared via ROP of CL at room temperature using BnOH as the initiator and methanesulfonic acid as the catalyst. Once the CL conversion reached 90%, the cross-linker BOD was added to the reaction to induce star formation. Using this approach, CCS 3.2 (Figure 3.1F) was prepared with targeted MI and BOD degree of polymerization (DP) values of 100 and 30, respectively. GPC analysis of CCS 3.2 provided a \( M_{n,GPC} \) of 295 kDa, PDI of 1.23, and an arm-to-star conversion of 95%, which is comparable to CCS 3.1a prepared using a similar MW MI (Table 3.1). No further improvements in arm-to-star conversion were observed after the addition of excess amounts of BOD or BnOH initiator (results not shown).

3.3.2 Synthesis of Alkyne End-functional Polyester-based CCS Polymer

The GPC characterization of CCS 3.1a-d and 3.2 indicates the presence of side-reactions that prevent 100% incorporation of the linear MIs into star polymers. In general, for the synthesis of CCS polymers via controlled radical polymerization (CRP), the loss of chain end functionality through radical termination events results in unincorporated linear polymers remaining, although it has been demonstrated that the selection of a catalytic system with low propagating radical concentration can suppress these termination events to give higher star yields.\(^5\)\(^,\)\(^6\) For the synthesis of CCS polymers via living cationic polymerization, the selection of initiation system (e.g., the base-stabilizing system rather than the counter ion system to ensure a more stable living chain end) was the key to achieving the quantitative synthesis of CCS polymers.\(^8\)

Motivated by these CCS synthetic systems, it was speculated that the unincorporated polymers in the designed ROP system must result from loss of the active hydroxy terminus of these polymers during star formation. To test this hypothesis as well as to demonstrate the versatility of the organic catalyst-mediated ROP system, CCS 3.3 – a novel alkyne end-functional CCS polymer was prepared using an \( \alpha\)-alkyne, \( \omega\)-hydroxy
PCL MI, HC≡C-PCL-OH 3.3 (Table 3.1), which was synthesized via ROP of CL using propargyl alcohol (PgOH) as the initiator and Sn(Oct)$_2$ as the catalyst at 110 ºC in toluene. PgOH was selected as the initiator due to its MW (55.6 g/mol), which is significantly different to the MW of the CL repeat unit (114.14 g/mol), as opposed to BnOH, which has a MW of 108.14 g/mol. This is particularly important when conducting end-group analysis of polymers via matrix assisted laser desorption/ionization time-of-flight (MALDI ToF) mass spectrometry, since cyclic PCL (c-PCL) impurities can be more easily identified as there would not be the overlapping mass peaks between HC≡C-PCL-OH and c-PCL series, whereas this complication might arise in the case of Bn-PCL-OH. CCS 3.3 was prepared using the same reaction conditions used for CCS 3.1a, and after 24 h a final arm-to-star conversion of 94 % was achieved. Similar to CCS 3.1a-d and 3.2 (Figure 3.1), the GPC RI chromatogram of CCS 3.3 revealed a trimodal peak profile (Figure 3.2A), with the peak corresponding to the star polymers at a retention time of 19–24 min also being accompanied by peaks at higher retention times of 23–27 and 28–30 min.

In order to identify the species responsible for the peaks at 23–27 and 28–30 min, CCS 3.3 was fractionated utilizing a fractional precipitation technique (see Appendix 2) to isolate the unincorporated polymers into two fractions (Figure 3.2A (ii) and (iii)). The fractionated polymers were subsequently analyzed via MALDI ToF mass spectroscopy and compared with the MALDI ToF mass spectrum of the MI HC≡C-PCL-OH (Figure 3.2B). The MALDI ToF mass spectrum of the MI HC≡C-PCL-OH revealed two apparent oligomeric mass series: the major series correspond to HC≡C-PCL-OH and the minor series correspond to linear PCL with an α-carboxylic acid end group (i.e., HOOC-PCL-OH) (Figure 3.2B (iii)).
Figure 3.2 (A) GPC RI chromatograms of (i) CCS 3.3, (ii) fractionated unincorporated cyclic PCL (c-PCL), (iii) fractionated unincorporated linear PCL (l-PCL) and (iv) MI HC≡C-PCL-OH 3.3; $M_n$, GPC = 11.8 kDa, PDI = 1.15 (Table 3.1, Entry 5), and (B) MALDI-ToF mass spectra of (i) fractionated unincorporated cyclic PCL (c-PCL), (ii) fractionated unincorporated linear PCL (l-PCL) and (iii) MI HC≡C-PCL-OH 3.3. MALDI ToF mass spectra were acquired in linear/positive mode using $\alpha$-cyano-4-hydroxycinnamic acid and potassium trifluoroacetate (KTFA) as the matrix and cationisation agent, respectively.
The presence of HOOC-PCL-OH could potentially originate from the ROP of CL initiated by water present in the PgOH initiator, or water produced from esterification of PgOH with octanoic acid liberated from the Sn(Oct$_2$) catalyst at elevated temperatures (>100 °C).$^{22}$ Another plausible explanation for the presence of HOOC-PCL-OH is the fragmentation of propargylic ester end groups of the MI HC≡C-PCL-OH during the mass spectroscopy ionization process, as the relative peak intensity of the HOOC-PCL-OH oligomeric series varies in the MALDI ToF mass spectra under different acquisition conditions, e.g., matrix and laser power (see Appendix 3, Figure A3.2). Mass peaks observed corresponding to the c-PCL oligomeric series were negligible (< 0.5 % of the total peak area) compared to the HC≡C-PCL-OH and HOOC-PCL-OH oligomeric series (Figure 3.2B (iii)).

In comparison, the mass peaks corresponding to the c-PCL oligomeric series can be clearly observed in the mass spectra of the fractionated unincorporated PCL polymers (Figure 3.2B (i) and (ii)). For example, c-PCL is the dominant oligomeric series in the MALDI ToF mass spectrum (Figure 3.2B (i)) of the unincorporated PCL polymers with a GPC RI retention time of 27.5–30 min (Figure 3.2A (ii)), and accounts for ca. 50 % of the sample composition as determined by peak area integration. These results suggest that the intramolecular transesterification or back-biting process$^{13}$ of MIs takes place during the star formation process, leading to the formation of low MW c-PCL, which cannot be integrated into stars. Surprisingly, the MALDI ToF mass spectra of both fractionated unincorporated polymers (Figure 3.2B (i) and (ii)) revealed oligomeric series corresponding to the telechelic PCL polymers, HC≡C-PCL$_n$-OH and HOOC-PCL$_n$-OH. The presence of unincorporated telechelic PCL with ‘active’ hydroxyl termini can only result from the intramolecular transesterification of the performed star polymers, during which the hydroxyl functional groups embedded in the core of the CCS polymers attack the ester groups on the linear arms to cleave and liberate l-PCL polymer (Scheme 3.2: Process 4).
3.3.3 Star Formation Mechanism via Organic Catalyst-mediated ROP

Based upon the previously obtained results, a mechanism of PCL CCS polymer formation via ROP can be proposed (Scheme 3.2), whereby four distinct and sequential processes occur: (1) reactive block polymer formation (i.e., chain-extension of MI with BOD); (2) polymer linking to form CCS polymers; (3) growth of CCS polymers, and; (4) cleavage of \textit{l-PCL} arms as a result of intramolecular transesterification. The cleaved \textit{l-PCL} can either attack the preformed star polymers through (5) intermolecular transesterification with the arms, which leads to the generation of new \textit{l-PCL} chains without any overall change in the amount of \textit{l-PCL}, or (6) intramolecular back-biting to give \textit{c-PCL} and another \textit{l-PCL} with lower MW.
Scheme 3.2 Proposed mechanism of CCS polymer formation via ROP.

3.3.4 Organic Vs. Organometallic Catalyst-mediated ROP for CCS Polymer Synthesis

To demonstrate the effectiveness of the organic catalyst-mediated ROP for star polymer synthesis, CCS 3.4 was prepared via ROP catalyzed by Sn(Oct)$_2$ in toluene at 110 ºC over 48 h (whilst keeping all other reaction conditions constant) and compared to CCS 3.1a (Table 3.1). Comparison of the GPC results for both CCS 3.4 and CCS 3.1a (Figure...
3.3) reveals several important differences. For example, the GPC RI chromatogram of CCS 3.4 shows a large shoulder peak (Figure 3.3A (i)) and a higher percentage of unincorporated polymers (Figure 3.3 (ii) and (iii)). The large shoulder peak most likely corresponds to high MW star-star coupled products that were formed as a result of elevated reaction temperature (110 ºC) and long reaction time (48 h) (Figure 3.3A).\textsuperscript{23} Since Sn(Oct)\textsubscript{2} has a high rate of transesterification even at relatively low monomer conversions,\textsuperscript{12} transesterifications are more pronounced in Sn(Oct)\textsubscript{2}-catalyzed star formation, which leads to a larger amount of the unincorporated polymers (i.e., cyclic oligomers \textit{c}-PCL and cleaved linear polymers \textit{l}-PCL) (Figure 3.3(ii) and (iii)). Therefore, CCS 3.4 only contains approximately 85 % star polymers, even taking the star-star coupled products into account. In contrast, CCS 3.1a synthesis was completed within 24 h, the GPC RI chromatogram shows no formation of star-star coupled products (Figure 3.3B), and the final yield of star was 95 %. Overall, this comparison reveals that by performing star polymer synthesis using organic catalysts (e.g., methanesulfonic acid) with low rates of transesterification, at low reaction temperatures, the amount of unconverted \textit{l}-PCL and \textit{c}-PCL (Figure 3.3 (ii) and (iii)) caused by inter- or intramolecular transesterification reactions can be significantly reduced, but not completely eliminated (Figure 3.3B).
Figure 3.3 GPC RI chromatograms for (A) CCS 3.4 prepared via ROP using Sn(Oct)$_2$ as catalyst ([Bn-PCL-OH 3.1a]/[BOD]/[Sn(Oct)$_2$]$_0$ = 1/30/0.5; [Bn-PCL-OH 3.1a]$_0$ = 0.15 mM; toluene; 110 °C), and (B) CCS 3.1a prepared via ROP using CH$_3$SO$_3$H as catalyst ([Bn-PCL-OH 3.1a]/[BOD]/[CH$_3$SO$_3$H]$_0$ = 1/30/3; [Bn-PCL-OH 3.1a]$_0$ = 0.15 mM; DCM; r. t). Peak (i) with retention time ($t_{ret}$) = 16 – 18 min corresponds to high molecular polymers resulting from star-star coupling, peak (ii) ($t_{ret}$ = 24 – 26 min) and peak (iii) ($t_{ret}$ = 28 – 30 min) correspond to unconverted L-PCL and c-PCL, respectively.
3.4 Conclusion

The facile and efficient synthesis of PCL-based star polymers via the organic catalyst (i.e., methanesulfonic acid)-mediated ROP and the arm-first approach was demonstrated in this chapter. The mild reaction temperature, fast reaction rate and low transesterification rate of the ROP star synthesis system that suppress inter- and intramolecular transesterification side-reactions lead to the near-quantitative star polymer yields (upto 96%). Although being significantly suppressed, transesterification side-reactions are still responsible for the formation of trace amounts of low MW linear and cyclic impurities in the products, preventing the stars’ yields to reach 100%. The versatility and robustness of the innovative star synthesis system was demonstrated through the synthesis of a novel alkyne end-functional polyester-based CCS polymer in high yield (95%).

This study provides a facile, metal-free, and high yielding approach for the synthesis of CCS polymers via organic catalyst-mediated ROP, which requires far less demanding reaction conditions than other controlled polymerization techniques. Hence, it is anticipated that the reported synthetic approach will be applicable to the synthesis of wide variety of polyester-based functional star polymers, and aid in the development of advanced materials, commercial applications and academic research.
3.5 Experimental Section

3.5.1 Materials

Propargyl alcohol (PgOH, 99 %), urea hydrogen peroxide (CO(NH$_2$)$_2$.H$_2$O$_2$, 97 %), stannous 2-ethylhexanoate (Sn(Oct)$_2$, 95 %), potassium trifluoroacetate (KTFA, 98 %) and methanesulfonic acid (CH$_3$SO$_3$H, 98 %) were purchased from Aldrich and used as received. Methanol (MeOH, AR, Chem-Supply), formic acid (97 %, Chem-Supply) and α-cyano-4-hydroxycinnamic acid (≥99%, Fluka) were also used as received. Tetrahydrofuran (THF, RCI Labscan, HPLC) was distilled from sodium benzophenone ketyl before use. Toluene (Scharlau, HPLC), ε-caprolactone (CL, 99+ %, Aldrich), benzyl alcohol (BnOH, AR grade, Ajax) and dichloromethane (99.8 %, Merck) were distilled from calcium hydride (95 %, Aldrich) before use. 4,4′-bioxepanyl-7,7′-dione (BOD) was synthesized according to a previously published procedure. 3

3.5.2 Instrumentation

Gel permeation chromatography (GPC) was performed on a Shimadzu liquid chromatography system fitted with a Wyatt DAWN EOS multangle laser light scattering (MALLS) detector (690 nm, 30 mW) and a Wyatt OPTILAB DSP interferometric refractometer (690 nm), using three Phenomenex Phenogel columns (500, 10$^4$, and 10$^6$ Å porosity; 5 μm bead size) operated at 1 mL/min using THF as the mobile phase and with the column temperature set at 30 ºC. Astra software (Wyatt Technology Corp.) was used to process the data to determine the MWs either using known dn/dc values or based on the assumption of 100 % mass recovery of the polymer where the dn/dc value was unknown. $^1$H NMR spectroscopic analysis was performed on a Varian Unity Plus 400 MHz spectrometer using the deuterated solvent as reference. Gas chromatography was performed on a Shimadzu GC 17-A gas chromatograph equipped with an Agilent J+W DB-5 capillary column (30 m, 5% phenyl siloxane) and coupled to a GCMS-QP50000 mass spectrometer (injector temperature = 250 ºC; initial column initial temperature = 40 ºC; heat ramp = 10
°C/min; final column temperature = 320 °C). MALDI ToF MS was performed on a Bruker Autoflex III Mass Spectrometer operating in positive linear mode; the analyte, matrix (α-cyano-4-hydroxycinnamic acid) and cationisation agent (KTFA) were dissolved in THF at concentrations of 10, 10 and 1 mg/mL, respectively, and then mixed in a ratio of 10:1:1. Subsequently, 0.3 μL of this solution was spotted onto a ground steel target plate and the solvent was allowed to evaporate prior to analysis. Flex Analysis (Bruker) was used to analyze the data.

**Synthesis of Bn-PCL-OH macrorinitiator 3.1a.** Sn(Oct)_2 (0.20 g, 0.50 mmol, 0.5 equiv.) was added to a flask purged with argon. CL (10.07 mL, 100 mmol, 100 equiv.) and BnOH (105 μL, 1.01 mmol, 1 equiv.) were then added via syringe. The reaction solution was stirred at 110 °C under argon for 1 h, cooled to room temperature, diluted with THF (50 mL) and then precipitated into cold MeOH (600 mL). The precipitate was collected by vacuum filtration and dried in vacuo to yield a white powder, 8.44 g (92.0 %). GPC-MALLS: \(M_n = 9.9\) kDa, PDI = 1.08; \(^1H\) NMR (400 MHz, CDCl\(_3\)): \(\delta_H 1.34-1.46\) (\(m\), -CH\(_2\)CH\(_2\)CH\(_2\)–), 1.61-1.72 (\(m\), -CH\(_2\)CH\(_2\)CH\(_2\)–), 2.32 (\(t\), -CH\(_2\)CH\(_2\)CO–), 3.66 (\(t\), CH\(_2\)CH\(_2\)OH end group), 4.07 (\(t\), -CH\(_2\)CH\(_2\)O–), 5.11 (\(s\), PhCH\(_2\)O- end group), 7.31-7.39 (\(m\), Ph end group) ppm. **Bn-PCL-OH** Mls 3.1b-c with different MWs were prepared by variation of the monomer to initiator ratio. **HC≡C-PCL-OH MI 3.3** was prepared using the same experimental procedure but with PgOH as the initiator to afford 3.3 as a white solid, 7.50 g (94 %). GPC-MALLS: \(M_n = 11.8\) kDa, PDI = 1.15; \(^1H\) NMR (400 MHz, CDCl\(_3\)): \(\delta_H 1.34-1.46\) (\(m\), -CH\(_2\)CH\(_2\)CH\(_2\)–), 1.61-1.72 (\(m\), -CH\(_2\)CH\(_2\)CH\(_2\)–), 2.32 (\(t\), -CH\(_2\)CH\(_2\)CO–), 2.53 (\(s\), C ≡ CH end group), 3.66 (\(t\), CH\(_2\)CH\(_2\)OH end group), 4.07 (\(t\), -CH\(_2\)CH\(_2\)O–), 4.58 (\(s\), -CO\(_2\)CH\(_2\)– end group) ppm. See Table A3.1 in Appendix 3 for more details.

**Synthesis of PCL star polymer CCS 3.1a.** Bn-PCL-OH MI 3.1a (\(M_n = 9.9\) kDa, PDI = 1.08; 0.5 g, 0.051 mmol, 1 equiv.) and BOD (0.34 g, 1.50 mmol, 30 equiv.) were added to a
flask under argon and dissolved in dichloromethane (10 mL). Methanesulfonic acid (14.8 µL, 0.15 mmol, 3 equiv.) was added via syringe and the reaction mixture was stirred at room temperature for 24 h (BOD conversion via GC = 99+ %). The crude reaction solution was diluted with dichloromethane (10 mL) and then precipitated into cold MeOH (50 mL) twice to afford CCS 3.1a as a white powder, 0.80 g (94.0 %). GPC-MALLS: $M_n = 326$ kDa, PDI = 1.25; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$H 1.30-1.45 (m, -CH$_2$CH$_2$CH$_2$-), 1.52-1.72 (m, -CH$_2$CH$_2$CH$_2$-), 2.32 (t, -CH$_2$CH$_2$CO-), 4.07 (t, -CH$_2$CH$_2$O-), 5.11 (s, PhCH$_2$O- end group), 7.31-7.39 (m, Ph end group) ppm. CCS 3.1b-d and CCS 3.3 were prepared by variation of the corresponding MI to cross-linker BOD ratio (refer to Table 3.1).

**One-pot synthesis of PCL star polymer CCS 3.2.** CL (0.49 mL, 4.47 mmol, 100 equiv.) and BnOH (4.7 µL, 0.045 mmol, 1 equiv.) were added via syringe to an argon purged flask and dissolved in dichloromethane (4.5 mL). Methanesulfonic acid (3.0 µL, 0.046 mmol, 1.02 equiv) was added and the solution was stirred at room temperature for 8 h (CL conversion via GC = 93.4 %; GPC-MALLS: $M_n = 12.2$ kDa, PDI = 1.12). Subsequently, a solution of BOD in dichloromethane (0.26 M, 5.7 mL, 30 equiv. BOD) was added, followed by methanesulfonic acid (6 µL, 0.092 mmol, 1.04 equiv) and the solution was stirred for 24 h (BOD conversion via GC = 99.0+ %). The reaction solution was diluted with dichloromethane (10 mL) and then precipitated into cold MeOH (50 mL) twice to afford CCS 3.2 as a white powder, 0.78 g (91.2 %). GPC-MALLS: $M_n = 295$ kDa, PDI = 1.23; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$H 1.30-1.45 (m, -CH$_2$CH$_2$CH$_2$-), 1.52-1.72 (m, -CH$_2$CH$_2$CH$_2$-), 2.32 (t, -CH$_2$CH$_2$CO-), 4.07 (t, -CH$_2$CH$_2$O-), 5.11 (s, PhCH$_2$O- end group), 7.31-7.39 (m, Ph end group) ppm.

**Synthesis of PCL star polymer CCS 3.4.** Bn-PCL-OH MI 3.1a ($M_n = 9.9$ kDa, PDI = 1.08; 0.52 g, 0.053 mmol, 1 equiv.), BOD (0.36 g, 1.59 mmol, 30 equiv.) and Sn(Oct)$_2$ (11.0 mg, 0.027 mmol, 0.5 equiv.) were added to a flask under argon. Toluene (10 mL) was
then added via syringe and the reaction mixture was stirred at 110 ºC for 48 h (BOD conversion via GC = 99+ %). After cooling to room temperature the reaction solution was diluted with dichloromethane (10 mL), filtered and then precipitated into cold MeOH (50 mL) twice to afford CCS 3.4 as a white powder, 0.71 g (80.6 %). GPC-MALLS: $M_n = 364$ kDa, PDI = 1.20; $^1$H NMR (400 MHz, CDCl$_3$): $\delta_H$ 1.30-1.45 ($m$, -CH$_2$CH$_2$CH$_2$-), 1.52-1.72 ($m$, -CH$_2$CH$_2$CH$_2$-), 2.30 ($t$, -CH$_2$CH$_2$CO-), 4.05 ($t$, -CH$_2$CH$_2$O-), 5.11 ($s$, PhCH$_2$O- end group), 7.31-7.39 ($m$, Ph end group) ppm.
3.6 Reference


PART 2

Synthesis and Characterization of Novel Poly(pseudo)rotaxane Supramolecular Architectures
Chapter 4

Synthesis of Novel Core Cross-linked Star (CCS)-based Polyrotaxane

4.1 Chapter Perspective

Functionalization of CCS polymers is often achieved through covalent chemistry; for example, the use of functional monomers, cross-linkers or initiators through polymerization to insert functional moieties into the CCS macromolecule, as demonstrated in Chapters 2 and 3. Functionalization of CCS polymers via supramolecular chemistry through non-covalent interactions has been less explored. In this chapter, the functionalization of a PCL-based CCS polymer with the cyclic oligosaccharide α-CD via non-covalent inclusion complexation was explored. The PCL arms of the CCS polymers were found to be capable of threading through discrete α-CDs in spite of the high steric hindrance. The threaded α-CDs were effectively locked onto the CCS polymers by installing bulky end-caps to the arm chain ends via click chemistry. This leads to the formation of an unprecedented CCS supramolecular polymer with radiating polyrotaxane arms. The inclusion complexation gives rise to some unusual physical properties and characteristics exhibited by the α-CD complexed CCS polymers, which includes a remarkably increased size (or hydrodynamic volume) compared to the PCL CCS polymer precursor.
4.2 Introduction

In the past, cyclodextrin (CD)-based polyrotaxane supramolecular structures have attracted significant attention as new building blocks to construct advanced nanomaterials with novel properties and functions. As a result of their low cytotoxicity, controllable size and unique structure, CD-based polyrotaxanes demonstrate a diverse range of potential applications in life sciences and biotechnology, including polymer therapeutics, gene delivery and tissue engineering. For example, CD-based polypseudorotaxane hydrogels have been utilized as a promising injectable drug delivery system for sustained and controlled drug release. Furthermore, biodegradable polyrotaxanes with drug-conjugated CDs and degradable end caps may serve as supramolecular prodrugs for controlled and targeted drug delivery. A cationic polyrotaxane prepared from dimethylaminoethyl modified CDs and poly(ethylene glycol) (PEG) with benzyloxy carbonyl-L-tyrosine end-caps was exploited as a DNA carrier. In addition, hydrolyzable hydrogels prepared from cross-linked α-CD-PEG polyrotaxanes could potentially serve as desirable tissue engineering scaffold.

