

**Design, synthesis and material property
investigation of degradable block copolymers
prepared via the combination of ROCOP and
ROP**

Yunqing Zhu

**A thesis submitted in partial fulfilment of the requirements for the degree of Doctor of
Philosophy in Chemistry**

Department of Chemistry
Imperial College London
September 2016

For my Nearest and Dearest Family and Friends

Declaration

The work described in this thesis was conducted in the Department of Chemistry, Imperial College London, between October 2013 and September 2016 and is the work of the author unless otherwise stated.

The copyright of this thesis rests with the author and is made available under a Creative Commons Attribution-Non Commercial-No Derivatives licence. Researchers are free to copy, distribute or transmit the thesis on the condition that they attribute it, that they do not use it for commercial purposes and that they do not alter, transform or build upon it. For any reuse or distribution, researchers must make clear to others the licence terms of this work.

Acknowledgements

Sponsored by the Imperial-China Scholarship Council Scholarship, I started my Ph.D. study in 2013. I want to express my gratitude to both the Imperial College and the China Scholarship Council for funding and supporting me.

During my Ph.D. study, I have been guided and supported by many people. Particularly, I would like to thank my supervisor Professor Charlotte Williams. I have learnt a lot from her and she has been very supportive to me. She gave me a lot of freedom to do research in different areas, like thermoplastic elastomers and polymer self-assemblies and helped me find collaborators in these areas. Besides research, I also benefited a lot from her career advices. I couldn't have asked for a more supportive supervisor. My gratitude to Charlotte is beyond words.

Many people from the Chemistry Department of Imperial College London have been very helpful during the past three years. I would like to thank Peter Haycock for conducting several NMR experiments for me; Lisa Haigh for her mass spectrometry service. I would also like to thank Patricia Carry at the Chemical Engineering Department for letting me use DSC and Richard Sweeney at the Materials Department for his WAXS service. Additionally, I want to express my gratitude to my collaborators, Prof. Giuseppe Battaglia, Dr. Jens Gaitzsch, Dr. Alessandro Poma, Dr. Loris Rizzelloto from the University College of London for helping me conduct cell tests and TEM analyses, and Prof. Marc A. Hillymer, Dr. Madalyn R. Radlauer, Deborah K. Schneiderman, from the University of Minnesota for helping me run SAXS characterizations and TEM analyses.

I would also like to show my gratitude to all the members of the Williams group, past and present, for all the help they have been giving me, especially Dr Charles Romain. As my co-supervisor, I learnt a lot from him. Without his help and guidance, I would not be able to start my research projects smoothly and certainly would not be able to get so many results.

The other post-doctoral researchers in the group, past and present, have all been very helpful to me. Thanks to Dr. Valentin Poirier, Dr. Junjuda Unruangsri, Dr. Prabhjot Saini, Dr. Anish Cyriac, Dr. Clare Bakewell, Dr. Jenni Garden, Dr. Neil Brown, Dr. Seb Pike, Dr. Andrés Garcia Trencó, Dr. Sumesh Kureppadathu Raman and Dr. Giulia Fiorani. I also enjoyed

working with other Ph.D. students and would like to thank Ni Yi, Arnaud Thevenon, Shyeni Paul, Dom Myers, Jameel Marafie, Gemma Trott, Alice Leung, Rachel Brooks, Charlie Coleman, Tim Stoesser, Arron Deacy, Matthew Allinson and Jonathan Weiner.

Finally, I would like to thank my whole family, especially my beloved wife. I love her so much and it is her support that encouraged me to overcome so many difficulties over the past three years. I feel like I can fight against the whole world with her at my side.

Abstract

The thesis focuses on the synthesis of (multi)block copolyesters using combinations of the ring-opening copolymerization of anhydrides/epoxides and the ring-opening polymerization of lactones. All the new block copolyesters are fully characterized and in depth investigations of the materials' properties include evaluations as thermoplastic elastomers, shape memory polymers and polymers for biomedicine.

Chapter 2 describes the polymerization of ϵ -caprolactone, using a di-zinc catalyst and various diols. A mixture of two polymer chain architectures is observed when using diols featuring secondary hydroxyls: these comprise chains which are either chain extended or chain terminated by the diol. This observation highlights the importance of analyzing the polymer architecture, the analysis may be achieved using a combination of NMR spectroscopic techniques, in the ring-opening polymerization of ϵ -caprolactone and refutes the common assumption that a single chain extended structure is produced in all cases.

Chapter 3 uses di-zinc catalysts to selectively polymerize mixtures of lactones, epoxides and cyclic anhydrides to form multiblock copolyesters. By controlling the chemistry of the Zn-OP (P represents polymer chain) it is possible to select for a particular polymerization route and thereby allow access to multiblock copolymers having both alternating polyester blocks and aliphatic polyester blocks. The switchable catalysis is established to be generally applicable to a range of lactone/epoxide/cyclic anhydride combinations. The unusual catalyst selectivity is proposed to arise due to both kinetic and thermodynamic factors.

Chapter 4 applies the selective catalysis to make multiblock copolymers which are subsequently chain-extended by reactions with diisocyanates. This method allows the preparation of amorphous multiblock copolymers comprising hard blocks from the ring-opening copolymerization of phthalic anhydride (PA) and cyclohexene oxide (CHO) and soft blocks from the ring-opening polymerization of ϵ -decalactone (DL). The obtained multiblock polymers function as thermoplastic elastomers, and shape memory materials, which are fully characterized and various application areas are proposed.

Chapter 5 reports the synthesis of amphiphilic block copolymers, featuring hydrophobic poly(ϵ -caprolactone) blocks and hydrophilic blocks produced by the alternating copolymerization of maleic anhydride and epoxides featuring ether chains. The block copolyesters are designed to be both biodegradable and biocompatible. Block copolymers

with different hydrophilic/hydrophobic ratios are processed to form self-assembled nanostructures in aqueous solutions, and show a range of different morphologies. The (bio)degradability, biocompatibility and drug release profiles are studies.

List of Publications

1. **Zhu, Y.**; Romain, C.; Williams, C. K. Sustainable polymers using renewable resources for today and tomorrow. *Nature*, **2016**, *accepted*. (IF: 38.14) [Dr Charles Romain and I contributed equally in writing this review paper]
2. Romain, C.; **Zhu, Y.**; Dingwall, P.; Paul, S.; Rzepa, H. S.; Buchard, A.; Williams, C. K. Chemoselective polymerizations from mixtures of epoxide, lactone, anhydride, and carbon dioxide. *Journal of the American Chemical Society* **2016**, *138*, 4120-4131. (IF: 13.04) [My contribution to this paper is that I provided all the experimental data related to the polyester-*b*-polyester block polymer to support the DFT simulations]
3. **Zhu, Y.**; Romain, C.; Williams, C.K. Sequence selective polymerization catalysis: controlling the metal chain end group to prepare block copolyesters. *Journal of the American Chemical Society*, **2015**, *137*, 12179–12182. (IF: 13.04) [I did all the experiment and wrote the paper. Dr Charles Romain was listed as a co-author because I frequently discuss my results with him]
4. **Zhu, Y.**; Romain, C.; Poirier, V.; Williams, C. K. Influences of a dizinc catalyst and bifunctional chain transfer agents on the polymer architecture in the ring-opening polymerization of ϵ -caprolactone. *Macromolecules* **2015**, *48*, 2407-2416. (IF: 5.55) [I did all the experiment and wrote the paper. Dr Charles Romain was listed as a co-author because I frequently discuss my results with him. Dr Valentin Poirier was listed as another co-author because he suggested apply the kinetic equation to determine the rate constants of both initiation and propagation]
5. **Zhu, Y.**; Paul, S. (co-first); Romain, C.; Brooks, R.; Saini, P. K.; Williams, C. K. Ring-opening copolymerization (ROCOP): synthesis and properties of polyesters and polycarbonates. *Chemical Communication* **2015**, *51*, 6459-6479. (IF: 6.57) [Shyeni Paul and I contribute equally in this review paper. I wrote the part related to the polyesters prepared *via* ring-opening copolymerization and their corresponding thermal and mechanical properties]
6. Saini, P. K.; Romain, C.; **Zhu, Y.**; Williams, C. K. Di-magnesium and zinc catalysts for the copolymerization of phthalic anhydride and cyclohexene oxide. *Polymer Chemistry* **2014**, *5*, 6068-6075. (IF: 5.69) [My contribution to this paper is that I suggested a new approach to identify the signals of ether linkage and end groups in ^1H NMR spectroscopy]

Patent

1. **Zhu Y.**, Williams C.K., Biodegradable thermoplastic elastomer from multi-block copolyester, UK Priority Patent Application Number 1514506.3

List of Abbreviations

ATR-IR	Attenuated Total Reflectance Infrared
BDI	β -diiminate
β M δ VL	β -Methyl- δ -valerolactone
BPA	Bisphenol A
Cell-g-P(BA- <i>co</i> -DAEMA)]	Cellulose-g-poly(n-butyl acrylate- <i>co</i> -dehydroabietic ethyl methacrylate)
Cell-g-P(LMA- <i>co</i> -DAEMA)	Cellulose-g-poly(lauryl methacrylate- <i>co</i> -dehydroabietic ethyl methacrylate)
ϵ -CL	ϵ -Caprolactone
CHD	Cyclohexane-1,2-diol
CHO	Cyclohexene Oxide
COSY	Homonuclear Correlation Spectroscopy
CPrA	Cyclopropane-1,2-dicarboxylic acid <i>anhydride</i>
CPA	Cyclopentane-1,2-dicarboxylic acid <i>anhydride</i>
Cy	1,2-Cyclohexylene
D	Domain Spacing
DCM	Dichloromethane
DCTB	Trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propeny lidene]malononitrile
DEPT	Distortionless Enhancement by Polarization Transfer
DFT	Density Functional Theory
D_h	Hydrodynamic Diameter
ϵ -DL	ϵ -Decalactone
DLE	Drug Loading Efficiency
DLS	Dynamic Light Scattering
DMAP	Dimethylaminopyridine
DMF	Dimethyl Formamide

DMSO	Dimethyl Sulfoxide
DNA	Deoxyribonucleic Acid
DOX•HCl	Doxorubicin Hydrochloride
DSC	Differential Scanning Calorimetry
EG	Ethylene Glycol
FFT	<i>Fast Fourier Transform</i>
HDF	<i>Human Dermal Fibroblasts</i>
HLCMs	Hydrated Large Compound Micelles
HSQC	Heteronuclear Single Quantum Coherence
IR	Infrared
L	Ligand
<i>rac</i> -LA	<i>rac</i> -Lactide
LCST	Lower critical solution temperature
LCMs	Large Compound Micelles
LCVs	Large Compound Vesicles
M	Lewis Acidic Metal Centre
MA	Maleic Anhydride
MALDI	Matrix Assisted Laser Desorption Ionisation
MCVs	Multicompartment Vesicles
MDI	Methylene Diphenyl Diisocyanate
Me	Methyl
MeOH	Methanol
MEMO	2-((2-methoxyethoxy)methyl)oxirane
ME ₂ MO	2-((2-(2-methoxyethoxy)ethoxy)methyl)oxirane
ME ₃ MO	2-((2-(2-(2-methoxyethoxy)ethoxy)ethoxy)methyl)oxirane
M_n	Number Average Molecular Weight
MPD	2-Methyl-1,3-Propanediol
MTT	3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide
M_w	Weight Average Molecular Weight
MW	Molecular Weight

Nf-kB	Nuclear Factor Kappa-Light-Chain-Enhancer of Activated B Cells
NMR	Nuclear Magnetic Resonance
N-MeIm	N-methylimidazole
Nu	Nucleophile
OAc	Acetoxy
PA	Phthalic Anhydride
PBS	Phosphate-Buffered Saline
PC	Polycarbonate
PCHC	Poly(cyclohexene) Carbonate
PCHPE	Poly(cyclohexylene phthalate)
PCL	Poly(ϵ -caprolactone)
PD	1,2-Propanediol
PDI	Polydispersity Index
PDL	Poly(ϵ -decalactone)
PET	Polyethylene terephthalate
PEG	Polyethylene Glycol
PEO- <i>b</i> -PEE	Poly(ethylene oxide)- <i>block</i> -polyethylethylene
PEO- <i>b</i> -PBD	Poly(ethylene oxide)- <i>block</i> -polybutadiene
PGMA- <i>b</i> -PHPMA	Poly(glycerol monomethacrylate)- <i>b</i> -poly(2-hydroxypropylmethacrylate)
PHA	Poly(hydroxyl alkanoates)
PICsomes	Polyion complex polymersomes
PISA	Polymerization-induced Self-assembly
PLA	Poly lactide
PlimC	Poly(limonene carbonate)
PMPC- <i>b</i> -PDPA	poly[2-(methacryloyloxy)ethyl phosphorylcholine]- <i>b</i> -poly[2-(diisopropylamino)ethyl methacrylate]
PNIPAAM	Poly(<i>N</i> -isopropylacrylamide)
PO	Propylene Oxide
PPC	Poly(propylene) Carbonate
PPF	Poly(propylene fumarate)

PPM	Poly(propylene maleate)
PPNCl	Bis(triphenylphosphene)iminium chloride
PS- <i>b</i> -PSBA- <i>b</i> -PS	Poly(styrene- <i>b</i> -soybean oil acrylate- <i>b</i> -styrene)
PS- <i>b</i> -PSBMA- <i>b</i> -PS	Poly(styrene- <i>b</i> -soybean oil methacrylate- <i>b</i> -styrene)
PvCHPE	Poly(4-vinyl-1-cyclohexylene phthalate)
PVL	Poly(δ -valerolactone)
RAFT	Reversible Addition-Fragmentation Chain Transfer
ROCOP	Ring Opening Copolymerisation
ROP	Ring Opening Polymerisation
SA	Succinic Anhydride
SAS	Poly[styrene- <i>b</i> -(lauryl acrylate- <i>co</i> -stearyl acrylate)- <i>b</i> -styrene]
SAXS	Small-Angle X-ray Scattering
SBS	Polystyrene- <i>b</i> -Polybutadiene- <i>b</i> -Polystyrene
SEC	Size Exclusion Chromatography
SIS	Polystyrene- <i>b</i> -Polyisoprene- <i>b</i> -Polystyrene
^t Bu	<i>Tert</i> -butyl
TBAHS	Tetrabutylammonium Hydrogen Sulphate
TCE	1,1,2,2-Tetrachloroethane
T_d	Decomposition Temperature
TEM	Transmission Electron Microscopy
TFA	Trifluoroacetic Acid
T_g	Glass Transition Temperature
TGA	Thermogravimetric Analysis
THF	Tetrahydrofuran
T_m	Melting Temperature
ToF	Time of Flight
TOF	Turnover Frequency
TON	Turnover Number
TPE	Thermoplastic Elastomer
T_{trans}	Transition Temperature
UPy	2-Ureido-4[1H]-pyrimidinone
vCHO	4-vinyl-1-cyclohexene 1,2-epoxide
δ -VL	δ -Valerolactone

List of Figures, Schemes and Tables

Chapter 1

- Figure 1.1:** Schematic illustration of the generic reactions occurring during ring-opening copolymerization (ROCOP) prepare alternating polyesters and polycarbonates.
- Figure 1.2:** Illustration of the elementary steps occurring during epoxide/anhydride ring-opening copolymerizations (ROCOP).
- Figure 1.3:** Illustration of the structures of some typical metalloporphyrin complexes.
- Figure 1.4:** The structures of some typical β -diiminate zinc catalysts.
- Figure 1.5:** The structures of some typical metal salen and salophen complexes.
- Figure 1.6:** The structures of some typical dinuclear catalysts.
- Figure 1.7:** Proposed mechanism for the formation of copoly(ester-*b*-carbonate), as reported by Coates and co-workers.
- Figure 1.8:** Illustration of the combined ROCOP and ROP reactions, using a single catalyst as reported by Williams and co-workers.
- Figure 1.9:** (a) Ring-opening copolymerization of maleic anhydride with propylene oxide; (b) isomerization of poly(maleic anhydride-*co*-propylene oxide) catalyzed by morpholine.
- Figure 1.10:** The formation of stereocomplex poly(propylene succinate) by co-crystallisation of poly(*(S)*-propylene succinate) and poly(*(R)*-propylene succinate).
- Figure 1.11:** The synthesis of the thermo-response polyesters prepared by ROCOP. Reagents and Conditions: (a) $\text{Al}(\text{O}^i\text{Pr})_3$.
- Figure 1.12:** Using terpenes to make renewable TPEs.
- Figure 1.13:** Structures of the monomers (AMMS and myrcene) and representative triblock polymer.
- Figure 1.14:** Production of a semi-renewable network material using recycled polystyrene.
- Figure 1.15:** Synthetic route of soybean oil derived monomers, soybean oil methacrylate (SBMA) and soybean oil acrylate (SBA) monomers.
- Figure 1.16:** (A) The biosynthetic pathway of $\beta\text{M}\delta\text{VL}$. (B) Synthesis of $\beta\text{M}\delta\text{VL}$ from

mevalonate. (C) TPE comprises β M δ VL.

Figure 1.17: Schematic illustration of cellulose based graft copolymers.

Figure 1.18: Common morphologies of self-assembled amphiphilic block copolymers: spherical micelles, cylindrical micelles and vesicles (also known as polymersomes).

Table 1.1: Comparison of mechanical properties of various bio-derived oxygenated polymers.

Table 1.2: The thermal properties of some representative ROCOP polyesters described in section 1.6.1.

Table 1.3: Mechanical properties of known TPEs.

Scheme 1.1: The immortal ring-opening polymerization of ϵ -caprolactone, initiated by a di-zinc complex and different diol chain transfer agents.

Scheme 1.2: (A) Diagram illustrating the chemoselective sequence controlled polymerization; (B) Reactions corresponding to the steps illustrated in (A).

Scheme 1.3: Preparation of sustainable thermoplastic elastomer using $\{PDL_m\text{-}b\text{-}PCHPE_n\text{-}b\text{-}PDL_m\}_y$ multi-block copolyesters.

Scheme 1.4: Schematic illustration of the proposed preparation of amphiphilic block copolyesters, PCL-*b*-P(SA-*alt*-ME₃MO), and the self-assembly procedure.

Chapter 2

Figure 2.1: The molecular weights (MWs) for different PCL samples (entry 1-4 in Table 2.1, obtained by SEC using polystyrene calibration), and the molecular weight can be controlled by tuning the molar ratio of $[\epsilon\text{-CL}]/[\text{CHD}]$.

Figure 2.2: A representative MALDI-ToF spectrum of the PCL synthesized with CHD as the CTA (Table 2.1, entry 2).

Figure 2.3: (A) Schematic diagram showing the two PCL architectures (Type I & II) using cyclohexane diol (CHD) as the CTA; (B) Typical ^1H - ^{13}C HSQC NMR spectrum of PCL₃₀ (Table 2.1, entry 1) and (C) Enlarged HSQC NMR spectrum (Y axis: ^{13}C DEPT 135°) corresponding to the selected area in (B) and showing the correlation between the ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR signals for each of the junction/end groups (A).

Figure 2.4: ^1H - ^1H COSY spectrum of PCL₃₀ (Table 2.1, entry 1) containing chains of architecture Type II (the signal at 3.95 ppm is assigned to methylene protons

in the polymer backbone).

Figure 2.5: ^1H NMR spectra of PCL in CDCl_3 with (upper) or without (below) D_2O addition.

Figure 2.6: (A) Schematic diagram illustrating the reaction between the polymer end groups and 2-chloro-4,4,5,5-tetramethyl dioxaphospholane, used for the determination of the end groups; (B) ^{31}P NMR spectrum of PCL_{30} (Table 2.1, entry 1) after reacted with 2-chloro-4,4,5,5-tetramethyl dioxaphospholane (Bisphenol A was used as an internal standard).

Figure 2.7: ^1H NMR spectrum of PCL_{70} (see Table 2.3, entry 3).

Figure 2.8: ^1H NMR spectrum of PCL polymerized using ethylene glycol (EG) as the chain transfer agent (Table 2.1, entry 6).

Figure 2.9: (A) ^1H NMR spectra of both PEG and PEG-*b*-PCL (Table 2.1, entry 8), the polymerization was run in neat cyclohexene oxide as the reaction solvent at 80 °C, for 2.5 hours; (B) $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of PEG, PEG-*b*-PCL (Table 2.1, entry 8) and a mixture of PEG/ PEG-*b*-PCL after reaction with 2-chloro-4,4,5,5-tetramethyl dioxaphospholane (using bisphenol A as an internal standard).

Figure 2.10: ^1H - ^1H COSY spectrum of PEG-*b*-PCL (Table 2.1, entry 8).

Figure 2.11: Typical plot of monomer conversion vs. time for the ROP of ϵ -CL in neat CHO at 80 °C catalyzed by bimetallic zinc catalyst.

Figure 2.12: Curve-fitting at low monomer conversion (initiation stage, monomer conversion < 25%) catalyzed by bimetallic zinc catalyst using the kinetic model developed by Wang *et al.*

Figure 2.13: ^1H NMR spectrum of PCL_{30} (PD as CTA, see Table 2.1, entry 7).

Figure 2.14: MALDI-ToF spectrum of the PCL synthesized with 1,2-propane diol as CTA (Table 2.1, entry 7).

Figure 2.15: (A) A schematic diagram of the two architectures (Type I & II) of PCL formed using 1,2-propanediol as the CTA; (B) A typical ^1H - ^1H COSY spectrum of the PCL (PD as CTA) and (C) An enlarged ^1H - ^1H COSY spectrum corresponding to the selected area in (B) and the correlative hydrogens in (A).

Figure 2.16: (A) A schematic diagram of the two architectures (Type I & II) of PCL formed using 2-methyl-1,3-propanediol (MPD) as the CTA (Table 2.1, entry

9); (B) A typical ^1H - ^1H COSY spectrum of the PCL (MPD as CTA) and (C) An enlarged ^1H - ^1H COSY spectrum corresponding to the selected area in (B) and the correlative hydrogen in (A).

- Table 2.1:** The immortal ROP of ϵ -CL, at different molar ratios, using trans cyclohexane diol (CHD), ethylene glycol (EG), 1,2-propanediol (PD), poly(ethylene glycol) (PEG) and 2-methyl-1,3-propanediol (MPD) as the chain transfer agents.
- Table 2.2:** The normalized integrals of peaks a and b in PCL₇₀.
- Table 2.3:** The relative contents of Type I and II in PCL synthesized with various chain transfer agents.
- Table 2.4:** The relative contents of Type I and II chains present in a sample of PCL₉₀ over time
- Table 2.5:** The immortal ROP of ϵ -CL using mono-functional alcohols as the chain transfer agents.
- Table 2.6:** The normalized integrals of peaks c, f and i, in PCL₃₀ (PD as CTA).
- Scheme 2.1:** The immortal ring-opening polymerization of ϵ -caprolactone, initiated by a di-zinc complex and different diol chain transfer agents.
- Scheme 2.2:** The schematic diagram illustrating the process of the in situ catalyst formation and the initiation, propagation and exchange reactions.

Chapter 3

- Figure 3.1:** Scheme of the ring-opening copolymerization (ROCOP) of the PCHPE catalyzed by di-zinc acetate catalyst.
- Figure 3.2:** ^1H NMR spectrum of PCHPE in CDCl_3 .
- Figure 3.3:** 2D HSQC NMR spectrum of PCHPE in CDCl_3 .
- Figure 3.4:** ^1H NMR spectra of (A) a mixture of PCHPE and poly(cyclohexene oxide), (B) poly(cyclohexene oxide) and (C) PCHPE in $\text{DMSO}-d_6$.
- Figure 3.5:** Typical ^1H NMR DOSY spectrum of PCHPE-*b*-PCL prepared using the sequential method.
- Figure 3.6:** Time-resolved ATR-IR spectra showing the formation of polymer (PCHPE & PCL) and the consumption of monomers (PA & ϵ -CL).
- Figure 3.7:** Typical ^1H NMR DOSY spectrum of PCHPE-*b*-PCL prepared from the mixed monomer feedstock method.

- Figure 3.8:** The $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the PCHPE-*b*-PCL copolyester.
- Figure 3.9:** SEC traces of PCHPE-*b*-PCL and PCHPE block.
- Figure 3.10:** ^1H NMR spectra of PCHPE homopolymer and PCHPE-*b*-PCL block copolyesters.
- Figure 3.11:** Preparation of di-zinc phenyl complex, $[\text{LZn}_2(\text{Ph})_2]$, in THF using ZnPh_2 as the precursor.
- Figure 3.12:** The *in situ* catalyst forming reaction between $[\text{LZn}_2(\text{Ph})_2]$ and cyclohexanediol (used as CTAs).
- Figure 3.13:** The ROCOP and ROP reactions catalyzed by $[\text{LZn}_2(\text{Ph})_2]$, where CHD is 1,2-cyclohexanediol.
- Figure 3.14:** ^1H NMR spectrum of PCHPE homopolymer. No signal appears at 3.6 ppm, indicating no ether linkages.
- Figure 3.15:** Plots showing the molecular weight of PCHPE.
- Figure 3.16:** The MALDI-ToF spectrum of the polyester (**Table 3.5**, entry 2).
- Figure 3.17:** The MALDI-ToF spectrum of the polyester (**Table 3.6**, entry 5).
- Figure 3.18:** Plots showing the fit between molecular weight of PDL.
- Figure 3.19:** Representative ATR-IR spectrum acquired during (PDL-*b*-PCHPE-*b*-PDL) formation (**Table 3.7**, entry 2).
- Figure 3.20:** ^1H NMR spectrum of the aliquot taken before the complete conversion of phthalic anhydride (ca. 73 mol%).
- Figure 3.21:** The SEC traces of the polymer aliquots before and after propagation of the PDL block (**Table 3.7**, entry 3).
- Figure 3.22** $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of PCHPE, PDL-*b*-PCHPE-*b*-PDL (**Table 3.7**, entry 4) after reaction with 2-chloro-4,4,5,5-tetramethyl dioxaphospholane (using bisphenol A as an internal standard), in CDCl_3 .
- Figure 3.23** ^1H NMR DOSY spectra of (A) PDL-*b*-PCHPE-*b*-PDL (**Table 3.7**, entry 3) and (B) a blend of PCHPE/PDL homopolymers with the similar chain length as the blocks in PDL-*b*-PCHPE-*b*-PDL, respectively, in toluene- d_8 .
- Figure 3.24** The typical $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the PDL-*b*-PCHPE-*b*-PDL copolyester. Inset: magnified region of the carbonyl signals from both the PCHPE and PDL blocks.
- Figure 3.25** The SEC traces of the polymer aliquots of multi-block polyesters (**Table 3.9**).
- Figure 3.26** The $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the (A) PCHPE-*b*-PDL heptablock

copolyester (**Table 3.9**, entry 4).