Since the discovery of CD-based polyrotaxanes by Harada and co-workers in 1992, most studies have focused on the development of polyrotaxanes with simple linear structures (i.e., polyrotaxane prepared from threading CDs onto a linear polymer). Limited examples of CD-based poly(pseudo)rotaxanes with complex three-dimensional (3D) supramolecular architecture have been prepared to date. This might be due to either the synthetic complexity of synthesizing suitable 3D polymer architecture as the guest macromolecule, or the inefficient end-capping reactions preventing the threaded CD from being permanently locked onto the guest polymer to afford a stable supramolecular assembly.

Previously in Chapter 3, the near-quantitative synthesis of a novel PCL-based alkyne end-functional CCS polymer was described. It is well-known that polyesters, including PCL, are capable of forming poly(pseudo)rotaxane with α-CD through the host-guest inclusion complexation. Therefore, the alkyne end-functional CCS polymer may serve as a suitable 3D polymeric scaffold to construct a novel polyrotaxane supramolecular architecture. To provide a fundamental understanding of the characteristic properties of 3D polyrotaxane supramolecules, and explore their potential applications, the synthesis of a novel well-defined CCS-based polyrotaxane is described in this chapter. The 3D
polyrotaxane supramolecular structure was constructed through the inclusion complexation of the alkyne end-functional CCS polymer scaffold (prepared via organic-catalyst mediated ROP) with α-CDs. The terminal alkyne functionality of the CCS polymer was reacted with a bulky azido anthracene compound to effectively end-cap the threaded α-CDs via click chemistry. The formation of the CCS polyrotaxanes was confirmed by various characterization techniques, and some distinct and interesting characteristics and properties of the CCS polyrotaxane supramolecule were elucidated.

4.3 Results and Discussion

4.3.1 Synthesis of PCL-based Alkyne End-functional CCS Polymers

The PCL-based alkyne end-functional CCS polymer precursor was prepared via methanesulfonic acid (MSA)-mediated ROP of 4,4′-bioxepanyl-7,7′-dione (BOD) (i.e., the cross-linker) using an α-alkyne, ω-hydroxyl telechelic PCL macroinitiator (PCL-MI) (see Chapter 3, Scheme 3.1). The number average molecular weight (MW) of the PCL-MI determined by GPC (\(M_{n,\text{GPC}}\)) was 11.8 kDa with a narrow monomodal molecular weight distribution (MWD) (PDI < 1.1) (Figure 4.1a). The \(M_n\) of the PCL-MI was also determined by \(^1\)H NMR spectroscopic analysis (\(M_{n,\text{NMR}}\)) using the ratio of the integrals of the resonances at 4.02-4.10 ppm (‘f’, -CH\(_2\)O- of CL repeating unit) and 4.68 ppm (‘b’, CH≡CCH\(_2\)- of end-group), according to Equation A4.1 (see Appendix 4, Table A4.1). PCL-MI has a \(M_{n,\text{NMR}}\) of 10.9 kDa, which is good agreement with its \(M_{n,\text{GPC}}\) as well as its theoretical average MW (\(M_{n,\text{dheo}} = 10.6\) kDa, based upon the monomer conversion via GC-MS analysis).
Figure 4.1 GPC (THF) differential refractive index (DRI) chromatograms of (a) PCL-MI and (b) PCL CCS polymer with arm-to-star conversion > 94% (determined via the deconvolution of the GPC chromatogram using a Gaussian distribution function).

After the star-formation reaction, the GPC differential refractive index (DRI) trace revealed a peak at low elution time relative to the initial PCL-MI peak (Figure 4.1), indicating the formation of CCS polymers with high MWs. The $M_n$ of the PCL CCS was determined to be 286 kDa with a narrow MWD (PDI < 1.3). The GPC trace of the PCL CCS polymer also revealed a small shoulder peak at a retention time of ca. 24.5 min corresponding to the unconverted MI (Figure 4.1b). The average arm number per star polymer ($N_{arm}$) was calculated to be 15 according to the previously published calculation method. The $^1$H NMR spectrum of the PCL CCS polymer revealed two unique resonance, ‘a’ ($\text{CH}=\text{C}$, $\delta = 2.61$ ppm) and ‘b’ ($\text{CH}=\text{CH}_2$, $\delta = 4.68$ ppm) (Figure 4.2a), which correspond to the alkyne and methylene protons, respectively, of the terminal propargylic functionalities, verifying the end group fidelity of the PCL CCS polymer.
4.3.2 Synthesis of PCL CCS Polypseudorotaxane via Inclusion Complexation

The CCS polypseudorotaxane was prepared via the inclusion complexation of the PCL CCS polymer with \( \alpha \)-CD (Scheme 4.1(i)). Initially, a solution of the PCL CCS polymer in acetone was slowly added to an aqueous solution of \( \alpha \)-CD, resulting in the immediate formation of a turbid mixture. The turbid suspension results from the precipitation of the high MW CCS polypseudorotaxane. The resulting CCS polypseudorotaxanes were isolated via centrifugation, washed repeatedly with acetone/H\(_2\)O (1/3, v/v) to remove any uncomplexed CD, and then characterized via \(^1\)H and 2D-ROESY NMR spectroscopic analysis, X-ray powder diffraction (XRD) and thermogravimetric analysis (TGA). The \(^1\)H NMR spectrum of the CCS polypseudorotaxane is shown in Figure 4.2b.
Scheme 4.1 Schematic for the synthesis of PCL CCS-based polyrotaxane: (i) inclusion complexation of alkyne end-functional CCS polymer and $\alpha$-CD, and (ii) end-capping click reaction between the alkyne end functionalities of the CCS polymer and azido anthracene derivatives.
The stoichiometry of α-CD to CL repeat units (i.e., α-CD : CL molar ratio) in the CCS polypseudorotaxane were determined from $^1$H NMR spectroscopic analysis via the ratio of the integral of resonance ‘1’ at 4.78 ppm (-C(CH$_2$)HO-, α-CD) over that of resonance ‘f’ at 3.96 - 4.02 ppm (-CH$_2$O-, PCL) (Figure 4.2b, and see also Appendix 4, Table A4.2). The α-CD to CL ratio was found to be 0.74, which is less than the theoretical 1:1 stoichiometry. This result is unsurprising as the threading of α-CD onto the arms, along the radial direction towards the core of the star, becomes increasingly difficult and less thermodynamically favorable as a result of steric congestion. Thus, it can be concluded that the 3D macromolecular structure of the polymer scaffold plays an effect on the composition of the resultant polypseudorotaxane.

4.3.3 Synthesis of PCL CCS Polyrotaxane via Click End-capping Reaction

The CCS polypseudorotaxane was end-capped via copper-catalyzed azide-alkyne cycloaddition (CuAAC) click chemistry, through the reaction of the terminal alkyne functionalities of the CCS polypseudorotaxane with a bulky azido anthracene derivative (Scheme 4.1(ii)), resulting in the formation of the CCS polyrotaxane. The resultant CCS polyrotaxane was characterized by $^1$H and 2D-ROESY NMR spectroscopic analysis, UV-vis spectrophotometry, XRD, TGA, Dynamic light scattering (DLS) and Transmission electron microscopy (TEM). The $^1$H NMR spectrum of the CCS polyrotaxane (Figure 4.2c) revealed a series of resonances between 8.75-7.55 ppm (‘j-m’ 9 AtH and ‘n’ -NCH=C-), which are attributed to the aromatic protons of anthracene and the proton on the triazole ring. The presence of these characteristic resonances confirms the successful click end-capping reaction and formation of the polyrotaxane. The α-CD : CL ratio in the CCS polyrotaxane was then re-calculated via $^1$H NMR spectroscopic analysis using the same method as for the CCS polypseudorotaxane (Figure 4.2c, and see also Appendix 4, Table A4.2). For the CCS polyrotaxane, the α-CDs : CL ratio was found to be 0.68, which is comparable to that for the un-capped PCL CCS polypseudorotaxane (α-CD : CL = 0.72). This result suggests that as a result of the robust and efficient nature of CuAAC, dethreading of the complexed α-CDs from the PCL CCS polymer was minimal during the end-capping reaction.
To determine the end-capping efficiency of the CCS polyrotaxane, the extinction coefficient of the azido anthracene derivative was determined by UV-vis spectrophotometry (Figure 4.3). The absorption of various concentration solutions at 366 nm was measured to generate a concentration-absorbance calibration curve, from which the extinction coefficient was found to be 5000 M\(^{-1}\) cm\(^{-1}\) (Figure 4.3b). Utilizing this excitation coefficient, the number of anthracene molecules ‘clicked’ onto each CCS polyrotaxane was calculated to be ca. 14, which is very close to the arm number of the PCL CCS polymer (\(N_{\text{arm}} = 15\)). Based upon this result, the ‘click’ end-capping efficiency was calculated to be 92 %. Furthermore, as a result of the fluorescent nature of the anthracene derivative, the CCS polyrotaxane was found to give blue fluorescence under UV irradiation (\(\lambda = 254 \text{ nm}\)) (Figure 4.3a, (ii)), which provides additional evidence for the successful end-capping of the CCS polypseudorotaxanes via click chemistry.

**Figure 4.3** (a) UV-vis spectra of anthracene end-capped CCS polyrotaxane and azido anthracene at various molar concentrations in DMSO, *Inset*: DMSO solutions of CCS polyrotaxane under (i) white light and (ii) UV irradiation at \(\lambda = 254 \text{ nm}\), and (b) absorption calibration curve for azido anthracene to determine the anthracene loading of the CCS polyrotaxane.
The formation of the CCS polyrotaxane was also proven by XRD analysis. Figure 4.4 shows the X-ray powder diffractograms of (a) α-CD, (b) PCL CCS polymer, (c) CCS polypseudorotaxane, and (d) CCS polyrotaxane, respectively.

Figure 4.4 X-ray powder diffractograms of (a) α-CD, (b) PCL CCS polymer, (c) CCS polypseudorotaxane, and (d) CCS polyrotaxane.

The X-ray diffractogram of α-CD shows the typical α-CD crystallite diffraction pattern with multiple diffraction peaks resulting from the randomly orientated α-CD with cage-type structure (Figure 4.4a). In the diffractogram of the PCL CCS polymer, only the characteristic PCL crystallite peaks at 2θ = 21.3° and 23.6° were observed (Figure 4.4b). For both the CCS polypseudorotaxane and polyrotaxane, the diffractograms reveal the distinct α-CD and PCL inclusion complex diffraction pattern (Figure 4.4c and d, respectively). In both the CCS polypseudorotaxane and polyrotaxane supramolecular structures, the threaded α-CD rings were stacked along the PCL arms to form a channel-type or tunnel structure. The X-ray diffraction of the crystallite that is formed from the
close packing of the channel-type inclusion complexes give the characteristic diffraction peaks at $2\theta = 19.8^\circ$ and $22.6^\circ$.

The 2D-ROESY NMR spectroscopic analysis provides additional evidence for the formation of the CCS polypseudorotaxane and polyrotaxane supramolecular polymers. The 2D-ROESY NMR spectrum of the CCS polypseudorotaxane (Figure 4.5b) clearly shows the correlations resulting from non-bonding interactions through space, between the protons on the PCL arms (resonances ‘c-f’) and the $\alpha$-CD (resonances ‘1-9’). Furthermore, this proves that the arms of the PCL CCS polymer are physically included in the cavities of the $\alpha$-CDs to afford a unique star-shaped 3D polyrotaxane supramolecular assembly. Similar correlations were observed in the 2D-ROESY NMR spectrum of the CCS polyrotaxane (Figure 4.5a), and these findings are in good agreement with the previously published literatures.\textsuperscript{8d, 12}
Figure 4.5 2D-ROESY NMR spectra of (a) CCS polyrotaxane and (b) CCS polypseudorotaxane in DMSO-$d_6$.

The thermal decomposition profiles of the PCL-MI, PCL CCS polymer, CCS polypseudorotaxane, CCS polyrotaxane, and $\alpha$-CD were studied via TGA (Figure 4.6). $\alpha$-CD exhibited the lowest thermal stability of all the compounds studied (Figure 4.6e).
Judging from the thermal decomposition profiles, the PCL CCS polymer has a higher initial decomposition temperature than the PCL-MI (Figure 4.6b and a, respectively). The enhanced thermal stability of the star polymers is attributed to the strong inter- and intramolecular van der Waals interactions amongst the PCL arms.\textsuperscript{8a} The profiles for the CCS polypseudorotaxane and CCS polyrotaxane (Figure 4.6c and d, respectively) reveal a two-step thermal decomposition mode, in which the first and second weight loss steps can be attributed to the decomposition of the α-CDs and the CCS polymers, respectively.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{TGA_curves.png}
\caption{Thermogravimetric curves for (a) PCL-MI, (b) PCL CCS polymer, (c) CCS polypseudorotaxane, (d) CCS polyrotaxane, and (e) α-CD. The samples were heated from 70 to 700 °C at a rate of 10 °C/min under a N\textsubscript{2} flow of 20 mL/min.}
\end{figure}

Based upon their respective thermal decomposition profiles, it was estimated that the threaded α-CDs constitute 72 wt% of the CCS polypseudorotaxane, which is higher than that of the CCS polyrotaxane (59 wt%) and is in agreement with the \textsuperscript{1}H NMR results (see Appendix 4, Table 4.2). The TGA results suggest during the end-capping reaction, some of the threaded α-CDs (approx. 13 wt%) are liberated from the CCS polypseudorotaxanes, most probably as a result of the low association constant of α-CD-
PCL inclusion complexes in DMSO, the solvent which was used for the click end-capping reaction.

The typical TEM micrographs for the PCL CCS polymer and CCS polyrotaxane are shown in Figure 4.7a and b, respectively. From TEM, the PCL CCS polymer appears to adopt a globular morphology with an average diameter of ca. 70 nm (Figure 4.7a), which agrees well with the hydrodynamic diameter ($D_h$) of the CCS polymer obtained from DLS analysis (Figure 4.8a). In comparison, the CCS polyrotaxane showed an enlarged or ‘swollen’ spherical morphology with a clear core-shell structure and an average diameter of ca. 200 nm (Figure 4.7b, and see also Figure A4.1 in Appendix 4). Thus, upon inclusion complexation, the CCS polymer experiences a significant size expansion which can be attributed to: 1) the original randomly coiled PCL arms of the CCS polymer adopt a stretched conformation, and 2) the threaded α-CDs substantially increase the volume of the arms; hence the steric repulsions amongst the polyrotaxane arms cause the overall volume expansion of the CCS structure.

**Figure 4.7** Transmission electron microscopy (TEM) images of (a) PCL CCS polymer and (b) CCS polyrotaxane. The scale bars represent 200 nm

It is worth noting that the average diameter of the CCS polyrotaxane determined from the TEM images was ca. 100 nm smaller than the $D_h$ obtained from DLS analysis (Figure 4.8a). During the TEM sample preparation, evaporation of the solvent caused the arm polymers of the CCS polyrotaxane to collapse onto the core and this leads to a
considerable shrinkage in its size. When DLS measurements were taken, the arms of the CCS polyrotaxane was fully dissolved in DMSO and expected to stretch out radially from the core due to the solvation effect. Such effect provides a rational explanation for the discrepancy between the $D_h$ and averaged diameter of the CCS polyrotaxane observed under TEM.

The hydrodynamic diameter of the CCS polyrotaxane was found to be 300 nm, which is very close to the estimated diameter of the PCL CCS polymer with the core and arm components at maximum extension (ca. 280 nm, see Appendix 4). The slight discrepancy can be attributable to the size expansion of the star polymer after the inclusion complexation with $\alpha$-CD. Furthermore, the hydrodynamic diameter of the CCS polyrotaxane remained constant upon dilution (Figure 4.8b). These characterization results strongly suggested the core/shell nanoparticles observed under TEM as well as characterized by DLS are single particles of CCS polyrotaxane, not their random aggregates.

![Figure 4.8](image)

**Figure 4.8** (a) DLS measurement plots of PCL CCS polymer, CCS polypseudorotaxane and CCS polyrotaxane (0.5 mg/mL in DMSO), and (b) DLS measurement plots of the CCS polyrotaxane at various concentrations in DMSO.
4.4 Conclusion

In this chapter, the synthetic strategy to prepare a novel 3D CCS polyrotaxane was described. The CCS polyrotaxane was synthesized via the inclusion complexation of α-CD and a PCL CCS polymer scaffold, followed by end-capping via click chemistry to permanently lock the threaded α-CDs in position. The formation of the CCS polyrotaxane was confirmed via \(^1\)H and 2D-ROSEY NMR spectroscopic analysis, XRD, TGA and UV-vis spectrophotometry. The characterization results revealed some interesting characteristics and properties of the CCS polyrotaxane. Compared to the PCL polymer precursor, the CCS polyrotaxane has a unique two-step thermal decomposition profile, which results from the thermal degradation of the threaded α-CD, and that of the PCL polymer scaffold, respectively. The TEM images showed remarkable supramolecular images of the CCS polyrotaxane with a clear core-shell structure. The CCS polyrotaxane has a significantly larger size than the PCL CCS polymer judging from the TEM images and DLS analysis. This size expansion is caused by the increase in structural stiffness and volume of the arms of the CCS nanoparticle upon inclusion complexation. The procedure reported herein, which combines the application of organic catalyst-mediated ROP, inclusion complexation and click chemistry has led to the first successful synthesis of CD-based CCS poly(pseudo)rotaxanes. It is anticipated that such a facile and versatile synthetic protocol would aid in the development of advanced nanomaterials for applications in life sciences and nanotechnology.
4.5 Experimental Section

4.5.1 Materials

e-Caprolactone (CL, >99%), methanesulfonic acid (MSA, 97%), propargyl alcohol (99.5%), anthracene-9-carboxylic acid (>96%), 3-chloropropanol (98%), sodium ascorbate (>98%), N,N,N′,N′′,N′′-pentamethyldiethylenetriamine (PMDETA, 99%), thionyl chloride (SOCl₂, ≥99%), and α-cyclodextrin (α-CD, 98%) were purchased from Sigma-Aldrich and used as received. Deuterated dimethyl sulfoxide (DMSO-d₆, 99.8%) and deuterated chloroform (CDCl₃, 99.9%) were purchased from Cambridge Isotope Laboratories, Inc and used as received. Dichloromethane (DCM) was distilled from calcium hydride under argon before use. Tetrahydrofuran (THF) were distilled from benzophenone and sodium metal under argon before use. AR grade acetone, methanol, and dimethyl sulfoxide (DMSO) were purchased from Chem-Supply Pty. Ltd. and used as received.

4.5.2 Instrumentation

Gel permeation chromatography (GPC) (THF as eluent) was performed on a Shimadzu liquid chromatography system fitted with a Wyatt DAWN EOS multi-angle laser light scattering (MALLS) detector (690 nm, 30 mW) and a Wyatt OPTILAB DSP interferometric refractometer (690 nm), using three Phenomenex Phenogel columns (500, 10⁴ and 10⁶ Å porosity; 5 µm bead size) operated at 1 mL/min with column temperature set at 30 °C. Astra software (Wyatt Technology Corp.) was used to process the data to determine the MWs either using known dn/dc values or based on the assumption of 100% mass recovery of the polymer where the dn/dc value was unknown. Gas chromatography was performed on a Shimadzu GC 17-A gas chromatograph equipped with an Agilent J+W DB-5 capillary column (30 m, 5% phenyl siloxane) and coupled to a GCMS-QP50000 mass spectrometer (injector temperature = 250 °C; initial column initial temperature = 40 °C; heat ramp = 10 °C/min; final column temperature = 320 °C). ¹H NMR and 2D ROSEY NMR spectroscopic analysis was performed on a Varian Unity (400 MHz) spectrometer using the deuterated solvent as reference. Dynamic light scattering (DLS) measurements were performed using a Malvern high performance particle sizer (HPPS) with a 3.0 mW He-Ne laser operated at 633 nm. Analysis was performed at an angle of 173° and a constant
temperature of 25 ± 0.1 °C. Thermogravimetric analysis (TGA) was performed on a PerkinElmer Pyris-1 thermogravimetric analyzer, and the samples were heated from 70 to 700 °C at a rate of 10 °C·min⁻¹ under a nitrogen flow (20 mL·min⁻¹). X-ray diffraction (XRD) patterns of the samples were recorded on a Bruker D8 Advance instrument with Cu Kα radiation (40 kV, 40 mA) and a nickel filter, and the samples were exposed at a scanning rate of 2θ = 0.020 °·s⁻¹ in the range of 3-50 °. Transmission electron microscopy (TEM) images were taken using a Tecnai TF30 transmission electron microscope (FEI Co., Eindhoven, The Netherlands) operated at 200 kV. Images were acquired digitally with a Gatan US1000 2k × 2k CCD Camera (Pleasanton, CA). The TEM samples were prepared by dissolving at a concentration of 0.5 mg mL⁻¹ and then spin-coating the sample solution on TEM copper grid (strong carbon film, 300 mesh). UV-vis spectrophotometry was performed on a Shimadzu UV-1800 spectrometer using quartz cuvettes with a 1 cm path length.

**Synthesis of 3-azidopropyl anthracene-9-carboxylate.** 3-Azidopropyl anthracene-9-carboxylate was prepared according to the synthetic procedure described in Chapter 2 (Section 2.5). ¹H NMR (400 MHz, CDCl₃): δH 8.48 (s, 1H, ArH), 7.95-8.14 (m, 1H, 4ArH), 7.44-7.54 (m, 4H, 4ArH), 4.67 (t, 2H, J = 5.2 Hz, -CH₂N₃), 3.45 (t, 2H, J = 5.2 Hz, -OCH₂-), 2.09 (quin, 2H, J = 6.4 Hz, -CH₂-) ppm. ³¹C NMR (100 MHz, CDCl₃): δC 169.6 (C=O), 131.0 (ArCH), 129.5 (2ArCH), 128.7 (2ArCH), 128.5 (ArCC=O), 127.7 (ArCH), 127.2 (2ArCH), 125.6 (2ArCH), 124.7 (2ArCH), 62.5 (OCH₂), 48.2 (CH₂N₃), 8.3 (CH₂) ppm.

**Synthesis of PCL CCS polymer.** The PCL CCS polymer was synthesized according to the synthetic procedure described in Chapter 3 (Section 3.5). GPC-MALLS (THF): Mₙ,GPC = 286.0 kDa, Mₙ/Mₙ = 1.29; ¹H NMR (400 MHz, CDCl₃): δH 4.83 (m, 2H, CH=CCH₂-), 4.21 (m, 2H, -CH₂O- protons of BOD moiety), 4.12-4.02 (m, 2H, -CH₂O- protons of PCL), 3.70-3.62 (t, 2H, J = 6.4 Hz, -CH₂OH), 2.61 (m, 1H, CH=CH), 2.35-2.22 (m, 2H, -C(=O)CH₂-), 1.72-1.56 (m, 4H, -CH₂CH₂CH₂-), 1.42-1.33 (m, 2H, -CH₂CH₂CH₂-) ppm.

**Synthesis of CCS polypseudorotaxane through inclusion complexation of α-CD and PCL CCS polymer.** PCL CCS (Mₙ,GPC = 286.0 kDa, 0.143 g, 5 × 10⁻⁴ mmol) and α-CD
(1.5 g, 1.54 mmol) were dissolved in acetone (5 mL) at 50 °C and distilled water (15 mL) at 60 °C, respectively. The polymer solution was added dropwise to the aqueous solution of α-CD at 60 °C for 6 h with rigorous stirring, and the reaction mixture was then cooled to room temperature and stirred for further 42 h. The precipitate was collected via centrifugation, washed with acetone/H2O (1/3, v/v, 10 mL) thrice, and dried in vacuo at 40 °C for 24 h to give a white powder, 0.45g (68%). 1H NMR (400 MHz, DMSO-d6): δH 5.40-5.52 (m, 12H, -CHOH, protons of α-CD), 4.78 (d, 6H, -OCH(CH)O-, protons of α-CD), 4.45 (m, 6H, -CH2OH, protons of α-CD), 3.94-3.98 (m, 2H, -CH2O-, protons of PCL), 3.72-3.78 (m, 6H, -CHOH, protons of α-CD), 3.52-3.68 (m, 18H, -CH2OH and -CHCHOH, protons of α-CD), 3.20-3.40 (m, 12H, -CHOH and -CH-, protons of α-CD), 2.20-2.26 (m, 2H, -C(=O)CH2- protons of PCL), 1.45-1.52 (m, 4H, -CH2CH2CH2- protons of PCL), 1.25-1.28 (m, 2H, -CH2CH2CH2- protons of PCL) ppm.

Synthesis of CCS polyrotaxane through click end capping CCS polypseudorotaxane. Initially a catalyst stock solution was prepared by dissolving CuSO4·5H2O (50 mg, 0.2 mmol), sodium ascorbate (200 mg, 1.0 mmol) and PMDETA (70 mg, 0.4 mmol) in degassed H2O/DMSO (95/5 %v/v, 2 mL). In a Schlenk tube, CCS polypseudorotaxane (128 mg, 1.4 × 10⁻³ mmol of alkyne) and 3-azidopropyl anthracene-9-carboxylate (30 mg, 0.1 mmol, 70 equiv. to alkyne) were dissolved in DMSO (4 mL). The mixture was degassed via two freeze-pump-thaw cycles, backfilled with argon and the catalyst stock solution (1 mL, 70 equiv. to alkyne) was then added. The reaction solution was subjected to one additional freeze-pump-thaw cycle, backfilled with argon and stirred at r.t. for 48 h. The product was precipitated in cold acetone (10 mL × 2) and was washed with H2O (10 mL × 3). The precipitate was collected via centrifugation and dried in vacuo at 40 °C for 24 h to give a brown powder, 96 mg (75%). 1H NMR (400 MHz, DMSO-d6): δH 8.75 (s, 1H, ArH), 8.12-8.18 (m, 2H, 2ArH), 7.90-7.96 (m, 2H, 2ArH), 7.72-7.77 (m, 1H, -NCH=C-, proton of triazole ring), 7.52-7.62 (m, 4H, 4ArH), 5.40-5.52 (m, 12H, -CHOH of α-CD), 4.78 (d, 6H, -OCH(CH)O- of α-CD), 4.45 (m, 6H, -CH2OH of α-CD), 3.94-3.98 (m, 2H, -CH2O- of PCL), 3.72-3.78 (m, 6H, -CHOH of α-CD), 3.52-3.68 (m, 18H, -CH2OH and -CHCHOH of α-CD), 3.20-3.40 (m, 12H, -CHOH and -CH- of α-CD), 2.20-2.26 (m, 2H, -C(=O)CH2- of

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PCL), 1.45-1.52 (m, 4H, -CH<sub>2</sub>CH<sub>2</sub> of PCL), 1.25-1.28 (m, 2H, -CH<sub>2</sub>CH<sub>2</sub>-CH<sub>2</sub>- of PCL) ppm.
4.5 Reference


Chapter 5

Novel Cylindrical Bottlebrush Polypseudorotaxane

5.1 Chapter Perspective

In the previous chapter, a core cross-linked star (CCS)-based polyrotaxane was successfully prepared and a unique conformational expansion of the CCS polymer was observed upon inclusion complexation. In this chapter, a high density bottlebrush polymer with PCL grafts (i.e., branches) was prepared and complexed with α-cyclodextrin (CD). Complementary to the previous study (Chapter 4), this research provides new insights into the effect of macromolecular architecture, branch length and branch density on inclusion complexation. Self-assembly of the bottlebrush polymer and α-CD through inclusion complexation gives rise to the formation of a novel bottlebrush with polypseudorotaxane side-chains. The resulting polypseudorotaxane and the bottlebrush precursor displayed clear differences in physical properties and characteristics. Similar to the CCS polymer system, an inclusion-induced conformational transition of the bottlebrush polymer was observed, although the mode of the transition is substantially different from that of the CCS polymer.
5.2 Introduction

In the past decades, supramolecular chemistry\(^1\) has attracted significant attention from various scientific disciplines including chemistry, physics and biology, as a powerful method to construct functional nanomaterials with controlled dimension, unique architectures and novel properties.\(^2\) Different from molecular chemistry based on covalent bonds, supramolecular chemistry replies on non-covalent forces such as hydrogen bonding, electrostatic interactions, \(\pi-\pi\) interactions and other types of van der Waals forces to assemble molecular components to form supramolecular assemblies. Recently, supramolecular self-assembly systems that utilize the inclusion complexation of CD with guest molecules through non-covalent host-guest interactions as the assembling mode have attracted great interest.\(^3\) In particular, supramolecules prepared by threading CD onto polymer guests (i.e., CD-based poly(pseudo)rotaxanes\(^4\)), have demonstrated a wide scope of potential applications in drug\(^5\) and gene delivery,\(^6\) and tissue engineering.\(^7\)

Previously, most investigations have focused on the design, synthesis and characterization of linear polypseudorotaxanes.\(^8\) As a result of recent developments in controlled/living polymerization techniques, polymer chemists have succeeded in preparing novel well-defined polypseudorotaxanes with more complex molecular architectures, and explored their exciting new functions and properties.\(^9\) In Chapter 4, the first syntheses of well-defined 3D CCS-based polypseudorotaxane and polyrotaxane were described. In this chapter, a facile and highly efficient synthetic route towards a novel bottlebrush polypseudorotaxane is presented. Although the synthesis of graft polymer-based polypseudorotaxane has been previously reported by Huang et al.,\(^10\) the resultant supramolecular polymer has a limited number of side-chains (\(\leq 20\)). The bottlebrush polypseudorotaxane reported herein is constructed through the inclusion complexation of a densely-grafted bottlebrush polymer with \(\alpha\)-CD, and is therefore expected to have a large number of polypseudorotaxane side-chains (approx. 200) and exhibit unusual properties and characteristics compared to the previously reported graft polypseudorotaxane.

It has been demonstrated that other than ring opening metathesis polymerization (ROMP), molecular brush polymers prepared via controlled/living polymerization techniques such as living radical\(^11\) and anionic\(^12\) polymerization and the grafting-through approach often suffer from a low degree of polymerization (DP). This results from strong
stERIC repulsion between the propagating brush polymer and incoming macromonomers (MMs) during the polymerization. Several distinctive advantages of ROMP enable it to synthesize molecular brush polymers with high DPs via the grafting-through approach.\textsuperscript{13} Firstly, norbornenyl MMs result in larger spacing between side-chains and provide a more kinetically favourable environment for propagation reactions. In addition, ring strain in the norbornenyl functionality enhances the thermodynamic driving force for the polymerization. Furthermore, highly robust and efficient metathesis catalysts (e.g., Ru-based Grubbs’ catalysts) possess high functional group tolerance that enables well-defined bottlebrush polymers to be efficiently prepared using various types of functional norbornenyl MMs.\textsuperscript{14}

In this study, a high density $\varepsilon$-caprolactone (PCL) bottlebrush polymer was firstly prepared via the ROMP of norbornenyl PCL MMs using the robust and highly active 2\textsuperscript{nd} Generation Grubbs’ catalyst as initiator. Inclusion complexation of the high density PCL-based bottlebrush polymer scaffold and $\alpha$-CD afforded a novel bottlebrush polypseudorotaxane. Characterization by nuclear magnetic resonance (NMR) spectroscopic analysis, dynamic light scattering (DLS), differential scanning calorimetry (DSC), thermogravimetric analysis (TGA) and transmission electron microscopy (TEM) confirmed the formation of the bottlebrush polypseudorotaxane and identified some unique characteristics and properties of this unprecedented supramolecular polymer.

\section*{5.3 Results and Discussion}

The overall strategy for the synthesis of the bottlebrush polypseudorotaxane BB-IC is presented in Scheme 5.1. The PCL bottlebrush polymer BB, which serves as the macromolecular scaffold for BB-IC was first prepared via the ROMP of norbornenyl PCL MMs initiated by the pyridine-modified 2\textsuperscript{nd} Generation Grubbs’ catalyst (5.1) (Scheme 5.1(ii)).\textsuperscript{13}\textsuperscript{a} The DP of BB was controlled by the MM to the Grubbs’ catalyst 5.1 feeding ratio. MM was synthesized via the ring-opening polymerization (ROP) of $\varepsilon$-caprolactone using stannous octoate (Sn(Oct)$_2$) as the catalyst and 5-norbornene-2-ol as the initiator (Scheme 5.1(i)). The inclusion complexation of the BB with $\alpha$-CD results in the formation of BB-IC (Scheme 5.1(iv)). The linear polypseudorotaxane (MM-IC) (Scheme 5.1(iii)) was also prepared via the inclusion complexation of MM and $\alpha$-CD. The characterization
results for the MM-IC were compared against that of BB-IC to evaluate the effect of architecture on the properties of polypseudorotaxanes.

Scheme 5.1 Schematics for the synthesis of the linear polypseudorotaxane MM-IC and bottlebrush polypseudorotaxane BB-IC.

5.3.1 Synthesis of Norbornenyl PCL Macromonomers

The α-norbornenyl functionalized PCL MMs were prepared by the ROP of ε-CL in toluene at 110 °C using Sn(Oct)$_2$ as the catalyst and 5-norborne-2-ol as the initiator (Scheme 5.1(i)). PCL MMs with five different molecular weights (MW)s were prepared by varying the initial monomer to initiator (i.e., [M]$_0$/[I]$_0$) ratio (Table 5.1). The resultant MMs were characterized via GPC (solid traces: MM$_1$ to MM$_5$, Figure 5.1), $^1$H NMR spectroscopic analysis and MALDI-TOF MS, and the results are summarized in Table 5.1.
Table 5.1 Characterization of PCL MMs, PCL bottlebrush polymers, and linear and bottlebrush polypseudorotaxanes.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Monomer Conversion (%)</th>
<th>$M_{n,\text{theo}}$ (kDa)</th>
<th>$M_{n,\text{GPC}}$ (kDa)</th>
<th>$M_{n}/M_{n}$ (kDa)</th>
<th>$M_{n,NMR}$ (kDa)</th>
<th>$M_{n,MAL}$ (kDa)</th>
<th>$N_{\alpha-\text{CD}}/N_{\text{CL}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>MM₁</td>
<td>98</td>
<td>2.1</td>
<td>2.0</td>
<td>1.20</td>
<td>2.2</td>
<td>2.4</td>
<td>0.67</td>
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<tr>
<td>MM₂</td>
<td>97</td>
<td>4.0</td>
<td>3.9</td>
<td>1.17</td>
<td>3.9</td>
<td>4.0</td>
<td>0.53</td>
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<tr>
<td>MM₃</td>
<td>98</td>
<td>6.1</td>
<td>6.0</td>
<td>1.24</td>
<td>6.3</td>
<td>6.5</td>
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<tr>
<td>MM₄</td>
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<td>9.8</td>
<td>9.5</td>
<td>1.15</td>
<td>9.8</td>
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</tr>
<tr>
<td>MM₅</td>
<td>96</td>
<td>19.2</td>
<td>18.6</td>
<td>1.17</td>
<td>19.5</td>
<td>17.7</td>
<td>-</td>
</tr>
<tr>
<td>BB₁</td>
<td>99</td>
<td>420</td>
<td>418.7</td>
<td>1.24</td>
<td>-</td>
<td>-</td>
<td>0.26</td>
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<tr>
<td>BB₂</td>
<td>99</td>
<td>800</td>
<td>770.0</td>
<td>1.25</td>
<td>-</td>
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<td>1,346</td>
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<td>-</td>
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<td>BB₄</td>
<td>94</td>
<td>1,842</td>
<td>1,686</td>
<td>1.24</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>BB₅</td>
<td>78</td>
<td>2,995</td>
<td>2,554</td>
<td>1.34</td>
<td>-</td>
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<td>-</td>
</tr>
</tbody>
</table>

The CL monomer and PCL MM conversions were determined by GC-MS and GPC analysis, respectively.

$M_{n,\text{theo}} = \text{MW}_{\text{NB}} + \text{MW}_{\text{CL}} \times \text{Conv.} \times ([M_0]/[I_0])$, where $\text{MW}_{\text{NB}}$, $\text{MW}_{\text{CL}}$ and $\text{Conv.}$ are the MWs of 5-norbornen-2-ol, CL and CL monomer conversion, respectively. $[M_0]$ and $[I_0]$ are the initial concentration of monomer and the initiator 5-norbornene-2-ol. For BB, $M_{n,\text{theo}} = \text{MW}_{\text{MM}} \times ([\text{MM}_0]/[I_0])$, where $\text{MW}_{\text{MM}}$, $[\text{MM}_0]$ and $[I_0]$ are the $M_{n,NMR}$ of NB-PCL, the initial concentration of MM and the initial concentration of the catalyst 5.1, respectively.

Determined by GPC based on the assumption of 100% mass recovery of polymers.

$M_{n,NMR} = \text{MW}_{\text{NB}} + \text{MW}_{\text{CL}} \times \frac{I_j}{I_b + I_d}$ (Equation 5.1), where, $I_j$, $I_b$ and $I_d$ represent the integral values of peak ‘j’ (methylen protons on PCL repeating units), ‘b’ and ‘d’ (allylic protons of norbornenyl end group), respectively (Figure 5.2a).

Determined by MALDI-TOF MS.

$N_{\alpha-\text{CD}}/N_{\text{CL}} = N_1 / 3I_j$ (Equation 5.2), where $N_{\alpha-\text{CD}}/N_{\text{CL}}$ is the stoichiometric ratio of $\alpha$-CD to CL monomer unit in the resultant inclusion complexes, $I_1$ represents the integral values of peak ‘1’ (methine group protons of $\alpha$-CDs) (Figure 5.2b).
The GPC differential refractive index (DRI) chromatograms of the MM$_1$S all show monomodal peaks with narrow molecular weight distributions (MWD)$s$ $(M_n/M_w \leq 1.24)$. The series of characteristic resonances (‘a-f’) in the $^1$H NMR spectrum of the MM confirms the fidelity of the ROMP polymerizable norbornenyl chain end (Figure 5.2a). The $M_{n,NMR}$ of the PCL MM$_1$S was calculated via comparison of the integral of the resonance at 4.02-4.10 ppm (‘j’, methylene protons of PCL) with those at 2.82 and 3.13 ppm (‘b’ and ‘d’, allylic protons of the norbornenyl end-group) according to Equation 5.1 (Table 5.1). The $M_{n,NMR}$ of the MM$_1$S was compared with the $M_{n,GPC}$ and $M_{n,MAL}$, as well as the theoretical MW ($M_{n,th}$) (Table 5.1), which revealed that the number average MWs determined by the different methods are all in good agreement with slight differences within error of the measurements.
Figure 5.2 $^1$H NMR spectra of (a) PCL MM (MM$_1$) in CDCl$_3$, (b) linear polypseudorotaxane (MM$_1$-IC) in DMSO-$d_6$, (c) PCL brush polymer (BB$_1$) in CDCl$_3$ and (d) bottlebrush polypseudorotaxane (BB$_1$-IC) in DMSO-$d_6$. 

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5.3.2 Synthesis of PCL Bottlebrush Polymers

The high density BBs were prepared via ROMP of the corresponding MMs with different MWs. The reactions were terminated by the addition of ethyl vinyl ether\textsuperscript{15} to detach the Ru-based catalyst from the bottlebrush polymer end-group (Scheme 1(ii)). As a result of the robust and highly active nature of the catalyst 5.1 and the low critical MM concentration required in the ROMP system, high MM conversions (≥ 79\%) were achievable, even for high MW MMs.\textsuperscript{13b} For MMs with \(M_{n,GPC} \leq 6\) kDa, quantitative MM-to-BB conversions were obtained, as determined via GPC analysis (Figure 5.1). The GPC traces of the corresponding PCL bottlebrush polymers BB\textsubscript{1} to BB\textsubscript{3} reveal monomodal peaks with narrow MWDs (\(M_w/M_n \leq 1.27\)). In comparison, the GPC trace of BB\textsubscript{4} revealed a small peak at an elution time of \(ca. 26\) mins, which corresponds to unconverted MM\textsubscript{4}. The final conversion of MM\textsubscript{4} (\(M_{n,GPC} = 9.5\) kDa) was estimated to be 94\% via devolution of the GPC trace using Gaussian function. For the large MW MM, MM\textsubscript{5} (\(M_{n,GPC} = 18.6\) kDa), the GPC trace of the resultant bottlebrush polymer BB\textsubscript{5} has a relatively large peak at a retention time of \(ca. 24.5\) min, resulting from a considerable amount of unconverted MM\textsubscript{5}. The conversion of MM\textsubscript{5} plateaued at \(ca. 80\%\) (determined via GPC analysis) even after a prolonged reaction time of 24 h. The increase in the MW of the MM ultimately leads to a decrease in MM conversion, as well as the DP of the resultant bottlebrush polymer, as a result of steric hindrance. This is evident by the incomplete MM conversions in the ROMP of MM\textsubscript{4} and MM\textsubscript{5}. Nevertheless, as demonstrated by this series of polymerizations, ROMP is a potent synthetic method to prepare high MW bottlebrush polymers via the grafting-through approach.

The conversion of the PCL MMs was also monitored via \(^1\)H NMR spectroscopic analysis. For example, the \(^1\)H NMR spectrum of BB\textsubscript{1} shows the total disappearance of the norbornenyl resonances of the MM between 6.35 and 5.95 ppm (Figure 5.2a, resonance a), which confirms the quantitative consumption of MM\textsubscript{1} in agreement with the GPC result. In addition, the trans/cis alkene proton resonances of the PCL BB backbone were observed between 5.0 to 5.4 ppm (Figure 5.2c, resonance a’), confirming successful ROMP.
5.3.3 Preparation of Bottlebrush Polypseudorotaxanes

The bottlebrush polypseudorotaxanes (BB-ICs) were prepared via the inclusion complexation of the BB with α-CD (Scheme 5.1(iv)). Acetone solutions of the bottlebrush polymers were added dropwise to aqueous solutions of α-CD, resulting in immediate turbidity as a result of the precipitation of the bottlebrush polypseudorotaxane supramolecules. Following isolation, this was further verified via NMR spectroscopic analysis (vide infra). The acetone solution system is the optimal system we have found for the inclusion complexation of high molecular weight (MW) PCL with α-CD. It has been utilized by a number of research groups to prepare α-CD/PCL poly(pseudo)rotaxanes with high MW and complex macromolecular architectures, despite of that the final product precipitates out of the reaction solution. Precipitation of the α-CD/PCL poly(pseudo)rotaxane was in fact observed for all the previously reported synthetic systems using various solvents. This is the direct result of the poly(pseudo)rotaxane’s poor solubility in most organic solvents and water-organic solvent mixtures. The corresponding linear polypseudorotaxanes (MM-IC)s were also prepared from the MMs and α-CD following the same procedure (Scheme 5.1(iii)). The linear/bottlebrush polypseudorotaxanes were isolated by centrifugation, repeatedly washed with H₂O/acetone to remove the uncomplexed CDs, and then characterized via ¹H NMR spectroscopic analysis, TGA and DSC. The results obtained for the bottlebrush and linear polypseudorotaxanes were compared to determine what effect molecular architecture has on the physical and chemical properties of the polypseudorotaxanes.

The ¹H NMR spectra of the linear (MM₁-IC) and bottlebrush (BB₁-IC) polypseudorotaxane allowed the composition (i.e., α-CD : CL stoichiometric ratio) of the polypseudorotaxanes to be calculated from the integral ratio of resonances ‘1’ at 4.78 ppm (protons of methine group of CDs) to ‘j’ at 3.96-4.02 ppm (methylene protons of PCL MMs) (Figure 5.2b and d, respectively) according to Equation 5.2 (Table 5.1). Previously, it has been proposed that for linear polypseudorotaxanes constructed from telechelic PCL and α-CD, the theoretical stoichiometric ratio of the threaded α-CD to the CL monomer unit is 1 : 1. However, for the norbornenyl PCL MMs the α-CD to CL ratios were significantly lower, ranging from 0.29 to 0.67 depending on the MW of the linear PCL precursor (Table 5.1). This is a direct result of low dispersability of PCL MMs in the
aqueous reaction mixtures, which prevents them from diffusing effectively into α-CDs’ cavities reducing the amount of the threaded α-CD in the MM-ICs below the theoretical 1:1 stoichiometry of α-CD to CL. The low α-CD to CL stoichiometric ratio can also be attributed to the poor solubility of the partially-threaded polypseudorotaxane in the complexation solvent, which reduced the threading efficiency of α-CD. Besides, the bulky α-norbornenyl terminus of MM's has a molecular size of approx. 0.7 nm, which is larger than the internal diameter of α-CD (0.45 nm). Therefore, the threading of α-CD becomes less effective as it can only take place at the α-hydroxyl chain end of the MM's further lowering the α-CD to CL ratios. Evidently, α-CD : CL ratio was found to decrease with increasing MM chain length (Table 5.1). The higher threading efficiency for short chain MM's is attributed to steric effects 9b as well as the better dispersability of the short chain MM's in the reaction solution. This phenomenon is more pronounced in the reported poly(pseudo)rotaxane systems where threading of α-CD can only take place from a single polymer chain end.