Figure 3.27 ^1H NMR DOSY spectrum of PCHPE-*b*-PDL heptablock copolyester (**Table 3.9**, entry 4) in toluene- d_8 .

Figure 3.28 DSC thermograms (*exothermal up*) of (A) PDL-*b*-PCHPE-*b*-PDL (**Table 3.7**, entry 3 with 42 wt% of PCHPE) and (B) PCHPE/PDL blend (**Table 3.7**, entry 1 and 6, composition: 1/1, m/m).

Figure 3.29 Epoxide and cyclic esters used in this section.

Figure 3.30 ^1H NMR spectrum of the aliquot taken before the complete conversion of phthalic anhydride (ca. 66 mol%) during the polymerization of PA/CHO/ δ -VL.

Figure 3.31 (A) The SEC traces of the copolyesters prepared from PA/vCHO/ ϵ -DL, before and after the polymerization of the cyclic ester, ϵ -DL (**Table 3.10**, entry 1). (B) The corresponding ^1H NMR DOSY spectrum of the PA/vCHO/ ϵ -DL block copolyester, in toluene- d_8 . (C) The corresponding $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the PA/vCHO/ ϵ -DL block copolyester, in CDCl_3 .

Figure 3.32 (A) The SEC traces of the copolyester prepared from PA/CHO/*rac*-LA, before and after the polymerization of the cyclic ester, *rac*-LA (**Table 3.10**, entry 2). (B) The corresponding ^1H NMR DOSY spectrum of the PA/CHO/*rac*-LA block copolyester, in toluene- d_8 . (C) The corresponding $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the PA/CHO/*rac*-LA block copolyester, in CDCl_3 .

Figure 3.33 (A) The SEC traces of the copolyester prepared from PA/CHO/ δ -VL, before and after the polymerization of the cyclic ester, δ -VL (**Table 3.10**, entry 3). (B) The corresponding ^1H NMR DOSY spectrum of the PA/CHO/ δ -VL block copolyester, in toluene- d_8 . (C) The corresponding $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the PA/CHO/ δ -VL block copolyester, in CDCl_3 .

Figure 3.34 (A) The SEC traces of copolyester prepared from PA/vCHO/ δ -VL, before and after the polymerization of the cyclic ester, δ -VL (**Table 3.10**, entry 4). (B) The corresponding ^1H NMR DOSY spectrum of the PA/vCHO/ δ -VL block copolyester, in toluene- d_8 . (C) The corresponding $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the PA/vCHO/ δ -VL block copolyester, in CDCl_3 .

Table 3.1: The M_n of various PCHPE samples.

Table 3.2 The sequential addition synthesis of PCHPE-*b*-PCL using different monomer ratio.

Table 3.3	The synthesis of PCHPE- <i>b</i> -PCL from a mixed monomer feedstock of PA and ϵ -CL.
Table 3.4	Preparation of PDL- <i>b</i> -PCHPE- <i>b</i> -PDL using the di-zinc acetate complex, $[\text{LZn}_2(\text{OAc})_2]$.
Table 3.5	The ROCOP of phthalic anhydride and cyclohexene oxide, using $[\text{LZn}_2(\text{Ph})_2]$ and cyclohexane diol.
Table 3.6	The ROP of ϵ -decalactone, using $[\text{LZn}_2(\text{Ph})_2]$ and cyclohexanediol.
Table 3.7	Sequence controlled block copolyester syntheses.
Table 3.8	Ring-opening polymerization of ϵ -DL using $[\text{LZn}_2(\text{OAc})_2]$.
Table 3.9	Molecular weight of block copolyesters with different block numbers.
Table 3.10	Block copolyesters prepared using other epoxides and cyclic esters: 4-vinyl-1-cyclohexene 1,2-epoxide (vCHO), <i>rac</i> -lactide (<i>rac</i> -LA) and δ -valerolactone (δ -VL).
Scheme 3.1	General idea of the chemoselective sequence controlled polymerization method and typical block copolyesters investigated in this chapter
Scheme 3.2	(A) Diagram illustrating the chemoselective sequence controlled polymerization; (B) Reactions corresponding to the steps illustrated in (A).
Scheme 3.3	Reactions proposed to occur during sequence-selective polymerizations.

Chapter 4

Figure 4.1:	Synthetic route of $\{\text{PDL}_m\text{-}b\text{-PCHPE}_n\text{-}b\text{-PDL}_m\}_y$ multi-block copolyesters.
Figure 4.2:	SAXS profiles of PDL- <i>b</i> -PCHPE- <i>b</i> -PDL multiblock copolyesters.
Figure 4.3:	TEM images of PCHPE- <i>b</i> -PDL multi-block samples sectioned by ultramicrotome and stained with RuO_4 .
Figure 4.4:	(A) Stress-strain curves of the multi-block copolyesters (#1~4 in Table 4.1). (B) hysteresis study on the multi-block polyester with 26 wt% of PCHPE (6 cycles from 0% to 200% strain at the velocity of 10 mm/min, showing excellent elasticity.
Figure 4.5:	Strain stress curves and schematic illustration of the plastic-to-rubber transition observed in PCHPE- <i>b</i> -PDL 42 wt%, confirming the bicontinuous phase separation morphology.
Figure 4.6:	Thermal induced shape memory effect of PCHPE- <i>b</i> -PDL 59 wt% multiblock (#4 in Table 4.1).

- Figure 4.7:** DSC analysis of pre-stretched PCHPE-*b*-PDL multiblock with 59 wt% of PCHPE (#4 in **Table 4.1**).
- Figure 4.8:** Images of the uniaxial reversible shape memory effect of PCHPE-*b*-PDL 59 wt% multiblock (#4 in **Table 4.1**).
- Figure 4.9:** SAXS profiles of PCHPE-*b*-PDL 59 wt% multi-block (#4 in **Table 4.1**) with different fixed strain value.
- Figure 4.10:** TGA profile of the multiblocks with different PCHPE content.
- Figure 4.11:** Overlay of the storage modulus E' , loss modulus E'' and $\tan(\delta)$ of the multi-block copolyesters with (A) 26 wt% of PCHPE, (B) 42 wt% of PCHPE, (C) 49 wt% of PCHPE and (D) 59 wt% of PCHPE
- Table 4.1:** Characterization data for the block copolyester materials.
- Table 4.2** Mechanical properties of the multi-block copolyesters as a function of the different block compositions.
- Table 4.3** Mechanical properties of the multi-block copolyesters with different compositions, at ambient temperature (22 °C) measured *via* DMTA.

Chapter 5

- Figure 5.1** ^1H NMR data of the hydrophilic epoxide monomer, ME_3MO .
- Figure 5.2** Typical ^1H NMR spectrum of (A) PCL-OH macroinitiator (**Table 5.1**, entry 1) and (B) PCL-*b*-P(SA-*alt*- ME_3MO) (**Table 5.1**, entry 3).
- Figure 5.3** SEC traces of PCL-*b*-P(SA-*alt*- ME_3MO), corresponding to polymers listed in **Table 5.1**.
- Figure 5.4** A representative ^1H NMR DOSY spectrum of PCL-*b*-P(SA-*alt*- ME_3MO) in toluene- d_8 . (**Table 5.1**, entry 5).
- Figure 5.5** (A) A typical $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum in CDCl_3 of (a) PCL-OH (**Table 5.1**, entry 1) and (b) PCL-*b*-P(SA-*alt*- ME_3MO) (**Table 5.1**, entry 5) after being reacted with 2-chloro-4,4,5,5-tetramethyl dioxaphospholane (using bisphenol A as internal reference); (B) the enlarged $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum corresponding to the highlighted area in (A).
- Figure 5.6** Dynamic light scattering analyses of PCL-*b*-P(SA-*alt*- ME_3MO) self-assemblies.
- Figure 5.7** (A) Cumulant fit and (B) Correlation functions of DLS studies of the self-assemblies.

- Figure 5.8** TEM images of representative block copolymer self-assemblies.
- Figure 5.9** Lipase catalyzed biodegradation of polyester vesicles monitored by DLS.
- Figure 5.10** SEC traces of the biodegradation products during block copolyester reacting with lipase.
- Figure 5.11** The fluorescence spectrum (A) and calibration curve (B) of DOX•HCl in PBS solution (10.0 mM, pH 7.4).
- Figure 5.12** Cumulative drug release profiles of DOX-loaded copolyesters vesicles at 37 °C in PBS buffer (10.0 mM, pH 7.4).
- Figure 5.13** Cell viability tests using 3 different cell lines, including cancer cells, FaDu and HeLa, and normal cells, HDF and quantified by an MTT assay.
- Figure 5.14** Cytotoxicity tests quantified by the cell counting method, using HDF cells treated with the degradation products, micelles, and polymersomes, respectively.
- Figure 5.15** Confocal microscopy images of the nuclear translocation process observed for Nf-kB in HDF cells treated with degradation products, micelles, and polymersomes, respectively for 48 hours.
- Table 5.1** Synthesis of the amphiphilic block copolyesters with different compositions.
- Table 5.2** DLS analysis of the self-assemblies of the block copolyesters, prepared as per Table 5.1.
- Table 5.3** Molecular weights and dispersities of the block copolyesters during biodegradation experiments.
- Table 5.4** Signal overlap values for the nucleus and Nf-kB in control cells and cells treated with degradation products, micelles, and polymersomes, respectively.
- Scheme 5.1** Schematic illustration of the proposed preparation of amphiphilic block copolyesters, PCL-*b*-P(SA-*alt*-ME₃MO), and the self-assembly procedure.
- Scheme 5.2** Synthetic route of the hydrophilic epoxide monomer.

Chapter 6

- Figure 6.1** The structures of some typical metal-salen and metal-porphyrin complexes.
- Figure 6.2** Potential monomers which can be used to make block copolyesters *via* chemoselective polymerization method.
- Figure 6.3** Schematic illustration of the synthesis, post-polymerization modification and degradation of metabolite polymers.

- Figure 6.4** Proposed post-polymerization modification routes to afford metabolite polymers with various functionalities.
- Figure 6.5** Proposed route to afford metabolite polymers with the neighbouring dual functionality.
- Scheme 6.1** Copolyesters with sequence controlled architecture for information coding.

Chapter 7

- Figure 7.1** ^1H NMR spectrum of 4-tert-butyl-2,6-diformylphenol in CDCl_3 .
- Figure 7.2** ^1H NMR spectrum of $[\text{H}_4\text{L}^{1'}](\text{ClO}_4^-)_2$ in $\text{DMSO}-d_6$.
- Figure 7.3** ^1H NMR spectrum of $[\text{H}_2\text{L}^1]$ in CDCl_3 .
- Figure 7.4** ^1H NMR spectrum of $[\text{L}^1\text{Zn}_2(\text{OAc})_2]$ in toluene- d_8 at 110 °C.
- Figure 7.5** The formation of the zinc alkoxide intermediate.
- Figure 7.6** Synthetic route of PCL in the presence of chain transfer agent, CHD.
- Figure 7.7** Synthesis of PCHPE-*b*-PCL *via* the sequential method.
- Figure 7.8** Synthetic route to PCHPE.
- Figure 7.9** Synthesis of PCHPE-*b*-PDL using a mixed monomer feedstock.
- Figure 7.10** Synthesis of the hydrophilic epoxide monomer, ME_3MO .
- Figure 7.11** Ring-opening polymerization of $\epsilon\text{-CL}$, in toluene, using TBD as the catalyst and 1-hexanol as the chain transfer agent.
- Figure 7.12** Ring-opening copolymerization of SA and ME_3MO , in toluene, using a $[\text{SalenCrCl}]/\text{PPNCl}$ catalyst system and monofunctional PCL as macroinitiator.
- Scheme 7.1** Synthetic route of bimetallic zinc catalyst $[\text{L}^1\text{Zn}_2(\text{OAc})_2]$.

Appendices

- Figure A1** SEC traces of PCHPE-*b*-PCL and PCHPE.
- Figure A2** Plots of differential refractive index against the concentration of the alternating polyester (PCHPE) in THF at 25 °C.
- Figure A3** ^1H NMR spectrum of PDL homopolymer (Table 3.6, entry 5) in CDCl_3 .
- Figure A4** Plots (Table 3.6, entry 2) of the differential refractive index against the concentration of the polyester, poly(decalone) (PDL) in THF at 25 °C.
- Figure A5** The thermoresponsive behavior monitored by the change in zeta potential at

different temperature.

Figure A6 The chemical structure of the di-zinc complex with acetate co-ligand.

Figure A7 ^1H NMR spectrum of $[\text{LZn}_2(\text{Ph})_2]$ in $\text{TCE-}d_2$ at 403 K.

Figure A8 $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of $[\text{LZn}_2(\text{Ph})_2]$ in $\text{TCE-}d_2$ at 403 K.

Figure A9 $^1\text{H-}^{13}\text{C}$ HSQC spectrum of $[\text{LZn}_2(\text{Ph})_2]$ in $\text{TCE-}d_2$ at 403 K.

Table of contents

Chapter 1 Introduction	1
1.1 Fossil Fuel Depletion	2
1.2 Sustainable Polymers	2
1.3 Biorenewable Oxygenated Polymers: Polyesters and Polycarbonates	4
1.4 Catalysts development for Ring-Opening Copolymerization	7
1.4.1 Polymerization Pathway	7
1.4.2 Early Catalyst Discoveries	8
1.4.3 Well-Defined Metal Catalysts	9
1.4.4 Major classes of well-defined catalysts	9
1.5 Using Catalysis Ring-opening (Co)polymerization to make block copolymers	14
1.5.1 ROCOP Terpolymerizations	14
1.5.2 Combining ROCOP and ROP: Switch Catalysis and Tandem Methods	16
1.6 ROCOP: Polyester Properties	17
1.6.1 Thermal Properties	18
1.6.2 Amphiphilic Polyesters	22
1.6.3 Mechanical Properties	23
1.7 Renewable Thermoplastic Elastomers	24
1.8 Potential Application as Biomedical Materials	30
1.8.1 Polymeric Self-assemblies	30
1.8.2 Preparation Methods	31
1.8.3 Current Development of Polymer Vesicles	34
1.8.4 Future Challenges in Developing Polymeric Self-assembled Structures	35
1.9 Outlook	36
1.10 Aims and Objectives	37
1.11 References	41
Chapter 2 The Influences of a Di-zinc Catalyst and Bifunctional Chain Transfer Agents on the Polymer Chain End in the Ring-Opening Polymerization of ϵ -Caprolactone	51
2.1 Background and Aims	52
2.2 Results and Discussion	53
2.2.1 General Mechanism of the Ring-Opening Polymerization Catalyzed by Di-zinc bis(acetate) Complex with the Presence of Chain Transfer Agents	54
2.2.2 Ring-Opening Polymerization of ϵ -CL using Di-zinc bis(acetate) Complex with CHD as the Diol Chain Transfer Agent	57
2.2.3 Probing into the True Structure of the Obtained PCL with Both Chain Ends Functionalized	59
2.2.4 Calculation of the Relative Content of Type I and Type II in Different PCL Samples	65

2.2.5 Monitoring the Relative Quantities of Type I and Type II During the ROP of ϵ -CL	68
2.2.6 Investigation of the PCL Structure Using Different Types of Diol Chain Transfer Agent.....	69
2.2.7 How Kinetics Affect the Nature of the Polymer Chain End Groups.....	72
2.3 Conclusions.....	82
2.4 References.....	83
Chapter 3 Selective Polymerization Catalysis: Controlling the Metal Chain End Group to Prepare Block Copolyesters.....	86
3.1 Background and Aims.....	87
3.2 Results and Discussion	88
3.2.1 The ROCOP of Epoxide and Anhydride	88
3.2.2 Synthesis of PCHPE- <i>b</i> -PCL	93
3.2.3 Synthesis of PCHPE- <i>b</i> -PDL Block Copolymers	102
3.3 Conclusions.....	127
3.4 References.....	129
Chapter 4 Renewable and Degradable Multiblock Polyesters with Tunable Elasticity or as Shape Memory Materials.....	131
4.1 Background and Aims.....	132
4.2 Results and Discussion	134
4.2.1 Chain Extension Reaction of PDL- <i>b</i> -PCHPE- <i>b</i> -PDL Triblock Copolyesters.....	134
4.2.2 Microphase Separation of the PDL- <i>b</i> -PCHPE- <i>b</i> -PDL Multiblocks	136
4.2.3 Multiblocks Exhibiting Thermoplastic Elastomeric Properties.....	140
4.2.4 Multiblocks Exhibiting Shape Memory Effects	144
4.2.5 Thermal Stability and Thermo Mechanical Properties of the Multiblocks.....	150
4.3 Conclusions.....	153
4.4 References.....	155
Chapter 5 Non-toxic and Degradable Amphiphilic Polyesters for Drug Delivery Applications	158
5.1 Background and Aims.....	159
5.2 Results and Discussion	161
5.2.1 Synthesis of the Hydrophilic Epoxide Monomer.....	161
5.2.2 Preparation of the Amphiphilic Block Copolyesters with Different Block Ratios	162
5.2.3 Characterization of the Block Copolymer Architecture	166
5.2.4 Investigation of the Self-assembly of the Amphiphilic Block Copolyesters.....	169
5.2.5 TEM Characterization of the Self-assembled Block Copolyesters.....	171
5.2.6 Thermal Stability of the Vesicles.....	173

5.2.7 <i>In vitro</i> Lipase Catalyzed Biodegradation of the Polyester Vesicles.....	174
5.2.8 Model Drug Release Experiments	176
5.2.9 Cytotoxicity Tests	178
5.3 Conclusions.....	184
5.4 References.....	185
Chapter 6 Conclusions	188
6.1 Overviews	189
6.2 Conclusions.....	190
6.3 Future Outlook.....	193
6.4 References.....	197
Chapter 7 Experimental	Error! Bookmark not defined.
7.1 General Procedures	199
7.1.1 Materials	199
7.1.2 Syntheses of Polymers and Catalysts.....	200
7.2 References.....	222
Chapter 8 Characterization Techniques	223
8.1 Techniques and methods.....	224
8.2 References.....	241
Appendices.....	243
Appendix A – Data	244
Appendix B – Permissions	252

Chapter 1

Introduction

1.1 Fossil Fuel Depletion

Fossil oil, including crude oil, coal and natural gas, is the foundation of both the economy and modern life.¹ Besides being used as a fuel, it is also the major source of chemicals, both commodity and specialty.² According to the peak oil theory, the extraction of petroleum will reach the maximum rate, followed by a terminal decline.³ Although many attempts have been made to predict the timing of the peak oil, it is still open to debate.³ However, it is accepted that fossil oil is not an infinite resource, considering that it requires millions of years to form and it is likely to become depleted in the future.⁴ Moreover, its usage leads to problems of pollution. Therefore, it is of particular value to start developing alternative resources for preparing chemicals prior to the peak, to avoid serious economic and social consequences.

1.2 Sustainable Polymers

By definition, sustainability is ‘meeting the needs of the present without compromising the ability of future generations to meet their needs.’⁵ Therefore, a sustainable polymer should be able to meet the needs of the consumers and not harmful to the environment, economy and the health of human beings. The raw materials for sustainable polymers should be renewable, for example being sourced from plants. Compared to the production of non-sustainable polymers, the production of sustainable polymers should use less non-renewable energy and net water, with less emission of greenhouse gases and smaller carbon footprint.⁶ Moreover, the sustainable polymer should also be economically viable. It is noteworthy that the measurement of sustainability requires complete life cycle assessment which is out of the scope of this thesis. Therefore, only biorenewable polymers are discussed in this thesis, these can be defined as a resource which can be reproduced to overcome usage and consumption, through naturally recurring processes within a short period of time; though the goal is to achieve sustainability.⁵

Currently, the polymer industry relies heavily on fossil oil resources and so will suffer the effects of reduced supply and increased price of the fossil oil resources in the future. Modern life relies on polymers, from the materials in our clothing, houses, cars, and airplanes through to applications in medicine, diagnostics and electronics. Many polymers also contribute significantly to a better quality of life and environment, for example as materials enabling water purification or as improved fuel-economy polymer composites in aerospace.^{7,8} Even though only ~6% of worldwide oil production is used to produce polymers, there are environmental concerns associated with both the raw materials used to make them⁹ and end-of-life options.¹⁰ There are also economical concerns associated with the cost of

transportation.⁹ Whilst there is no panacea to these complex environmental problems, one option is to develop more ‘sustainable’ polymers. Research activities have primarily focused on both replacement of fossil raw materials with renewable alternatives, the products being known as bioderived polymers, and on end-of-life options, including materials suitable for recycling or (bio)degradation. It is worth pointing out that bioderived polymers are not necessarily sustainable polymers because using renewable raw materials to make polymers only partly fits the definition of sustainable polymers. Also, it is important to note that simply because a material is bioderived does not guarantee its biodegradation, and that a few polymers derived from petrochemicals are biodegradable.¹¹ The potential for sustainable polymers is stimulated by recent policy, legislation and international agreements, such as Paris COP21.¹² Nonetheless, any commercial application of bioderived polymers may benefit from improved environmental performance (as well as supporting policy or legislation) but it will require favourable economics and equivalent or better material properties, including features such as thermal resistance, mechanical strength, processibility and compatibility.

Taken together, these are tough criteria and may explain in part why there are currently rather few commercially successful biorenewable polymers. To quantify this, in 2014, for an annual polymer production of over 300 Mt, only 1.7 Mt of biorenewable polymers were produced, with the three major products, by volume, being polyethylene terephthalate (PET), polyethylene (PE) and polylactide (PLA).¹³ There are generally two approaches to preparing more ‘sustainable’ polymers: 1) to improve the environmental impacts of current monomer and polymer production, for example by using biomass to make known monomers/polymers, such as the PET or PE or 2) to prepare new ‘sustainable’ material structures, such as oxygenated polymers derived from renewable raw materials like PLA. Polyesters and polycarbonates are amongst the most widely applied oxygenated polymers.¹⁴ The majority of commercial materials are prepared by condensation polymerizations and include well-known polymers such as poly(ethylene terephthalate) (PET) and polycarbonate (PC) (from bisphenol A). These oxygenated polymers are important commodity materials with good thermal (e.g. T_g of PET is ca. 70 °C and T_g of PC is ca. 145 °C, for commercialized products), mechanical properties (e.g. the tensile strength and elongation at break value of PET are 55-75 MPa and 50-150%, respectively; the tensile strength and elongation at break value of PC are 55-75 MPa and 80-150%, respectively)¹⁵⁻¹⁷ and have been widely applied in packaging, fibres, rigid plastics and engineering materials.¹⁴ Therefore, it is of great value to develop new renewable oxygenated polymers to replace the petrochemical derived analogues. It is noteworthy that

the development of renewable olefin monomers is also of great value due to huge demand of polyolefin (e.g. polyethylene: 88.1 million ton/year).¹⁸ However, it is out of the scope of this thesis.

1.3 Biorenewable Oxygenated Polymers: Polyesters and Polycarbonates

One interesting oxygenated polyester, produced on a several hundred thousand tonnes/annum scale, is poly(lactic acid) (PLA) (~\$2.2/kg).¹⁹ It is attracting considerable attention as a renewable and degradable alternative polymer for packaging, fibres, medical sutures/stents and in controlled release of active compounds.²⁰⁻²³ Another promising class of polyesters are the poly(hydroxyl alkanoates) (PHAs), once again applied for both commodity and niche medical applications.²⁴⁻²⁶

Alternating polyesters and polycarbonates prepared by the ring-opening copolymerization (ROCOP) of cyclic anhydrides, epoxides and carbon dioxide are also very attractive due to the fact that many cyclic anhydrides (e.g. succinic anhydride, maleic anhydride) and epoxides (e.g. limonene oxide, methane oxide) can be acquired from biorenewable resources,²⁷ and commercialization ventures are reported to be operating at pilot scale.²⁸ The recent focus and development of ring-opening copolymerization (ROCOP) catalysts is significant because the product polyesters and polycarbonates differ considerably in backbone structure and functionality compared to those accessible by ring-opening polymerization (ROP). Most importantly, simply by changing the combination of cyclic anhydride, epoxide and CO₂, the properties of the resulting material can be easily controlled, including the thermal properties [e.g. glass transition temperature (T_g), melting temperature (T_m) and thermal decomposition temperature (T_d)] as well as properties such as the lower critical solution temperature (LCST) and UV-stability.^{26,29-32} These materials are desirable as potential substitutes for conventional petrochemical polyols. Indeed, a recent detailed life cycle analysis shows that these materials consume ~20% less petrochemical raw materials and reduce carbon dioxide emissions by approximately 20% compared to the use of conventional petrochemicals.³³

Table 1.1 Comparison of mechanical properties of various bioderived oxygenated polymers.

Bioderived oxygenated polymers	Bio-based monomers	Molecular weight (kDa)	$\bar{D}$	T_g (°C) ^a	E modulus (MPa)	Elongation at break (%)
PLA ³⁴	Lactic acids	50-500	1.8-2.6	60	2000-3000	2.4-5.2
PHA ³⁵	Hydroxyalkanoates	100-10000	1.2-6.0	-50-4	Flexible	2-1000

PPC ³⁶	CO ₂	50-360	1.7-2.8	31-41	993-6900	3-5
PET ³⁷	Bioethylene glycol	20-30	2.0-5.0	69-115	2000-2700	180
PLimC ³⁸	Limonene oxide & CO ₂	25-109	1.1-1.2	130	950	15

^{a)} T_g : glass transition temperature.

Another major focus in the field is the development of ‘controlled’ polymerizations, namely reactions where the molecular weights, molecular weight dispersities, compositions, architectures and end-group functionalities are predictable and tunable.³⁹⁻⁴⁹ Fundamentally, the interest in understanding and developing such routes started in academic study. However, such routes could be of significant value in the production of copolymers with sophisticated architectures (e.g. block, graft, stereochemistry controlled and monomer sequence controlled polymers).⁴⁰⁻⁴⁹

There are several living/controlled polymerization methods to afford polyesters and polycarbonates. According to the IUPAC definition, living polymerization is a chain polymerization from which chain transfer and chain termination are absent and in many cases, the rate of chain initiation is fast compared with the rate of chain propagation, so that the number of kinetic-chain carriers is essentially constant throughout the polymerization.⁵⁰ As a result, the growth rate of the polymer chains is more constant than that observed in the traditional chain growth polymerization, leading to very narrow molecular weight distribution.⁵⁰ Different from the living polymerization, controlled polymerization is defined as polymerization in which chain termination is merely suppressed rather than eliminated.⁵¹ An immortal polymerization also affords a polymer with a narrow molecular weight distribution and the number of polymer chains being higher than the number of initiator molecules.⁵² Instead of being an irreversible side reaction, a chain transfer reaction in an immortal polymerization is reversible and so happens faster than the chain growth, leading to narrow molecular weight distribution.⁵² Therefore, rapid exchange between the alkoxide complex and –OH is the key to immortal polymerization. The most commonly used two methods, in terms of making polyesters, are the ring-opening polymerization (ROP) of cyclic esters/carbonates^{20-23,42,53-72} and the ring-opening copolymerization (ROCOP) of epoxides, cyclic anhydrides and CO₂ (**Figure 1.1**). It is the second method which is the primary target of this thesis, although ROP is also relevant.