The α-CD : CL ratios determined using 1H NMR spectroscopic analysis were found to be significantly lower for the BB-ICs compared to the corresponding MM-ICs. The α-CD : CL ratios ranged from 0.26 to 0.18 for the bottlebrush polypseudorotaxanes (BB1-IC to BB3-IC) depending on the MW of the PCL BB precursors (Table 5.1), in contrast to 0.67 to 0.29 for the corresponding linear polypseudorotaxanes (MM1-IC to MM3-IC). This suggests that the threading of α-CD may be affected by both the MW and architecture of the guest macromolecules. The BBs may possess lower dispersability in the complexation solution compared to the MM's as result of their high MWs, and the PCL side-chains of BBs are therefore expected to have much reduced α-CD threading efficiency. Additionally, the increasing steric congestion along the radial axis of the bottlebrush polymer towards the core prevents the threading of α-CD onto the CL units close to the backbone. 10 Thus, the α-CD : CL ratios for the BB-ICs are lower than those for the corresponding MM-ICs.

2D-ROESY NMR spectroscopic analysis was utilized to verify the formation of BB-ICs. The partial 2D-ROESY 1H NMR spectrum of BB1-IC clearly shows cross-peaks resulting from the non-bonding interaction through space between the methylene protons ‘h, i and g’ on the PCL side chains [C(=O)CH2CH2CH2CH2CH2O] and the protons ‘1-4, 7 and 8’ on the threaded α-CDs (Figure 5.3). These results confirm that the PCL side-chains of
BB₁ are included in the cavities of α-CDs through non-covalent interactions, and preclude the possibility of other types of physical association between the α-CD and the BB polymer.⁹d

**Figure 5.3** Partial 2D-ROESY ¹H NMR spectrum of the bottlebrush polypseudorotaxane BB₁-IC in DMSO-ｄ₆.

Solid-state ¹³C CP-MAS NMR spectroscopic analysis was employed to provide additional evidence for the bottlebrush polypseudorotaxane structure. It has been reported that uncomplexed α-CD adopts a less symmetrical conformation in its pure crystalline
form,\textsuperscript{9b} and therefore in its $^{13}$C CP-MAS NMR spectrum the carbon atoms ‘1’ and ‘4’ adjacent to the conformally strained 1,4-glucosidic linkage show additional resonances at 98.0 and 80.7 ppm, respectively (Figure 5.4a). However, in the spectrum of the bottlebrush polypseudorotaxane BB$_1$-IC, these resonances are completely absent and all carbon atoms on the α-CD show single resonances (Figure 5.4b). This result is consistent with the threaded α-CDs adopting a more symmetrical cyclic conformation as a consequence of the inclusion of the PCL side-chains.\textsuperscript{16}

![Figure 5.4 13C CP-MAS NMR spectra of (a) α-CD and (b) bottlebrush polypseudorotaxane BB$_1$-IC.](image)

The formation of the bottlebrush polypseudorotaxane supramolecular architecture was also verified by X-ray powder diffraction (XRD) (Figure 5.5). For the uncomplexed α-CD in the solid state, the XRD pattern is typical of α-CD crystallites, with multiple diffraction peaks resulting from their randomly-orientated cage-type structure (Figure
The XRD pattern of the PCL bottlebrush polymer revealed characteristic PCL crystallite peaks at $2\theta = 21.3$ and $23.6^\circ$ (Figure 5.5c).\(^{16}\) In comparison, the XRD pattern of the bottlebrush polypseudorotaxane has two distinct crystallite peaks at $2\theta = 19.8$ and $22.6^\circ$ (Figure 5.5a), which results from the $\alpha$-CDs stacking along the PCL side-chains to form ordered column or channel-type supramolecular structures. The crystallites formed from the close packing of such channel-type structures lead to this unique XRD pattern, which is substantially different from the XRD patterns of the uncomplexed $\alpha$-CD and PCL bottlebrush polymer.\(^{17}\)

Figure 5.5 X-ray diffraction patterns for (a) bottlebrush polypseudorotaxane $BB_1$-IC, (b) PCL bottlebrush polymer $BB_1$, and (c) $\alpha$-CD.

5.3.4 Thermal Properties of Bottlebrush Polypseudorotaxanes.

The differential scanning calorimetry (DSC) melting and cooling curves for the PCL MM $MM_1$, the corresponding linear polypseudorotaxane $MM_1$-IC, the PCL bottlebrush polymer $BB_1$ and the corresponding bottlebrush polypseudorotaxane $BB_1$-IC are shown in Figure 5.6a-d, respectively. The linear and bottlebrush polypseudorotaxanes
possess much smaller endothermic and exothermic peaks as compared with their PCL linear and bottlebrush polymer counterparts. For the polypseudorotaxanes, a large proportion of the CL repeat units are locked in the cavities of \( \alpha \)-CDs, and therefore the original melting and crystallization behaviour of the PCL polymer precursors is significantly suppressed.\(^{10}\) This reduced the melting and crystallization behaviour indirectly suggests the successful formations of the linear and bottlebrush polypseudorotaxanes.

Figure 5.6 The crystallization (top) and melting (bottom) DSC curves of (a) PCL macromonomer MM\(_1\), (b) linear polypseudorotaxane MM\(_1\)-IC, (c) PCL bottlebrush polymer BB\(_1\) and (d) bottlebrush polypseudorotaxane BB\(_1\)-IC.

The thermal decomposition profiles of the linear and bottlebrush polypseudorotaxanes and their corresponding PCL polymer precursors were characterized via thermogravimetric analysis (TGA) (Figure 5.7). It is found that the PCL bottlebrush polymer (Figure 5.7b) has a higher initial decomposition temperature than the PCL MMs (Figure 5.7a). The enhanced thermal stability of the bottlebrush polymers is attributed to the strong inter- and intramolecular association of the side chains through van der Waals interaction.\(^{9b}\) The TGA curves of linear polypseudorotaxane and bottlebrush
polypseudorotaxane (Figure 5.7c and d) present two-step thermal decomposition profiles, in which the first step weight loss is attributed to the decomposition of the α-CDs, and the second step results from the decomposition of the PCL.

![Thermogravimetric curves](image)

**Figure 5.7** Thermogravimetric curves for (a) linear PCL MM₁, (b) PCL brush polymer BB₁, (c) linear polypseudorotaxane MM₁-IC, and (d) bottlebrush polypseudorotaxane BB₁-IC.

Based upon the thermal decomposition profiles of the polypseudorotaxanes (Figure 5.7c and d), the α-CD content of the linear and bottlebrush polypseudorotaxanes was calculated. The linear polypseudorotaxane was found to have a higher α-CD content (86.2 % wt, α-CD : CL = 0.71) than that of bottlebrush polypseudorotaxane (69.9 % wt, α-CD : CL = 0.24), which is in good agreement with results obtained from ¹H NMR spectroscopic analysis (Table 5.1). The bottlebrush polypseudorotaxane displays a higher initial decomposition temperature than the linear polypseudorotaxane counterpart (Figure 5.7c and d, respectively), which is attributed to the strong intra- and intermolecular side-chain association of the bottlebrush polypseudorotaxane through van der Waals interactions as previously discussed.
5.3.5 Morphology of Bottlebrush Polypseudorotaxanes

The PCL bottlebrush polymers and their corresponding bottlebrush polypseudorotaxanes were characterized via DLS and their volume-average hydrodynamic diameters ($D_h$) were determined (Table 5.2). The PCL bottlebrush polymers (BB$_1$ to BB$_3$) have $D_h$ values ranging from 29.5 to 71.5 nm depending on the side-chain MW ($M_{n,GPC} = 2 – 6$ kDa, Table 5.1). The $D_h$ values of the bottlebrush polypseudorotaxanes (BB$_1$-IC to BB$_3$-IC) ranged from 223.9 to 347.9 nm, which are approximately 4 to 6 times larger than that of their corresponding PCL bottlebrush precursors. Upon inclusion complexation, the side-chains of the bottlebrush polymers experience a significant size/volume increase as a result of the threading of $\alpha$-CD, which creates strong steric repulsion between adjacent polypseudorotaxane side-chains. The direct consequence of this side-chain repulsion is that the side-chains and backbone of the bottlebrush polypseudorotaxane stretch and assume an extended conformation to minimize steric energy, causing a substantial increase in $D_h$.

<table>
<thead>
<tr>
<th>Sample</th>
<th>$D_h^a$ (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BB$_1$</td>
<td>29.5</td>
</tr>
<tr>
<td>BB$_2$</td>
<td>40.4</td>
</tr>
<tr>
<td>BB$_3$</td>
<td>71.5</td>
</tr>
<tr>
<td>BB$_1$-IC</td>
<td>223.9</td>
</tr>
<tr>
<td>BB$_2$-IC</td>
<td>268.7</td>
</tr>
<tr>
<td>BB$_3$-IC</td>
<td>347.9</td>
</tr>
</tbody>
</table>

$^a$ Determined by DLS, sample concentration = 0.2 mg mL$^{-1}$ (DMSO at 25 ± 0.1 °C).

TEM provided clear evidence for the inclusion complexation-induced conformational change of the bottlebrush polymers. The TEM image of the PCL bottlebrush polymer MM$_1$ revealed globular morphologies with an average diameter of approx. 27.5 nm (Figure 5.8c), which correlates well with the $D_h$ obtained from the DLS analysis ($D_h = 29.5$ nm, Figure 5.8a). In comparison, the bottlebrush polypseudorotaxane
possess a cylindrical conformation with dimensions of 400 nm in length and 60 nm in width (Figure 5.8d). Upon inclusion complexation, the increased steric repulsion between the adjacent polypseudorotaxane side-chains causes a conformational transition of the bottlebrush polymer from a soft sphere to a stiff cylinder.\(^{18}\) It is noteworthy that the length of the bottlebrush polypseudorotaxane BB\(_1\)-IC (L = 400 nm) observed from TEM is twice of its average hydrodynamic diameter (\(D_h = 223.9 \text{ nm, Table 5.2}\)). In the DLS measurement, the \(D_h\) was determined based upon the assumption that the bottlebrush polypseudorotaxane adopts a spherical conformation according to the Stokes-Einstein equation; however, if a rod-like structure was considered, a larger \(D_h\) value would have been expected.\(^{19}\)

![Figure 5.8](image)

**Figure 5.8** Volume-average hydrodynamic diameter distribution curves of (a) the PCL bottlebrush polymer BB\(_1\) and (b) the bottlebrush polypseudorotaxane BB\(_1\)-IC, and TEM images of (c) BB\(_1\) and (d) the bottlebrush polypseudorotaxane BB\(_1\)-IC.
5.4 Conclusion

High density PCL bottlebrush polymers with DP of approx. 200 were synthesized via ROMP initiated by the pyridine modified 2\textsuperscript{nd} Generation Grubbs’ catalyst and the grafting-through approach. The GPC and \textsuperscript{1}H NMR spectroscopic analysis results confirmed that well-defined PCL bottlebrush polymers with narrow MWDs were obtained in high yields of 78 – 99% (MM-to-brush conversion) using various norbornenyl PCL MMs with MW ranging 2.0 to 18.6 kDa. The MM-to-brush conversion was dependent upon the MW of the PCL MM and limited by the degree of steric repulsion between the propagating brush polymer and the MM during ROMP.

The resultant PCL bottlebrush polymers served as macromolecular scaffolds to construct novel bottlebrush polypseudorotaxanes through inclusion complexation with \(\alpha\)-CD. The formation of the bottlebrush polypseudorotaxanes were confirmed via various characterization techniques including \textsuperscript{1}H NMR, 2D-ROSEY NMR and \textsuperscript{13}C CP-MAS NMR spectroscopic analysis, and XRD. The stoichiometric ratios of \(\alpha\)-CD to CL in the bottlebrush polypseudorotaxanes were determined via \textsuperscript{1}H NMR spectroscopic analysis and were found to range from 0.18 to 0.26, which is lower than the theoretical stoichiometry of 1:1. This results from the molecular architecture as well as high MW of the PCL bottlebrush polymer precursors. Interestingly, the \(\alpha\)-CD to CL ratios for the bottlebrush polypseudorotaxanes were much lower than that of the CCS polypseudorotaxane (\(\alpha\)-CD to CL = 0.72, Chapter 4), and this implies that the bottlebrush polymers possesses much higher branch densities than the CCS polymer counterpart. The thermal properties of the polypseudorotaxane were analyzed via DSC and TGA, which revealed enhanced thermal stability and reduced melting and crystallization behaviour compared to the PCL bottlebrush precursor. TEM revealed the bottlebrush polypseudorotaxanes possess a rigid cylindrical conformation upon the inclusion complexation in contrast to a collapsed globular conformation of the PCL bottlebrush precursors.

The simple procedure reported herein, which combines the highly efficient synthetic methodologies of ROP and ROMP with inclusion complexation chemistry, provides a versatile approach towards supramolecular polymers with high MW, controlled dimensions and well-defined architectures. It is envisioned that the bottlebrush polypseudorotaxane
constructed from biocompatible and biodegradable PCL and α-CD could potentially have a wide scope of applications in gene delivery, polymer therapeutics and tissue engineering.
5.5 Experimental Section

5.5.1 Materials

\(\varepsilon\)-Caprolactone (\(\varepsilon\)-CL, >99%), stannous 2-ethylhexanoate (Sn(Oct)\(_2\)), 5-norbornene-2-ol (99.5%), dithranol (>90%, HPLC) and \(\alpha\)-cyclodextrin (\(\alpha\)-CD, 98%) were purchased from Sigma-Aldrich and used as received. Deuterated dimethyl sulfoxide (DMSO-\(d_6\), 99.8 %) and deuterated chloroform (CDCl\(_3\), 99.9 %) were purchased from Cambridge Isotope Laboratories, Inc. Dichloromethane (DCM) and toluene were distilled from calcium hydride under argon. Tetrahydrofuran (THF) was distilled from benzophenone and sodium metal under argon. AR grade acetone, methanol and hexane were purchased from Chem-Supply Pty. Ltd. and used as received. The pyridine modified 2\(^{nd}\) generation Grubbs’ catalyst 5.1 was synthesized according to the literature procedure used as freshly prepared.\(^{13b}\)

5.5.2 Instrumentation

Gel permeation chromatography (GPC) (THF as eluent) was performed on a Shimadzu liquid chromatography system fitted with a Wyatt DAWN EOS multi-angle laser light scattering (MALLS) detector (690 nm, 30 mW) and a Wyatt OPTILAB DSP interferometric refractometer (690 nm), using three Phenomenex Phenogel columns (500, 10\(^4\) and 10\(^6\) \(\text{Å}\) porosity; 5 \(\mu\)m bead size) operated at 1 mL/min with column temperature set at 30 \(^\circ\)C. Astra software (Wyatt Technology Corp.) was used to process the data to determine the MWs either using known \(dn/dc\) values or based on the assumption of 100% mass recovery of the polymer where the \(dn/dc\) value was unknown. Gas chromatography was performed on a Shimadzu GC 17-A gas chromatograph equipped with an Agilent J+W DB-5 capillary column (30 m, 5% phenyl siloxane) and coupled to a GCMS-QP50000 mass spectrometer (injector temperature = 250 \(^\circ\)C; initial column initial temperature = 40 \(^\circ\)C; heat ramp = 10 \(^\circ\)C /min; final column temperature = 320 \(^\circ\)C). \(^{1}H\) NMR and 2D ROSEY NMR spectroscopic analysis was performed on a Varian Unity (400 MHz) spectrometer using the deuterated solvent as reference. Dynamic light scattering (DLS) measurements were performed using a Malvern high performance particle sizer (HPPS) with a 3.0 mW He-Ne laser operated at 633 nm. Analysis was performed at an angle of 173\(^{o}\) and a constant temperature of 25 ± 0.1 \(^\circ\)C. Thermogravimetric analysis (TGA) was performed on a
PerkinElmer Pyris-1 Thermogravimetric analyzer, and the samples were heated from 70 to 700 °C at a rate of 10 °C·min⁻¹ under a nitrogen flow (20 mL·min⁻¹). X-ray diffraction (XRD) patterns of the samples were recorded on a Bruker D8 Advance instrument with Cu Kα radiation (40 kV, 40 mA) and a nickel filter, and the samples were exposed at a scanning rate of 20 = 0.020 °·s⁻¹ in the range of 3-50 °. Transmission electron microscopy (TEM) images were taken using a Tecnai TF30 transmission electron microscope (FEI Co., Eindhoven, The Netherlands) operated at 200 kV. Images were acquired digitally with a Gatan US1000 2k × 2k CCD Camera (Pleasanton, CA). The TEM samples were prepared by dissolving at a concentration of 0.5 mg mL⁻¹ and then spin-coating the sample solution on TEM copper grid (strong carbon film, 300 mesh). UV-vis spectrophotometry was performed on a Shimadzu UV-1800 spectrometer using quartz cuvettes with a 1 cm path length. MALDI-TOF MS was performed on a Bruker Autoflex III Mass Spectrometer operating in positive reflex mode. The analyte, matrix (dithranol) and caternisation agent (sodium iodide) were dissolved in THF at concentration of 10 mg mL⁻¹, 10 mg mL⁻¹ and 1 mg mL⁻¹, respectively, and then mixed in a ratio of 10:1:1. 0.3 μL of this solution was then spotted onto a ground steel target plate and the solvent was allowed to evaporate prior to analysis. FlexAnalysis (Bruker) was used to analyse the acquired data.

**Synthesis of PCL macromonomers (MM) via ROP.** A typical procedure to synthesize the PCL MMs was as follows: 5-Norbornen-2-ol (0.644 g, 5.85 mmol, 1 equiv.) and CL (11.4 g, 100 mmol, 17.1 equiv.) were dissolved in toluene (20 mL) in a dried 50 mL Schlenk tube. Stannous 2-ethylhexanoate in toluene (3 mL, 0.97 M, 0.5 equiv.) was added under argon via syringe and the reaction was stirred at 110 °C for 24 h ([M]₀/[I]₀ = 17.1; monomer conversion = 98 % via GCMS, $M_n$tho = 2.1 kDa). After cooling to room temperature, the solution was diluted with THF (10 mL) and precipitated into cold methanol (400 mL). The precipitate was isolated by filtration and dried in vacuo at 40 °C for 24 h to give MM₁, 9.8 g (83 %); GPC (THF): $M_n$ = 2.0 kDa, $M_w/M_n$ = 1.20; MALDI-ToF: $M_n$ = 2.5 kDa, $M_w/M_n$ = 1.07; $^1$H NMR (400 MHz, CDCl₃): δ$_H$ 6.33, 6.22 and 5.94 (m, 2H, norbornenyl alkenyl protons), 5.27 (m, 1H, -CHOC(=O)-), 4.12-4.02 (m, 2H, -CH₂O-, protons of the fifth methylene group of PCL), 3.70-3.62 (t, $J$ = 6.4 Hz, 2H, -CH₂OH, protons of PCL), 3.12 (s, 1H, allylic proton of norbornenyl group), 2.83 (s, 1H, allylic
proton of norbornenyl group), 2.35-2.24 (m, 2H, -C(=O)CH₂-protons of the first methylene group of PCL), 2.12 (m, 1H, -CH₂-norbornenyl methylene proton), 1.72-1.56 (m, 4H, -CH₂CH₂CH₂-, protons of the second and fourth methylene groups of PCL) and (1H, -CH₂-norbornenyl methylene proton), 1.42-1.33 (m, 2H, -CH₂CH₂CH₂-, protons of the third methylene group PCL) and (1H, -CH₂-norbornenyl methylene proton), 0.87-0.94 (m, 1H, -CH₂- norbornenyl methylene proton) ppm.

**Preparation of linear polypseudorotaxane (MM-IC).** A typical synthetic procedure to prepare the linear polypseudorotaxane from a PCL MM and α-CD is described as follows: MM₁ (Mₙ,GPC = 2.0 kDa, 0.105 g, 0.05 mmol) and α-CD (1.0 g, 1.03 mmol) were dissolved in acetone (2 mL) at 50 °C and distilled water (5 mL) at 60 °C, respectively. The MM₁ solution was added dropwise to the aqueous solution of α-CD at 60 °C for 6 h with stirring. The mixture was then cooled to room temperature and stirred for a further 42 h. The precipitate was isolated by centrifugation, washed with water (10 mL × 3) and acetone (10 mL × 3), and dried in vacuo at 40 °C for 24 h to afford MM₁-IC, 0.45 g (67 %); ¹H NMR (400 MHz, DMSO-d₆): δH 1.25-1.28 (m, 2H, -CH₂CH₂CH₂- of PCL), 1.45-1.52 (m, 4H, -CH₂CH₂CH₂- of PCL), 2.20-2.26 (m, 2H, -C(=O)CH₂- of PCL), 3.20-3.40 (m, 12H, -CHOH and -CH- of α-CD), 3.52-3.68 (m, 18H, -CH₂OH and -CHCHOH of α-CD), 3.72-3.78 (m, 6H, -CHOH of α-CD), 3.94-3.98 (m, 2H, -CH₂O- of PCL), 4.45 (m, 6H, -CH₂OH of α-CD), 4.78 (d, 6H, -OCH(CH)O- of α-CD), 5.40-5.52 (m, 12H, -CHOH of α-CD) ppm.

**Synthesis of high density PCL bottlebrush polymers (BB) via ROMP.** The general procedure for ROMP was as follows: to a THF solution of the catalyst 5.1 (4.88 × 10⁻³ M, 0.5 mL, 1 equiv.) under argon in a scintillation vial capped with septum was added the MM₁ (Mₙ = 2.0 kDa, 0.976 g, 0.488 mmol, 200 equiv.) in THF (4.0 mL) via syringe. The reaction was allowed to stir at room temperature for 1 h, and then quenched by addition of ethyl vinyl ether (a few drops). The crude reaction was precipitated in methanol (50 mL × 2) and the precipitates were isolated by filtration and dried in vacuo at 40 °C for 24 h to give BB₁ as a white powder, 0.8 g (82 %); GPC (THF): Mₙ = 418.7 kDa, Mₘ/Mₙ = 1.20; ¹H NMR (400 MHz, CDCl₃): δH 1.33-1.42 (m, 2H, -CH₂CH₂CH₂- of PCL), 1.56-1.72 (m, 4H, -
CH$_2$CH$_2$CH$_2$- of PCL), 2.24-2.35 (m, 2H, -C(O)CH$_2$- of PCL), 3.62-3.70 (t, 2H, -CH$_2$OH of PCL), 4.02-4.12 (m, 2H, -CH$_2$O- of PCL) ppm.