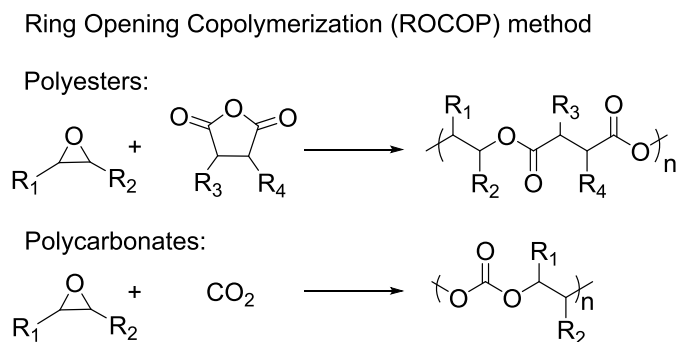


Figure 1.1 Schematic illustration of the generic reactions occurring during ring-opening copolymerization (ROCOP) prepare alternating polyesters and polycarbonates.

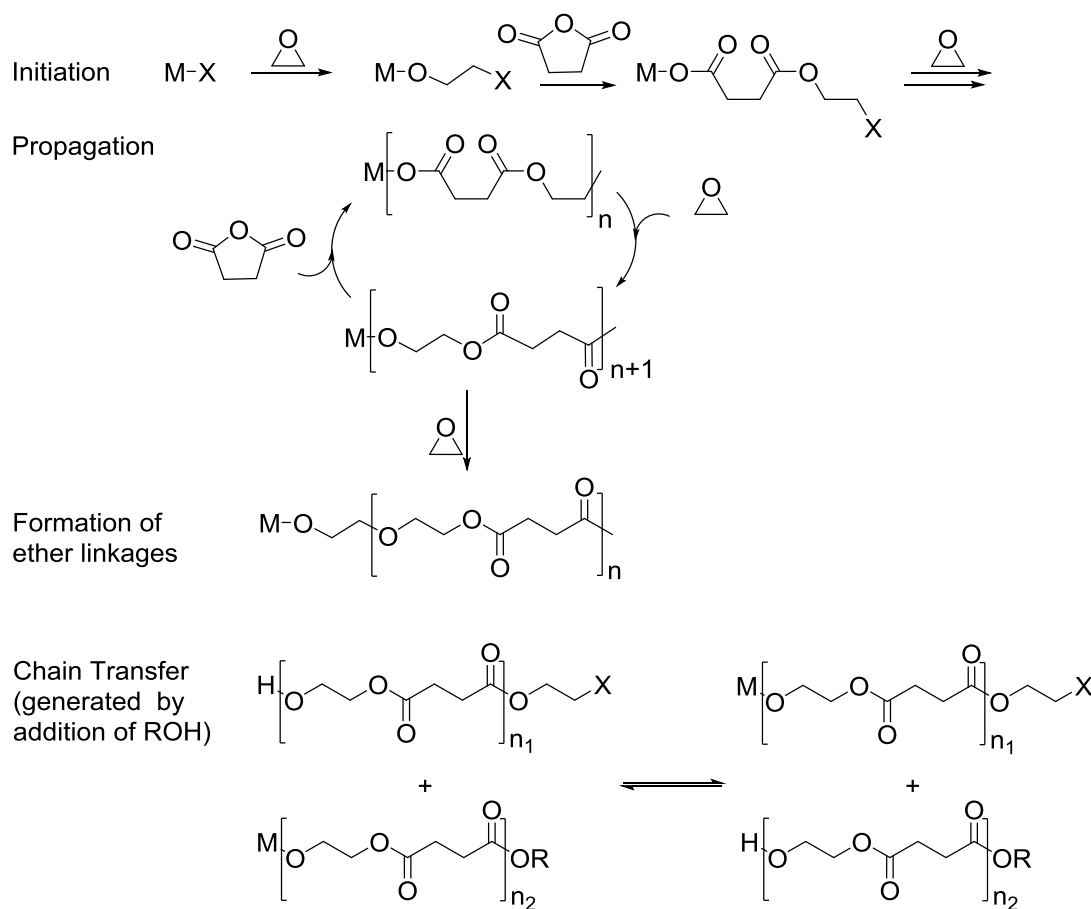
While the ROP is a well developed, controlled polymerization for many applications, it has some limitations, including the rather limited monomer pool.^{73,74} In contrast, ROCOP has received far less attention, yet has a much broader available range of monomers. Although most of the monomers for ROCOP are still derived from petrochemicals, some of them can be acquired from renewable resources.²⁷ The most attractive aspect of ROCOP is that the properties of the polymers can be easily tailored to meet the requirements of different applications. Such tuning can be achieved by changing the monomer compositions: for example, the glass transition temperatures of such polyesters/polycarbonates can be manipulated over the range from -26 °C to 123 °C,^{31,75} which is similar to the polyesters prepared *via* the ring-opening polymerization, for instance, polylactide with different substituents.⁷⁶ This facility to substitute different epoxides, using the same or similar catalysts and reaction conditions, stands in stark contrast to ROP methodologies, where changing the polymer repeat unit requires the preparation of new, functionalized lactones/cyclic carbonates.⁵⁴ It is important to emphasize that synthesizing functionalized lactones or cyclic carbonates can be complex, in terms of the need to protect certain functionalities (e.g. hydroxyl) to prevent side reactions.^{54,77} Furthermore, the addition of substituents to 6- or 7-membered rings reduces ring strain and thereby limits the thermodynamic driving force to polymerization.⁵⁴ The addition of substituents might also cause steric effect during the polymerization.⁷⁸ Another limitation of ROP is that polymers containing aromatic groups in the backbone are very hard to make.⁷⁹ ROCOP can overcome these limitations and it represents an attractive means to prepare semi-aromatic polyesters/polycarbonates.^{29,30,80-84} Addition of aromatic backbone is attractive as a means to thermal and mechanical performance: both are current limitations for aliphatic polyesters produced by ROP.^{79,85}

1.4 Catalysts development for Ring-Opening Copolymerization

Since ROCOP offers promise for the synthesis of oxygenated polymers (especially polyesters) with tuneable properties and functionalities, it is important to understand how the ROCOP reaction occurs. Most of the ROCOP processes are catalyzed by metal catalysts, with or without the addition of co-catalysts. The following section outlines the relationship between different catalyst systems for epoxide/anhydride polymerizations and evaluates their performances, in terms of the turnover frequencies (TOF), turnover number (TON), ether linkage content, polymer selectivity, co-catalysts, molecular weights of the final products.

1.4.1 Polymerization Pathway

Ring-opening copolymerization (ROCOP) requires the use of complexes which perform as both the catalysts and/or initiators. These complexes usually have the LMX structure, where L is the ligand, M is the metal centre at which catalysis occurs and X is the initiating group (**Figure 1.2**).



X= Halide, carboxylate, alkoxide; OR = alkoxide

Figure 1.2 Illustration of the elementary steps occurring during epoxide/anhydride ring-opening copolymerization (ROCOP).

Initiation involves the insertion of monomers into the MX bond to generate metal alkoxide/carboxylate intermediates. The initiating group is commonly a carboxylate, alkoxide or halide group and, during controlled polymerization, this group becomes one of the chain end groups. **Propagation** occurs as monomers are sequentially enchainned, this involves sequential formation of metal-alkoxide and carboxylate intermediates. The metal alkoxide intermediate attacks the anhydride to generate the metal carboxylate intermediate. The metal carboxylate intermediate attacks and ring-opens the epoxide co-monomer to (re-)generate the metal alkoxide. For this class of polymerizations, it is also important to consider **chain transfer reactions**. These are reactions in which the growing polymer chain equilibrates with added protic compounds, for example alcohols. The chain transfer reactions are typically assumed to occur more rapidly than propagation reactions. Addition of protic compounds can be used to control the polymer molecular weight and to control dispersity. However, if the chain transfer reactions do not occur more rapidly than propagation, the molecular weight will be less controlled and the dispersity will be broad. Other side reactions that can occur include sequential epoxide enchainment, leading to ether linkages. The **termination** of polymerization is frequently achieved by manipulating the conditions (reducing temperature, monomer removal).

1.4.2 Early Catalyst Discoveries

The first reports of the alternating copolymerization of epoxides and anhydrides were in the 1960s.⁸⁶ A range of catalyst systems including inorganic salts, tertiary amines or metal-alkyl initiators were reported.⁸⁷⁻⁹⁴ However, these copolymerizations were hampered by poor performance characteristics including low levels of polymerization control, poor activity and low molecular weight products; additionally, in some cases, the catalysts exhibited poor selectivity resulting in significant quantities of ether linkages. In the mid-1960s, Inoue *et al.*, investigated the preparation of polyesters using organometallic complexes.^{88,89,92} After that, several metal complexes, together with added alcohol or water, were applied. An important mechanistic proposal, for phthalic anhydride/cyclohexene oxide ROCOP initiated by dialkyl zinc, was that polymerization proceeded by sequential formation of zinc-carboxylate and -alkoxide species.⁹² By 1973, Heisch *et al.* investigated the terpolymerization of epoxides, oxiranes and anhydrides, initiated by tri(alkyl)aluminium complexes.⁹³ The resulting

polymers consisted of alternating ABC blocks featuring ether-ester-ester linkages. In 1980, Kuran *et al.* reported maleic anhydride/propylene oxide copolymerization, using a series of organozinc catalysts of general formula $RZnEt$ (R = alkoxide, aryloxide, carboxylate).⁹⁴ Polyesters containing only 53 mol% incorporation of propylene oxide (PO) and of low molecular weight ($M_n < 2.0$ kDa) were produced. These early discoveries set the foundation for future designing organometallic complexes to catalyze ROCOP.

1.4.3 Well-Defined Metal Catalysts

The next generation catalysts applied well-defined metal complexes, either mononuclear or binuclear complexes. The mononuclear species usually need co-catalysts, such as organic salts (ammonium, phosphonium halides), or Lewis bases [N-methylimidazole, dimethylaminopyridine (DMAP)]. The true role of the co-catalyst remains complex, but it is generally proposed that either the Lewis base or the anion coordinates to the metal catalyst, resulting in the labilizing of the initiating group, X, or the propagating polymer chain and accelerating polymerization. In addition, bimetallic or dinuclear catalysts frequently show superior performance compared to mononuclear complexes even without any co-catalysts.^{75,95-116} This is proposed to be due to an improved facility to accommodate the monomers and lower barriers for metal carboxylate or carbonate attack on bound epoxide molecules.

1.4.4 Major classes of well-defined catalysts

1.4.4.1 Metalloporphyrins

In 1985, Inoue *et al.*, reported the combination of porphyrinato aluminium complexes (**1a-b**, **Figure 1.3**) with quaternary ammonium/phosphonium co-catalysts, as catalytic systems to afford perfectly alternating polyesters with narrow molecular weight distributions ($PDI < 1.1$).^{117,118} These early works were very important contributions to the field because the catalyst undergoes living polymerization and almost no ether linkages were formed. It was also reported that the same metalloporphyrin complexes were active for both the ROCOP of epoxides/cyclic anhydrides and the ROP of cyclic esters.¹¹⁸ More recently, Duchateau *et al.* re-visited the porphyrinato catalysts and reported that chromium complex **1c**, in the presence of DMAP or N-MeIm as co-catalysts, were effective for the copolymerization of cyclohexene oxide with different anhydrides.⁸² The catalyst system exhibited high activity (bulk: TOF = 95 h^{-1} at $100\text{ }^{\circ}\text{C}$) and selectivity ($>99\%$ ester linkages). Concurrently, Chisholm and

co-workers successfully applied the same porphyrin complex (**1c**) in styrene oxide/cyclic anhydride copolymerization, using PPNCI as the co-catalyst.¹¹⁹ Other porphyrin complexes with different metal centres were also investigated by the same group, including Al(III), Cr(III), Co(III). For propylene oxide/anhydride copolymerization,¹²⁰ Cr(III) catalysts were significantly more active ($\text{TOF} = 52 \text{ h}^{-1}$) than the Co(III) and Al(III) analogues ($\text{TOF} = 19 \text{ h}^{-1}$ and 25 h^{-1} , respectively). In these porphyrin complexes, the high activity of Cr(III) complex was rationalized by the relative affinity to achieve six-coordination: $\text{Cr(III)} > \text{Al(III)} \sim \text{Co(III)}$. Metalloporphyrin complexes are excellent catalysts but to reach high TOF and low ether linkage contents, co-catalysts are needed. Furthermore, the ROP of cyclic esters catalyzed by metalloporphyrin complexes exhibited low TOF values.¹¹⁸

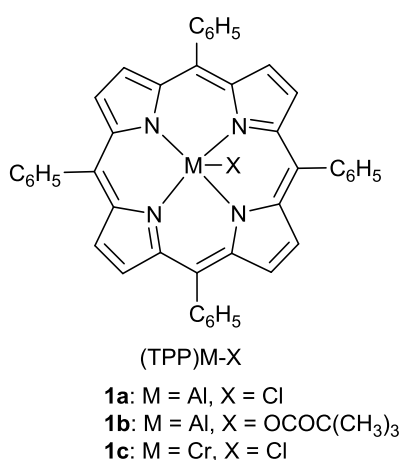


Figure 1.3 Illustration of the structures of some typical metalloporphyrin complexes.

1.4.4.2 β -Diiminate (BDI) Zinc Complexes

In 2007, Coates and co-workers reported the use of β -diiminate zinc [(BDI)Zn] catalysts (**2a-2e**, **Figure 1.4**) for the ROCOP of cyclic anhydrides/epoxides.²⁹ They were already known to be effective catalysts for a range of polymerizations, including CO₂/epoxide copolymerization,^{103-105,121} cyclic ester¹²²⁻¹²⁴ and cyclic carbonate ring-opening polymerization. The ligands' backbone and aryl substituents affected the stability and activity of the catalysts during polymerization.¹²¹ Complexes with R₃ = CN (**2b**, **2d**, **2e** in **Figure 1.4**) were among the fastest and most tolerant.²⁹ In addition, a wide range of epoxides/anhydrides were investigated, leading to a library of polyesters which showed some promising features, including relatively high degradation temperatures ($\sim 290^\circ\text{C}$) and moderate glass transition temperatures ($50\text{-}60^\circ\text{C}$). Although studies using [(BDI)Zn] complexes to catalyze the ROP of cyclic esters have already been reported by Coates and co-workers,^{122,124} the most active [(BDI)Zn] catalyst (R₃ = H) for ROP was the least effective catalyst for ROCOP of epoxides

and anhydrides.²⁹ They hypothesized that the cyclic anhydride reacts with the BDI ligand at the carbon beside R_3 and destroyed the complex.¹²⁵⁻¹²⁷ The electron withdrawing nature of the nitrile group also prevented the degradation of the ligand.

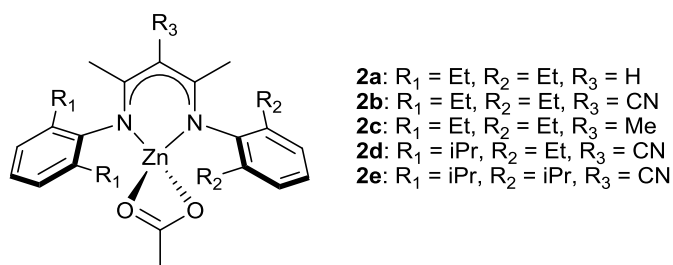


Figure 1.4 The structures of some typical β -diiminate zinc catalysts.

1.4.4.3 Metal Salen and Salan catalysts

Metal(III) salen catalysts (**Figure 1.5**) have been widely applied in CO_2 /epoxide copolymerizations.¹²⁸ Duchateau and co-workers reported the chromium salphen complex (**3a**)/DMAP system (**Figure 1.5**) for cyclohexene oxide/anhydride copolymerizations.⁸² The catalyst was ineffective without the addition of a co-catalyst. Coates and co-workers reported the successful use of cobalt and chromium salen complexes, **4a** and **4b**, for epoxides/maleic anhydride copolymerization and the catalysts were effective without any co-catalysts.³¹ Poly(propylene maleate) (PPM) of moderate molecular weight was produced ($M_n = 5,000$ g/mol; 17,000 g/mol, **4a** and **4b**, respectively). The PPM was then successfully converted to poly(propylene fumarate) PPF by controlled *cis-trans* isomerization in the presence of diethylamine. Darensbourg and co-workers found that **4b** on its own was inactive for CHO/PA copolymerization.¹²⁹ Duchateau and co-workers also reported an extensive study of metal salen/co-catalyst combinations for cyclohexene oxide/anhydride copolymerizations.¹³⁰ Chromium complexes outperformed cobalt and aluminium analogues. They also reported the ROCOP of limonene oxide/phthalic anhydride catalyzed by metal salophen complexes (**3a**, **3b**, **3c**, **3e**), to yield partially renewable polyesters.³⁰ Coates and co-workers recently discovered that by tuning the Lewis acidity of the aluminium complex (**3f**),¹³¹ side reactions (e.g. transesterification, epimerization) can be eliminated during the ROCOP of epoxides and cyclic anhydrides. Using the best aluminium complex (**3f**), the amount of PPNCl co-catalyst could be reduced to a substoichiometric level. With excess of propylene oxide, the remaining species are likely to be an aluminium alkoxide and a $[\text{PPN}]^+$ alkoxide, in equilibrium with a hexacoordinate dialkoxide aluminate, after the full

consumption of the anhydride monomer. By increasing the Lewis acidity of the aluminium complex, the equilibrium can be pushed towards the hexacoordinate dialkoxide aluminate. This strategy results in a reduced concentration of $[\text{PPN}]^+$ alkoxide which is proposed to be the highly reactive species causing the side reactions. Furthermore, aluminium salen catalysts have also shown an extensive history as catalysts for the ROP of cyclic esters.¹³²

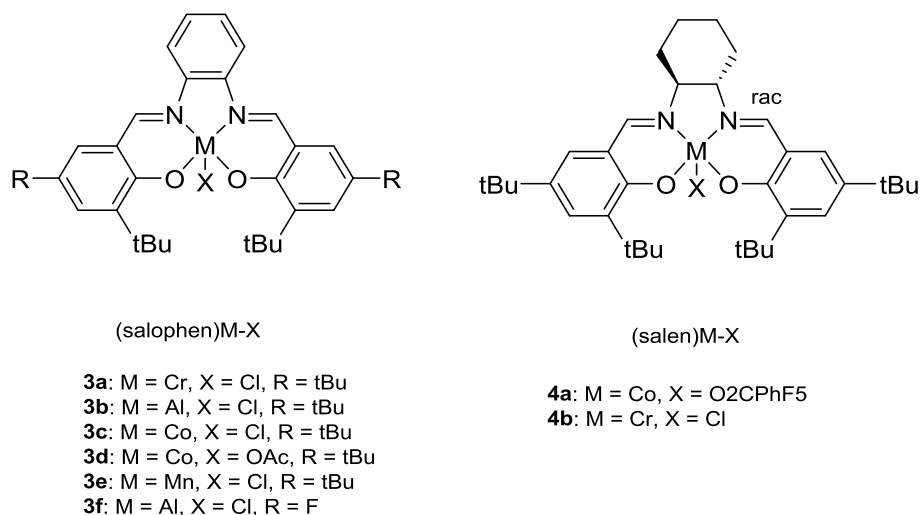


Figure 1.5 The structures of some typical metal salen and salophen complexes.

1.4.4.4 Dinuclear Catalysts

For the ROCOP of epoxides/ CO_2 , dinuclear catalysts frequently show superior performance to mononuclear analogues.^{75,95-116} This is proposed to be due to improvement in accommodating the monomers thereby reducing the barriers for metal carbonate bond attack on the coordinated epoxides. It is possible that an analogous rationale could be applied to the ROCOP of epoxides/cyclic anhydrides and therefore testing of dinuclear catalysts was the logical next step (**Figure 1.6**). Lu *et al.* found the dinuclear catalyst, **5**, was much more active than its mononuclear analogues for the ROCOP of epoxides/maleic anhydride.¹³³ Williams and co-workers also reported di-zinc and di-magnesium catalysts (**6a** and **6b**) for CO_2 /epoxide copolymerizations,^{75,95-102} which were also effective for epoxide/anhydride copolymerization.¹³⁴ The geometry of the complexes **6a** and **6b** is not conclusive and requires further investigation based on the previous research conducted by my colleagues.^{99,101,102} Therefore, the complex geometry is not displayed in **Figure 1.6**. Di-zinc complex **7**, with DMAP, as a co-catalyst was shown to selectively copolymerise cyclohexene oxide and maleic anhydride at 110 °C.¹³⁵ Recently, Nozaki and co-workers reported a dinuclear metal-corrole complex **8** (**Figure 1.6**) for the ROCOP of epoxides/anhydrides or epoxides/ CO_2 .¹⁰⁷ In the presence of a co-catalyst, $(\text{PPN})\text{OBzF}_5$, **8** showed slow activity for

propylene oxide/glutaric anhydride copolymerization ($\text{TOF} = 3 \text{ h}^{-1}$, in bulk, at 30°C), affording perfectly alternating polyesters. However, a poly(ester-*co*-ether) was formed in toluene, whereas no activity was observed in THF. Recently, a series of dinuclear zinc salen complexes were developed by Williams and co-workers, and applied in the ROCOP of epoxides, cyclic anhydrides and CO_2 . The best catalyst (**9**) shows higher activity ($\text{TOF} = 44 \text{ h}^{-1}$) for CO_2/CHO ROCOP than other dizinc salen catalyst and a better activity ($\text{TOF} = 198 \text{ h}^{-1}$) for PA/CHO ROCOP than other reported catalysts. The dizinc catalysts, developed by Williams and co-workers, (**6a**) also exhibits good activity in catalyzing the ROP of cyclic esters,¹³⁶ suggesting it might be a good candidate for the investigation of switchable catalysis.

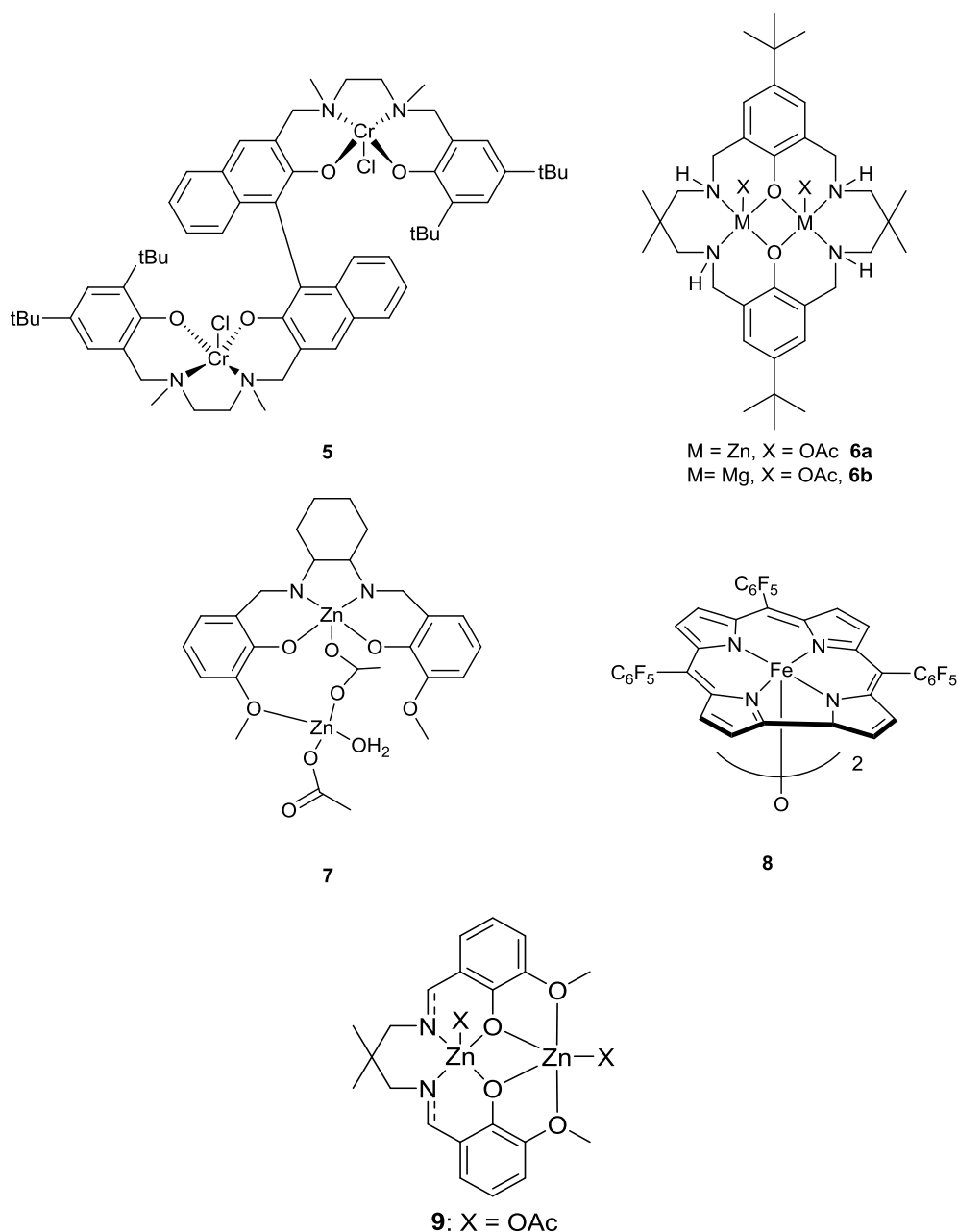


Figure 1.6 The structures of some typical dinuclear catalysts.

1.5 Using Catalysis Ring-opening (Co)polymerization to make block copolymers

Besides developing catalysts for the synthesis well-defined alternating polyesters and polycarbonates, efforts have also been made to afford block copolymers and/or polymers with more complex architectures. There has been a particular focus on the development of so-called ‘one-pot’ methods, i.e. where all monomers are combined and copolymer selectivity results from catalysts control methods.