**Synthesis of bottlebrush polypseudorotaxane (BB-IC).** The general procedure to prepare the BB-IC is as follows: the PCL bottlebrush polymer BB$_1$ ($M_{n\text{GPC}} = 418.7$ kDa, 0.100 g, $2.4 \times 10^{-4}$ mmol) and α-CD (1.0 g, 1.03 mmol) were first dissolved acetone (2.5 mL) at 50 °C and distilled water (5 mL) at 60 °C, respectively. The BB$_1$ solution was added dropwise into the aqueous solution of α-CD at 60 °C for 6 h with vigorous stirring. The turbid mixture was then cooled to room temperature and stirred for further 48 h. The precipitate in the reaction mixture was isolated by centrifugation, washed with water (10 mL × 3) and acetone (10 mL × 3), and then dried in vacuo at 40 °C for 24 h to give BB$_1$-IC as a white powder, 0.24 g (78%); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$H 1.25-1.28 (m, 2H, -CH$_2$CH$_2$CH$_2$- of PCL), 1.45-1.52 (m, 4H, -CH$_2$CH$_2$CH$_2$- of PCL), 2.20-2.26 (m, 2H, -C(O)CH$_2$- of PCL), 3.20-3.40 (m, 12H, -CHOH and -CH- of α-CD), 3.52-3.68 (m, 18H, -CH$_2$OH and -CHOH of α-CD), 3.72-3.78 (m, 6H, -CHOH of α-CD), 3.94-3.98 (m, 2H, -CH$_2$O- of PCL), 4.45 (m, 6H, -CH$_2$OH of α-CD), 4.78 (d, 6H, -OCH(CH)O- of α-CD), 5.40-5.52 (m, 12H, -CHOH of α-CD) ppm.
5.6 References


Part 3.

Synthesis and Characterization of Novel Stereospecific Cyclic Polymers and Their Supramolecular Assembly through Stereocomplexation
Chapter 6

Stereospecific Cyclic Poly(methyl methacrylate) (PMMA) and Its Topology-guided Hierarchically-controlled Supramolecular Assemblies

6.1 Chapter Perspective

In Parts 1 and 2 of this thesis, novel macro(supra)molecular architectures based on CCS and bottlebrush structures have been successfully prepared and characterized. In Part 3 (Chapter 6), cyclic polymer – one of the most intriguing and synthetically challenging macromolecular structures was explored. In Chapter 6, a synthetic route towards a novel stereospecific cyclic vinyl polymer i.e., cyclic syndiotactic (st-)PMMA is described. The stereocomplex helix formations between cyclic st-PMMA s with various MWs and the complementary linear isotactic it-PMMA s were investigated. Surprising new insights into the effects of topology (i.e., end-groups), size and tacticity of assembling components on the helix stereocomplex formation were obtained. Characterization results revealed that the self-assembly of cyclic st-PMMA s with appropriate ring sizes and linear it-PMMA s resulted in the formation of an unprecedented ‘polypseudorotaxane-type’ supramolecular assembly through stereocomplexation. Such a stereocomplex exhibits remarkably different physical properties as compared to the conventional triple-helix PMMA stereocomplex as a result of the cyclic topology of the st-PMMA assembling component.
6.2 Introduction

Naturally-occurring macromolecules possess a precisely-regulated molecular weight (MW), composition, monomer sequence, and stereochemistry (i.e., tacticity). The meticulous structural controls grant them unique structure, distinct properties and the ability to form intricate and exquisite supramolecular assemblies (e.g., DNA\textsuperscript{1} and proteins\textsuperscript{2}), which regulate important bioprocesses within living organisms. The ultimate goal in polymer chemistry is to match and emulate nature by synthesizing macromolecules with precisely controlled primary structure, which may serve as basic building blocks to assemble advanced nanostructured functional materials with novel properties and functions.\textsuperscript{3} So far, limited success has been achieved towards this end, and the synthesis of polymers with highly-controlled primary structure still remains challenging.

Cyclic polymers present in both natural\textsuperscript{4} and synthetic forms\textsuperscript{5} are one of the most fascinating classes of macromolecules. They possess simple molecular structures but exhibit intriguing chemical and physical properties\textsuperscript{6} as a consequence of the topology control imposed by the tethering of chain ends. Recently, remarkable progress in the development of synthetic techniques offering efficient routes to well-defined cyclic polymers with high purity has been reported.\textsuperscript{7} Cyclic polymers with well-defined MWs and compositions (i.e., homopolymer, copolymers, and gradient polymers) have been extensively investigated.\textsuperscript{8} However, with the exception of cyclic poly(oligo)peptides,\textsuperscript{9} cyclic polymers that consist of monomeric units with controlled stereochemical arrangement have been less explored.\textsuperscript{10} In this chapter, the synthesis of a novel cyclic syndiotactic poly(methyl methacrylate) (\textit{c-st}-PMMA) with simultaneous controls over MW, tacticity and topology through polymerization of the vinyl monomer methyl methacrylate (MMA) is presented. The synthesis of well-defined stereospecific cyclic polymers constructed from ‘non-optically active’ building blocks has not been previously demonstrated. Furthermore, the controlled tacticity endows the cyclic \textit{st}-PMMA with the ability to stereocomplex with complementary linear isotactic (\textit{ii}-) PMMA, resulting in an unprecedented ‘polypeseudorotaxane-type\textsuperscript{11} supramolecular assembly with controlled crystallization mode dictated by the topology of the \textit{st}-PMMA component.
6.3 Results and Discussion

The fabrication of the novel cyclic  

st-PMMA was achieved using a combination of stereospecific living radical polymerization (SLRP)$^{12}$ and ‘click’ end-to-end cyclization.$^{7a}$ The cyclic  
st-PMMAs were obtained in high purity (cyclic purity $> 93\%$) through cyclization of the heterotelechelic  
st-PMMA precursors containing alkyne and azide end-groups (Scheme 6.1).

![Scheme 6.1 Schematic illustration for the preparation of cyclic syndiotactic poly(methyl methacrylate) (c-st-PMMA) via (i) stereospecific living radical polymerization (SLRP), (ii) azidation, and (iii) ‘click’ cyclization.](image)

In this study, a copper-catalyzed (Cu-)SLRP was devised (Figure 6.1) and exploited for the preparation of heterotelechelic polymer precursors. The implemented Cu-SLRP system provided living  
st-PMMAs with triad syndiotacticy ($rr$) values of up to 72\%. Although living anionic polymerization$^{13}$ is able to provide  
st-PMMAs with higher levels of syndiotacticy ($rr$ up to 96\%) compared to the Cu-SLRP, the asymmetric functional groups at the polymer chain-ends could be introduced conveniently in the Cu-SLRP, via the use of a functional initiator and end-group substitution (Scheme 6.1).$^{14}$
Figure 6.1 Polymerization of MMA at 0 °C in 1,1,1,3,3,3-hexafluoro-2-phenyl-2-propanol (PhC(CF$_3$)$_2$OH); [MMA]/[PgBr]/[CuBr]/[Cu$_2$Br]/[Bpy] (mM) = 2000/20/20/2/40. Based on these conditions, the synthesis of α-alkyne, ω-bromine heterotelechelic syndiotactic PMMA (l-st-PMMA-Br) was performed on large scales and isolated at low MMA conversions to ensure high ω-end-group fidelity.

For the Cu-SLRP, the bulky cumyl fluoroalcohol (PhC(CF$_3$)$_2$OH) was used as the solvent, which coordinates to the carbonyl groups of MMA and the growing polymer side-chain to generate a syndiospecific environment for living polymerization to proceed (Scheme 6.2). The dual control of MW and tacticity is therefore simultaneously achieved. The cyclization of heterotelechelic st-PMMA was performed after quantitatively transforming the ‘living’ ω-bromine chain-end into an azide through azidation (see Appendix 6, Figure A6.1).
Scheme 6.2 Schematic model for solvent-mediated syndiospecific radical polymerization of methyl methacrylate (MMA).

The ring-closure of the ‘clickable’ heterotelechelic st-PMMA was verified by gel permeation chromatography (GPC), matrix-assisted laser desorption ionization time-of-flight (MALDI ToF) mass spectrometry, $^1$H NMR spectroscopy (Figure 6.2), differential scanning calorimetry (DSC) and FT-IR spectroscopy (Figure 6.3). Using the c-st-PMMA st-C$_{2k}$ ($M_n = 1.9$ kDa, $M_w/M_n = 1.28$, $mmlmr/rr$ 2:26:72, cyclic purity = 96 %) as example, the GPC differential refractive index (DRI) chromatogram of st-C$_{2k}$ (peak retention time ($t_p$) = 20.5 min) after cyclization shifted to a high retention time region compared to that of the linear precursor st-L$_{2k}$ ($t_p$ = 19.8 min) (Figure 6.2a). This result reveals that st-C$_{2k}$ possesses a smaller hydrodynamic volume than st-L$_{2k}$, as intramolecular cyclization leads polymers into a more compact conformation. The MALDI-ToF mass spectra of st-C$_{2k}$ and st-L$_{2k}$ (Figure 6.2b) demonstrate that the MW and molecular weight distribution (MWD) of the st-PMMA did not vary after the cyclization. Higher MW impurities such as macrocyclic dimers, catenanes, and longer chain linear impurities resulting from oligomerization, were totally absent in the spectrum of st-C$_{2k}$. These results suggest that the end-to-end coupling of the st-L$_{2k}$ proceeded intramolecularly to afford st-C$_{2k}$ in high purity, and the same conclusion was drawn based upon the GPC results (Figure 6.2a).
Figure 6.2 (a) GPC differential refractive index (DRI) response and molecular weight distribution, respectively, (b) MALDI-ToF mass spectra, and (c) $^1$H NMR spectra of cyclic syndiotactic poly(methyl methacrylate) ($st$-$C_{2k}$) and its linear polymer precursor ($st$-$L_{2k}$).
Moreover, the $^1$H NMR spectra (Figure 6.2c) indicate the quantitative conversion of the terminal alkyne (characteristic resonance ‘a’ and ‘b’ at 2.4 and 4.6 ppm, respectively) and azide chain ends of $st$-$L_{2k}$ into the triazole ring (characteristic resonance at ‘a’ and ‘b’ at 7.8 and 5.2 ppm, respectively) in $st$-$C_{2k}$. Further evidence for the quantitative trizole ring formation was obtained from the FT-IR spectroscopic analysis (Figure 6.3b), as the total disappearance of the azide peak (at 2160 cm$^{-1}$) was seen in the spectrum of $st$-$C_{2k}$ after the cyclization. Since MALDI-ToF and GPC results have already ruled out the possible formation of high MW side-reaction products, the quantitative yield of the triazole rings indicate the successful transformation of the linear precursor $st$-$L_{2k}$ into the corresponding cyclic product $st$-$C_{2k}$. It has been previously demonstrated that intramolecular cyclization (i.e., topological constraint) imparts changes in the bulk properties of polymers, for instance, the glass transition temperature ($T_g$). The DSC traces clearly show $st$-$C_{2k}$ possesses a higher $T_g$ than $st$-$L_{2k}$ due to a reduction in configurational entropy upon cyclization (Figure 6.3a), and this result provides additional evidence for the successful ‘click’ ring-closure.

**Figure 6.3** (a) DSC profiles and (b) FT-IR spectra of cyclic syndiotactic poly(methyl methacrylate) ($st$-$C_{2k}$) and its linear polymer precursor ($st$-$L_{2k}$). Cyclization conditions: [l-$st$-PMMA-$N_3$]/[CuBr]/[PMDETA] (mM) = 0.1/2.0/2.0 at 90 °C in DMF.

It is well-known that linear PMMAs are able to form a triple-stranded helical supramolecule consisting of an inter-twined double-stranded helix of $it$-PMMAs wrapped by a single strand of $st$-PMMA in an $it$-$st$- 1:2 stoichiometry. In the present study, we
initially anticipated that the c-st-PMMA would not be able to form a conventional stereocomplex$^{18}$ with the complementary linear it-PMMA since the absence of chain-ends on the c-st-PMMA component would hinder molecular wrapping. To test this hypothesis, two linear (l-)it-PMMAs (it-L$^{10k}$: $M_n = 10.3$ kDa, $M_w/M_n = 1.12$, mm/l/rr 93:3:4, and it-L$^{44k}$: $M_n = 44.3$ kDa, $M_w/M_n = 1.30$, mm/l/rr 97:2:1) (see Appendix 6, Figure A6.2 and Table A6.1) were synthesized via living anionic polymerization to stereocomplex with the c-st-PMMAs.

Previously, it has been demonstrated that st-PMMAs with low syndiotacticity (rr < 80 %) are capable of forming stereocomplexes, whilst the complementary it-PMMAs with high degrees of isotacticity are essential for stereocomplex formation to occur.$^{18a,18c}$ The l-it-PMMAs were prepared by anionic rather than living radical polymerization as a synthetic route to highly isotactic (mm > 90 %) polymers through the latter method has not been established. The PMMA stereocomplexes were prepared by the simple mixing of the separately dissolved it- and st-PMMA components in an it-st- 1:2 stoichiometry, using acetonitrile/water 9:1 as the complexation solvent.$^{17c,19}$ Unexpectedly, the DSC and X-ray diffraction (XRD) profiles (Figure 6.4a) of the stereocomplex sample prepared from c-st-PMMA (st-C$^{4k}$: $M_n = 3.2$ kDa, $M_w/M_n = 1.32$, mm/l/rr 2:26:72, cyclic purity = 93 % via $^1$H NMR spectroscopic analysis) and l-it-PMMA (it-L$^{10k}$) revealed a crystalline structure that is essentially different from the individual PMMA precursors (Figure 6.4c and d).
Figure 6.4 DSC thermo diagram and X-ray powder diffraction (XRD) patterns of (a) \(\text{st-C}_4/\text{it-L}_{10k}\) stereocomplex, (b) linear \(\text{st-L}_{4k}/\text{it-L}_{10k}\) stereocomplex, (c) linear \(\text{it-PMMA \it-L}_{10k}\), (d) cyclic \(\text{st-PMMA \it-C}_4\), and (e) linear \(\text{st-PMMA \it-L}_{4k}\).

Furthermore, large nanoscale objects (100 × 100 nm\(^2\)) were observed in the 1:2 stoichiometric mixture of \(\text{it-L}_{10k}\) and \(\text{st-C}_4\) via atomic force microscopy (AFM), as a direct result of the aggregation of complexed supramolecules through strong Van der Waals interaction.\(^{18a, 18c}\) Such phenomena were entirely absent in the samples of individual stereoregular PMMAs (Figure 6.5). This set of important results indicates that the \(c\)-\(\text{st-PMMA}\) is able to stereocomplex with complementary \(l\)-\(\text{it-PMMA}\) in spite of its cyclic topology.
Figure 6.5 Atomic force microscope (AFM) height images of (a) linear \textit{it}-PMMA (\textit{it}-L_{10k}), (b) cyclic \textit{st}-PMMA (\textit{st}-C_{4k}), and (c) \textit{st}-C_{4k}/\textit{it}-L_{10k} stereocomplex (a mixture of \textit{it}-L_{10k} and \textit{st}-C_{4k} in \textit{it-}/\textit{st-} 1:2 stoichiometry).

More interestingly, the \textit{st}-C_{4k}/\textit{it}-L_{10k} stereocomplex and the \textit{st}-L_{4k}/\textit{it}-L_{10k} (i.e., the stereocomplex that is constructed from \textit{it}-L_{10k} and \textit{st}-L_{4k} ($M_n = 4.0$ kDa, $M_w/M_n = 1.32$, \textit{mml/mr/rr} 2:26:72) - the corresponding linear polymer precursor of \textit{st}-C_{4k}) - share similar XRD profiles (Figure 6.4a and b) with a characteristic PMMA stereocomplex \textit{d}-spacing value at 2.08 nm. The \textit{d}-spacing value correlates well with the chain-chain lateral spacing ($2.4 \pm 0.1$ nm) of the linear PMMA triple-helix stereocomplexes observed by AFM.\textsuperscript{16} Furthermore, the unit quantity of complexed sequence formed in the \textit{st}-C_{4k}/\textit{it}-L_{10k} stereocomplex is less than in the \textit{st}-L_{4k}/\textit{it}-L_{10k} stereocomplex, as supported by the DSC thermograms (the total endothermic heat released ($\Delta H_{tot}$) from melting of the stereocomplex upon heating) (see Appendix 6, Table A6.2, Entry 1 and 5, respectively).\textsuperscript{20}
Based upon these results, we hypothesized that the $c$-st-$l$-it-PMMA stereocomplex possesses a distinct ‘polypseudorotaxane-type’ or ‘molecular necklace’ structure that is comprised of a double-stranded helix of $it$-PMMAs,\textsuperscript{21} onto which discrete $st$-PMMA rings are threaded (Figure 6.6a, (i)).

**Figure 6.6** (a) Schematic illustration of two possible stereocomplexes prepared from $l$-it-PMMA and $c$-st-PMMA with (i) ‘polypseudorotaxane-type’, and (ii) ‘double wrapping’ arrangement, respectively, and (b) XRD profiles of (i) $st$-$C_{2k}$/$it$-$L_{10k}$ stereocomplex, the simulated $c$-st-$l$-it-PMMA stereocomplexes with (ii) ‘polypseudorotaxane-type’ and (iii) ‘double wrapping’ arrangement ($c$-st-PMMA with degree of polymerization = 18).

Further evidence for the proposed ‘polypseudorotaxane-type’ stereocomplex structure was attained after carefully examining the effect of $c$-st-PMMA ring size on stereocomplex formation. In the conventional linear PMMA triple-helix stereocomplex, each helical turn of the wrapping $st$-PMMA consists of ca. 18 MMA repeat units (MW: 1.8 kDa).\textsuperscript{16} Hence, it was expected that as the MW of $c$-st-PMMA approaches this limiting value, reduced complex formation would arise from ineffective threading of the $c$-st-PMMA as a result of steric restrictions. In fact, a decrease in MW below the limiting value may result in no
stereocomplex formation since the threading of c-st-PMMA is impossible (see Appendix 6, Scheme A6.1a).

To verify this prediction, c-st-PMMAs st-C\textsubscript{2k} ($M_n = 1.9$ kDa, $M_w/M_n = 1.28$, \textit{mm/mr/rr} 2:26:72, cyclic purity = 96 %) and st-C\textsubscript{1k} ($M_n = 1.0$ kDa, $M_w/M_n = 1.36$, \textit{mm/mr/rr} 2:27:71, cyclic purity = 97 %) were synthesized and stereocomplexed with \textit{it-L}\textsubscript{10k}. The DSC and XRD results of the resulting stereocomplexes match our prediction rather well. The \textit{st-C\textsubscript{2k}/it-L\textsubscript{10k}} stereocomplex has a lower $\Delta H_{\text{tot}}$ value than the \textit{st-C\textsubscript{4k}/it-L\textsubscript{10k}}, which is indicative of a lower degree of (crystalline) complex formation (Figure 6.7b and a, respectively, also see Appendix 6, Table A6.2). This is also confirmed by the observation that the XRD profile of \textit{st-C\textsubscript{2k}/it-L\textsubscript{10k}} shows weakened peak intensity compared to that of \textit{st-C\textsubscript{4k}/it-L\textsubscript{10k}} (Figure 6.7b and a, respectively). No stereocomplex was formed using \textit{st-C\textsubscript{1k}} and \textit{it-L\textsubscript{10k}} as precursors, as supported by both the DSC and XRD profiles (Figure 6.7d).

In contrast, the variation in chain length of \textit{l-st-PMMA} has negligible impact on the amount of stereocomplexes formed with the same \textit{it-PMMA} (Figure 6.7e and f). However, the only exception is where the average chain length of the \textit{l-st-PMMA} component is shorter than 18 MMA units, in which case only the partially-stabilized PMMA stereocomplex can be prepared (see Appendix 6, Scheme A6.1b). One typical example of the partially stabilized stereocomplex is \textit{st-L\textsubscript{1k}/it-L\textsubscript{10k}}, which has lower thermal stability and crystallinity compared with the other PMMA stereocomplexes, as indicated by its DSC and XRD profiles (Figure 6.7h). Although these results cannot rule out the possibility that $c$-$st$-PMMA forms a partially-stabilized stereocomplex with the \textit{l-it-PMMA} (i.e., the ‘double wrapping’ stereocomplex; Figure 6.6a, (ii)), they suggest the stereocomplexation of $c$-$st$-PMMA and \textit{l-it-PMMA} predominantly affords the ‘polypseudorotaxane-type’ complex in support of the proposed model.
Figure 6.7 DSC and X-ray powder diffraction profiles of the e-st/-it-PMMA stereocomplexes (a) \( st\-C_{4k}/it\-L_{10k} \), (b) \( st\-C_{2k}/it\-L_{10k} \), (c) \( st\-C_{2k}/it\-L_{44k} \), and (d) \( st\-C_{1k}/it\-L_{10k} \), and the l-st/-it-PMMA stereocomplex counterparts (e) \( st\-L_{4k}/it\-L_{10k} \), (f) \( st\-L_{2k}/it\-L_{10k} \), (g) \( st\-L_{2k}/it\-L_{44k} \), and (h) \( st\-L_{1k}/it\-L_{10k} \).
Additionally, the degree of complexation of \( c-st/l-l-it \)-PMMA stereocomplex varies with the chain length of \( l-it \)-PMMA (Figure 6.7b and c), whereas that in the linear stereocomplex remains almost constant (Figure 6.7f and g). The increased chain length of the molecular axle would lead to a reduced number of threaded cyclic components due to steric effects.\(^2\) These results provide additional evidence that \( c-st/l-l-it \)-PMMA stereocomplexes adopt the proposed ‘polypseudorotaxane-type’ supramolecular structure. The present system elucidates one possible formation mechanism for the conventional PMMA triple-helix stereocomplex, in which a double-stranded helix of \( it \)-PMMAs is included in a preformed single-stranded helix of \( st \)-PMMA, and the termini of the \( st \)-PMMA are not essential in facilitating stereocomplexation.

Previous studies have demonstrated that the conventional linear stereocomplex can also be prepared by solvent-free thermal annealing at reaction temperatures above the glass transition temperatures (\( \Delta T_g \)) of the PMMA components.\(^{20b}\) In this study, the amount of stereocomplexes formed via thermal annealing, determined by means of DSC (\( \Delta H_m \)), is less than prepared in solvent (see Appendix 6, Figure A6.3 and Table A6.2) as a direct consequence of reduced system mobility, which is in good agreement with literature.\(^{[20]}\) Notably, no \( c-st/l-l-it \)-PMMA stereocomplex can be obtained by thermal annealing under the same conditions. We propose two possible explanations for this observation. Firstly, the stereocomplexation system involving cyclic polymer has a higher system immobility compared to the linear counterpart, which originates from the imposed topology constraint. Secondly, in the absence of solvent media, the \( c-st \)-PMMA component is not able to form the ‘opened ring’ (solvated) structure, hence they cannot thread the complementary \( it \)-PMMAs to afford the ‘polypseudorotaxane-type’ stereocomplex.

Two-dimensional rotating frame nuclear Overhauser effect spectroscopy (2D ROESY) – a common characterization technique for inclusion complexes\(^{23} \) – was utilized to characterize the resultant \( c-st/l-l-it \)-PMMA stereocomplexes. However, no cross-peak interactions were detected between nuclei on the complementary \( st \)- and \( it \)-PMMA components due to their low mobility and solubility upon stereocomplexation.

A subtle difference between the DSC profiles of the \( c-st/l-l-it \)-PMMA stereocomplex and that of the linear stereocomplex is noteworthy. Except for \( st-L_{1k}/it-L_{10k} \), all of the linear stereocomplexes have two melting temperatures (\( T_m^1 \) and \( T_m^3 \)) – one extra high temperature
melting point \( T_m^3 \) than the corresponding \( c-st/l-it \)-PMMA stereocomplexes \( T_m^1 \) only) (Figure 6.7). This is ascribed to the different crystallization modes of the two stereocomplexation systems. Schomaker and Challa have investigated the origin of the multiple endothermic peaks of the PMMA stereocomplex in detail and proposed that \( T_m^1 \) and \( T_m^3 \) could be assigned to the formation of fringed-micellar structures (clusters of stereocomplexes) and lamellar crystallites, respectively (Figure 6.8).\(^{20, 24}\) In the linear system, the \( st \)-PMMA component has free chain-ends that might bridge\(^{25}\) between adjacent stereocomplexes aiding the formation of lamellar superstructures (see Appendix 6, Scheme A6.2). In contrast, the bridging is suppressed by the cyclic topology of \( c-st \)-PMMA in the \( c-st/l-it \)-PMMA stereocomplexes, so its crystallization mechanism follows the fringed-micellar growth only. This difference accounts for the observation that the linear stereocomplexation solution became turbid immediately after mixing of the two complementary PMMA components, whilst that of \( c-st/l-it \)-PMMA stereocomplex remained clear even after prolonged reaction times (170 h), which is attributed to the suppressed inter-complex interactions (see Appendix 6, Figure A6.4 and A6.5). The average hydrodynamic radius \( (R_h) \) of dispersed particles in the diluted \( st-L_{4k}/it-L_{10k} \) stereocomplex solution is significantly (approx. 15 times) larger than that in the diluted \( st-C_{4k}/it-L_{10k} \) stereocomplex solution (Figure 6.8).
Figure 6.8 Sample solutions (acetonitrile/water 9:1 at a concentration of 2 mg/ml) of (a) st-L_{4k}/it-L_{10k} stereocomplex (inset: illustration of suspending particles resulting from lamellar crystallization mode), and (b) st-C_{4k}/it-L_{10k} stereocomplex (inset: illustration of suspending particles resulting from micellar crystallization mode), and dynamic light scattering (percentage intensity) distributions of (c) st-L_{4k}/it-L_{10k}, and (d) st-C_{4k}/it-L_{10k} stereocomplex (acetonitrile/water 9:1 at a concentration of 0.1 mg/ml).

The difference in crystallization mode is also reflected in the XRD profiles of the c-st-ll-it-PMMA stereocomplexes (Figure 6.7). Their XRD profiles showed relative weak intensity of the diffraction peaks with \( d \) spacing values at 2.08 and 0.57 nm suggesting low ordering perpendicular to the helix axis in the absence of lamellar crystallite growth, which is in agreement with the DSC analysis.\[^{20a}\]

It is difficult to design experiments to observe the exact structure of the c-st-ll-it-PMMA stereocomplex. Therefore, we constructed molecular models of the two proposed structures of the c-st-ll-it-PMMA stereocomplex (Figure 6.6a, (i) and (ii), also see Figure 6.9 and 6.10).
**Figure 6.9** Molecular model of the ‘polypseudorotaxane-type’ PMMA stereocomplex. The *it*-PMMA fibers are colored in orange and red and the cyclic *st*-PMMA are colored in dark blue. Dashed lines indicate the dimensions of the unit cell (x = 3.98 nm, y = 2.36 nm, and z = 1.81 nm). The light blue lines represent spacing in the xy plane (left) and the pitch spacing of the *st*-PMMA rings (right).

**Figure 6.10** Molecular model of the ‘double wrapping’ PMMA stereocomplex. The *it*-PMMA fibers are colored in orange and red and the cyclic *st*-PMMA are colored in dark blue. Dashed lines indicate the dimensions of the unit cell (x = 3.62 nm, y = 2.71 nm, and z = 1.78 nm).
The XRD profiles (Figure 6.6b) of the corresponding crystal structures of those proposed stereocomplexes were simulated and compared with the experimental result. The simulations demonstrated that the ‘polypseudorotaxane-type’ arrangement reproduces the experimental XRD pattern of the st-C\textsubscript{2k}/it-L\textsubscript{10k} stereocomplex. Such configuration produces three diffraction peaks with \(d\)-spacing values at 2.08, 0.79 and 0.57 nm (Figure 6.6b, (ii)), in good agreement with the experimental \(d\)-spacing values at 2.08, 0.78 and 0.60 nm (Figure 6.6b, (i)), respectively. The peak at 2.08 nm was assigned to the spacing between \textit{it}-PMMA double helices in the x and xy planes. The peaks at 0.79 nm and 0.57 nm arise from multiple contributions, including the pitch spacing of \textit{st}-C\textsubscript{2k} rings and the distance between individual \textit{it}- and \textit{st}-PMMA fibers in the xy plane, respectively (Figure 6.9). The ‘double wrapping’ model failed to reproduce experimental \(d\)-spacings, particularly the peak at 2.08 nm (Figure 6.6b, (iii)). The ‘double wrapping’ model has a unique diffraction peak at 1.29 nm, which is associated with the spacing of the \textit{st}-C\textsubscript{2k} rings in the xy plane (Figure 6.10). Additionally, the ‘double wrapping’ configuration has a lower calculated density (1.20 g cm\(^{-3}\)) and solubility parameter (19.1 J\(^{1/2}\)cm\(^{3/2}\)) than the ‘polypseudorotaxane-type’ configuration (1.22 g cm\(^{-3}\) and 20.7 J\(^{1/2}\)cm\(^{3/2}\), respectively) (see Appendix 6, Table A6.3). Through an examination of both structural and thermodynamic characteristics, the simulation results indicate that the ‘polypseudorotaxane-type’ configuration is the most plausible way the stereocomplex of the \textit{c-st}-PMMA and the complementary \textit{it}-PMMA double helix could be arranged and support the experimental evidence.

Finally, it is anticipated that the stereocomplexation between the \textit{l-it}-PMMA and \textit{c-st}-PMMA with a significantly high degree of polymerization (DP) (e.g., DP > 200) may afford the ‘cross-linked’ triple-stranded and/or the quadruple-stranded\textsuperscript{[16]} helix stereocomplex (see Appendix 6, Scheme A6.3), as a direct effect of the diminished rigidity of \textit{c-st}-PMMA with large ring size. The resultant \textit{c-st-l-it}-PMMA stereocomplexes are expected to crystallize in both the fringed-micellar and lamellar modes similar to the corresponding linear stereocomplex counterparts, since the suppression of inter-complex cross-linking by topological constraint of the \textit{c-st}-PMMA will be compensated by its chain length and mobility.
6.4 Conclusion

In summary, we have described a synthetic route for the preparation of a syndiospecific cyclic vinyl polymer (upto 40 repeat units). The highly regulated microstructure enables the cyclic polymer to form an unprecedented supramolecular assembly with linear isospecific counterparts through stereocomplexation. It is proposed that the resulting stereocomplex has a ‘polypseudorotaxane-type’ structure. The presented self-assembly system demonstrates a hierarchical control over the microstructure of the polymers, their supramolecular assembly as well as the morphology of the resulting crystalline structure. The hierarchical control imposed by topological restriction of the macromolecular building blocks is anticipated to provide new directions of research in supramolecular chemistry. Practically, it is emphasized that the reported synthetic strategy may pave the way for the development of a novel class of cyclic inclusion materials for molecular separation, catalytic, and electronic and optoelectronic applications. Further investigations, including the AFM imaging of the present individual stereocomplex are currently underway.
6.5 Experimental Section

6.5.1 Materials

The initiator, propan-2-yne 2-bromo-2-methylpropanoate (PgBr) was prepared using a previously published synthetic method.\textsuperscript{26} Copper(I) bromide (CuBr, 99.999 %), copper(II) bromide (Cu\textsubscript{2}Br, 99.999 %), magnesium turnings (> 99.5 %), anhydrous dimethyl sulfoxide (DMSO, > 99.9 %), \(t\)-butylbromide (> 99 %) and 2,2′-bipyridine (bpy, ≥ 99 %) were purchased from Aldrich and used as received. All solid compounds were handled in a glovebox (VAC Nexus) under a moisture- and oxygen-free argon atmosphere (\(H_2O < 0.1\ ppm\) and \(O_2 < 0.1\ ppm\)). Methyl methacrylate (MMA, TCI, > 99.8 %), 1,1,1,3,3,3-hexafluoro-2-phenylpropan-2-ol (PhC(CF\textsubscript{3})\textsubscript{2}OH, Wako, > 99 %) and \(N,N,N',N''\)-pentamethyldiethylenetriamine (PMDETA, Aldrich, 99 %) were distilled from calcium hydride under reduced pressure before use. Toluene (Kishida, > 99 %) was distilled from sodium benzophenone ketyl and bubbled with dry nitrogen for 15 min just before use. Acetonitrile (MeCN, Shameleon Reagent, > 99.5 %), diethyl ether (DEE, ChemSupply, 98 %), ethyl acetate (EtOAc, ChemSupply, AR), \(n\)-hexane (TCI, > 99 %), and anhydrous methanol (ChemSupply, > 99 %) were used as received.

6.5.2 Instrumentation

\(^1\)H and \(^{13}\)C NMR spectroscopy measurements were conducted in CDCl\textsubscript{3} at 25 °C or 55 °C (polymer analysis) on a JEOL ECS-400 spectrometer operating at 400 and 100 MHz for \(^1\)H and \(^{13}\)C, respectively. The triad tacticity of PMMAs was determined by the integration of area under the C=O carbon resonance at 175-180 ppm in the \(^{13}\)C NMR spectrum. IR spectra were recorded with a JASCO Fourier Transform IR-620 spectrophotometer. The X-ray measurements were performed on a Rigaku R-AXIS IV detector system equipped with a Rigaku FR-E rotating-anode generator and confocal mirror monochromated CuK radiation (0.15418 nm) focused through a 0.5 mm pinhole collimator, which was supplied at 45 kV voltage and 45 mA current, equipped with a flat imaging plate having a specimen-to-plate distance of 200.0 mm. The dried powders were placed in a borosilicate glass capillary tube, and their X-ray diffractograms were taken at ambient temperatures (20 – 25 °C) from the edge-view position. The number-average molecular weight (\(M_n\)) and weight-average molecular weight (\(M_w\)) of the product polymers were
determined by GPC in THF at 40 °C using two polystyrene gel columns [Shodex KF-805L (pore size: 20–1000 Å; 8.0 mm i.d. × 30 cm) × 2; flow rate 1.0 mL/min] connected to Jasco PU-980 precision pump and a Jasco RI-2031 detector. The columns were calibrated against 10 standard PMMA samples (Agilent Technologies; \( M_p = 875–1677000 \) Da; \( M_w/M_n = 1.02–1.09 \)). Differential scanning calorimetry (DSC) was performed on a TA Instruments model 2920 modulated DSC under nitrogen flow. DSC calibration was performed using certified indium and sapphire. For determination of glass transition temperatures (\( T_g \)) of PMMA, samples were first heated to 200 °C at 5 °C/min, equilibrated at this temperature for 5 min, and cooled to -50 °C at 5 °C/min. After being held at -50 °C for 5 min, the sample was then reheated to 200 °C at 5 °C/min. For determination of melting temperatures (\( T_m \)) and heat of melting (\( \Delta H_m \)) of PMMA stereocomplexes, samples were heated to 200 °C at 10 °C/min, and cooled down to 40 °C at 10 °C/min before the next measurement. PMMA stereocomplex samples were dried under vacuum (0.05 mmHg) for 12 h prior to DSC analysis.

**Synthesis of \( \alpha \)-alkyne, \( \omega \)-bromine heterotelechelic syndiotactic PMMA (\( l-st \)-PMMA-Br).** The procedure for synthesis of \( l-st \)-PMMA-Br was adopted from previously published literature with modifications.\(^{27}\) CuBr (30.0 mg, 0.21 mmol) and CuBr\(_2\) (4.7 mg, 0.021 mmol) were added to a dry round-bottom flask equipped with a 3-way stopcock in a glovebox, followed by the addition (under dry \( N_2 \)) of PhC(CF\(_3\))\(_2\)OH (7.0 mL), MMA (2.25 mL, 21 mmol), bpy (495 mM in toluene, 0.85 mL) and PgBr (503 mM in toluene, 0.42 mL) and 1 mL aliquots of the reaction mixture were extracted and flame-sealed in glass ampoules under an \( N_2 \) atmosphere. The ampoules were then immersed in a thermostatic methanol bath at 0 °C. At predetermined intervals the reaction ampoules were removed from the bath and terminated by cooling the reaction to -78 °C. A sample was extracted for \(^1\)H NMR spectroscopic analysis and the remaining polymeric product was diluted with toluene (to approximately 10 mL) and mixed with an absorbent (Kyowaad-2000G-7 (Mg\(_{0.7}\)Al\(_{0.3}\)O\(_{1.15}\)); Kyowa Chemical). The absorbent was filtered off and the filtrate was washed with 1 M HCl (10 mL × 3) and water (10 mL × 3). The organic phase was evaporated to dryness to give the product polymer (68 %); (example: \( st \)-PMMA isolated at
Large-scale synthesis of α-alkyne, ω-bromine heterotelechelic syndiotactic PMMA (l-st-PMMA-Br). CuBr (36.0 mg, 0.25 mmol) and CuBr$_2$ (5.6 mg, 0.025 mmol) were added to a dry round-bottom flask equipped with a 3-way stopcock in a glovebox, followed by addition (under dry N$_2$) of PhC(CF$_3$)$_2$OH (8.4 mL), MMA (2.7 mL, 25.2 mmol), bpy (495 mM in toluene, 1.0 mL) and PgBr (503 mM in toluene, 0.50 mL). The reaction was conducted at 0 °C with samples taken periodically under N$_2$. The polymerization was terminated after 11 h by cooling the reaction to -78 °C. A sample was extracted for $^1$H NMR spectroscopic analysis, and the remaining product was diluted with EtOAc (200 mL), washed with 1 M HCl (100 mL × 2), then distilled water (150 mL × 2). The extracted product was collected, concentrated and then precipitated in hexane, followed by drying in vacuo to afford the l-st-PMMA-Br (st-L$_{2k}$-Br) as a white solid, 0.28 g (85.1 %); $^1$H NMR: MMA conversion = 10 % (theoretical $M_n$ = 1.2 kDa); GPC: $M_n = 2.25$ kDa, $M_w/M_n = 1.25$; $^{13}$C NMR: mm/mr/rr (%) = 2/26/72.

Synthesis of α-alkyne, ω-azide heterotelechelic syndiotactic PMMA (l-st-PMMA-N$_3$). The general procedure employed for the preparation of l-st-PMMA-N$_3$ was as follows.$^{7h}$ A dry round-bottom flask equipped with a 3-way stopcock was charged with α-alkyne, ω-bromine heterotelechelic syndiotactic PMMA (0.28 g, 0.12 mmol) and NaN$_3$ (0.25 g, 3.8 mmol). The reaction vessel was evacuated and back filled with N$_2$. Anhydrous DMSO (5.3 mL) was then added and the reaction mixture was allowed to stir at 40 °C for 24 h. The product mixture was precipitated into distilled H$_2$O (100 mL), and extracted with EtOAc (50 mL × 2). The organic extracts were combined and dried over MgSO$_4$ for 2 h. The solution was then filtered and concentrated under reduced vacuum to afford the product l-st-PMMA-N$_3$ (st-L$_{2k}$) as a white powder, 255 mg (91 %); $^1$H NMR: bromine end-group conversion = 99 %$^+$; GPC: $M_n = 2.4$ kDa, $M_w/M_n = 1.29$. The $^1$H NMR spectrum and GPC chromatogram for st-L$_{2k}$ are provided in Figure A6.1 (Appendix 6). The FT-IR spectrum is provided in Figure 6.3.
Synthesis of cyclic syndiotactic PMMA (c-st-PMMA). The general procedure employed for the synthesis of c-st-PMMA was as follows: l-st-PMMA (st-L2k) (GPC: $M_n = 2.4$ kDa, $M_w/M_n = 1.29$, 100 mg, 0.042 mmol) and DMF (409 mL) were added to a dry 1000 mL round-bottom flask, and the polymer solution was degassed by bubbling $N_2$ for 1 hr. CuBr/PMDETA (1:1) catalyst solution (100 mM in degassed DMF, 9.9 mL) was then added, and the reaction mixture was stirred at 90 °C for 48 h. The mixture was concentrated in vacuo to ca. 2 mL in volume, diluted with EtOAc (200 mL) and washed with 1 M HCl (200 mL × 2) and distilled H$_2$O (200 mL × 2). The organic phase was dried (MgSO$_4$), filtered and concentrated in vacuo to afford c-st-PMMA (st-C2k) as a white powder, 63 mg (63 %); $^1$H NMR: $M_n = 2.57$ kDa, cyclic purity = 96 %; GPC: $M_n = 1.97$ kDa, $M_w/M_n = 1.28$. The GPC DRI chromatogram, $^1$H NMR spectrum and MALDI-ToF mass spectrum for st-C2k are provided in Figure 6.2. The DSC and FT-IR spectra are provided in Figure 6.3.

Synthesis of linear isotactic PMMA (l-it-PMMA). l-it-PMMA was synthesized by anionic polymerization according to previously published procedures. The Grignard reagent, t-C$_4$H$_9$MgBr, was prepared as follows: anhydrous DEE (28 mL) and t-butylbromide (14 g, 0.10 mol) were added consecutively into a dry addition funnel under N$_2$. Separately, Mg turnings (3.72 g, 0.15 mol) were added to a dry round bottom flask under N$_2$ via a funnel with a flushing adapter, followed by the addition of anhydrous DEE (60 mL). The t-butylbromide solution was then added slowly at 25 °C over 1 h. The solution was stirred for a further hour and then left to stand for 12 hours. The Grignard reagent ([t-C$_4$H$_9$MgBr]$_{eff}$ = 286 mM determined via polymerization) was stored in a dry round-bottom flask equipped with a 3-way stopcock under Ar atmosphere at 0 °C before use.

The general procedure employed for the synthesis of l-it-PMMA was as follows: The initiator solution (0.39 mL) was added to anhydrous toluene (5.4 mL) in a Schlenk tube at -78 °C under Ar. MMA was then added slowly (1.2 mL in 5 min) causing the mixture to turn orange. The polymerization solution was kept at -78 °C for 126 h, and then anhydrous methanol (1 mL) was added to the Schlenk flask to quench the reaction. The reaction solution was diluted with toluene (20 mL), washed with 1 M HCl (20 mL × 3) and distilled
water (20 mL × 3), dried (MgSO₄), filtered and precipitated into hexane to afford l-it-PMMA (it-L₁₀k) as a white powder, 0.95 g (85 %); GPC: $M_n = 10.3$ kDa, $M_w/M_n = 1.12$; $^1$H NMR: $mm/mr/rr$ (%) = 93/3/4. Polymerization data and NMR spectra are provided in Figure A6.2 (Appendix 6).

**Synthesis of PMMA stereocomplexes in dilute solution.** The general procedure employed for the synthesis of PMMA stereocomplexes was as follows:¹⁹ the corresponding st-PMMA (10 mg) and it-PMMA (10 mg) precursors were separately dissolved in MeCN:H₂O (9:1) at concentrations of 2 mg/mL and combined to an it:st molar ratio of 1:2. The solutions were left to stand at room temperature for 24 h. After removing the solvent in vacuo, the stereocomplexes were dried under reduced vacuum (0.05 mmHg) for 24 h before DSC and XRD analysis.

**Preparation of PMMA stereocomplexes via thermal annealing.**²⁰ᵃ The fully decomplexed DSC samples of the PMMA stereocomplexes (checked via a second DSC scan) prepared in solution was first re-homogenized at 220 °C for 5 mins and then annealed at 95 °C in an oven for 24 h. The annealed sample was then characterized via DSC analysis. The same experiment and characterization was also repeated with annealing at 120 °C. DSC thermograms are provided in Figure A6.3 (Appendix 6).

**Modelling of cyclic syndiotactic PMMA/linear isotactic PMMA stereocomplex.**

**Initial Model Construction.** Double-stranded helices of 9/1 it-PMMA (9 monomer units per turn, helical pitch of 1.84 nm) were constructed based on the bond lengths, bond angles and internal rotation angles reported in the previous published literatures.¹⁶ᵃ,²¹ᵃ The fiber axes of the chains were oriented in the z direction and to eliminate the terminal melting propensity of finite polymeric chains, each it-PMMA fragment was connected to its periodic image in the z direction, mimicking an infinite PMMA crystal. Multiple models of cyclic st-PMMA (DP = 18 units) complexed with linear it-PMMA double helices based on two possible packing motifs were constructed. The first arrangement has the it-PMMA double-helix threaded into discrete cyclic st-PMMAs (i.e., ‘polypseudorotaxane-type’
arrangement) (Figure 6.9), while the second arrangement has the it-PMMA double-helix wrapped with the cyclic st-PMMAs (i.e., ‘double wrapping’ arrangement) (see Figure 6.10).

**Computational Method.** Simulations were carried out using the LAMMPS\textsuperscript{29} software distributed by Sandia National Laboratories. Analysis was performed using the Materials Studio 6.1\textsuperscript{30} software from Accelrys Inc. The potential energy was calculated using the PCFF force field\textsuperscript{31} with the missing parameter for the C-O-C-C dihedral taken from the CFF91 force field.\textsuperscript{32} These potentials have been shown to reproduce structural and thermodynamic properties of condensed phase polymeric systems well.\textsuperscript{33} Short-range non-bonded interactions were calculated using the atom-based summation method, with a cut-off radius of 15.5 Å. A long-range tail correction was applied for van der Waals interactions larger than the cut-off radius. The PPPM (particle-particle-particle-mesh) method\textsuperscript{34} was applied for long-range coulomb interactions.