1.5.1 ROCOP Terpolymerizations

An early example of the terpolymerizations of PO, CO₂ and MA was reported in 2006, leading to the formation of a poly(ester-carbonate).¹³⁷ In 2008, Coates and co-workers reported that the terpolymerizations of diglycolic anhydride (DGA), CO₂ and cyclohexene oxide (CHO) using catalyst **2b** (X= OAc).¹³⁸ Detailed *in situ* ATR-IR spectroscopic analysis revealed that epoxide/anhydride ROCOP occurred first, and, only once the anhydride was nearly completely consumed, did epoxide/CO₂ ROCOP occur. This was surprising because when conducted independently the epoxide/CO₂ copolymerization occurred significantly faster than epoxide/anhydride copolymerization. It was proposed that the selectivity is due to a relative faster rate of anhydride insertion vs. CO₂ insertion into the zinc alkoxide intermediate; both reactions are pre-rate determining steps in the catalytic cycles. **Figure 1.7** illustrates the combination of polymerization cycles which are proposed to be occurring. During initiation, the [(BDI)ZnOAc] complex reacts with an equivalent of epoxide to generate the zinc alkoxide species (A). At this stage, the reaction with anhydride (B) is proposed to occur faster than the reaction with CO₂ (C), leading to the dominant intermediate in terpolymerizations being a zinc carboxylate species. This intermediate reacts with epoxide (D) to form a zinc-alkoxide and the polymerization cycle progresses around the ester cycle (steps B, D). Only when the anhydride is almost fully consumed, does the insertion of CO₂ into the zinc alkoxide intermediate (C) become competitive. Once this occurs, a zinc carbonate intermediate is formed, which ring opens an epoxide to re-generate an alkoxide (E). Therefore, in this polymerization the formation of the second block occurs faster than the first block because reaction E is faster than D.

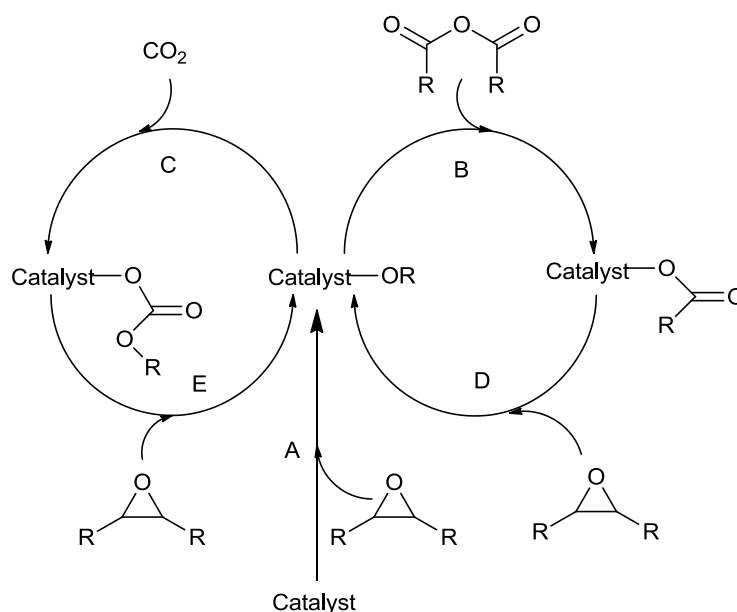


Figure 1.7 Proposed mechanism for the formation of copoly(ester-*b*-carbonate), as reported by Coates and co-workers.¹³⁸

Subsequently, other catalysts have also been shown to exhibit the same selectivity and produce copoly(ester-*b*-carbonates).^{80,82,129,134,137,139-141} Duchateau and co-workers used **3a** with DMAP as the co-catalyst for the terpolymerisation of CHO/anhydrides (SA/CPrA/CPA or PA) and CO₂.^{80,82} By monitoring the reaction, they found that ~90 % of the anhydride is converted before any carbonate functionalities are formed. Darensbourg and co-workers also prepared block copolymers from CHO/PA/CO₂, using a chromium salen catalyst **4b** with PPNCI/N₃ as the co-catalyst, in this case two glass transition temperatures were observed, indicating phase separation between blocks ($T_g = 48\text{ }^{\circ}\text{C}$ and $115\text{ }^{\circ}\text{C}$).¹⁴² A Cr(III)salen catalyst with a tethered ammonium co-catalyst, was also successfully applied, by the Darensbourg group, to copolymerize PO/NA/CO₂.¹³⁹ Duchateau and co-workers reported that metal porphyrin catalyst **1c** with DMAP (as co-catalyst), was effective for the terpolymerisation of CHO, anhydrides (SA/CPrA/CPA or PA) and CO₂.⁸² However, carbonate linkages formed concurrently during the enchainment of ester linkages, leading to non-defined block structures. In contrast, Chisholm *et al.* also used the **1c** with PPNCI for the terpolymerization of PO/SA/CO₂ and reported the formation of diblock copoly(ester-carbonates).¹²⁰ Di-zinc and di-magnesium catalysts reported by the Williams group, **6a/b**, are also selective in the terpolymerizations of CHO, PA and CO₂ producing block copoly(ester-carbonates).¹³⁴ Heterogeneous catalysts such as zinc glutarate or double metal cyanides (DMC) have also been investigated for PO/MA/CO₂ copolymerization to produce poorly defined block copoly(ester-carbonates), due to the similarity in the insertion

rate of the cyclic anhydride and CO₂.¹⁴⁰ A similar result occurs using double metal cyanide catalysts.¹⁴¹ In the heterogeneous catalysis, the phase of the catalyst is different from that of the reactant. Generally, the activity of the heterogeneous catalyst depends on the crystal morphology, particle size, size distribution and also impurities.¹⁴³

1.5.2 Combining ROCOP and ROP: Switch Catalysis and Tandem Methods

Another interesting method is to combine ROCOP and ROP for the copolymerization of epoxides, CO₂ and lactones. This is conceptually distinct and advantageous *versus* the terpolymerization of CO₂, epoxides and cyclic anhydrides and also offers a broader access to properties and monomers as it requires the combination of two different polymerization catalytic cycles. There have been a few reports of the use of heterogeneous catalysts for such transformations, including zinc glutarate and double metal cyanides,¹⁴⁴⁻¹⁴⁷ in all cases leading to undefined polymer structure with low/random lactone enchainment. A [(BDI)ZnOAc] catalyst was reported for the terpolymerisation of CO₂/CHO/lactide (LA), resulting in the formation of a statistical copolymer.¹⁴⁸ It was the first time that a catalyst was reported to give poly(cyclohexyl carbonate-*co*-lactide) from the terpolymerization of CO₂, cyclohexene oxide and lactide. Although blocky structures were not observed, the composition of the terpolymers could be tuned by changing the monomer feed ratio.

Williams and co-workers reported the first example of ‘Switch’ catalysis which enabled the two polymerization cycles to be combined and controlled using a single catalyst.¹³⁶ The di-zinc catalyst, **6a**, allowed the copolymerization of CHO, CO₂ and ϵ -caprolactone (CL) and led to the selective formation of block poly(ester-*co*-carbonates) (**Figure 1.8**).¹³⁶ ATR-IR spectroscopy showed that the ROCOP occurred first leading to the formation of pure polycarbonate, subsequently, after CO₂ removal, the lactone ROP occurred, leading to a poly(carbonate-*b*-ester). The selectivity was interesting and unexpected because the rate of ROCOP was significantly slower than that of ROP. However, it was controlled by the pre-rate determining step, the insertion of carbon dioxide into the zinc alkoxide bond (**Figure 1.8**). This is comparable to the earlier findings on epoxide/anhydride/CO₂ copolymerisation reported by Coates and co-workers.¹³⁸ It was discovered that the catalyst selectivity could be easily manipulated, thus under a nitrogen atmosphere the combination of CHO and CL led to the exclusive formation of polyester. When the gas atmosphere was changed to CO₂, the only product was the polycarbonate. The polymerizations were easily controlled, in one-pot, by

adding different monomers at selected time points and this enabled the production of block copolymers.

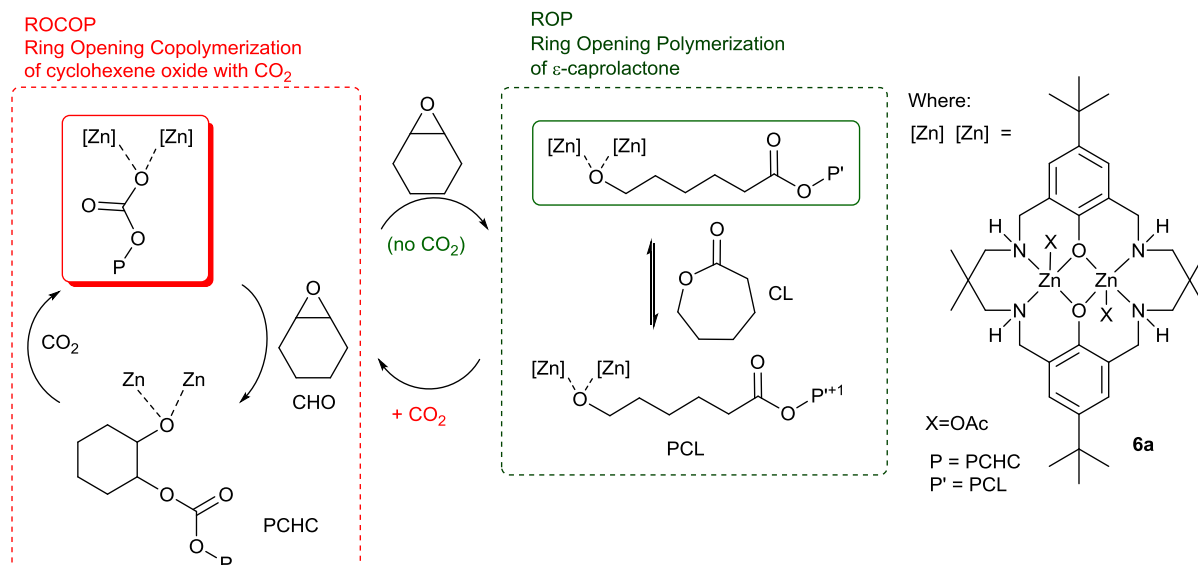


Figure 1.8 Illustration of the combined ROCOP and ROP reactions, using a single catalyst as reported by Williams and co-workers.¹³⁶

An alternative route to such copolymers is the tandem method, either using a macroinitiator to initiate the ROCOP or using the alternating polyesters/polycarbonates as the macroinitiator to initiate the ROP. In 2010, Lee and co-workers carried out an extensive study of CO₂/epoxide ROCOP, using cobalt salen catalysts, and the in presence of various macromolecular chain transfer agents.¹⁴⁹ Alternatively, our group and the Darensbourg group have both applied polycarbonate macro-initiators in the ring-opening polymerization of lactones or cyclic phosphoesters.^{97,129,150,151}

1.6 ROCOP: Polyester Properties

The recent focus and development of ring-opening copolymerization (ROCOP) catalysts is significant because its capability to enchain a wide range of renewable monomers (cyclic anhydrides, epoxides, and CO₂) into polymers. Additionally, the obtained polyesters/polycarbonates differ considerably in backbone structure and functionality compared to that prepared by ROP. Simply by changing the epoxide or cyclic anhydride, the properties of the resulting material can be easily tuned, including the thermal properties, mechanical properties, amphiphilicity and stimuli-responsiveness.²⁹⁻³² Because the polymer properties of the ROCOP polycarbonates from CO₂ and epoxides are out of the scope of this thesis, they are not discussed in this section. It is still worth mentioning that great progress

has been made in the field to change the polycarbonate properties by using different epoxides and it is envisaged similar tuning could be feasible for alternating polyesters.^{38,152-159}

1.6.1 Thermal Properties

Understanding the influence of the polymer structure on the thermal properties (T_g and T_m) is of particular interest, due to the correlation with mechanical properties and processing conditions. One limitation for aliphatic polyesters is their low glass transition temperatures (T_g) observed for many materials. It is difficult using ROP to prepare polyesters with glass transition temperatures higher than 100 °C. Where this has proved possible the monomer syntheses are often challenging.⁷⁶ For example, polymandelide prepared by the ring-opening polymerization of mandelide can reach a T_g value of ca. 100 °C. However, the yield of mandelide is relatively low (~ 45%) and the synthesis of the polymer suffers from the poor monomer stability.¹⁶⁰ Also, the methane protons are highly reactive because they are α protons to both the carbonyl and the benzene ring, resulting in the yellowing during melt processing.¹⁶⁰ This can be overcome by direct hydrogenation to form the cyclohexyl derivatives [poly(cyclohexylglycolide), T_g = ca. 98 °C].⁷⁶ One attraction of ROCOP is the facility to prepare materials with tuneable glass transition temperatures, including those approaching or exceeding 100 °C.¹²⁹ Thus, by selecting the epoxide/anhydride combination, it is relatively straightforward to modify the thermal properties of the resulting polyester.

The nature of the polymer backbone linkages plays key role in determining their glass transition temperature and the presence of ether linkages may introduce backbone flexibility leading to a lower glass transition temperature. Nishimura and co-workers, reported that for poly(itaconic anhydride-*co*-1,2-epoxybutane), the T_g decreased upon the increasing the content of ether linkages (from 11 to -9 °C).¹⁶¹ It is notable that although isomerization from the itaconic to citraconic configuration occurred during the polymerization, the molar ratio of the two configurations hardly affected the T_g . In addition, it was noted that the T_g of the polyester could be further increased by crosslinking the polymer through the itaconic units, however, this complicated the processibility. Therefore, catalysts that feature higher ester linkage selectivity should be the primary choice to reach materials with higher glass transition temperatures.

ROCOP, using maleic anhydride, has been widely investigated due to its potential of post-polymerization modification.^{31,94,141,162,163} Poly(maleic anhydride-*alt*-propylene oxide)

has only a Z-configuration of the C=C bonds (**Figure 1.9a**). However, these can be isomerized to the E-configuration, by reaction with morpholine (**Figure 1.9b**). In addition, by varying the isomerization reaction time, the ratio of Z- to E- was easily controlled. The T_g increased from -14 °C to 4 °C with the increasing content of the E-configuration (from 0 to 92 mol%).

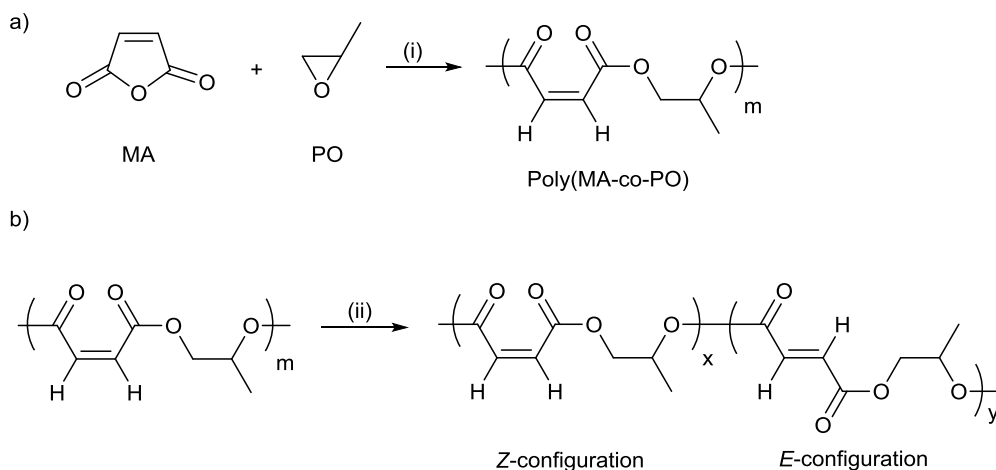


Figure 1.9 (a) Ring-opening copolymerization of maleic anhydride with propylene oxide; (b) isomerization of poly(maleic anhydride-co-propylene oxide) catalyzed by morpholine.¹⁶³ Reagents and conditions: (i) $\text{Mg}(\text{OEt})_2$, toluene; (ii) Morpholine, dichloroethane.

As mentioned, Coates and co-workers reported a range of polyesters synthesized from maleic anhydride and various epoxides, including PO, epichlorohydrin, glycidyl ethers, perfluoroalkyl substituted epoxides, *via* ROCOP.³¹ The T_g of the poly(alkylene maleate) was tuned from -26 °C to 41 °C, by changing the epoxide co-monomer. The highest T_g was observed using perfluoro alkyl substituted epoxides, whilst epoxides with diethylene glycol substituents afforded materials with the lowest T_g . Furthermore, the isomerization of poly(propylene maleate) to poly(propylene fumarate) slightly increased the T_g of the polyesters when diethylamine was used as the isomerisation catalyst.

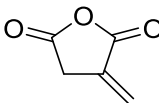
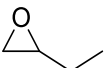
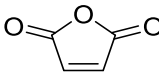
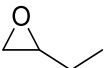
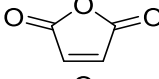
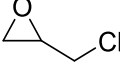
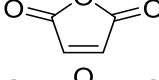
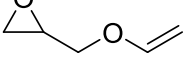
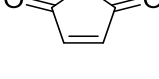
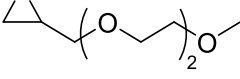
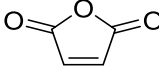
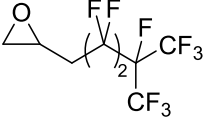
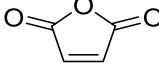
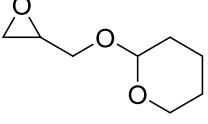
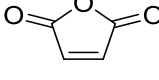
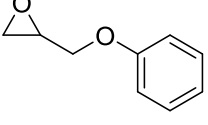
Since the monomer combinations affect the T_g of the corresponding polyesters, a range of epoxides/cyclic anhydrides combinations were investigated by Darensbourg and co-workers.¹⁴² They pointed out that for a particular anhydride, the T_g of the obtained polyesters increase in the order $\text{PO} < \text{SO} < \text{CHO}$, whilst for a particular epoxide, the T_g increases in the order $\text{SA} < \text{MA} < \text{CHA} \leq \text{PA} < \text{CHE}$. As expected, the steric effect of the pendant groups and the rigidity of the repeat unit exert a significant influence on the T_g of

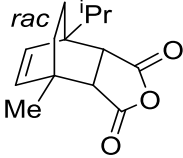
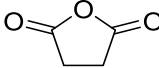
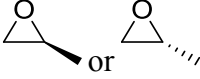
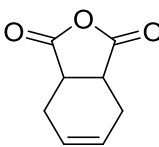
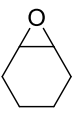
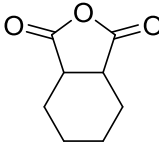
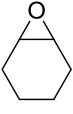
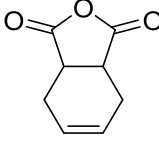
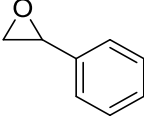
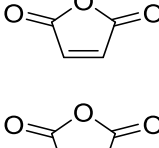
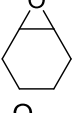
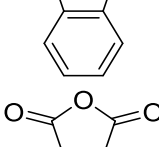
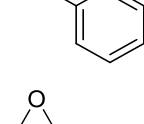
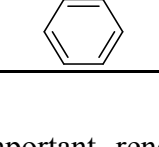
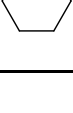
polyesters [from -39 °C (SA/PO) to 95 °C (CHE/CHO)]. Moreover, two different T_g values were obtained for MA/PO copolymer due to photo-isomerization reactions.

A further influence on the polyesters T_g is the molecular weight of the polymer. Duchateau and co-workers, reported that the T_g of poly(styrene oxide-*alt*-phthalic anhydride) increases from 43 to 73 °C as the molecular weight increases from 4,500 to 9,000 g/mol.⁸¹

Polyesters derived from renewable resources with promising properties are also a hot topic in the field. In 2015, Coates and co-workers reported a range of polyesters prepared by ROCOP of terpene-based cyclic anhydrides and propylene oxide (**Table 1.2**, entry 9) using metal salen catalysts. One of the polyesters exhibits a T_g value up to 109 °C, suggesting a potential renewable alternative to petrochemical-based high T_g polymers.¹⁶⁴

Table 1.2 The thermal properties of some representative ROCOP polyesters described in section 1.6.1.

#	anhydrides	epoxides	T_g (°C)	T_g (°C) after isomerization	T_m (°C)
1 ¹⁶¹			-9	-3	N.A.
2 ³¹			11	-14	N.A.
3 ³¹			33	45	N.A.
4 ³¹			-10	-6	N.A.
5 ³¹			-26	-29	N.A.
6 ³¹			40	53	N.A.
7 ³¹			35	36	N.A.
8 ³¹			41	50	N.A.

#	anhydrides	epoxides	T_g (°C)	T_g (°C) after isomerization	T_m (°C)
9 ¹⁶⁴			109	N.A.	N.A.
10 ¹⁶⁵			-4	N.A.	120 (after forming stereocomplex)
11 ¹⁴²			95	N.A.	N.A.
12 ¹⁴²			85	N.A.	N.A.
13 ¹⁴²			53	N.A.	N.A.
14 ¹⁴²			53	N.A.	N.A.
15 ¹⁴²			46	N.A.	N.A.
16 ¹⁴²			48	N.A.	N.A.

One important renewable monomer, succinic acid, is derived from a highly efficient fermentation process of glucose and produced on 170 kt/annum scale.¹⁶⁶ Polyesters featuring succinic acid repeat units can be prepared by ROCOP of epoxides and succinic anhydride.²⁹ The method is attractive as it is controlled, may obviate the need for precise control of reagent stoichiometry and it yields materials with predictable molecular weights. Coates and co-workers reported a new class of stereocomplex formed using isotactic and enantiomeric poly(propylene succinate) chains (**Figure 1.10**). The enantiomeric polyesters [poly((*S*)-propylene succinate) and poly((*R*)-propylene succinate)] were synthesized from succinic anhydride and enantiopure (*R*) or (*S*)-propylene oxide, using the ring-opening copolymerization.¹⁶⁵ The stereocomplex forms by co-crystalline of the 2 enantiomers. Its melting temperature (120 °C) is 40 °C higher than either isotactic polyesters and comparable

to low density polyethylene. However, the limitation of this method lies in the requirements for enantiopure epoxide usage.

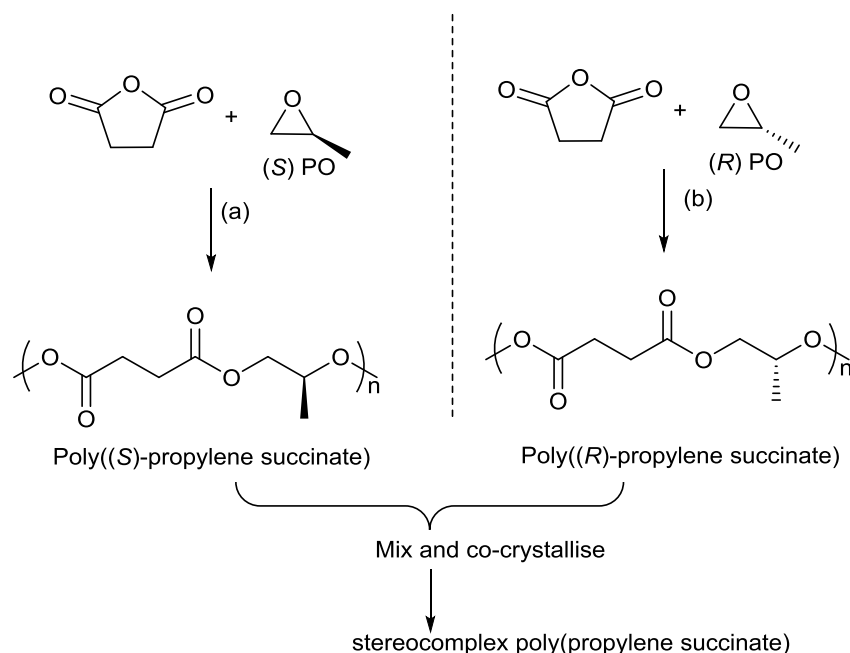


Figure 1.10 The formation of stereocomplex poly(propylene succinate) by co-crystallisation of poly((*S*)-propylene succinate) and poly((*R*)-propylene succinate). Reagents and conditions: (a) [(*R,R*)-(Cl-salcy)CoNO₃], [PPN][NO₃], 30 °C, 36 h. (b) [(*S,S*)-(Cl-salcy)CoNO₃], [PPN][NO₃], 30 °C, 36 h.¹⁶⁵

1.6.2 Amphiphilic Polyesters

Amphiphilic polymers exhibiting thermo-responsive behaviour such as poly(*N*-isopropylacrylamide) (PNIPAAm) are of particular interest in bio-medical applications.¹⁶⁷⁻¹⁷⁰ However, so far, the common thermo-responsive materials are not degradable, and PNIPAAm has been implicated in some cytotoxic mechanisms.¹⁷¹ It would be of significant value to design polyesters exhibiting thermo-responsiveness. However, though there has been some recent progress in preparing amphiphilic or hydrophilic polycarbonates from CO₂ and epoxides,¹⁷²⁻¹⁷⁴ reports on amphiphilic or hydrophilic ROCOP polyesters are still limited. One example of thermo-responsive polyester was reported by Hao and coworkers.¹⁷⁵ Epoxides bearing oligo-ethylene glycol pendant chains (with different chain lengths) were copolymerized with succinic anhydride (**Figure 1.11**). A lower critical solution temperature (LCST) was observed in all three samples, with a narrow transition temperature window; the temperature was dependent on the chain length (*m* = 1, 2, 3 corresponding to LCST values of 17.8 °C, 49.2 °C and 73.3 °C, respectively). Under

physiological pH conditions, the polyesters displayed comparable degradation rates to some clinically applied materials. Interestingly, the degradation rate also depended on the ether side chain length, a finding that has been attributed to the increase in hydrophilicity and aqueous solubility. Although these initial results are promising, the successive tuning of the LCST cannot be easily achieved. In order to achieve finer degrees of control, a mixture of 2-((2-methoxyethoxy)methyl)oxirane/2-((2-(2-methoxyethoxy)ethoxy)methyl)oxirane (MEMO/ME₂MO) epoxides were copolymerized with SA.³² By changing the molar ratio of MEMO/ME₂MO (from 0 to 100 mol %), fine control of the LCST of the polyester was possible over the range 17.8 to 49.2 °C. Importantly, a linear increase of LCST was observed with the increasing ME₂MO content in the initial feed.