For the initial stereocomplex models, the geometry optimization (energy minimization) of atomic positions and unit cell dimensions were performed using the Polak-Ribiere version of the conjugate gradient algorithm.\textsuperscript{35} Following energy minimization, molecular dynamics (MD) simulations in the NPT ensemble (constant number of particles, pressure and temperature) were undertaken for a total of 12 ns with the temperature and pressure maintained at 298 K and 1 atm respectively using the Nose-Hoover thermostat and barostat.\textsuperscript{36} A time step of 1 fs was implemented, with atomic coordinates and thermodynamic quantities recorded every 10,000 steps. The models were considered equilibrated when the energy and density attained a steady value (standard deviation within 1%), which occurred within the first few nanoseconds. Equilibrated models were then energy minimized again with a convergence criteria of 0.001 kcal/mol/Å. The optimized structures were then utilized for analysis of density and solubility parameters, as well as the calculation of x-ray diffraction spectra. The simulation result summary is provided in Table A6.3 (Appendix 6).
6.6 Reference and Notes


(17) For the first report on the PMMA stereocomplex see: Fox, T. G.; Garrett, B. S.; Goode, W. E.; Gratch, S.; Kincaid, J. F.; Spell, A.; Stroupe, J. D., J. Am. Chem. Soc. 1958, 80, 1768; the crystal structure was initially proposed to be nonhelical see: Liquori, A. M.; Anzuino, G.; Coiro, V. M.; D’Alagni, M.; De Santis, P.; Savino, M., Nature 1965, 206, 358; later, a double-stranded helix was proposed see: Schomaker, E.; Challa, G., Macromolecules 1989, 22, 3337; a recent AFM study showed that the PMMA stereocomplex is most likely a triple- or quadruple-stranded helix.16


Chapter 7

Conclusion and Future Work

7.1 Conclusion

The properties and functions of polymeric materials are dictated by their composition as well as structural configurations. Construction of macromolecules with unprecedented architectures has become an ongoing research theme in polymer science towards the discovery of (nano)materials with novel functions, properties and applications. Recent advances in polymer chemistry have offered practical and efficient synthetic methods to prepare and assemble simple polymeric building blocks into sophisticated molecular architectures with controllable sizes, compositions and functional group placements. Utilizing a judicious combination of modern synthetic techniques including controlled/living polymerization, click chemistry and/or supramolecular interactions, an array of novel macro(supra)molecular architectures has been constructed via a ‘bottom-up’ approach in this research work. Valuable understandings on the molecular-level behavior of the resultant macro(supra)molecules in crystal and solution states, upon chemical modification and physical stimuli were obtained. With well-defined composition and hierarchical arrangement of assembled components and functionalities, these macro(supra)molecules exhibit remarkable characteristics and properties, which may be suitable for a diverse spectrum of applications in materials science and nanotechnology.

A facile and efficient approach that provides access to a diverse range of highly corona-functionalized CCS polymers was devised in Chapter 2. In this approach, a polyester-based CCS polymer with high coronal alkyne functionality was exploited as a scaffold to create a library of highly corona-functionalized star macromolecular architectures. This was achieved by grafting the CCS scaffolds with various azido functional compounds. These functional star macromolecular architectures include fluorescent, saccharide and amphiphilic polyester-based CCS polymers. Factors affecting the grafting efficiency (i.e., click efficiency) of azido compounds onto the CCS scaffolds were identified, which include the molecular size and structure of the azido compounds,
their compatibility with the CCS scaffold and other synergistic driving forces, such as the potential formation of inclusion complexes. As a result, a valuable molecular model for the high density functionalization of complex 3-D nanostructures was established.

In Chapter 3, the near-quantitative synthesis of polyester-based CCS polymer was demonstrated through methanesulfonic acid-mediated ROP. Novel polyester-based CCS polymers with a high number of benzyl or alkyne end-group functionalities ranging from 8 to 21 units were prepared using either a two-pot, or a one-pot two-step strategy in high yields (90 - 96%) at ambient temperatures. The mild reaction temperatures, fast reaction rates and low extent of transesterification in this polymerization system, which collectively minimize inter- and intramolecular transesterification side-reactions during the CCS syntheses, are responsible for the near-quantitative yields. Although significantly suppressed, transesterification reactions are still responsible for the formation of a small quantity of low MW linear and cyclic impurities in the product polymers. However, compared to other high-yielding CCS polymer synthesis systems, the new system involves no toxic metal catalysts or additives, operates at ambient temperature, and requires less stringent and demanding reaction conditions. Hence, it represents an attractive alternative synthetic route towards novel functional CCS macromolecular architectures.

In Chapter 4, functionalization of CCS polymers through supramolecular chemistry was demonstrated through the development of a novel method to prepare CCS-based polyrotaxanes via inclusion complexation and click chemistry. The self-assembly of a PCL-based CCS polymer and α-CDs through inclusion complexation gave rise to the formation of a novel star-shaped supramolecule with radiating polyrotaxane arms. Using a similar approach, unprecedented bottlebrush supramolecular polymers with α-CD/PCL polypseudorotaxane side-chains were prepared (Chapter 5). The molecular architecture (star vs. bottlebrush), branch (side-chains for bottlebrush and ‘arm’ for CCS) length and density of the PCL macromolecular precursors were found to affect the threading efficiency of α-CD, as determined by calculation of the inclusion ratio (i.e., α-CD : CL stoichiometric ratio) in the resulting poly(pseudo)rotaxane supramolecular structures. It was found that the α-CD inclusion complexation not only modifies the chemical and physical properties of the guest macromolecules, but also causes them to undergo significant volume expansion and conformational transitions.
In Chapter 6, another type of non-covalent complexation was investigated to complement the CD inclusion complexation studies. These studies involved the synthesis of a novel cyclic st-PMMA via SLRP and click ring-closure. Stereocomplex formation between st-PMMAs with various ring sizes and the complementary linear it-PMMAs were investigated. With an appropriate ring size, cyclic st-PMMA appears to self-assemble with linear it-PMMA into an unprecedented ‘polypseudorotaxane-type’ supramolecular structure through stereocomplexation, which is substantially different from the conventional triple-helix stereocomplex prepared from linear st-/it-PMMAs. In this study, it was determined that the topology (cyclic versus linear) of the st-PMMA component does not affect its ability to form stereocomplexes, and therefore the end-groups of st-PMMA do not play an essential role in facilitating the stereocomplexation. Rather, the topology of the st-PMMA component dictates the microstructure as well as the physical characteristics and properties of the resulting supramolecular assemblies, which include crystallization mechanisms, crystal structures and melting behaviour.

7.2 Future work

The research presented in this thesis represent a series of fundamental studies on the synthesis and characterization of polymers with novel macro(supra)molecular architectures. However, the ultimate goal of these fundamental studies is to develop novel materials suitable for various practical applications. The following section outlines some future directions of the presented research, which are considered of great importance and will potentially lead to the development of valuable advanced functional nanomaterials.

7.2.1 Degradable and Biocompatible End-functional Core Cross-linked Star (CCS) Polymers

As highlighted in Chapter 1 of this thesis, CCS polymers are potential candidates for in vivo drug delivery systems. Towards this goal a synthetic strategy was devised for the near-quantitative synthesis of well-defined degradable polyester-based CCS polymers via the organic-catalyst mediated ROP (Chapter 3). CCS polymers with hydrophilic shell and degradable hydrophobic core domains can be fabricated by the reported strategy using a
bis-cyclic ester (e.g., BOD) and biocompatible water-soluble heterotelechelic polymers (e.g., PEG) as the cross-linker and macroinitiator, respectively (Scheme 7.1).

Scheme 7.1 Amphiphilic end-functional CCS polymers for targeted drug delivery.

The resulting CCS polymer represents a highly attractive drug delivery device, with the core acting as a site for the encapsulation of therapeutic agents through hydrophobic interactions and the hydrophilic shell providing solubility in physiological environments (e.g., the blood stream). The major advantages of the proposed delivery device include: i) their facile and high-yielding synthesis without the need for toxic metal catalysts, ii) potential biocompatibility and degradability, which may be utilized to control the drug release kinetics and facilitate the post-delivery body clearance, and iii) targeting moieties can be easily installed through reaction with the end-group functionalities (introduced by the functional chain end of macroinitiator) of the star to realize site-specific delivery.

7.2.2 Amphiphilic Core Cross-linked Star (CCS) Polyrotaxane ‘Sliding-ring’ Hydrogels

CD-based poly(pseudo)rotaxanes are important building blocks for the construction of ‘sliding-ring’ (SR) hydrogels with application as tissue engineering scaffolds, scratch resistant materials, and as artificial skin and vessels. Amphiphilic CCS supramolecular polymers with a polyester core domain and polyrotaxane radiating arms (e.g., α-CD/PEG or α-CD/PCL inclusion complex) may be designed and incorporated into SR hydrogels to improve their mechanical as well as their functional properties (Scheme 7.2). The benefits of this approach are three-fold. As previously discussed (Section 7.2.1), the hydrophobic
polyester core domains may serve as drug loading sites where hydrophobic guests may be loaded prior to the formation of cross-linked networks. Depending on the pH of the physiological environment, the degradability of the polyester nano-domain can also be tuned by varying the type (e.g., lactide vs. lactone) and/or composition (e.g., homopolymer vs. block copolymer) of the polyester to achieve ‘controlled’ drug release kinetics. Furthermore, it is anticipated that the CCS polyrotaxanes would provide extra mechanical strength to the SR hydrogel network, as the unique cross-linked structure of its core would increase the cross-linking density of the gel. If a small quantity of CCS polyrotaxane is introduced, other desirable features of the SR hydrogel, such as large extensibility and high elasticity\(^2\) would be marginally affected.

**Scheme 7.2** Amphiphilic CCS polyrotaxane sliding-ring hydrogel.
7.2.3 Stereocomplex-templated Synthesis of Cyclic Poly(alkyl methacrylate)s

The research described in Chapter 6 has demonstrated that both linear and cyclic st-PMMAs are capable of forming stereocomplexes with the complementary linear it-PMMAs. The resultant stereocomplexes are believed to adopt a ‘polypseudorotaxane-type’ supramolecular structure consisting of a double-stranded it-PMMA helix onto which discrete cyclic st-PMMAs are threaded. Based upon this discovery, surface-initiated it-PMMA brush polymers may potentially be employed as a template for the cyclization of linear st-PMMA with complementary reactive chain ends (Scheme 7.3).

**Scheme 7.3** Process cycle for the stereocomplex-templated synthesis of cyclic poly(alkyl methacrylate)s: (i) stereocomplexation, (ii) cyclization via end-to-end coupling approach, and (iii) decomplexation to remove cyclic syndiotactic poly(alkyl methacrylate)s (st-PMA)s.
Slow addition of the heterotelechelic \( st \)-PMMA into a strong stereocomplexation solvent, in which the surface-grafted \( it \)-PMMA brush polymers are immersed, would result in immediate stereocomplex formation. The stereocomplexation would bring the complementary reactive chain ends of linear \( st \)-PMMAs into close proximity. Using a highly efficient coupling chemistry (e.g., click chemistry), intramolecular cyclization of the linear \( st \)-PMMA will be expected to occur rapidly. The resulting cyclic polymers would be expected to remain complexed with the \( it \)-PMMA double-helices while fresh linear PMMA precursor is added. Hence, the possible formations of by-products such as macrocyclic dimers or catenanes are minimized. High dilution techniques that are essential in the conventional end-to-end coupling cyclization system to avoid the polycondensation of linear precursors are unnecessary in the proposed approach.\(^3\)

At the end of the reaction, the cyclic products can be conveniently separated from the \( it \)-PMMA brush polymer templates by extraction using a non-stereocomplexation solvent after decomplexation. As such, the templates can be easily recycled and re-used in the next batch reaction.

Other than \( st \)-PMMA, \( st \)-poly(alkyl methacrylate)s having primary and secondary ester groups (e.g., poly(EMA) and poly(\( i \)-PMA)) are also capable of forming stereocomplexes with linear \( it \)-PMMAs.\(^4\) Therefore, this innovative approach may be versatile and applicable to the synthesis of cyclic \( st \)-polymethacrylates with a variety of pendent functionalities.

### 7.2.4 Stereospecific Radical Polymerization via Dual Segregation and Templating

Previously, stereocomplex formation has been exploited in stereospecific templated polymerizations of \( st \)- and \( it \)-PMMA in solution,\(^5\) and within nanoporous films.\(^6\) These two existing stereospecific templated polymerization approaches display several disadvantages. The solution approach lacks effective means of separating the produced polymers from the template polymers. Whereas the difficulty of product isolation is overcome in the film templating approach by selective solvent extractions, the construction of the stereoregular polymeric template film, however, involves an iterative and time-consuming layer-by-layer (LBL) assembly process. Both approaches failed to give well-defined stereoregular daughter polymers with narrow MWD (PDI ~ 2.0). McHale et al. recently demonstrated an
elegant biomimetic segregation and templating approach to fabricate a nucleic acid analogue poly(vinylbenzyl adenine) with narrow MWD (PDI = 1.05). Inspired by this, a segregation and templating approach towards the synthesis of PMMA with dual control over MW and tacticity is proposed and illustrated in **Scheme 7.4**.

![Scheme 7.4 Schematic illustration of the stereospecific radical polymerization of MMA via a dual segregation and templating approach.](image)

In selected aqueous-organic solvent mixtures, micelles assembled from amphiphilic diblock copolymers consisting of *it*-PMMA and poly(ethylene glycol) (*it*-PMMA-*b*-PEG) may serve as a compartmentalized nanoreactor for the syndiospecific radical polymerization of MMA. The monomers (i.e., MMAs) added to the reaction solution would
either diffuse into the core domains of the preformed micelles or associate with \textit{it}-PMMA blocks of the residual un-micellized copolymer templates through hydrophobic interactions. Free radicals generated by a conventional initiator (e.g., 4,4’-azobis(4-cyanovaleric acid) (ACVA)) can easily access the MMAs associated with the ‘free’ \textit{it}-PMMA-\textit{b}-PEG as compared to the encapsulated MMAs within the performed micelles due to steric effects. Hence, the propagation step of the polymerization would take place in vicinity of the ‘free’ diblock copolymer template.

It has been demonstrated that conventional radical polymerization can afford syndiotactic-rich PMMAs with syndiotactic triad (\textit{rr}) upto 65\%,\textsuperscript{8} and the resultant PMMAs are capable of stereocomplexation in spite of the moderate degree of syndiotacticty.\textsuperscript{9} Also, as demonstrated in \textbf{Chapter 6} and the literature,\textsuperscript{10} the end-group functionality of the stereoregular PMMAs does not affect their ability to form stereocomplexes. Once the propagating syndiotactic-rich PMMA reaches a critical chain length,\textsuperscript{9a} stereocomplexation between the syndiotactic-rich PMMA and the \textit{it}-PMMA-\textit{b}-PEGs would take place resulting in the formation of a three-armed star polymer consisting of a triple-helix PMMA stereocomplex (SC) and two PEG arms.

As a result of the amphiphilic nature, the resulting three-armed star polymer will be incorporated into the preformed micelles. Within the core domain of the star incorporated micelles, the syndiotactic-rich PMMA macroradical will continue to propagate in direct contact with the \textit{it}-PMMA matrix to afford a longer polymer with a much higher level of syndiotacticity. As a combined result of the segregated environment and high local monomer concentration, the syndiospecific polymerization would proceed along a defined number of \textit{it}-PMMA templates within the micelle at a fast rate, with minimal termination events. The resulting polymers would therefore be anticipated to have an unprecedented dual control over MW and tacticity. Also, they can be easily separated from the diblock copolymer templates (i.e., \textit{it}-PMMA-\textit{b}-PEGs) based upon the difference in solubility characteristics.
7.3 Reference


Appendices

Appendix 2: Additional Data for Chapter 2

Calculation of star CCS 2.2 average number of arms ($N_{arms}$):

The average number of linear polymeric arms ($N_{arms}$) incorporated into the CCS polymers was calculated using Equation A2.1:

$$N_{arms} = \frac{WF_{arms}M_{w,CCS}}{M_{w,arms}} \quad (A2.1)$$

where the CCS molecular weight (MW) ($M_{w,CCS}$) and the MW of the linear arms ($M_{w,arms}$) were determined by GPC-MALLS. The weight fraction of arms ($WF_{arms}$) can be determined using Equation A2.2:

$$WF_{arm} = \frac{m(arms)x_a}{m(XL)x_x + m(arms)x_a} \quad (A2.2)$$

where the conversion of cross-linker ($\chi_c$) was determined by GC-MS and the conversion of arm ($\chi_a$) was determined by GPC. $m(arms)$ and $m(XL)$ are the amount (g) of macronitiator and cross-linker employed in the CCS polymer synthesis.

$$WF_{arm} = \frac{2.51 \times 0.61}{2.51 \times 0.61 + 0.647 \times 0.90} = 0.724$$

$$f = \frac{0.724 \times 300000}{8660} = 25.0$$

Therefore, each alkyne functional CCS polymer has 25 arms and 450 alkyne groups, since each arm consists of 18 propargyl methacrylate repeat units on average (Table 2.1).
Figure A2.1 MALDI ToF MS spectrum of PEG$_{400}$-N$_3$ in linear/positive mode using dithranol/NaI. The numbers on the MS spectrum denote the number of repeat units (n, 44.05 m/z). Inset shows expanded section of MS spectrum complete with peak m/z values and m/z differences. Both the major and minor series corresponds to the expected PEG-N$_3$ with or without cationization agents.
Figure A2.2 MALDI ToF MS spectrum of PEG\textsubscript{1000}-N\textsubscript{3} in linear/positive mode using dithranol/KI.

The numbers on the MS spectrum denote the number of repeat units (n, 44.01 m/z). Inset shows expanded section of MS spectrum complete with peak m/z values and m/z differences. The major series correlates to the expected PEG-N\textsubscript{3} and the minor series corresponds to the unreacted poly(ethylene glycol) monomethyl ether (PEG-OH) - 92% azide substitution.
**Figure A2.3** MALDI ToF MS spectrum of PEG\(_{2000}\)-N\(_3\) in linear/positive mode using dithranol/KI.

The numbers on the MS spectrum denote the number of repeat units (n, 44.01 m/z). Inset shows expanded section of MS spectrum complete with peak m/z values and m/z differences. The major series correlates to the expected PEG-N\(_3\) and the minor series corresponds to the unreacted polyethylene glycol monomethyl ether (PEG-OH) - 85% azide substitution.
**Figure A2.4** MALDI ToF MS spectrum of PrBA-N₃ in linear/positive mode using DCTB/NaI.

The numbers on the MS spectrum denote the number of repeat units (n, 128.17 m/z). Inset shows expanded section of MS spectrum complete with peak m/z values and m/z differences. The major series correlates to the expected PrBA-N₃ and the minor series corresponds to PrBA-N₃ in which a t-butyl group has been lost through fragmentation.
Figure A2.5 $^1$H NMR spectra ($d_6$-DMSO, 400 MHz) of $\beta$-CD functionalized star CCS C6, $\beta$-galactopyranosyl functionalized star CCS C5, and alkyne functionalized star CCS 2.2. * Denotes solvent peaks.
Figure A2.6 $^1$H NMR spectra (CDCl$_3$, 400 MHz) of furan functionalized star CCS C4, decane functionalized star CCS C7, and alkyne functionalized star CCS 2.2; * Denotes solvent peaks.
Click efficiency (CE) of poly(tert-butyl acrylate) functionalized star CCS P4 was estimated using Equation A2.3:

\[
CE \approx \left( \frac{A1}{Total} \right)_{After} - \left( \frac{A1}{Total} \right)_{Before} \quad (A2.3)
\]

So for CCS P4 CE is estimated as:

\[
CE \approx \left( \frac{0.616}{2.951} \right)_{After} - \left( \frac{0.275}{2.415} \right)_{Before} \approx 10\%
\]
Figure A2.8 $^1$H NMR spectra (CDCl$_3$, 400 MHz) of PEG$_{400}$, PEG$_{1000}$ and PEG$_{2000}$ corona-functionalized stars CCS P1-3, respectively. * Denotes solvent peaks.
Figure A2.9 $^1$H NMR spectra (CDCl$_3$, 400 MHz) of PEG$_{1000}$ grafted linear polymer LP P2, anthracene grafted linear polymer LP C2 and deprotected macroinitiator HO-P(CL-$b$-PgMA)-Br LP 1; * Denotes solvent peaks.
Figure A2.10 $^1$H NMR spectra (CDCl$_3$, 400 MHz) of $\beta$-CD grafted linear polymer LP C6 and deprotected macroinitiator HO-P(CL-$b$-PgMA)-Br LP 1; * Denotes solvent peaks.
Figure A2.11. Dynamic light scattering (percentage number) traces for various click-functionalized CCS polymers: (a) alkyne functionalized star CCS 2.2 and naphthalene, anthracene and pyrene corona-functionalized stars CCS C1-3, respectively (THF as solvent), (b) alkyne functionalized star CCS 2.2 and furan and decane corona-functionalized stars CCS C4 and CCS C7, respectively (THF as solvent), (c) alkyne functionalized star CCS 2.2 and β-galactose and β-cyclodextrin corona-functionalized stars CCS C5 and CCS C6, respectively (DMF as solvent), and (d) alkyne functionalized star CCS 2.2 and PEG_{400}, PEG_{1000} and PEG_{2000} corona-functionalized stars CCS P1-3 (THF as solvent).
**Fractional precipitation**

Fractional precipitation was employed to separate the alkyne CCS polymers from unincorporated polymer. The technique involves the slow addition of a non-solvent, methanol, to a rapidly stirred solution of the polymer in a small amount of THF. After the addition of a certain amount of methanol the solution becomes cloudy as the largest molecular weight species precipitate out of solution. The mixture is then left to settle and the polymer is collected by filtration using a fine grade filter paper. The polymer is analyzed by GPC to check for purity and the filtrate is allowed to reach ambient temperature again, before being treated with further methanol. In this manner many fractions of polymer can be collected and analyzed, with each fraction containing polymer with low polydispersity and successively lower molecular weight polymer. The whole process of fractional precipitation can be repeated until satisfactory separation is obtained.
Appendix 3: Additional Data for Chapter 3

Summary of results for macroinitiator synthesis:

Table A3.1 Characterization of PCL macroinitiators.

<table>
<thead>
<tr>
<th>Sample</th>
<th>M/I Ratio</th>
<th>Conv. (%)</th>
<th>$M_{n,\text{theo}}$ (kDa)(^a)</th>
<th>$M_{n,\text{NMR}}$ (kDa)(^b)</th>
<th>$M_{n,\text{GPC}}$ (kDa)(^c)</th>
<th>DP(^d)</th>
<th>PDI(^e)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bn-PCL-OH 3.1a</td>
<td>100</td>
<td>79.5</td>
<td>9.2</td>
<td>10.0</td>
<td>9.9</td>
<td>86</td>
<td>1.08</td>
</tr>
<tr>
<td>Bn-PCL-OH 3.1b</td>
<td>200</td>
<td>60.7</td>
<td>14.0</td>
<td>14.8</td>
<td>15.6</td>
<td>136</td>
<td>1.04</td>
</tr>
<tr>
<td>Bn-PCL-OH 3.1c</td>
<td>300</td>
<td>58.8</td>
<td>20.2</td>
<td>24.0</td>
<td>24.8</td>
<td>216</td>
<td>1.06</td>
</tr>
<tr>
<td>Bn-PCL-OH 3.1d</td>
<td>400</td>
<td>62.8</td>
<td>28.8</td>
<td>34.0</td>
<td>36.2</td>
<td>316</td>
<td>1.08</td>
</tr>
<tr>
<td>Bn-PCL-OH 3.2</td>
<td>100</td>
<td>93.4</td>
<td>10.8</td>
<td>-</td>
<td>12.2</td>
<td>106</td>
<td>1.12</td>
</tr>
<tr>
<td>HC≡C-PCL-OH 3.3</td>
<td>100</td>
<td>92.0</td>
<td>10.6</td>
<td>10.9</td>
<td>11.8</td>
<td>102</td>
<td>1.15</td>
</tr>
</tbody>
</table>

\(^a\)Theoretical molecular weight calculated from monomer conversion as determined by GC-MS.