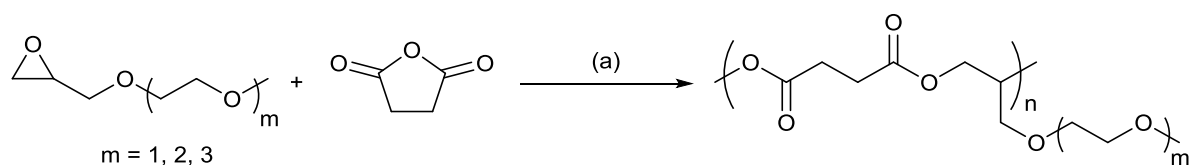


Figure 1.11 The synthesis of the thermo-response polyesters prepared by ROCOP. Reagents and Conditions: (a) Al(OⁱPr)₃.¹⁷⁵

1.6.3 Mechanical Properties

Although a few studies on the mechanical properties of ROCOP polycarbonates have been reported,^{38,152,157,158} the studies on the comparable alternating polyesters' mechanical properties have rarely been reported.¹⁷⁶ The mechanical properties should also be tailored by changing the combination of cyclic anhydrides/epoxides. Wang *et al.* studied three anhydrides: succinic anhydride (aliphatic), phthalic anhydride (aromatic), and maleic anhydride (unsaturated) and each was copolymerized with propylene oxide, using a double metal cyanide complex catalyst, to afford poly(ether-ester) (polyesters with ether linkages) polyols.¹⁷⁶ After a chain extension reaction, using 4,4'-diphenylmethanediisocyanate (forming a polyurethane segment), the mechanical properties of the three polyurethanes were investigated. By changing the aliphatic anhydride (succinic anhydride) to the aromatic one (phthalic anhydride), the tensile strength was significantly increased from 19.1 to 23.5 MPa. Also, high ester content in the soft segments was important to achieve the best mechanical performance of the polyurethanes. One interesting opportunity for such alternating polyester and block copolymers is as a thermoplastic elastomer.

1.7 Renewable Thermoplastic Elastomers

Thermoplastic elastomers (TPE), also known as thermoplastic rubbers, are important materials for various applications.¹⁷⁷⁻¹⁷⁹ TPEs usually consist of different, incompatible polymer blocks which phase-separate on the micro- or nano-scale. The intrinsic elastic property of a TPE usually derives from the presence of both ‘soft’ and ‘hard’ domains. The terms refer to the flexibility of the amorphous polymer block, where the T_g of the soft block should be lower than the operating temperature and the block should be amorphous at the operating temperature. The hard polymer block should show either a T_g or a T_m higher than the operating temperature. Furthermore, the hard domains are responsible for the physical crosslinking of the sample which is critical for it to show elasticity.¹⁸⁰

Two of the most successful commercial TPEs are polystyrene-*b*-polybutadiene-*b*-polystyrene (SBS) and polystyrene-*b*-polyisoprene-*b*-polystyrene (SIS). They are produced on a million tons scale annually for various applications.¹⁸¹⁻¹⁸⁴ However, SBS/SIS and their derivatives are petroleum-based and also non-degradable. Therefore the development of ‘green’ TPE has attracted increasing attention. Fully renewable thermoplastic elastomers can now be made from a range of renewable monomers, including terpenes, vegetable oils, sugars and CO₂.^{157,177,185-191} This is an exciting area both fundamentally, in terms of understanding block copolymers, and practically in terms of the high-end applications for elastomers.

As one of the pioneering groups in the field, Hillmyer and co-workers reported an early example of a fully renewable thermoplastic elastomer in 2012.¹⁷⁷ The TPE comprise a triblock copolymer, poly(α -methylene- γ -butyrolactone)-*b*-poly(menthene)-*b*-poly(α -methylene- γ -butyrolactone) (PMBL-*b*-PM-*b*-PMBL) (**Figure 1.12**). Both of the monomers are potentially biorenewable. Menthene can be derived from the plant *Mentha arvensis*, while α -methylene- γ -butyrolactone may be synthesized from levulinic acid (cellulosic biomass). Due to the high T_g value of the PMBL block (170 °C to 190 °C), the elasticity of the triblock copolymers remains even at elevated temperature. In 2014, new ABA triblock polymers were reported by Hillmyer and co-workers (**Figure 1.13**).¹⁸⁹ These polymers were synthesized using pinene-derived monomers α -methyl-*p*-methylstyrene (AMMS) and myrcene *via* the living anionic polymerization method. The obtained triblocks exhibited an upper service temperature at ca. 182 °C which is much higher than the traditional styrenic thermoplastic elastomers, such as SBS (T_g = ca. 100 °C). Furthermore, though the tensile strength is merely comparable to the traditional styrenic TPEs, the elongation at break

value reached up to 1300% which is one of the highest values reported in the field of renewable TPEs.

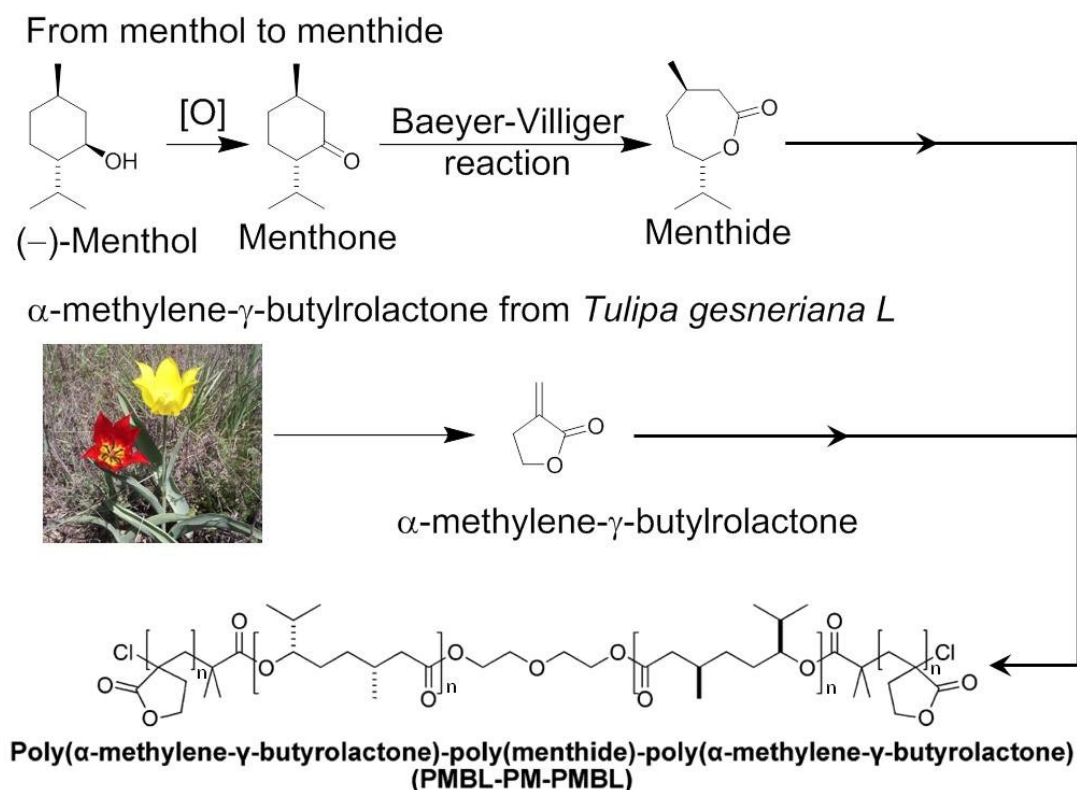


Figure 1.12 Using terpenes to make renewable TPEs.¹⁷⁷

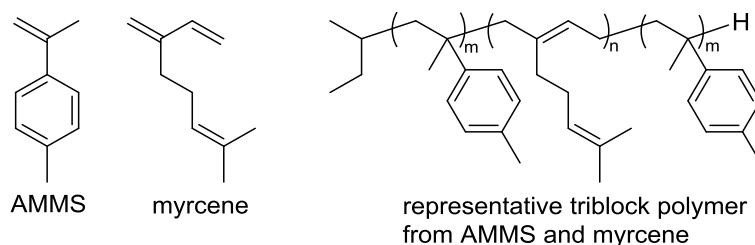


Figure 1.13 Structures of the monomers (AMMS and myrcene) and representative triblock polymer.¹⁸⁹

In 2014, a multicomponent elastomer which consists of recycled polystyrene and renewable polymer network was reported by Hearon, Wooley and co-workers (**Figure 1.14**).¹⁹² Renewable D-limonene was used as both the solvent to dissolve a recycled thermoplastic polystyrene drinking cup and as a monomer to form a new poly(thioether) network. The polymer network showed tuneable physical and mechanical properties, and this work offers an interesting demonstration of recycling waste to new product.

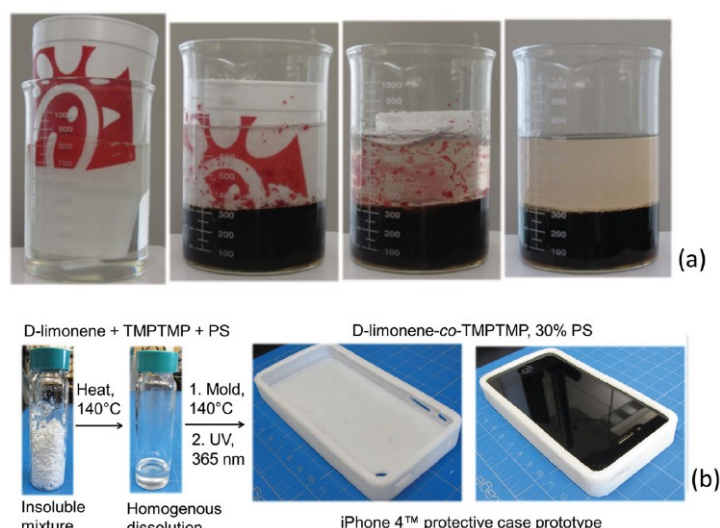


Figure 1.14 Production of a semi-renewable network material using recycled polystyrene.¹⁹²

a) The recycling of a waste cup by dissolving it in D-limonene. b) The fabrication of iPhone 4 protective case prototype made using the network material.

Triglycerides have been used to prepare thermoplastic elastomers, including even an example of a self-healing and thermo-reversible elastomer.¹⁹¹ The elastomer used reversible supramolecular hydrogen bonding interactions for cross-linking, which facilitated its processing and even allowed its recycling. Soybean oil derived monomers were also copolymerized with styrene to afford partly renewable thermoplastic elastomers, poly(styrene-*b*-soybean oil acrylate-*b*-styrene) (PS-*b*-PSBA-*b*-PS) and poly(styrene-*b*-soybean oil methacrylate-*b*-styrene) (PS-*b*-PSBMA-*b*-PS) (**Figure 1.15**).¹⁷⁹ Another example, reported by Robertson and co-workers, applied stearyl and lauryl acrylate (derived from vegetable oils) to prepare partly renewable triblock copolymers, poly[styrene-*b*-(lauryl acrylate-*co*-stearyl acrylate)-*b*-styrene] (SAS). The SAS triblocks form microphase-separated morphology and display elastomeric behaviour with an elongation at break value of less than 200%.¹⁹³ Fatty acids can also make vitrimers, which are polymers showing reversible temperature-induced thermoset to thermoplastic transitions, for example by thermally controllable transesterification reactions.^{194,195}

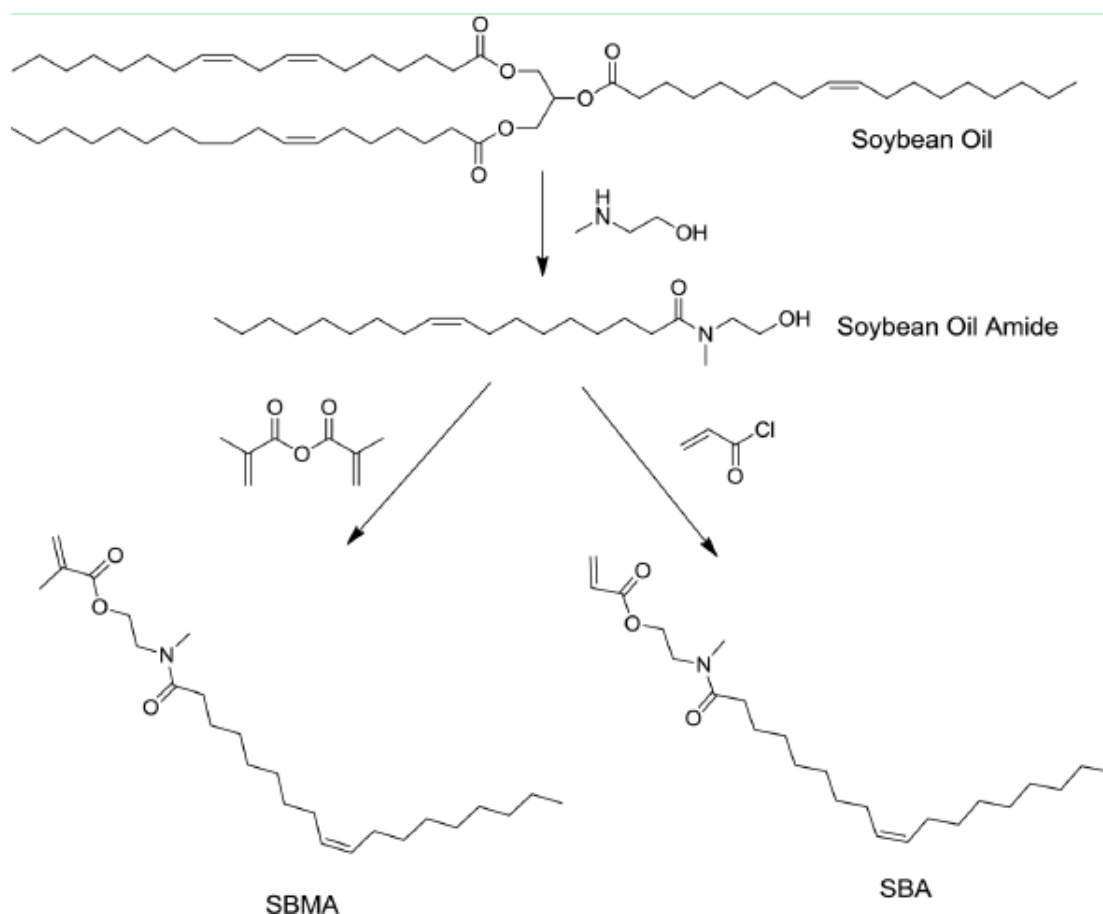


Figure 1.15 Synthetic route of soybean oil derived monomers, soybean oil methacrylate (SBMA) and soybean oil acrylate (SBA) monomers.¹⁷⁹

In addition, recent research shows the potential for block copolyester elastomers from carbohydrates. Engineered *E.Coli* was used to prepare a functionalized lactone in high efficiency (88 g/L in semi-batch mode), with monomer cost being estimated at ~\$2/kg, which is within the range for some commodity applications (**Figure 1.16**).¹⁹⁰ The lactone was polymerized using controlled ring-opening polymerization to produce an elastomer ($T_g = -50$ °C), and its copolymerization with lactide yielded a thermoplastic elastomer that could be stretched to 18 times its original length without breaking.

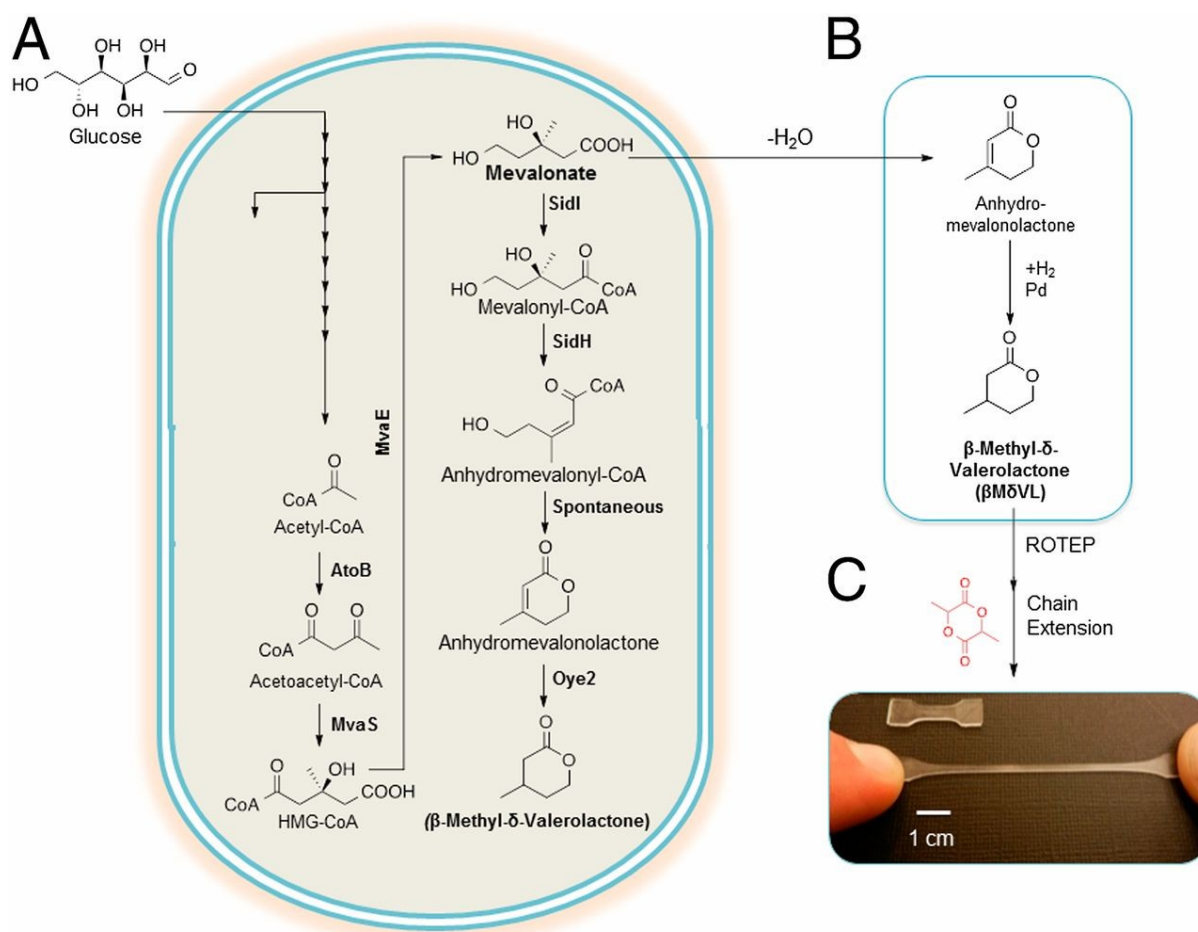


Figure 1.16 (A) The biosynthetic pathway of β M δ VL. (B) Synthesis of β M δ VL from mevalonate. (C) TPE comprises β M δ VL.¹⁹⁰

Completely renewable thermoplastic elastomers, derived from cellulose, rosin and fatty acids, were developed by Tang *et al.* in 2014 (**Figure 1.17**).¹⁹⁶ Two types of graft copolymers were prepared *via* the atom transfer radical polymerization (ATRP): cellulose-*g*-poly(*n*-butyl acrylate-*co*-dehydroabietic ethyl methacrylate) [Cell-*g*-P(BA-*co*-DAEMA)] and cellulose-*g*-poly(lauryl methacrylate-*co*-dehydroabietic ethyl methacrylate) [Cell-*g*-P(LMA-*co*-DAEMA)], in which DAEMA is derived from rosin and LMA is derived from fatty acids. The obtained graft copolymers showed excellent elasticity even at strain values higher than 500%.

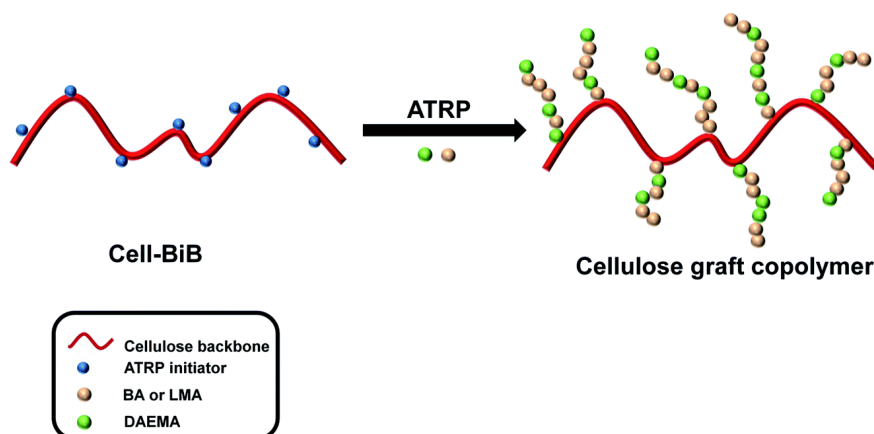


Figure 1.17 Schematic illustration of cellulose based graft copolymers.¹⁹⁶

Despite the fact that thermoplastic elastomers only account for a small portion of overall industrial polymer production, the market value of TPE is large due to the high-end properties. A range of TPEs comprising renewable components have been reported. However, the mechanical properties of these renewable TPEs are still inferior to those of many petrochemicals (**Table 1.3**). Furthermore, despite some progress having been achieved in making thermoplastic elastomers from renewable sources, degradable alternating polyesters derived from renewable cyclic anhydrides and epoxides have not yet been explored.

Table 1.3 Mechanical properties of known TPEs.¹⁹⁷

#	Polymer	Polymer type	Tensile strength at break (MPa)	ϵ at break (%)
1	Hytrel (Dupont)	Polyester based	10-31	200-375
2	Skypel (SK chemicals)	Polyester based	22-50	350-900
3	Riteflex (Celanese)	Polyester based	20-31	50-350
4	Pibiflex (SO.F.TER)	Polyester based	11-40	400-900
5	Kopel (Kolon)	Polyester based	25-39	400-850
6	RTP 1500 series (RTP)	Polyester based	8-40	200-550
7	Ecdel (Eastman Chemical Co.)	Polyester based	20-23	300-400
8	PEBAX (Arkema)	Poly(ether- <i>b</i> -amide)	34-63	300-640
9	Irogran (Huntsman)	Polyurethane based	35-45	550-700
10	Pearlthane (Merquinsa)	Polyurethane based	25-45	470-700
11	Pearlcoat (Lubrizol)	Polyurethane based	25-35	410-850
12	SBS	Polyolefin based	21-21	800-1100
13	PAMMS-PMYR-PAM MS ¹⁸⁹	Polyolefin based	0.5-4	500-1350
14	PMBL-PM-PMBL ¹⁷⁷	Poly(ester- <i>b</i> -olefin)	4-13	730-1800
15	PLA-PMCL-PLA ¹⁹⁸	Polyester based	10-14	1360-1880

1.8 Potential Application as Biomedical Materials

The need for renewable polymers in the biomedical industry may not appear as important due to the relatively small market size, but the high values and, therefore, high cost tolerance would facilitate the implementation of many new renewable materials. Moreover, many renewable raw materials derive from the metabolites of living organisms, suggesting the potential for biocompatibility which is difficult otherwise to achieve. Degradable polymers are especially interesting as they can break down, *via* hydrolytic or enzymatic process, into small molecules which can be excreted or absorbed rather than accumulating *in vivo* or being removed by surgery. Over the past fifty years, a range of degradable synthetic polymers with different backbone structure have been developed, such as polypeptides,¹⁹⁹⁻²⁰¹ polysaccharides,²⁰²⁻²⁰⁴ poly(α -esters),^{205,206} polyanhydrides,^{207,208} polycarbonates^{77,209-212} and polyphosphesters.²¹³⁻²¹⁵ However, reports on biocompatible polymers featuring both (bio)degradability and renewability are limited, especially in the field of colloidal or self-assembled polymers.

1.8.1 Polymeric Self-assemblies

Polymeric self-assemblies, especially polymer vesicles (also known as polymersomes, **Figure 1.18**) have experienced a blooming development over the past two decades.²¹⁶⁻²²⁴ Polymer vesicles are expected to be applied in the delivery and release of pharmaceuticals,²²⁵ gene therapies,^{226,227} magnetic resonance imaging agent (MRI) and in theranostics^{228,229} or cell mimicking.²³⁰⁻²³² Typically, polymer vesicles are nanoscale capsules featuring a hydrophobic membrane and a hydrophilic interior. Their structures are more complicated than polymer micelles which feature a simple core-shell nanostructure. Although lipid vesicles have been acting as the foundation of life for millions of years, polymer vesicles are more robust and stable. So far, they are commonly prepared from non-degradable poly(acrylates), poly(methacrylates) polypeptides, glycopeptides, starches, polyphosphesters and polycarbonates derived from ROP of six-membered cyclic carbonate are also known to undergo self-assembly.^{213,214,233-241}

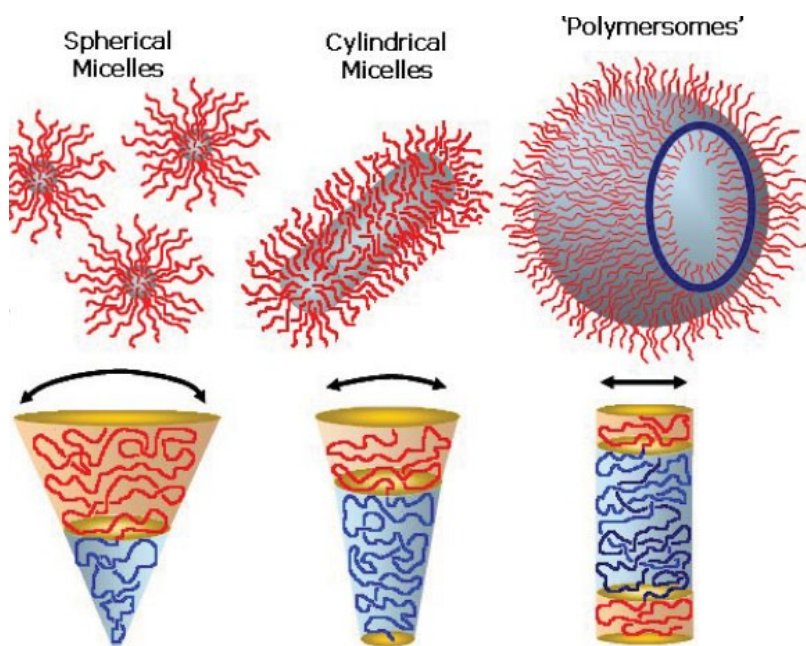


Figure 1.18 Common morphologies of self-assembled amphiphilic block copolymers: spherical micelles, cylindrical micelles and vesicles (also known as polymersomes).²⁴²

1.8.2 Preparation Methods

1.8.2.1 Solvent-switch method

Solvent-switch techniques have been widely used for preparing polymer vesicles as most amphiphilic block copolymers are not directly soluble in water.²⁴³⁻²⁴⁶ Initially, polymers are dissolved in organic polar solvents first [e.g. N,N-dimethylformamide (DMF) and tetrahydrofuran (THF)], followed by the addition of the second solvent (usually water) to selectively induce the nano-precipitation (membrane forming process) of the solvophobic part of the polymer chain. The hydrophilic blocks are solvated to form vesicle corona. Alternatively, the solvent-switch method can be applied reversely (adding polymer organic solution into water). Sometimes the organic solvent/water mixture ratio significantly affect the resultant morphology of self-assembly and also the permeability of vesicle membrane. However, vesicles prepared by means of solvent-switch require purification to remove organic solvents prior to applications. This is both time-consuming and economically unfavourable.