\(^b\)Number average MW determined from $^1$H NMR spectroscopic analysis.

\(^c\)Number average MW ($M_n$) and polydispersity (PDI) determined from GPC using THF as eluent ($dn/dc = 0.078^1$).

\(^d\)Degree of polymerization (DP) calculated based upon the number average MW determined from GPC.
Calculation of CCS average number of arms ($N_{arms}$):

The average value of linear polymeric arm number ($N_{arms}$) incorporated into the CCS polymers was calculated using Equation A3.1:

$$N_{arms} = \frac{W_{arms}M_{w,CCS}}{M_{w,arms}}$$  \hspace{1cm} (A3.1)

where the CCS MW ($M_{w, CCS}$) and the MW of the linear arms ($M_{w, arms}$) were determined by GPC-MALLS.

The weight fraction of arms ($W_{Farms}$) was determined using Equation A3.2:

$$W_{Farms} = \frac{m(arms)x_a}{m(XL)x_c + m(arms)x_a}$$  \hspace{1cm} (A3.2)

where the conversion of cross-linker ($x_c$) was determined by GC-MS and the conversion of arm ($x_a$) was determined by GPC RI chromatogram deconvolution. $m(arms)$ and $m(XL)$ are the amount (g) of macroinitiator and cross-linker employed in the CCS polymer synthesis.
Deconvolution of CCS polymer GPC RI traces to determine macroinitiator conversion ($x_a$):

**Figure A3.1**: Deconvolution of CCS polymer GPC RI chromatogram based on Gaussian functions, using the GPC RI chromatogram of CCS 3.1c as an example: (a) the original GPC RI trace of CCS 3.1c, (b) the deconvoluted GPC RI chromatogram corresponding to the star polymer, and (c) the deconvoluted GPC RI chromatogram corresponding to the unincorporated polymers.

The conversion of arm ($x_a$) was estimated using **Equation A3.3**:

$$x_a = \frac{A1}{A1 + A2} \quad (A3.3)$$

where $A1$ and $A2$ are the areas under the deconvoluted GPC RI chromatogram corresponding to the star polymer and the unincorporated polymer, respectively (**Figure A3.1b** and c).
Figure A3.2: MALDI-ToF MS spectra for macroinitiator HC≡C-PCL-OH 3.3 acquired in linear/positive mode, using (A) α-cyano-4-hydroxycinnamic acid and potassium trifluoroacetate KTFA as the matrix and cationisation reagents, respectively, (B) trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) and potassium trifluoroacetate (KTFA) as the matrix and cationisation agents, respectively.
Appendix 4: Additional data for Chapter 4

Table A4.1 Characterization result summary of the PCL-MI and the PCL CCS polymer synthesized.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Monomer Conversion $^a$ ( %)</th>
<th>PCL-MI Conversion $^b$ ( %)</th>
<th>$M_{n,\text{theo}}$ $^c$ (kDa)</th>
<th>$M_{n,\text{GPC}}$ $^d$ (kDa)</th>
<th>$M_n/M_n^d$</th>
<th>$M_{n,\text{NMR}}$ $^e$ (kDa)</th>
<th>DP $^e$</th>
<th>$N_{\text{arms}}$ $^f$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCL-MI</td>
<td>92</td>
<td>-</td>
<td>10.6</td>
<td>11.8</td>
<td>1.08</td>
<td>10.9</td>
<td>95.1</td>
<td>-</td>
</tr>
<tr>
<td>PCL CCS</td>
<td>-</td>
<td>94.2</td>
<td>-</td>
<td>286</td>
<td>1.29</td>
<td>-</td>
<td>-</td>
<td>15</td>
</tr>
</tbody>
</table>

$^a$The CL monomer conversions were determined by GC-MS;

$^b$The PCL MM conversions were determined by the deconvolution of GPC RI chromatogram using Gaussian function (Figure 4.1b);

$^c$Theoretical number average MW, $M_{n,\text{theo}} = MW_i + MW_{\text{CL}} \times \text{Conv.} \times ([M_0]/[I_0])$, where $MW_i$, $MW_{\text{CL}}$ and Conv. are the MWs of initiator, $\varepsilon$-caprolactone and $\varepsilon$-caprolactone monomer conversion, respectively. [$M_0$] and [I0] are the initial concentration of monomer and initiator.

$^d$Determined from GPC analysis;

$^e$The number average MW determined from $^1$H NMR spectroscopic analysis using Equation A4.1: $M_{n,\text{NMR}} = 56 + 114 \times \frac{I_f}{I_b}$; where, $I_f$ represents the integral area under the resonance ‘f’ (methylene protons on PCL repeating units); $I_b$ represents the integral area under the resonances ‘b’ (methylene protons of propargyl alcohol); and the value 56 and 114 are the MW of the propargyl alcohol initiator and $\varepsilon$-caprolactone monomer, respectively (Figure 4.2a). The degree of polymerization (DP) was determined using Equation A4.2: $DP = \frac{I_f}{I_b}$.

$^f$The average number of arms ($N_{\text{arms}}$) incorporated into the CCS polymer was calculated using Equation A4.3: $N_{\text{arms}} = \frac{WF_{\text{arms}} \times MW_{\text{CCS}}}{MW_{\text{arms}}}$, where the CCS MW ($MW_{\text{CCS}}$) and the MW of the linear arms ($MW_{\text{arms}}$) were determined by GPC-MALLS. The weight fraction of arms ($WF_{\text{arms}}$) can be
determined using Equation A4.4: \[ W_{F_{arms}} = \frac{m_{arms} \times x_a}{m_{XL} \times x_c + m_{arms} \times x_a} \], where the conversion of cross-linker \((x_c)\) was determined by GC-MS and the conversion of arm \((x_a)\) was determined by the deconvolution of GPC RI chromatogram using Gaussian function. \(m_{arms}\) and \(m_{XL}\) are the amount (g) of macroinitiator and cross-linker employed in the CCS polymer synthesis.

**Table A4.2.** Characterization result summary of the CCS polypseudorotaxane and the CCS polyrotaxane.

<table>
<thead>
<tr>
<th>Sample</th>
<th>(R^a) ((\alpha)-CD : CL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCS polypseudorotaxane</td>
<td>0.74</td>
</tr>
<tr>
<td>CCS polyrotaxane</td>
<td>0.68</td>
</tr>
</tbody>
</table>

\(^a\)R is the stoichiometric ratio of \(\alpha\)-CDs to CL units in the resultant poly(pseudo)rotaxanes, determined from \(^1\)H NMR spectroscopic analysis using Equation A4.5: \[ R = \frac{I_1}{3I_f} \], where \(I_1\) represents the integral area under the resonance ‘1’ for the methine group protons of \(\alpha\)-CDs and \(I_f\) represents the integral area under the resonance ‘f’ for the methylene protons on PCL repeat units (**Figure 4.2b** and **c**, respectively).
Figure A4.1 Additional TEM images of the CCS polyrotaxane. The scale bars (inset) represent 200 nm.

Figure A4.2 2D-ROESY NMR spectrum of α-CD-PCL linear polypseudorotaxane in DMSO-$d_6$. 
Calculation for the maximum diameter of the PCL CCS polymer.

The contour length of the PCL arms of the CCS polymer is calculated to be approximately 106 nm according to the following Equation A4.6 and A4.7:

\[ L_{PCL} = L_{CL} \times DP_{PCL} = 1.06 \times 100 = 106 \text{ nm} \quad (A4.6) \]

where \( L_{PCL} \) is the contour length of the PCL arm polymer, \( L_{CL} \) is the estimated length of the monomer CL in the ring-opened form at its maximum extension, and \( DP_{PCL} \) is the degree of polymerization of the PCL arm.

\[ L_{CL} = L_{C-C} \times 5 + L_{C-O} \times 2 = 1.06 \text{ nm} \quad (A4.7) \]

where \( L_{C-C} \) is the bond length of a C-C bond (i.e., 0.153 nm) and \( L_{C-O} \) is the bond length of a C-O bond (i.e., 0.143 nm). Note: each CL repeating units of PCL consists of five C-C and two C-O bonds.

The contour length of the crosslinking block incorporated into the core of the CCS polymer is calculated according to Equation A4.8 and A4.9:

\[ L_{PBOD} = L_{BOD} \times DP_{BOD} = 1.06 \times 30 = 32 \text{ nm} \quad (A4.8) \]

where \( L_{PBOD} \) is the contour length of the crosslinking block, \( L_{BOD} \) is the length of crosslinker BOD in the ring-opened form at its maximum extension, and \( DP_{BOD} \) is the degree of polymerization of the crosslinking block.

\[ L_{BOD} = L_{CL} = 1.06 \text{ nm} \quad (A4.9) \]
Note: BOD is a bis-lactone consisting of two caprolactones jointed at the 4th carbon position. The estimated length of BOD is the same as that of CL in the ring-opened form at maximum extension.

The maximum diameter of the CCS polymer is therefore estimated to be approximately 280 nm according to Equation A4.10:

\[
D_{CCS,\text{max}} = (L_{BOD} + L_{PCL}) \times 2 \approx 280 \text{ nm} \quad (A4.10)
\]

where \(D_{CCS,\text{max}}\) is the estimated maximum diameter of the CCS polymer.
Appendix 6: Additional data for Chapter 6

Figure A6.1 $^1$H NMR spectra and GPC DRI chromatograms of $l$-$st$-$PMMA$-$Br$ ($st$-$L_{2k}$-$Br$) before, and $l$-$st$-$PMMA$-$N_3$ ($st$-$L_{2k}$) after azidation. Azidation conditions: $[l$-$st$-$PMMA$-$Br]/[NaN_3]$ (mM) = 20/650 at 40 °C in DMSO.

Figure A6.2 Polymerization of MMA at -78 °C in toluene using tBuMgBr as initiator; $[MMA]/[tBuMgBr]$ (mM) = 1340-1650/53.4-8.40. Based on these conditions, the synthesis of linear isotactic PMMA ($l$-$it$-$PMMA$) was performed on a gram-scale.
Figure A6.3 DSC profiles of the c-st/l-it-PMMA stereocomplexes (a) st-C_4k/l-t-L_{10k}, (b) st-C_{2k}/l-t-L_{10k}, (c) st-C_{2k}/l-t-L_{44k}, and (d) st-C_{1k}/l-t-L_{10k}, and the l-st/l-it-PMMA stereocomplex counterparts (e) st-L_{4k}/l-t-L_{10k}, (f) st-L_{2k}/l-t-L_{10k}, (g) st-L_{2k}/l-t-L_{44k}, and (h) st-L_{1k}/l-t-L_{10k} after annealing at 95 and 120 °C for 24 h.
Figure A6.4 (a) Linear it-PMMA (it-L_{10k}), (b) cyclic st-PMMA (st-C_{4k}), and (c) st-C_{4k}/it-L_{10k} stereocomplex (a mixture of it-L_{10k} and st-C_{4k} in it-/st- 1:2 stoichiometry). it-L_{10k} and st-C_{4k} were dissolved separately in MeCN:H_{2}O (9:1) at concentrations of 2 mg/mL and mixed at room temperature. Solutions of it-L_{10k} and st-C_{4k} remained transparent while st-C_{4k}/it-L_{10k} became slightly turbid after standing at room temperature for 24 h.

Figure A6.5 (a) Linear it-PMMA (it-L_{10k}), (b) linear st-PMMA (st-L_{4k}), and (c) st-L_{4k}/it-L_{10k} stereocomplex (a mixture of it-L_{10k} and st-L_{4k} in it-/st- 1:2 stoichiometry). it-L_{10k} and st-L_{4k} were dissolved separately in MeCN:H_{2}O (9:1) at concentrations of 2 mg/mL and mixed at room temperature. Solutions of it-L_{10k} and st-C_{4k} remained transparent while st-L_{4k}/it-L_{10k} became turbid immediately after mixing.
Table A6.1 Characterization summary for various stereoregular PMMAs.

<table>
<thead>
<tr>
<th>PMMA</th>
<th>$M_n$,[a]</th>
<th>$M_w$/$M_n$[a]</th>
<th>mm/mr/rr[b]</th>
<th>$T_g$[c]</th>
</tr>
</thead>
<tbody>
<tr>
<td>st-C_{4k}</td>
<td>3.2</td>
<td>1.32</td>
<td>2/26/72</td>
<td>113.8</td>
</tr>
<tr>
<td>st-C_{2k}</td>
<td>2.0</td>
<td>1.28</td>
<td>2/26/72</td>
<td>107.8</td>
</tr>
<tr>
<td>st-C_{1k}</td>
<td>1.0</td>
<td>1.36</td>
<td>2/27/71</td>
<td>82.4</td>
</tr>
<tr>
<td>st-L_{4k}</td>
<td>4.2</td>
<td>1.34</td>
<td>2/26/72</td>
<td>98.6</td>
</tr>
<tr>
<td>st-L_{2k}</td>
<td>2.4</td>
<td>1.29</td>
<td>2/26/72</td>
<td>98.6</td>
</tr>
<tr>
<td>st-L_{1k}</td>
<td>1.1</td>
<td>1.38</td>
<td>2/27/71</td>
<td>59.3</td>
</tr>
<tr>
<td>it-L_{10k}</td>
<td>10.3</td>
<td>1.12</td>
<td>93/4/3</td>
<td>53.6</td>
</tr>
<tr>
<td>it-L_{44k}</td>
<td>44.3</td>
<td>1.30</td>
<td>97/2/1</td>
<td>56.8</td>
</tr>
</tbody>
</table>

[a] Number average MW ($M_n$,[a]) and MW distribution ($M_w$/$M_n$) determined by gel permeation chromatography (GPC) calibrated with linear PMMA standards.

[b] Tacticity (triads) determined by $^{13}$C NMR spectroscopic analysis using CDCl$_3$ as the solvent at 55 °C.

[c] Glass transition temperature ($T_g$) determined by differential scanning calorimetry (DSC).
Table A6.2 DSC result summary for various PMMA stereocomplexation samples.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Stereocomplex</th>
<th>Method[^a] (^{(S/T)})</th>
<th>(T_{m1}^{\circ C})</th>
<th>(T_{m3}^{\circ C})</th>
<th>(\Delta H_1^{J/g})</th>
<th>(\Delta H_3^{J/g})</th>
<th>(\Delta H_{tot}^{J/g})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>st-C(<em>{4k})/it-L(</em>{10k})</td>
<td>S</td>
<td>129.7</td>
<td>17.7</td>
<td>-</td>
<td>-</td>
<td>17.7</td>
</tr>
<tr>
<td>2</td>
<td>st-C(<em>{2k})/it-L(</em>{10k})</td>
<td></td>
<td>121.6</td>
<td>14.3</td>
<td>-</td>
<td>-</td>
<td>14.3</td>
</tr>
<tr>
<td>3</td>
<td>st-C(<em>{2k})/it-L(</em>{44k})</td>
<td></td>
<td>125.6</td>
<td>9.3</td>
<td>-</td>
<td>-</td>
<td>9.3</td>
</tr>
<tr>
<td>4</td>
<td>st-C(<em>{1k})/it-L(</em>{10k})</td>
<td></td>
<td>-</td>
<td>-</td>
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<td>5</td>
<td>st-L(<em>{4k})/it-L(</em>{10k})</td>
<td></td>
<td>126.4</td>
<td>167.0</td>
<td>14.6</td>
<td>9.6</td>
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<td>st-L(<em>{2k})/it-L(</em>{10k})</td>
<td></td>
<td>113.1</td>
<td>135.5</td>
<td>16.5</td>
<td>7.4</td>
<td>23.9</td>
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<td>7</td>
<td>st-L(<em>{2k})/it-L(</em>{44k})</td>
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<td>116.3</td>
<td>133.8</td>
<td>6.9</td>
<td>14.8</td>
<td>21.7</td>
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<td>8</td>
<td>st-L(<em>{1k})/it-L(</em>{10k})</td>
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<td>85.3</td>
<td>7.3</td>
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<td>7.3</td>
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<td>9</td>
<td>st-C(<em>{4k})/it-L(</em>{10k})</td>
<td>T (^{\circ C}) @ 95</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>st-C(<em>{2k})/it-L(</em>{10k})</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>11</td>
<td>st-C(<em>{2k})/it-L(</em>{44k})</td>
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<td>-</td>
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<td>-</td>
<td>-</td>
<td>0</td>
</tr>
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<td>12</td>
<td>st-C(<em>{1k})/it-L(</em>{10k})</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>13</td>
<td>st-L(<em>{4k})/it-L(</em>{10k})</td>
<td>T (^{\circ C}) @ 95</td>
<td>125.9</td>
<td>6.6</td>
<td>-</td>
<td>-</td>
<td>6.6</td>
</tr>
<tr>
<td>14</td>
<td>st-L(<em>{2k})/it-L(</em>{10k})</td>
<td></td>
<td>114.3</td>
<td>2.1</td>
<td>-</td>
<td>-</td>
<td>2.1</td>
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<td>15</td>
<td>st-L(<em>{2k})/it-L(</em>{44k})</td>
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<td>122.2</td>
<td>4.9</td>
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<td>16</td>
<td>st-L(<em>{1k})/it-L(</em>{10k})</td>
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<td>-</td>
<td>-</td>
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<tr>
<td>17</td>
<td>st-C(<em>{4k})/it-L(</em>{10k})</td>
<td>T (^{\circ C}) @ 120</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
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<td>18</td>
<td>st-C(<em>{2k})/it-L(</em>{10k})</td>
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<td>-</td>
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<tr>
<td>19</td>
<td>st-C(<em>{2k})/it-L(</em>{44k})</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>st-C(<em>{1k})/it-L(</em>{10k})</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>21</td>
<td>st-L(<em>{4k})/it-L(</em>{10k})</td>
<td></td>
<td>-</td>
<td>150.5</td>
<td>-</td>
<td>14.3</td>
<td>14.3</td>
</tr>
<tr>
<td>22</td>
<td>st-L(<em>{2k})/it-L(</em>{10k})</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>23</td>
<td>st-L(<em>{2k})/it-L(</em>{44k})</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>24</td>
<td>st-L(<em>{1k})/it-L(</em>{10k})</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
</tbody>
</table>

\[^a\] The PMMA stereocomplexes were prepared via either solvent induction (S) or thermal annealing (T) methods.

\[^b\] First melting point \((T_{m1})\).

\[^c\] Second melting point \((T_{m3})\).

\[^d\] Endothermic heat released from the first melting peak \((\Delta H_1)\).

\[^e\] Endothermic heat released from the second melting peak \((\Delta H_3)\).

\[^f\] Total endothermic heat resulting from melting of stereocomplexes \((\Delta H_{tot})\) determined via differential scanning calorimetry (DSC).
Table A6.3. Molecular modeling result summary for various constructed cyclic \textit{st-}
PMMA/\textit{it-}PMMA stereocomplexes.

<table>
<thead>
<tr>
<th>System</th>
<th>Peak 1\textsuperscript{[a]} (nm)</th>
<th>Peak 2\textsuperscript{[a]} (nm)</th>
<th>Peak 3\textsuperscript{[a]} (nm)</th>
<th>Peak 4\textsuperscript{[a]} (nm)</th>
<th>Density (g cm\textsuperscript{-3})</th>
<th>S.P. (J\textsuperscript{1/2}cm\textsuperscript{-3/2})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expt.\textsuperscript{[b]}</td>
<td>2.08</td>
<td>-</td>
<td>0.78</td>
<td>0.60</td>
<td></td>
<td></td>
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<tr>
<td>PR\textsuperscript{[c]} 1</td>
<td>2.08</td>
<td>-</td>
<td>0.79</td>
<td>0.57</td>
<td>1.22</td>
<td>20.7</td>
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<tr>
<td>PR 2</td>
<td>2.06</td>
<td>-</td>
<td>0.82</td>
<td>0.58</td>
<td>1.21</td>
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<tr>
<td>PR 3</td>
<td>2.03</td>
<td>-</td>
<td>0.83</td>
<td>0.57</td>
<td>1.22</td>
<td>19.7</td>
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<tr>
<td>DW\textsuperscript{[d]} 1</td>
<td>2.56</td>
<td>1.29</td>
<td>0.72</td>
<td>0.61</td>
<td>1.20</td>
<td>19.1</td>
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<tr>
<td>DW 2</td>
<td>-</td>
<td>1.06</td>
<td>0.82</td>
<td>0.63</td>
<td>1.20</td>
<td>19.1</td>
</tr>
<tr>
<td>DW 3</td>
<td>2.13</td>
<td>1.36</td>
<td>0.74</td>
<td>0.60</td>
<td>1.08</td>
<td>17.4</td>
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</tbody>
</table>

\textsuperscript{[a]} Calculated peaks in the XRD patterns of the energy minimized PMMA stereocomplex crystal structures.

\textsuperscript{[b]} Experimental result obtained from the \textit{st-C\textsubscript{2}k/it-L\textsubscript{10k} stereocomplex sample.}

\textsuperscript{[c]} Molecular model of cyclic \textit{st-PMMA/linear it-PMMA stereocomplex with the ‘Polypseudorotaxane-type’ (PR) arrangement.}

\textsuperscript{[d]} Molecular model of cyclic \textit{st-PMMA/linear it-PMMA stereocomplex with the ‘double wrapping’ (DW) arrangement.}

Note: the bolded molecular modeling systems are presented in Figure 6.9 and 6.10, respectively and the results are discussed in the main text.
Scheme A6.1 Schematic illustration of the possible stereocomplexation between l-it-PMMA and the complementary low DP (average ≤ 18) (a) c-st-PMMA, and (b) l-st-PMMA.
Scheme A6.2 Schematic illustration of the proposed PMMA stereocomplex prepared from \(l\)-it-PMMA and \(c\)-st-PMMA with three possible supramolecular structures; (i) 'polypseudorotaxane', and (ii) 'double wrapping' (top), and that prepared from \(l\)-it-PMMA and \(l\)-st-PMMA (bottom).
Scheme A6.3 Schematic illustration of the possible stereocomplexation between \textit{l}-it-PMMA and the complementary \textit{c-st}-PMMA with a significantly high degree of polymerization (DP) (e.g., DP > 200) to afford the proposed (i) ‘cross-linked’ triple-stranded helix, and/or (ii) quadruple-stranded helix stereocomplex (top), and between \textit{l}-it-PMMA and the complementary \textit{l-st}-PMMA with a significantly high DP affords the triple-stranded helix stereocomplex (bottom).
Reference


Author/s: Ren, Jing Ming

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