1.8.2.2 Rehydration method

Rehydration can be achieved by either a film or bulk swelling method. During film swelling, polymers are firstly dissolved in an organic solvent (such as chloroform) and processed to afford a thin film, after the evaporation of the organic solvent. The subsequent addition of water or aqueous buffer solutions hydrate the polymer thin film to form vesicles.²⁴⁷ For

instance, both giant vesicles and monodisperse normal vesicles can be prepared using [poly(ethylene oxide)-*block*-polyethylethylene] (PEO-*b*-PEE) or [poly(ethylene oxide)-*block*-polybutadiene] (PEO-*b*-PBD).²⁴⁸ As the polymer vesicles are prepared in the absence of organic solvents, they can be used without further purifications.

In bulk swelling, no organic solvents are required during the vesicle preparation as the polymer can be directly dissolved in water to form nanostructures.^{249,250} However, vigorous agitation is usually required to fully hydrate the polymer sample and this usually results in structure defects and/or broad particle size distributions.²⁴⁷

1.8.2.3 pH tuning in pure water

The self-assembly of polymers with pH stimuli-responsiveness can be prepared by changing the pH value. For example, in 2005, Du and Armes reported a diblock copolymer vesicle self-assembled from poly[2-(methacryloyloxy)ethyl phosphorylcholine]-*b*-poly[2-(diisopropylamino)ethyl methacrylate] (PMPC-*b*-PDPA). This PMPC-*b*-PDPA block copolymer can dissolve in acidic solution (pH < 6) due to the protonation of the tertiary amine groups (pK_a ≈ 6.6) on the PDPA block. By simply increasing the pH value above 7.0, the deprotonation of the tertiary amine groups will then induce the formation of polymer self-assemblies.^{251,252} A similar approach can also be applied to polymers with other types of stimuli-responsiveness, such as temperature.²⁵³

1.8.2.4 Polyion complexation

PICsomes (polyion complex polymersomes) are formed by the complexation of two polyelectrolytes with opposite charges.²⁵⁴⁻²⁶¹ Kataoka *et al.* reported the PICsomes by mixing two types of polyelectrolytes, PEG-poly(α,β -aspartic acid) (anionic counterpart) and PEG-poly([2-aminoethyl]- α,β -aspartamide) (cationic counterpart), in the aqueous solution.²⁵⁵ The strong interaction between the two oppositely charged polyelectrolytes affords the hydrophobic domain, leading to the formation of vesicles. Recently, Yusa and co-workers reported another PICsome based on an anionic-neutral double-hydrophilic block copolymer and a cationic-neutral double-hydrophilic block copolymer. The morphology transition from vesicles to spherical micelles can be induced reversibly by simply adding either one of the block copolymers into the solutions.²⁵⁸

1.8.2.5 Polymerization-induced self-assembly: PISA

Conventional self-assembly procedures are usually performed at dilute polymer concentrations (< 1 w/v %). This limits the large scale production of polymer vesicles.²⁶² However, by applying polymerization-induced self-assembly (PISA), this limitation can be overcome. Recently, different polymeric nanostructures have been prepared through PISA with high polymer concentrations by Armes,²⁶³⁻²⁶⁶ Pan^{267,268} and Charleux.²⁶⁹ For instance, poly(glycerol monomethacrylate)-*b*-poly(2-hydroxypropylmethacrylate), PGMA-*b*-PHPMA, was polymerized in aqueous solution using reversible addition-fragmentation chain transfer (RAFT) method. The PGMA block remains hydrophilic during the polymerization, whereas the PHPMA block becomes increasingly hydrophobic due to the growth in the molecular weight. Self-assembly can thus take place during the polymerization. The morphology evolution was monitored by Transmission Electron Microscopy (TEM) and showed structures from branched worms to vesicles, owing to the continually changing ratio of hydrophilicity/hydrophobicity. This method can deliver polymer vesicle solutions with extremely high solid content (10 w/v %).²⁶³

1.8.2.6 Other methods

A centrifugation method can also be used to form polymeric self-assemblies with sophisticated morphologies. For example, nature-inspired polymer vesosomes (polymersomes in polymersomes) can be prepared *via* simple centrifugation.²⁷⁰ The same method has been used to form an artificial cell structure with ‘organelles’ and ‘model cytoplasm’.²³¹ In addition, by using a microfluid device giant vesicles, with monodisperse size distributions, were prepared.^{271,272} Further, the nanoprinting method was developed, by Förster *et al.*, which allows the direct ‘printing’ of vesicles through inkjets.²⁷³

In summary, depending on the types of the polymer building blocks, many preparation methods have been developed to afford polymeric self-assemblies with sophisticated morphologies as described above. Among them, the ‘solvent-switch’ method is the most commonly used and reliable method for most polymers. However, it requires the use of (toxic) organic solvents, which is not ideal for any biomedical applications. To address this issue, a range of organic-solvent-free methods were developed, where only water or buffer solutions are required as described in section 1.8.2.2 to 1.8.2.6. However, these methods may not be universally applicable to all amphiphilic polymers. Therefore, the ‘solvent-switch’ method is employed as the primary preparation method to afford amphiphilic block polyester self-assemblies in this thesis. Amphiphilic block polyesters and polycarbonates that undergo self-assembling in organic-solvent-free conditions are currently under investigation.

1.8.3 Current Development of Polymer Vesicles

So far, the most commonly selected building blocks for forming polymer vesicles are still synthetic block copolymers prepared *via* radical polymerization.²⁴⁷ However, the public concerns of the cytotoxicity and lack of degradability of these acrylates/methacrylates have motivated the investigation of other building blocks. Over the past decade, amphiphilic homopolymers, peptides, glycopeptides, starches and polycarbonates have all been developed and studied as replacements for polymers from radical polymerization methods.²³³⁻²⁴¹

In addition to the rapid development of building blocks during the past decade, the membrane structure of the polymer vesicle has been evolving significantly. Conventionally, the bilayer structure and interdigitated structure were believed to be the only packing options inside the polymer vesicle membrane. However, driven by high-end applications and accessibility (suitable for mass production), more packing structures have been identified, such as the bio-inspired multicompartment vesicles (MCVs) with compartmentalized/phase-separated membrane structures^{230,274,275} and homopolymer vesicles with H-bonding induced gradient membrane structure.^{233,234,276,277} Driven by the poor thermodynamic compatibility between two (or more) hydrophobic blocks [high Flory-Huggins interaction parameter (χ)],²⁷⁸ MCVs form compartmentalized membranes with separated hydrophobic domains, which are suitable for encapsulating multiple incompatible agents for clinical diagnosis/treatment.²⁷⁹ In 2004, Du and Chen reported organic-inorganic hybrid multicompartment vesicles, prepared by concentration-controlled self-assembly of a hydrolytically self-cross-linkable diblock copolymer.²⁸⁰ Thereafter, a spotted giant diblock copolymer vesicle was prepared, by Discher and co-workers, based on a phase segregation induced by calcium ion,²⁷⁵ Then, Armes *et al.* presented both micro- and nanosized MCVs, composed of two pre-mixed diblock copolymers with thermodynamically incompatible blocks.²⁷⁴ They also found that compartmentalization can be induced by post-cross-linking of the material due to kinetic trapping.²⁸¹ In the meantime, studies on amphiphilic homopolymer vesicles showed that the structure of the vesicle membrane was no longer limited to simple bilayers or interdigitated packing states. In 2013, Du and co-workers confirmed that amphiphilic homopolymers form vesicles with much complicated ‘gradient membrane’ structures, the formation of which are driven by secondary forces, such as inter/intra molecular hydrogen bonding.^{233,277} By tuning the degree of hydrogen bonding, a range of nanostructures were produced, including: hydrated large compound micelles (HLCMs); large compound vesicles (LCVs) and large compound micelles (LCMs).²³³

From the outset of the research on polymer vesicles, the stimuli-responsive behaviour has been of interest.²⁴⁷ Conventionally, polymer vesicles that respond to external stimulus are considered to be ‘smart’/‘intelligent’. There are examples of the use of external stimuli such as pH,²²⁵ temperature,²⁸² oxidation/reduction,²⁸³ and light.²⁸⁴ Additionally, the past decade has seen the development of a range of new stimuli-responsive approaches, including application of an electrical field,²⁸⁵ magnetic field,²⁸⁶ sugar molecules,²⁸⁷ gases,^{288,289} and ultrasound.²⁹⁰ Attempts have also been made to modify the corona of polymer vesicles affording biofunctionalized polymer vesicles which are capable of crossing the blood-brain barrier,²⁹¹ having strong cell adhesion^{292,293} or penetrating the cell membrane.^{294,295} The innovations and modifications applied to polymer vesicles have brought their biomedical applications much closer to clinical practice.

Although polymer self-assemblies are becoming increasingly sophisticated, the practical bioapplications are still rather limited mostly due to their poor or unknown biocompatibilities. Aliphatic polyesters and polycarbonates are FDA approved materials¹⁷⁴ and have been widely applied as the hydrophobic blocks in making polymeric self-assemblies. The key polymers include poly(ϵ -caprolactone), polylactide and poly(1,3-trimethylene carbonate).^{245,296,297} However, polyesters and polycarbonates prepared *via* ROCOP have rarely been studied as building blocks for self-assemblies.

1.8.4 Future Challenges in Developing Polymeric Self-assembled Structures

Despite the recent developments highlighted, there remains a significant gap between ‘proof-of-concept’ academic studies and clinical application. Future studies of polymer vesicles need to address one or more of the following challenges:²⁹⁸

- 1) The polymer building blocks must be both biocompatible and biodegradable *in vivo*. Attention should also be paid to the biocompatibility of the degradation products of these building blocks. The degradation products must not have cytotoxicity or cause immune responses, inflammations and carcinogenesis. Preferably, the degradation products shall have bioactivity, for example, acting as drugs.
- 2) Future polymer vesicles must show complementary or improved functionality compared to existing materials. Multiple functionalities should be integrated onto a single polymer vesicle, including chemistry to allow diagnosis, biosensing, targeting, triggered release, multiple stimuli-responsiveness and degradation.

- 3) Facile preparation methods are of great interest, not only for the synthesis of the polymer building blocks, but also to improve the methods of self-assembly, efficient drug loading and post-self-assembly modification.

1.9 Outlook

Significant effort has already been made to enchain monomers derived from renewable resources into well-defined polymers. There is good precedent for the preparation of polyesters by the alternating copolymerization of cyclic anhydrides and epoxides. Various mononuclear/dinuclear catalysts have been developed for the polymerizations and it is possible to make polymers with more complex architectures. Some potential applications have been demonstrated, including as heat resistant plastics or engineering materials. However, in terms of replacing commodity petrochemical polymers, research lacks the combination of synthesis and property optimization required to deliver successful new products.

There are several issues remaining to be addressed, for instance, whether it is possible to prepare well-defined block copolyesters, incorporating a wide range of functionalized monomers? Although advances in catalysis have been realized, there is a lack of detailed feedback and investigation of (block)copolymer microstructures. For example, much of the current study on aliphatic polyesters overlooks the microstructure of the polymers and there is much less exploration of chain extension, end capping, cross-linking and initiation of other polymer blocks using these polymers.

A challenge in this thesis is to investigate the potential to prepare well-defined (multi-)block copolyesters from monomer mixtures by combining lactone ROP and epoxide/anhydride ROCOP. Block regulation provides a means to differentiate macroscopic thermal/mechanical performances using existing (renewable) monomers and of particular relevance for oxygenated polymers, degradation rates. Directing the block compositions in conventional polyester synthesis would be extremely difficult and more often impossible, due to the step-growth synthetic methods used to prepare them. Therefore, a polymerization method that could combine ROCOP and ROP offers an opportunity to control the block copolyester architecture. The potential for the route will be explored in Chapter 3.

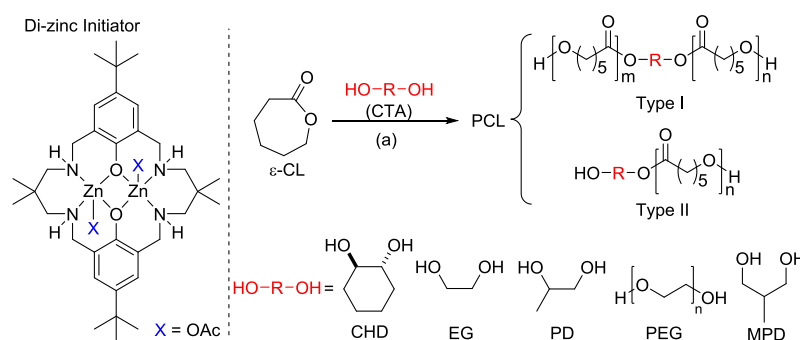
Moreover, although concerns associated with the sustainability and environmental impacts of petrochemicals have spurred the development polymers sourced from renewable resources, it is still important to improve the thermal/mechanical properties of these renewable polyesters so as to broaden application and access higher value products such as thermoplastic elastomers and shape-memory polymers. The properties for a series of multiblock copolymers will be explored in Chapter 4.

Finally, the block copolyesters will be applied as biomedical materials, which represents a very promising area for degradable polymers. Although approved by the FDA,¹⁷⁴ the bio-applications of aliphatic polyesters and polycarbonates, prepared by ring-opening polymerization, ROP, are limited due to their hydrophobicity and slow degradation. Theoretically, these limitations can be overcome by post-polymerization modification. However, due to the lack of functional monomers (cyclic esters and carbonates), studies on post-polymerization modification of these ROP polycarbonates and polyesters is limited.^{209,299} In contrast, functional ROCOP polyesters and polycarbonates should be more accessible due to the much bigger range of available (functionalized) monomers.¹⁴ The potential to use alternating polyesters for preparing biocompatible drug delivery vehicles will be explored in Chapter 5.

1.10 Aims and Objectives

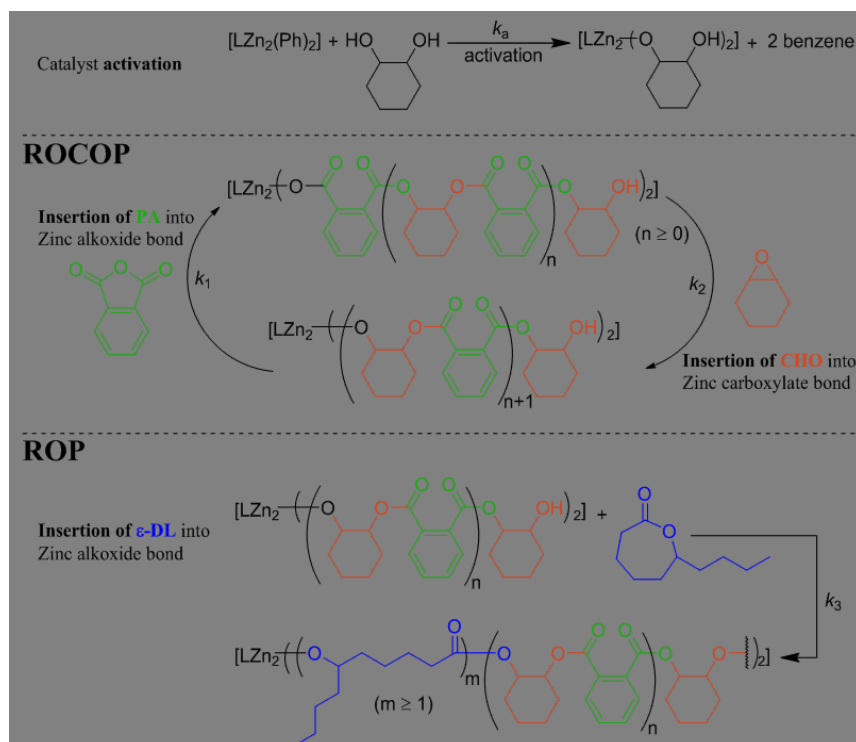
The aims and objectives of this thesis include:

1. To date, two main approaches have been developed to prepare telechelic polyesters: (i) the addition of a diol³⁰⁰⁻³⁰⁴ or (ii) the use of discrete metal borohydride initiators.³⁰⁵⁻³⁰⁷ The ‘diol’ approach is more widely applied due to its versatility and the PCL chains are believed to propagate from both hydroxyl groups due to the rather high chain transfer rate constant (k_c) usually observed in controlled ROP when using alcohols as chain transfer agents. However, the exact microstructure of the telechelic PCL, in particular the proportion of chains where the diol is a chain extender vs. those where it is a chain end group, is rarely quantified. This is of particular interest for ROP using multifunctional initiators. To gain in depth understanding of the microstructure of polyesters produced by lactone ROP. This will be achieved using di-zinc complex and telechelic chain transfer agents (**Scheme 1.1**). In particular, to understand the role of the diol structure and how the polymer architecture can be affected by it.



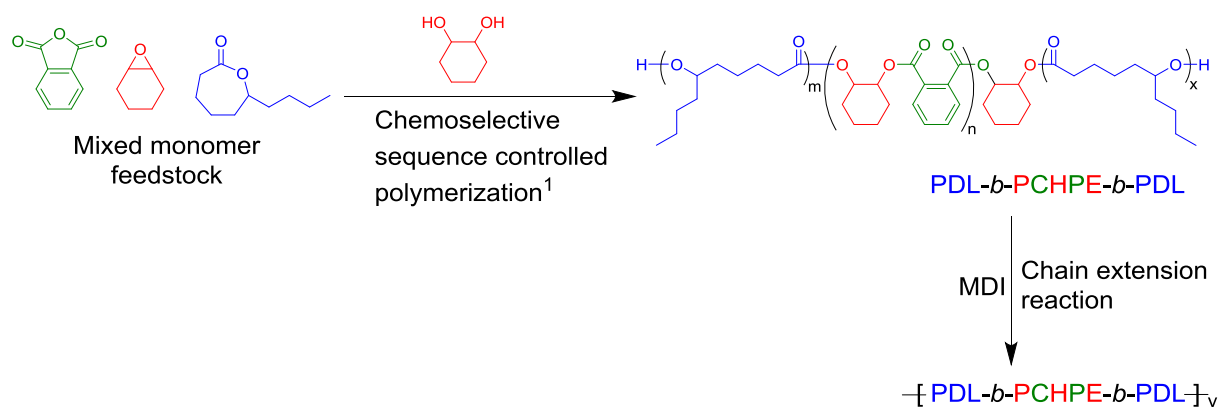
Scheme 1.1 The ring-opening polymerization of ϵ -caprolactone, initiated by a di-zinc complex and different diol chain transfer agents.

- Multi-block copolymers have the potential for significantly enhanced properties and functionality.¹⁸⁸ Block regulation provides a means to differentiate macroscopic thermal/mechanical performances and, of particular relevance for oxygenated polymers, degradation rates.³⁰⁸⁻³¹⁰ Directing the block compositions in conventional polyester synthesis would be extremely difficult and more often impossible, due to step-growth synthetic methods. In contrast, the ROP of lactones²¹ or ROCOP of epoxides/anhydrides^{29,81,130,134,138,142,154,311} allow the controlled syntheses.³¹² Currently, the catalysts used for these two processes have been reported separately and using these catalyst to catalyze both processes in one pot remains unexplored.. To address this issue, it is both of timely and novel to explore the possibility of using selective catalysis to prepare block copolyesters by combining ring-opening polymerization of lactones and ring-opening copolymerization of epoxides/anhydrides. (**Scheme 1.2**). A di-zinc complex will be used to investigate whether the method applies for block sequence selectivity from monomer mixtures.



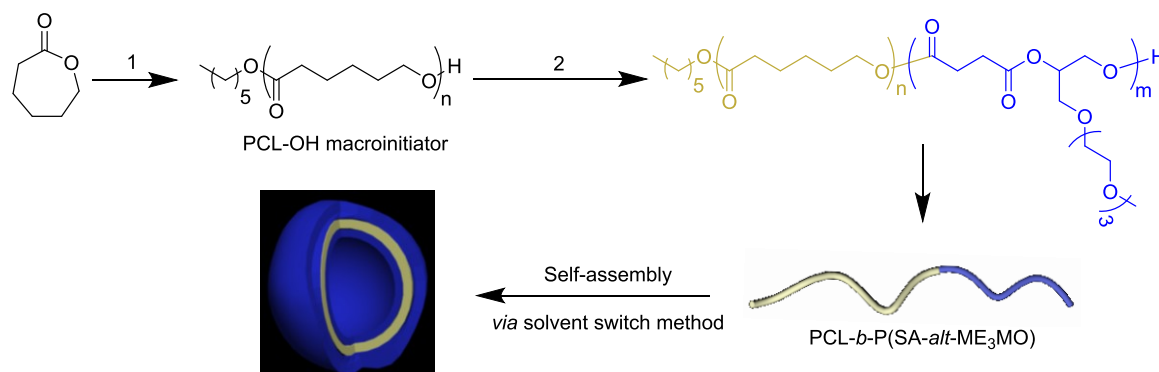
Scheme 1.2 (A) Diagram illustrating the chemoselective sequence controlled polymerization; (B) Reactions corresponding to the steps illustrated in (A).

- To investigate the thermal/mechanical properties of the (multi)block copolyesters obtained from the ‘chemoselective polymerization’ method. The goal is to develop simultaneously biorenewable and degradable polyesters suitable for high value applications (**Scheme 1.3**). The approach is to target a series of new multi-block copolyesters comprising rigid but amorphous hard blocks and soft, amorphous blocks. The materials will be prepared using switchable polymerization catalysis, although chain extension, e.g. with a diisocyanate, is likely to be necessary to overcome the low molecular weight achieved by ring-opening polymerizations. The low molecular weight results from the limited turnover number of the dizinc catalyst. The triblock copolymers comprise hard blocks from the ring-opening copolymerization of phthalic anhydride (PA) and cyclohexene oxide (CHO) and soft blocks from the ring-opening polymerization of ϵ -decalactone (DL).³¹³ Today these monomers are petrochemicals but routes from renewable sources have been pioneered: ϵ -decalactone from castor oil, phthalic anhydride from carbohydrates and cyclohexene oxide from fatty acids.^{154,314}



Scheme 1.3 Preparation of partly biorenewable thermoplastic elastomer using $\{ \text{PDL}_m\text{-}b\text{-PCHPE}_n\text{-}b\text{-PDL}_m \}_y$ multi-block copolyesters.

- To use metabolite-derived monomers to prepare partly renewable polyesters which can subsequently undergo self-assembly into drug delivery vehicles for potential biomedical applications (**Scheme 1.4**). The aim is to develop biocompatible polyesters which also generate non-toxic degradation products. The cytotoxicity of the degradation products will be carefully evaluated. The renewable component, succinic anhydride, is selected because its degradation product, succinic acid, is a metabolic intermediate in the Krebs cycle. The other comonomer, ME₃MO, affords PEG-like degradation product which is expected to show similar toxicity to glycerol ether.



Scheme 1.4 Schematic illustration of the proposed preparation of amphiphilic block copolyesters, PCL-*b*-P(SA-*alt*-ME₃MO), and the self-assembly procedure. Reaction conditions: (1) ring-opening polymerization of ϵ -caprolactone in toluene initiated from *n*-hexanol, using TBD as the catalyst at 25 °C; (2) ring-opening copolymerization of succinic anhydride and ME₃MO in toluene initiated from PCL-OH macroinitiator, using salenCrCl/PPNCl catalyst system at 80 °C.

1.11 References

- (1) Odell, P. R. *Why Carbon Fuels Will Dominate The 21st Century's Global Energy Economy*; Multi-Science Publishing: Essex, U.K., 2004.
- (2) Aresta, M. *Carbon Dioxide as Chemical Feedstock*; Wiley-VCH: Germany, 2010.
- (3) Hirsch, R. L.; Bezdek, R.; Robert, W. *Peaking of world oil production: impacts, mitigation, and risk management*, 2005.
- (4) Shafiee, S.; Topal, E. *Energy Policy* **2009**, 37, 181-189.
- (5) *Report of the World Commission on Environment and Development: Our Common Future* 1987.
- (6) <http://csp.umn.edu/about-us/sustainable-polymers-101/>.
- (7) Geise, G. M.; Lee, H.-S.; Miller, D. J.; Freeman, B. D.; McGrath, J. E.; Paul, D. R. *J. Polym. Sci. Pol. Phys.* **2010**, 48, 1685-1718.
- (8) Mouritz, A. P.; Leong, K. H.; Herszberg, I. *Composites Part A* **1997**, 28, 979-991.
- (9) van der Ploeg, F. J. *Econ. Lit.* **2011**, 49, 366-420.
- (10) Jambeck, J. R.; Geyer, R.; Wilcox, C.; Siegler, T. R.; Perryman, M.; Andrady, A.; Narayan, R.; Law, K. L. *Science* **2015**, 347, 768-771.
- (11) Ulery, B. D.; Nair, L. S.; Laurencin, C. T. *J. Polym. Sci. Pol. Phys.* **2011**, 49, 832-864.
- (12) Philp, J. C.; Bartsev, A.; Ritchie, R. J.; Baucher, M.-A.; Guy, K. *New Biotechnol.* **2013**, 30, 635-646.
- (13) Shen, L.; Worrell, E.; Patel, M. *Biofuels, Bioprod. Biorefin.* **2010**, 4, 25-40.
- (14) Paul, S.; Zhu, Y.; Romain, C.; Brooks, R.; Saini, P. K.; Williams, C. K. *Chem. Commun.* **2015**, 51, 6459-6479.
- (15) Mark, J. *Polymer Data Handbook*; Oxford University Press, Inc., 1999.
- (16) Wypych, G. In *Handbook of Polymers*; Elsevier: Oxford, 2012, p 308-314.
- (17) Wypych, G. In *Handbook of Polymers*; Elsevier: Oxford, 2012, p 385-390.
- (18) http://www.chemweek.com/lab/PEPP-2016-The-global-polyolefins-industry-has-a-bright-future_79771.html.
- (19) Madhavan Nampoothiri, K.; Nair, N. R.; John, R. P. *Bioresour. Technol.* **2010**, 101, 8493-8501.
- (20) Inkinen, S.; Hakkarainen, M.; Albertsson, A. C.; Sodergard, A. *Biomacromolecules* **2011**, 12, 523-532.
- (21) Platel, R. H.; Hodgson, L. M.; Williams, C. K. *Polym. Rev.* **2008**, 48, 11-63.
- (22) Tschan, M. J. L.; Brule, E.; Haquette, P.; Thomas, C. M. *Polym. Chem.* **2012**, 3, 836-851.
- (23) Auras, R.; Harte, B.; Selke, S. *Macromol. Biosci.* **2004**, 4, 835-864.
- (24) Sudesh, K.; Abe, H.; Doi, Y. *Prog. Polym. Sci.* **2000**, 25, 1503-1555.
- (25) Muller, H. M.; Seebach, D. *Angew. Chem., Int. Ed.* **1993**, 32, 477-502.
- (26) Lenz, R. W.; Marchessault, R. H. *Biomacromolecules* **2005**, 6, 1-8.
- (27) Zhu, Y.; Romain, C.; Williams, C. K. *Nature* **2016**, Accepted.
- (28) <http://www.empowermaterials.com/>; <http://www.novomer.com/>;
<http://www.materialscience.bayer.de/Projects-and-Cooperations/CO2-Project.aspx>;
<http://www.econic-technologies.com/>.
- (29) Jeske, R. C.; DiCiccio, A. M.; Coates, G. W. *J. Am. Chem. Soc.* **2007**, 129, 11330-11331.
- (30) Nejad, E. H.; Paoniasari, A.; van Melis, C. G. W.; Koning, C. E.; Duchateau, R. *Macromolecules* **2013**, 46, 631-637.
- (31) DiCiccio, A. M.; Coates, G. W. *J. Am. Chem. Soc.* **2011**, 133, 10724-10727.
- (32) Feng, L.; Liu, Y.; Hao, J.; Xiong, C.; Deng, X. *J. Polym. Sci. A: Polym. Chem.* **2012**, 50, 1812-1818.
- (33) von der Assen, N.; Bardow, A. *Green Chem.* **2014**, 16, 3272-3280.

- (34) Jem, K. J.; van der Pol, J. F.; de Vos, S. In *Plastics from Bacteria, Natural Functions and Applications*; Springer: Heidelberg, 2010, p 323-346.
- (35) Chen, G. Q. In *Plastics from Bacteria, Natural Functions and Applications*; Springer: Heidelberg, 2010, p 17-37.
- (36) Qin, Y.; Wang, X. *Biotechnol. J.* **2010**, *5*, 1164-1180.
- (37) Mialon, L.; Pemba, A. G.; Miller, S. A. *Green Chem.* **2010**, *12*, 1704-1706.
- (38) Hauenstein, O.; Reiter, M.; Agarwal, S.; Rieger, B.; Greiner, A. *Green Chem.* **2016**, *18*, 760-770.
- (39) Inoue, S. *J. Polym. Sci. A: Polym. Chem.* **2000**, *38*, 2861-2871.
- (40) Hawker, C. J. *Acc. Chem. Res.* **1997**, *30*, 373-382.
- (41) Coates, G. W. *Chem. Rev.* **2000**, *100*, 1223-1252.
- (42) Okada, M. *Prog. Polym. Sci.* **2002**, *27*, 87-133.
- (43) Lodge, T. P. *Macromol. Chem. Phys.* **2003**, *204*, 265-273.
- (44) Hadjichristidis, N.; Iatrou, H.; Pitsikalis, M.; Mays, J. *Prog. Polym. Sci.* **2006**, *31*, 1068-1132.
- (45) Braunecker, W. A.; Matyjaszewski, K. *Prog. Polym. Sci.* **2007**, *32*, 93-146.
- (46) Domski, G. J.; Rose, J. M.; Coates, G. W.; Bolig, A. D.; Brookhart, M. *Prog. Polym. Sci.* **2007**, *32*, 30-92.
- (47) Tsarevsky, N. V.; Matyjaszewski, K. *Chem. Rev.* **2007**, *107*, 2270-2299.
- (48) Moad, G.; Rizzardo, E.; Thang, S. H. *Acc. Chem. Res.* **2008**, *41*, 1133-1142.
- (49) Schrock, R. R. *Acc. Chem. Res.* **2014**, *47*, 2457-2466.
- (50) Halasa, A. F. *Rubber Chem. Technol.* **1981**, *54*, 627-640.
- (51) Odian, G. *Principles of Polymerization*; 4th ed.; A John Wiley & Sons, Inc.: New Jersey, 2004.
- (52) Aida, T.; Inoue, S. *Accounts. Chem. Res.* **1996**, *29*, 39-48.
- (53) Helou, M.; Miserque, O.; Brusson, J.-M.; Carpentier, J.-F.; Guillaume, S. M. *Adv. Synth. Catal.* **2009**, *351*, 1312-1324.
- (54) Williams, C. K. *Chem. Soc. Rev.* **2007**, *36*, 1573-1580.
- (55) Thomas, C. M.; Lutz, J. F. *Angew. Chem., Int. Ed.* **2011**, *50*, 9244-9246.
- (56) Stanford, M. J.; Dove, A. P. *Chem. Soc. Rev.* **2010**, *39*, 486-494.
- (57) Ajellal, N.; Carpentier, J. F.; Guillaume, C.; Guillaume, S. M.; Helou, M.; Poirier, V.; Sarazin, Y.; Trifonov, A. *Dalton Trans.* **2010**, *39*, 8363-8376.
- (58) Dechy-Cabaret, O.; Martin-Vaca, B.; Bourissou, D. *Chem. Rev.* **2004**, *104*, 6147-6176.
- (59) O'Keefe, B. J.; Hillmyer, M. A.; Tolman, W. B. *Dalton Trans.* **2001**, 2215-2224.
- (60) Dijkstra, P. J.; Du, H. Z.; Feijen, J. *Polym. Chem.* **2011**, *2*, 520-527.
- (61) Jaffredo, C. G.; Guillaume, S. M. *Polym. Chem.* **2014**, *5*, 4168-4194.
- (62) Tempelaar, S.; Mespouille, L.; Coulembier, O.; Dubois, P.; Dove, A. P. *Chem. Soc. Rev.* **2013**, *42*, 1312-1336.
- (63) Dagonne, S.; Normand, M.; Kirillov, E.; Carpentier, J.-F. *Coord. Chem. Rev.* **2013**, *257*, 1869-1886.
- (64) Brown, H. A.; Waymouth, R. M. *Acc. Chem. Res.* **2013**, *46*, 2585-2596.
- (65) Lecomte, P.; Jerome, C. In *Synthetic Biodegradable Polymers*; Rieger, B., Kunkel, A., Coates, G. W., Reichardt, R., Dinjus, E., Zevaco, T. A., Eds. 2012; Vol. 245, p 173-217.
- (66) Guillaume, S. M.; Carpentier, J.-F. *Cat. Sci. Tech.* **2012**, *2*, 898-906.
- (67) Dutta, S.; Hung, W.-C.; Huang, B.-H.; Lin, C.-C. In *Synthetic Biodegradable Polymers*; Rieger, B., Kunkel, A., Coates, G. W., Reichardt, R., Dinjus, E., Zevaco, T. A., Eds. 2012; Vol. 245, p 219-283.
- (68) Mespouille, L.; Coulembier, O.; Kawalec, M.; Dove, A. P.; Dubois, P. *Prog. Polym. Sci.* **2014**, *39*, 1144-1164.
- (69) Hillmyer, M. A.; Tolman, W. B. *Acc. Chem. Res.* **2014**, *47*, 2390-2396.

- (70) Yao, K.; Tang, C. *Macromolecules* **2013**, *46*, 1689-1712.
- (71) Labet, M.; Thielemans, W. *Chem. Soc. Rev.* **2009**, *38*, 3484-3504.
- (72) Arbaoui, A.; Redshaw, C. *Polym. Chem.* **2010**, *1*, 801-826.
- (73) Albertsson, A. C.; Varma, I. K. *Biomacromolecules* **2003**, *4*, 1466-1486.
- (74) Tian, H.; Tang, Z.; Zhuang, X.; Chen, X.; Jing, X. *Prog. Polym. Sci.* **2012**, *37*, 237-280.
- (75) Kember, M. R.; Buchard, A.; Williams, C. K. *Chem. Commun.* **2011**, *47*, 141-163.
- (76) Baker, G. L.; Vogel, E. B.; Smith, M. R. *Polym. Rev.* **2008**, *48*, 64-84.
- (77) Suriano, F.; Coulembier, O.; Hedrick, J. L.; Dubois, P. *Polym. Chem.* **2011**, *2*, 528-533.
- (78) Sawada, H. *J. Macromol. Sci., Polym. Rev.* **1970**, *5*, 151-173.
- (79) MacDonald, J. P.; Shaver, M. P. *Polym. Chem.* **2016**, *7*, 553-559.
- (80) Koning, C. E.; Sablong, R. J.; Nejad, E. H.; Duchateau, R.; Buijsen, P. *Prog. Org. Coat.* **2013**, *76*, 1704-1711.
- (81) Nejad, E. H.; Paoniasari, A.; Koning, C. E.; Duchateau, R. *Polym. Chem.* **2012**, *3*, 1308-1313.
- (82) Huijser, S.; HosseiniNejad, E.; Sablong, R. I.; Jong, C. D.; Koning, C. E.; Duchateau, R. *Macromolecules* **2011**, *44*, 1132-1139.
- (83) Darensbourg, D. J.; Wilson, S. J. *Macromolecules* **2013**, *46*, 5929-5934.
- (84) Darensbourg, D. J.; Wilson, S. J. *J. Am. Chem. Soc.* **2011**, *133*, 18610-18613.
- (85) Albertsson, A. C.; Varma, I. K. *Degradable Aliphatic Polyesters* **2002**, *157*, 1-40.
- (86) Fischer, R. F. *J. Polym. Sci.* **1960**, *44*, 155-172.
- (87) Schwenk, V. E.; Gulbins, K.; Roth, M.; Benzing, G.; Maysenhölder, R.; Hamann, K. *Makromol. Chem.* **1962**, *51*, 53-69.
- (88) Tsuruta, T.; Matsuura, K.; Inoue, S. *Makromol. Chem.* **1964**, *75*, 211-214.
- (89) Matsuura, K.; Tsuruta, T.; Terada, Y.; Inoue, S. *Makromol. Chem.* **1965**, *81*, 258-260.
- (90) Hilt, V. A.; Reichert, K. H.; Hamann, K. *Makromol. Chem.* **1967**, *101*, 246-270.
- (91) Schaefer, J.; Katnik, R. J.; Kern, R. J. *J. Am. Chem. Soc.* **1968**, *90*, 2476-2480.
- (92) Inoue, S.; Kitamura, K.; Tsuruta, T. *Makromol. Chem.* **1969**, *126*, 250-265.
- (93) Hsieh, H. L. *J. Macromol. Sci. Part A Pure Appl. Chem.* **1973**, *7*, 1525-1535.
- (94) Kuran, W.; Niestochowski, A. *Polym. Bull.* **1980**, *2*, 411-416.
- (95) Saini, P. K.; Romain, C.; Williams, C. K. *Chem. Commun.* **2014**, 4164-4167.
- (96) Kember, M. R.; Williams, C. K. *J. Am. Chem. Soc.* **2012**, *134*, 15676-15679.
- (97) Kember, M. R.; Copley, J.; Buchard, A.; Williams, C. K. *Polym. Chem.* **2012**, *3*, 1196-1201.
- (98) Buchard, A.; Jutz, F.; Kember, M. R.; White, A. J. P.; Rzepa, H. S.; Williams, C. K. *Macromolecules* **2012**, *45*, 6781-6795.
- (99) Jutz, F.; Buchard, A.; Kember, M. R.; Fredrickson, S. B.; Williams, C. K. *J. Am. Chem. Soc.* **2011**, *133*, 17395-17405.
- (100) Buchard, A.; Kember, M. R.; Sandeman, K. G.; Williams, C. K. *Chem. Commun.* **2011**, *47*, 212-214.
- (101) Kember, M. R.; Knight, P. D.; Reung, P. T. R.; Williams, C. K. *Angew. Chem., Int. Ed.* **2009**, *48*, 931-933.
- (102) Kember, M. R.; White, A. J. P.; Williams, C. K. *Inorg. Chem.* **2009**, *48*, 9535-9542.
- (103) Moore, D. R.; Cheng, M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2003**, *125*, 11911-11924.
- (104) Cheng, M.; Moore, D. R.; Reczek, J. J.; Chamberlain, B. M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2001**, *123*, 8738-8749.
- (105) Cheng, M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **1998**, *120*, 11018-11019.
- (106) Ellis, W. C.; Jung, Y.; Mulzer, M.; Di Girolamo, R.; Lobkovsky, E. B.; Coates, G. W. *Chem. Sci.* **2014**, *5*, 4004-4011.

- (107) Robert, C.; Ohkawara, T.; Nozaki, K. *Chem. Eur. J.* **2014**, 4789-4795.
- (108) Ohkawara, T.; Suzuki, K.; Nakano, K.; Mori, S.; Nozaki, K. *J. Am. Chem. Soc.* **2014**, *136*, 10728-10735.
- (109) Nakano, K.; Hashimoto, S.; Nozaki, K. *Chem. Sci.* **2010**, 369-373.
- (110) Noh, E. K.; Na, S. J.; S, S.; Kim, S.-W.; Lee, B. Y. *J. Am. Chem. Soc.* **2007**, *129*, 8082-8083.
- (111) Lee, B. Y.; Kwon, H. Y.; Lee, S. Y.; Na, S. J.; Han, S.-i.; Yun, H.; Lee, H.; Park, Y.-W. *J. Am. Chem. Soc.* **2005**, *127*, 3031-3037.
- (112) Liu, Y.; Ren, W.-M.; Liu, J.; Lu, X.-B. *Angew. Chem., Int. Ed.* **2013**, *52*, 11594-11598.
- (113) Anderson, C. E.; Vagin, S. I.; Hammann, M.; Zimmermann, L.; Rieger, B. *ChemCatChem* **2013**, *5*, 3269-3280.
- (114) Klaus, S.; Vagin, S. I.; Lehenmeier, M. W.; Deglmann, P.; Brym, A. K.; Rieger, B. *Macromolecules* **2011**, *44*, 9508-9516.
- (115) Vagin, S. I.; Reichardt, R.; Klaus, S.; Rieger, B. *J. Am. Chem. Soc.* **2010**, *132*, 14367-14369.
- (116) Klaus, S.; Lehenmeier, M. W.; Anderson, C. E.; Rieger, B. *Coord. Chem. Rev.* **2011**, *255*, 1460-1479.
- (117) Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1985**, *107*, 1358-1364.
- (118) Aida, T.; Sanuki, K.; Inoue, S. *Macromolecules* **1985**, *18*, 1049-1055.
- (119) Chatterjee, C.; Chisholm, M. H. *Chem. Rec.* **2013**, *13*, 549-560.
- (120) Bernard, A.; Chatterjee, C.; Chisholm, M. H. *Polymer* **2013**, *54*, 2639-2646.
- (121) Allen, S. D.; Moore, D. R.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 14284-14285.
- (122) Cheng, M.; Attygalle, A. B.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **1999**, *121*, 11583-11584.
- (123) Chamberlain, B. M.; Cheng, M.; Moore, D. R.; Ovitt, T. M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2001**, *123*, 3229-3238.
- (124) Rieth, L. R.; Moore, D. R.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 15239-15248.
- (125) Radzewich, C. E.; Coles, M. P.; Jordan, R. F. *J. Am. Chem. Soc.* **1998**, *120*, 9384-9385.
- (126) Yokota, S.; Tachi, Y.; Itoh, S. *Inorg. Chem.* **2002**, *41*, 1342-1344.
- (127) Carey, D. T.; Cope-Eatough, E. K.; Vilaplana-Mafe, E.; Mair, F. S.; Pritchard, R. G.; Warren, J. E.; Woods, R. J. *Dalton Trans.* **2003**, 1083-1093.
- (128) Darensbourg, D. J.; Mackiewicz, R. M.; Phelps, A. L.; Billodeaux, D. R. *Acc. Chem. Res.* **2004**, *37*, 836-844.
- (129) Wu, G. P.; Darensbourg, D. J.; Lu, X. B. *J. Am. Chem. Soc.* **2012**, *134*, 17739-17745.
- (130) Hosseini Nejad, E.; van Melis, C. G. W.; Vermeer, T. J.; Koning, C. E.; Duchateau, R. *Macromolecules* **2012**, *45*, 1770-1776.
- (131) Van Zee, N. J.; Sanford, M. J.; Coates, G. W. *J. Am. Chem. Soc.* **2016**, *138*, 2755-2761.
- (132) Pepels, M. P. F.; Bouyahyi, M.; Heise, A.; Duchateau, R. *Macromolecules* **2013**, *46*, 4324-4334.
- (133) Liu, J.; Bao, Y.-Y.; Liu, Y.; Ren, W.-M.; Lu, X.-B. *Polym. Chem.* **2013**, *4*, 1439-1444.
- (134) Saini, P. K.; Romain, C.; Zhu, Y.; Williams, C. K. *Polym. Chem.* **2014**, *5*, 6068-6075.
- (135) Wu, L. Y.; Fan, D. D.; Lü, X.-Q.; Lu, R. *Chin. J. Polym. Sci.* **2014**, *32*, 768-777.
- (136) Romain, C.; Williams, C. K. *Angew. Chem., Int. Ed.* **2014**, *53*, 1607-1610.
- (137) Liu, Y.; Huang, K.; Peng, D.; Wu, H. *Polymer* **2006**, *47*, 8453-8461.
- (138) Jeske, R. C.; Rowley, J. M.; Coates, G. W. *Angew. Chem., Int. Ed.* **2008**, *47*, 6041-6044.
- (139) Duan, Z.; Wang, X.; Gao, Q.; Zhang, L.; Liu, B.; Kim, I. *J. Polym. Sci. A: Polym. Chem.* **2014**, *52*, 789-795.

- (140) Liu, Y.; Xiao, M.; Wang, S.; Xia, L.; Hang, D.; Cui, G.; Meng, Y. *RSC Adv.* **2014**, *4*, 9503-9508.
- (141) Sun, X.-K.; Zhang, X.-H.; Chen, S.; Du, B.-Y.; Wang, Q.; Fan, Z.-Q.; Qi, G.-R. *Polymer* **2010**, *51*, 5719-5725.
- (142) Darensbourg, D. J.; Poland, R. R.; Escobedo, C. *Macromolecules* **2012**, *45*, 2242-2248.
- (143) Kim, J. S.; Kim, H.; Yoon, J.; Heo, K.; Ree, M. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 4079-4088.
- (144) Gu, L.; Qin, Y.; Gao, Y.; Wang, X.; Wang, F. *Chin. J. Chem.* **2012**, *30*, 2121-2125.
- (145) Hwang, Y.; Jung, J.; Ree, M.; Kim, H. *Macromolecules* **2003**, *36*, 8210-8212.
- (146) Hwang, Y.; Kim, H.; Ree, M. *Macromol. Symp.* **2005**, *224*, 227-238.
- (147) Liu, S.; Wang, J.; Huang, K.; Liu, Y.; Wu, W. *Polym. Bull.* **2011**, *66*, 327-340.
- (148) Kroger, M.; Folli, C.; Walter, O.; Doring, M. *Adv. Synth. Catal.* **2006**, *348*, 1908-1918.
- (149) Cyriac, A.; Lee, S. H.; Varghese, J. K.; Park, E. S.; Park, J. H.; Lee, B. Y. *Macromolecules* **2010**, *43*, 7398-7401.
- (150) Darensbourg, D. J.; Wu, G.-P. *Angew. Chem., Int. Ed.* **2013**, *52*, 10602-10606.
- (151) Wu, G.-P.; Darensbourg, D. J. *Macromolecules* **2016**, *49*, 807-814.
- (152) Luinstra, G. A. *Polym. Rev.* **2008**, *48*, 192-219.
- (153) Byrne, C. M.; Allen, S. D.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2004**, *126*, 11404-11405.
- (154) Winkler, M.; Romain, C.; Meier, M. A. R.; Williams, C. K. *Green Chem.* **2015**, *17*, 300-306.
- (155) Li, C.; Sablong, R. J.; Koning, C. E. *Eur. Polym. J.* **2015**, *67*, 449-458.
- (156) Auriemma, F.; De Rosa, C.; Di Caprio, M. R.; Di Girolamo, R.; Ellis, W. C.; Coates, G. W. *Angew. Chem., Int. Ed.* **2015**, *54*, 1215-1218.
- (157) Lee, S. H.; Cyriac, A.; Jeon, J. Y.; Lee, B. Y. *Polym. Chem.* **2012**, *3*, 1215-1220.
- (158) Chapman, A. M.; Keyworth, C.; Kember, M. R.; Lennox, A. J. J.; Williams, C. K. *ACS Catal.* **2015**, *5*, 1581-1588.
- (159) Darensbourg, D. J. *Chem. Rev.* **2007**, *107*, 2388-2410.
- (160) Liu, T.; Simmons, T. L.; Bohnsack, D. A.; Mackay, M. E.; Smith, M. R.; Baker, G. L. *Macromolecules* **2007**, *40*, 6040-6047.
- (161) Takasu, A.; Ito, M.; Inai, Y.; Hirabayashi, T.; Nishimura, Y. *Polym. J.* **1999**, *31*, 961-969.
- (162) Hua, Z.; Qi, G.; Chen, S. *J. Appl. Polym. Sci.* **2004**, *93*, 1788-1792.
- (163) Takenouchi, S.; Takasu, A.; Inai, Y.; Hirabayashi, T. *Polym. J.* **2002**, *34*, 36-42.
- (164) Van Zee, N. J.; Coates, G. W. *Angew. Chem., Int. Ed.* **2015**, *54*, 2665-2668.
- (165) Longo, J. M.; DiCiccio, A. M.; Coates, G. W. *J. Am. Chem. Soc.* **2014**, *136*, 15897-15900.
- (166) Delidovich, I.; Hausoul, P. J. C.; Deng, L.; Pfützenreuter, R.; Rose, M.; Palkovits, R. *Chem. Rev.* **2015**, *116*, 1540-1599.
- (167) Gil, E. S.; Hudson, S. M. *Prog. Polym. Sci.* **2004**, *29*, 1173-1222.
- (168) Loh, X. J.; del Barrio, J.; Toh, P. P. C.; Lee, T. C.; Jiao, D. Z.; Rauwald, U.; Appel, E. A.; Scherman, O. A. *Biomacromolecules* **2012**, *13*, 84-91.
- (169) Rossow, T.; Hackelbusch, S.; van Assenbergh, P.; Seiffert, S. *Polym. Chem.* **2013**, *4*, 2515-2527.
- (170) Zhang, Z. X.; Liu, K. L.; Li, J. *Macromolecules* **2011**, *44*, 1182-1193.
- (171) Vihola, H.; Laukkanen, A.; Valtola, L.; Tenhu, H.; Hirvonen, J. *Biomaterials* **2005**, *26*, 3055-3064.
- (172) Zhang, H.; Lin, X.; Chin, S.; Grinstaff, M. W. *J. Am. Chem. Soc.* **2015**, *137*, 12660-12666.
- (173) Darensbourg, D. J.; Tsai, F.-T. *Macromolecules* **2014**, *47*, 3806-3813.

- (174) Tsai, F.-T.; Wang, Y.; Darensbourg, D. J. *J. Am. Chem. Soc.* **2016**, *138*, 4626-4633.
- (175) Feng, L.; Liu, Y.; Hao, J.; Li, X.; Xiong, C.; Deng, X. *Macromol. Chem. Phys.* **2011**, *212*, 2626-2632.
- (176) Wang, D. X.; Zhang, G. J.; Zhang, Y. C.; Gao, Y. J.; Zhao, Y. H.; Zhou, C. Y.; Zhang, Q. Y.; Wang, X. K. *J. Appl. Polym. Sci.* **2007**, *103*, 417-424.
- (177) Shin, J.; Lee, Y.; Tolman, W. B.; Hillmyer, M. A. *Biomacromolecules* **2012**, *13*, 3833-3840.
- (178) Parulekar, Y.; Mohanty, A. K. *Green Chem.* **2006**, *8*, 206-213.
- (179) Wang, Z.; Yuan, L.; Trenor, N. M.; Vlaminck, L.; Billiet, S.; Sarkar, A.; Du Prez, F. E.; Stefik, M.; Tang, C. *Green Chem.* **2015**, *17*, 3806-3818.
- (180) Kraus, G.; Rollmann, K. W.; Gruver, J. T. *Macromolecules* **1970**, *3*, 92-96.
- (181) Hashimoto, T.; Fujimura, M.; Saijo, K.; Kawai, H.; Diamant, J.; Shen, M. In *Multiphase Polymers*; American Chemical Society: 1979; Vol. 176, p 257-275.
- (182) Lewis, P. R.; Price, C. *Polymer* **1972**, *13*, 20-26.
- (183) Campos-Lopez, E.; McIntyre, D.; Fetters, L. J. *Macromolecules* **1973**, *6*, 415-423.
- (184) McIntyre, D.; Campos-Lopez, E. *Macromolecules* **1970**, *3*, 322-327.
- (185) Du, Y. Z.; Yu, M.; Ge, J.; Ma, P. X.; Chen, X. F.; Lei, B. *Adv. Funct. Mater.* **2015**, *25*, 5016-5029.
- (186) Tran, C. D.; Chen, J.; Keum, J. K.; Naskar, A. K. *Adv. Funct. Mater.* **2016**, *26*, 2677-2685.
- (187) Wanamaker, C. L.; O'Leary, L. E.; Lynd, N. A.; Hillmyer, M. A.; Tolman, W. B. *Biomacromolecules* **2007**, *8*, 3634-3640.
- (188) Bates, F. S.; Hillmyer, M. A.; Lodge, T. P.; Bates, C. M.; Delaney, K. T.; Fredrickson, G. H. *Science* **2012**, *336*, 434-440.
- (189) Bolton, J. M.; Hillmyer, M. A.; Hoyer, T. R. *ACS Macro Lett.* **2014**, *3*, 717-720.
- (190) Xiong, M. Y.; Schneiderman, D. K.; Bates, F. S.; Hillmyer, M. A.; Zhang, K. C. *PNAS* **2014**, *111*, 8357-8362.
- (191) Cordier, P.; Tournilhac, F.; Soulie-Ziakovic, C.; Leibler, L. *Nature* **2008**, *451*, 977-980.
- (192) Hearon, K.; Nash, L. D.; Rodriguez, J. N.; Lonneck, A. T.; Raymond, J. E.; Wilson, T. S.; Wooley, K. L.; Maitland, D. J. *Adv. Mater.* **2014**, *26*, 1552-1558.
- (193) Wang, S.; Kesava, S. V.; Gomez, E. D.; Robertson, M. L. *Macromolecules* **2013**, *46*, 7202-7212.
- (194) Montarnal, D.; Capelot, M.; Tournilhac, F.; Leibler, L. *Science* **2011**, *334*, 965-968.
- (195) Altuna, F. I.; Pettarin, V.; Williams, R. J. J. *Green Chem.* **2013**, *15*, 3360-3366.
- (196) Liu, Y.; Yao, K.; Chen, X.; Wang, J.; Wang, Z.; Ploehn, H. J.; Wang, C.; Chu, F.; Tang, C. *Polym. Chem.* **2014**, *5*, 3170-3181.
- (197) Fakirov, S. *Handbook of Condensation Thermoplastic Elastomers*; WILEY-VCH Verlag GmbH & Co. KGaA: Weinheim, 2005.
- (198) Martello, M. T.; Hillmyer, M. A. *Macromolecules* **2011**, *44*, 8537-8545.
- (199) Kim, W.; Thevenot, J.; Ibarboure, E.; Lecommandoux, S.; Chaikof, E. L. *Angew. Chem., Int. Ed.* **2010**, *49*, 4257-4260.
- (200) Rhodes, A. J.; Deming, T. J. *J. Am. Chem. Soc.* **2012**, *134*, 19463-19467.
- (201) Rodriguez-Hernandez, J.; Lecommandoux, S. *J. Am. Chem. Soc.* **2005**, *127*, 2026-2027.
- (202) Schatz, C.; Lecommandoux, S. *Macromol. Rapid Commun.* **2010**, *31*, 1664-1684.
- (203) Guo, B.; Finne-Wistrand, A.; Albertsson, A.-C. *Biomacromolecules* **2011**, *12*, 2601-2609.
- (204) Gandini, A.; Lacerda, T. M.; Carvalho, A. J.; Trovatti, E. *Chem. Rev.* **2016**, *116*, 1637-1669.
- (205) Arrieta, M. P.; López, J.; Hernández, A.; Rayón, E. *Eur. Polym. J.* **2014**, *50*, 255-270.
- (206) Guillaume, C.; Ajellal, N.; Carpentier, J. F.; Guillaume, S. M. *J. Polym. Sci., Part A:*

Polym. Chem. **2011**, *49*, 907-917.

(207) Poetz, K. L.; Mohammed, H. S.; Snyder, B. L.; Liddil, G.; Samways, D. S. K.; Shipp, D. A. *Biomacromolecules* **2014**, *15*, 2573-2582.

(208) Tamada, J.; Langer, R. *J. Biomater. Sci.-Polym. Ed.* **1992**, *3*, 315-353.

(209) Engler, A. C.; Ke, X. Y.; Gao, S. J.; Chan, J. M. W.; Coady, D. J.; Ono, R. J.; Lubbers, R.; Nelson, A.; Yang, Y. Y.; Hedrick, J. L. *Macromolecules* **2015**, *48*, 1673-1678.

(210) Brignou, P.; Carpentier, J. F.; Guillaume, S. M. *Macromolecules* **2011**, *44*, 5127-5135.

(211) Darensbourg, D. J.; Choi, W.; Karroonnirun, O.; Bhuvanesh, N. *Macromolecules* **2008**, *41*, 3493-3502.

(212) Kricheldorf, H. R.; Rost, S. *Macromolecules* **2005**, *38*, 8220-8226.

(213) Zhang, S.; Zou, J.; Zhang, F.; Elsabahy, M.; Felder, S. E.; Zhu, J.; Pochan, D. J.; Wooley, K. L. *J. Am. Chem. Soc.* **2012**, *134*, 18467-18474.

(214) Liu, X.; Ni, P.; He, J.; Zhang, M. *Macromolecules* **2010**, *43*, 4771-4781.

(215) Clément, B.; Grignard, B.; Koole, L.; Jérôme, C.; Lecomte, P. *Macromolecules* **2012**, *45*, 4476-4486.

(216) Yu, K.; Eisenberg, A. *Macromolecules* **1996**, *29*, 6359-6361.

(217) Zhang, L. F.; Bartels, C.; Yu, Y. S.; Shen, H. W.; Eisenberg, A. *Phys. Rev. Lett.* **1997**, *79*, 5034-5037.

(218) Shen, H.; Eisenberg, A. *Macromolecules* **2000**, *33*, 2561-2572.

(219) Zhang, L.; Eisenberg, A. *J. Am. Chem. Soc.* **1996**, *118*, 3168-3181.

(220) Ding, J. F.; Liu, G. J. *Macromolecules* **1997**, *30*, 655-657.

(221) Yu, K.; Eisenberg, A. *Macromolecules* **1998**, *31*, 3509-3518.

(222) Yu, Y.; Zhang, L.; Eisenberg, A. *Macromolecules* **1998**, *31*, 1144-1154.

(223) Discher, B. M.; Won, Y. Y.; Ege, D. S.; Lee, J. C. M.; Bates, F. S.; Discher, D. E.; Hammer, D. A. *Science* **1999**, *284*, 1143-1146.

(224) Li, Z. C.; Liang, Y. Z.; Li, F. M. *Chem. Commun.* **1999**, 1557-1558.

(225) Du, J. Z.; Fan, L.; Liu, Q. M. *Macromolecules* **2012**, *45*, 8275-8283.

(226) Takemoto, H.; Ishii, A.; Miyata, K.; Nakanishi, M.; Oba, M.; Ishii, T.; Yamasaki, Y.; Nishiyama, N.; Kataoka, K. *Biomaterials* **2010**, *31*, 8097-8105.

(227) Liu, Z.; Zhang, Z.; Zhou, C.; Jiao, Y. *Prog. Polym. Sci.* **2010**, *35*, 1144-1162.

(228) Liu, Q. M.; Zhu, H. S.; Qin, J. Y.; Dong, H. Q.; Du, J. Z. *Biomacromolecules* **2014**, *15*, 1586-1592.

(229) Ren, T. B.; Liu, Q. M.; Lu, H.; Liu, H. M.; Zhang, X.; Du, J. Z. *J. Mater. Chem.* **2012**, *22*, 12329-12338.

(230) Zhu, Y. Q.; Wang, F. Y. K.; Zhang, C.; Du, J. Z. *ACS nano* **2014**, *8*, 6644-6654.

(231) Marguet, M.; Sandre, O.; Lecommandoux, S. *Langmuir* **2012**, *28*, 2035-2043.

(232) Zhang, X. Y.; Tanner, P.; Graff, A.; Palivan, C. G.; Meier, W. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 2293-2318.

(233) Zhu, Y. Q.; Liu, L.; Du, J. Z. *Macromolecules* **2013**, *46*, 194-203.

(234) Zhu, Y. Q.; Fan, L.; Yang, B.; Du, J. Z. *ACS nano* **2014**, *8*, 5022-5031.

(235) Holowka, E. P.; Pochan, D. J.; Deming, T. J. *J. Am. Chem. Soc.* **2005**, *127*, 12423-12428.

(236) Huang, J.; Bonduelle, C.; Thevenot, J.; Lecommandoux, S.; Heise, A. *J. Am. Chem. Soc.* **2012**, *134*, 119-122.

(237) Zhou, X.; Li, X. D.; Mao, T.; Zhang, J. X.; Li, X. H. *Soft Matter* **2011**, *7*, 6264-6272.

(238) Kukula, H.; Schlaad, H.; Antonietti, M.; Forster, S. *J. Am. Chem. Soc.* **2002**, *124*, 1658-1663.

(239) Kishimura, A.; Koide, A.; Osada, K.; Yamasaki, Y.; Kataoka, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 6085-6088.

(240) Tan, Y.; Xu, K.; Li, Y.; Sun, S. M.; Wang, P. X. *Chem. Commun.* **2010**, *46*, 4523-4525.

- (241) Sanson, C.; Diou, O.; Thévenot, J.; Ibarboure, E.; Soum, A.; Brûlet, A.; Miraux, S.; Thiaudière, E.; Tan, S.; Brisson, A.; Dupuis, V.; Sandre, O.; Lecommandoux, S. *ACS nano* **2011**, *5*, 1122-1140.
- (242) Blanazs, A.; Armes, S. P.; Ryan, A. J. *Macromol. Rapid Commun.* **2009**, *30*, 267-277.
- (243) Soo, P. L.; Eisenberg, A. J. *Polym. Sci. Pol. Phys.* **2004**, *42*, 923-938.
- (244) Liu, Q. M.; Chen, S.; Chen, J.; Du, J. Z. *Macromolecules* **2015**, *48*, 739-749.
- (245) Themistou, E.; Battaglia, G.; Armes, S. P. *Polym. Chem.* **2014**, *5*, 1405-1417.
- (246) Popescu, M.-T.; Korogiannaki, M.; Marikou, K.; Tsitsilianis, C. *Polymer* **2014**, *55*, 2943-2951.
- (247) Du, J. Z.; O'Reilly, R. K. *Soft Matter* **2009**, *5*, 3544-3561.
- (248) Lee, J. C. M.; Bermudez, H.; Discher, B. M.; Sheehan, M. A.; Won, Y. Y.; Bates, F. S.; Discher, D. E. *Biotechnol. Bioeng.* **2001**, *73*, 135-145.
- (249) Du, J. Z.; Armes, S. P. *Langmuir* **2009**, *25*, 9564-9570.
- (250) Du, J. Z.; Armes, S. P. *Langmuir* **2008**, *24*, 13710-13716.
- (251) Du, J. Z.; Tang, Y. Q.; Lewis, A. L.; Armes, S. P. *J. Am. Chem. Soc.* **2005**, *127*, 17982-17983.
- (252) Chen, J.; Liu, Q. M.; Xiao, J. G.; Du, J. Z. *Biomacromolecules* **2015**, *16*, 1695-1705.
- (253) Strandman, S.; Zhu, X. X. *Prog. Polym. Sci.* **2015**, *42*, 154-176.
- (254) Koide, A.; Kishimura, A.; Osada, K.; Jang, W. D.; Yamasaki, Y.; Kataoka, K. *J. Am. Chem. Soc.* **2006**, *128*, 5988-5989.
- (255) Anraku, Y.; Kishimura, A.; Oba, M.; Yamasaki, Y.; Kataoka, K. *J. Am. Chem. Soc.* **2010**, *132*, 1631-1636.
- (256) Schrage, S.; Sigel, R.; Schlaad, H. *Macromolecules* **2003**, *36*, 1417-1420.
- (257) Ohno, S.; Ishihara, K.; Yusa, S.-i. *Langmuir* **2016**, *32*, 3945-3953.
- (258) Takahashi, R.; Sato, T.; Terao, K.; Yusa, S.-i. *Macromolecules* **2016**, *49*, 3091-3099.
- (259) Yi, Q.; Sukhorokov, G. B.; Ma, J.; Yang, X.; Gu, Z. *Int. J. Polym. Sci.* **2015**, *2015*, 1-6.
- (260) Gao, H.; Goriacheva, O. A.; Tarakina, N. V.; Sukhorukov, G. B. *ACS Appl. Mater. Interfaces* **2016**, *8*, 9651-9661.
- (261) Hartig, S. M.; Greene, R. R.; DasGupta, J.; Carlesso, G.; Dikov, M. M.; Prokop, A.; Davidson, J. M. *Pharm. Res.* **2007**, *24*, 2353-2369.
- (262) Karagoz, B.; Esser, L.; Duong, H. T.; Basuki, J. S.; Boyer, C.; Davis, T. P. *Polym. Chem.* **2014**, *5*, 350-355.
- (263) Blanazs, A.; Madsen, J.; Battaglia, G.; Ryan, A. J.; Armes, S. P. *J. Am. Chem. Soc.* **2011**, *133*, 16581-16587.
- (264) Warren, N. J.; Mykhaylyk, O. O.; Mahmood, D.; Ryan, A. J.; Armes, S. P. *J. Am. Chem. Soc.* **2014**, *136*, 1023-1033.
- (265) Warren, N. J.; Armes, S. P. *J. Am. Chem. Soc.* **2014**, *136*, 10174-10185.
- (266) Gonzato, C.; Semsarilar, M.; Jones, E. R.; Li, F.; Krooshof, G. J. P.; Wyman, P.; Mykhaylyk, O. O.; Tuinier, R.; Armes, S. P. *J. Am. Chem. Soc.* **2014**, *136*, 11100-11106.
- (267) Wan, W. M.; Hong, C. Y.; Pan, C. Y. *Chem. Commun.* **2009**, 5883-5885.
- (268) Cai, W. M.; Wan, W. M.; Hong, C. Y.; Huang, C. Q.; Pan, C. Y. *Soft Matter* **2010**, *6*, 5554-5561.
- (269) Charleux, B.; Delaittre, G.; Rieger, J.; D'Agosto, F. *Macromolecules* **2012**, *45*, 6753-6765.
- (270) Marguet, M.; Edembe, L.; Lecommandoux, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 1173-1176.
- (271) Shum, H. C.; Kim, J. W.; Weitz, D. A. *J. Am. Chem. Soc.* **2008**, *130*, 9543-9549.
- (272) Matosevic, S.; Paegel, B. M. *J. Am. Chem. Soc.* **2011**, *133*, 2798-2800.
- (273) Hauschild, S.; Lipprandt, U.; Rumplecker, A.; Borchert, U.; Rank, A.; Schubert, R.; Förster, S. *Small* **2005**, *1*, 1177-1180.

- (274) LoPresti, C.; Massignani, M.; Fernyhough, C.; Blanazs, A.; Ryan, A. J.; Madsen, J.; Warren, N. J.; Armes, S. P.; Lewis, A. L.; Chirasatitsin, S.; Engler, A. J.; Battaglia, G. *ACS nano* **2011**, *5*, 1775-1784.
- (275) Christian, D. A.; Tian, A. W.; Ellenbroek, W. G.; Levental, I.; Rajagopal, K.; Janmey, P. A.; Liu, A. J.; Baumgart, T.; Discher, D. E. *Nat. Mater.* **2009**, *8*, 843-849.
- (276) Arumugam, S.; Vutukuri, D. R.; Thayumanavan, S.; Ramamurthy, V. *J. Am. Chem. Soc.* **2005**, *127*, 13200-13206.
- (277) Fan, L.; Lu, H.; Zou, K.; Chen, J.; Du, J. *Chem. Commun.* **2013**, *49*, 11521-11523.
- (278) Kubowicz, S.; Baussard, J.-F.; Lutz, J.-F.; Thünemann, A. F.; von Berlepsch, H.; Laschewsky, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 5262-5265.
- (279) Gensel, J.; Betthausen, E.; Hasenohrl, C.; Trenkenschuh, K.; Hund, M.; Boulmedais, F.; Schaaf, P.; Muller, A. H. E.; Fery, A. *Soft Matter* **2011**, *7*, 11144-11153.
- (280) Du, J. Z.; Chen, Y. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 5084-5087.
- (281) Chambon, P.; Blanazs, A.; Battaglia, G.; Armest, S. P. *Langmuir* **2012**, *28*, 1196-1205.
- (282) Qin, S. H.; Geng, Y.; Discher, D. E.; Yang, S. *Adv. Mater.* **2006**, *18*, 2905-2909.
- (283) Cerritelli, S.; Velluto, D.; Hubbell, J. A. *Biomacromolecules* **2007**, *8*, 1966-1972.
- (284) Babin, J.; Pelletier, M.; Lepage, M.; Allard, J.-F.; Morris, D.; Zhao, Y. *Angew. Chem., Int. Ed.* **2009**, *48*, 3329-3332.
- (285) Yan, Q.; Yuan, J.; Cai, Z.; Xin, Y.; Kang, Y.; Yin, Y. *J. Am. Chem. Soc.* **2010**, *132*, 9268-9270.
- (286) Louguet, S.; Rousseau, B.; Ephère, R.; Guidolin, N.; Goglio, G.; Mornet, S.; Duguet, E.; Lecommandoux, S.; Schatz, C. *Polym. Chem.* **2012**, *3*, 1408-1417.
- (287) Kim, H.; Kang, Y. J.; Kang, S.; Kim, K. T. *J. Am. Chem. Soc.* **2012**, *134*, 4030-4033.
- (288) Yan, Q.; Zhou, R.; Fu, C.; Zhang, H.; Yin, Y.; Yuan, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 4923-4927.
- (289) Yan, Q.; Zhao, Y. *J. Am. Chem. Soc.* **2013**, *135*, 16300-16303.
- (290) Chen, W.; Du, J. *Sci. Rep.* **2013**, *3*, Doi: 10.1038/srep02162.
- (291) Pang, Z.; Feng, L.; Hua, R.; Chen, J.; Gao, H.; Pan, S.; Jiang, X.; Zhang, P. *Mol. Pharmaceutics* **2010**, *7*, 1995-2005.
- (292) Egli, S.; Nussbaumer, M. G.; Balasubramanian, V.; Chami, M.; Bruns, N.; Palivan, C.; Meier, W. *J. Am. Chem. Soc.* **2011**, *133*, 4476-4483.
- (293) Robbins, G. P.; Lee, D.; Katz, J. S.; Frail, P. R.; Therien, M. J.; Crocker, J. C.; Hammer, D. A. *Soft Matter* **2011**, *7*, 769-779.
- (294) Lai, M.-H.; Jeong, J. H.; DeVolder, R. J.; Brockman, C.; Schroeder, C.; Kong, H. *Adv. Funct. Mater.* **2012**, *22*, 3239-3246.
- (295) Yasayan, G.; Redhead, M.; Magnusson, J. P.; Spain, S. G.; Allen, S.; Davies, M.; Alexander, C.; Fernandez-Trillo, F. *Polym. Chem.* **2012**, *3*, 2596-2604.
- (296) Wang, M.; Zhou, C.; Chen, J.; Xiao, Y.; Du, J. *Bioconjug. Chem.* **2015**, *26*, 725-734.
- (297) Le Hellaye, M.; Fortin, N.; Guilloteau, J.; Soum, A.; Lecommandoux, S.; Guillaume, S. M. *Biomacromolecules* **2008**, *9*, 1924-1933.
- (298) Zhu, Y.; Yang, B.; Chen, S.; Du, J. *Prog. Polym. Sci.* **2016**, In press.
- (299) Wilson, J. A.; Hopkins, S. A.; Wright, P. M.; Dove, A. P. *Biomacromolecules* **2015**, *16*, 3191-3200.
- (300) Duda, A. *Macromolecules* **1994**, *27*, 576-582.
- (301) Duda, A. *Macromolecules* **1996**, *29*, 1399-1406.
- (302) Lendlein, A.; Neuenchwander, P.; Suter, U. W. *Macromol. Chem. Phys.* **2000**, *201*, 1067-1076.
- (303) Kricheldorf, H. R.; Rost, S. *Polymer* **2005**, *46*, 3248-3256.
- (304) Kricheldorf, H. R.; Behnken, G.; Schwarz, G. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 3175-3183.

- (305) Nakayama, Y.; Okuda, S.; Yasuda, H.; Shiono, T. *React. Funct. Polym.* **2007**, *67*, 798-806.
- (306) Guillaume, S. M.; Schappacher, M.; Soum, A. *Macromolecules* **2003**, *36*, 54-60.
- (307) Lin, J.-O.; Chen, W.; Shen, Z.; Ling, J. *Macromolecules* **2013**, *46*, 7769-7776.
- (308) Takizawa, K.; Tang, C.; Hawker, C. J. *J. Am. Chem. Soc.* **2008**, *130*, 1718-1726.
- (309) Lee, H. S.; Roy, A.; Lane, O.; Lee, M.; McGrath, J. E. *J. Polym. Sci., Part A: Polym. Chem.* **2010**, *48*, 214-222.
- (310) Lendlein, A.; Neuenchwander, P.; Suter, U. W. *Macromol. Chem. Phys.* **1998**, *199*, 2785-2796.
- (311) Harrold, N. D.; Li, Y.; Chisholm, M. H. *Macromolecules* **2013**, *46*, 692-698.
- (312) Brule, E.; Guo, J.; Coates, G. W.; Thomas, C. M. *Macromol. Rapid Commun.* **2011**, *32*, 169-185.
- (313) Zhu, Y.; Romain, C.; Williams, C. K. *J. Am. Chem. Soc.* **2015**, 12179-12182.
- (314) Mahmoud, E.; Watson, D. A.; Lobo, R. F. *Green Chem.* **2014**, *16*, 167-175.

Chapter 2

The Influences of a Di-zinc Catalyst and Bifunctional Chain Transfer Agents on the Polymer Chain End in the Ring-Opening Polymerization of ϵ -Caprolactone

2.1 Background and Aims

Due to its excellent biocompatibility and biodegradability, poly(ϵ -caprolactone) (PCL) is a widely applied biomaterial and thus has been thoroughly investigated.¹⁻⁹ So far, PCL and its copolymers have been used in biomedicine, including controlled release, tissue-engineering, medical devices and implants, amongst other applications.¹⁰⁻¹⁵ Furthermore, PCL is miscible, and so can be easily blended with a wide range of other polymers.¹⁶⁻¹⁸ Currently, PCL is usually prepared *via* the ring-opening polymerization (ROP) of ϵ -caprolactone using a range of anionic,¹⁹⁻²¹ cationic^{22,23} and coordination catalysts/initiators.^{3,6,24-26} There are also a few reports of its production by the free radical ring-opening polymerization of 2-methylene-1,3-dioxepane.²⁷⁻²⁹ Considering the ROP route, a range of lower-toxicity catalysts have been developed, including complexes of zinc,^{6,30} magnesium,^{31,32} aluminium^{33,34} and calcium.³⁵

Recently, successful polymerization of ϵ -CL using a di-zinc pre-catalyst (see **Scheme 2.1**) was reported.³⁶ The zinc carboxylate groups, on the pre-catalyst, were ineffective initiators, however, zinc alkoxides, which were generated *in situ* by the reaction with sub-stoichiometric amounts of epoxide, were active polymerization initiators. Most importantly, the di-zinc pre-catalyst is the only chemoselective complex which can catalyze ring-opening copolymerization (ROCOP) and ring-opening polymerization (ROP) in a mixed monomer feedstock.³⁶

As macromolecules with reactive end-groups, telechelic polymers have attracted much industrial interest, especially in producing thermoplastic elastomers or higher molecular weight polymers, such as polyurethanes/polyesters.³⁷⁻⁴⁴ Telechelic polymers with predictable molecular weights, narrow polydispersities (M_w/M_n), and controllable chain ends are also of value as cross-linkers, chain extenders and precursors for making block, graft copolymers or polymer networks.⁴⁵⁻⁴⁹ As mentioned in the introduction, two main approaches have been developed to prepare telechelic polyesters.^{46,47,50-52,38,53,54} The ‘diol’ approach is more widely applied due to its versatility and the PCL chains are believed to propagate from both hydroxyl groups due to the rather high chain transfer rate constant (k_e) usually observed in immortal ROP. However, the exact microstructure of the telechelic PCL, in particular the proportion of chains where the diol is a chain extender *vs.* those where it is a chain end group, is rarely quantified. For multifunctional initiators, which are widely applied in the preparation of star-shaped polymers, graft copolymers and H-shaped copolymers,⁵⁵⁻⁵⁹ the same

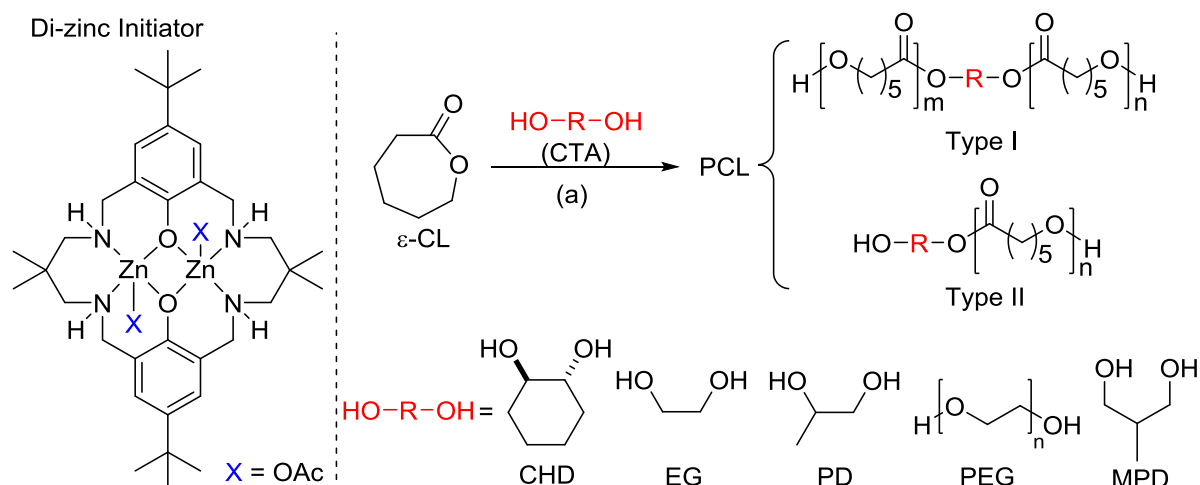
microstructure issue is frequently overlooked or unreported. There are very few specific reports on the nature of the end groups of telechelic PCL. In 2004, Chen *et al.* reported the application of an yttrium *tris*(2,6-di-*tert*-butyl-4-methylphenolate) catalyst with ethylene glycol and showed the production of polymer chains end-capped and chain extended from the diol. This resulted in bimodal molecular weight distributions.⁶⁰ Recently, Lin and co-workers applied the same yttrium initiator with 2-propanediol which led to an exclusive chain extended type of structure.⁶¹ However, the extent to which this result may be generalized to other catalyst systems remains unknown.

2.2 Results and Discussion

It is important to control telechelic polymer end groups for post-polymerization modification, such as chain extension. It was recently reported that a di-zinc catalyst shows an unusual ability to switch between ring-opening polymerization (ROP) and ring-opening copolymerization (ROCOP) using mixtures of caprolactone, epoxide and carbon dioxide.³⁶ This is important as it provides a means to control the polymer composition on the basis of the catalyst propagating chain chemistry. However, the precise nature of the polymer structures generated by the switch catalysis is not yet elucidated. In the context of this switch catalysis, it is important to understand the influence of the di-zinc catalyst in lactone ring-opening polymerization and the nature of the PCL chain end groups.⁶²

To address this deficiency, several bifunctional chain transfer agents: *trans*-1,2-cyclohexanediol (CHD) (as a good model for the end group of the polycarbonate prepared *via* ring-opening copolymerization), ethylene glycol (EG), 1,2-propanediol (PD), polyethylene glycol 1500 (PEG) and 2-methyl-1,3-propanediol (MPD) bearing either secondary or/and primary hydroxyl groups, were applied with the di-zinc pre-catalyst for the immortal polymerization of ϵ -CL (**Scheme 2.1**).

Scheme 2.1 The immortal ring-opening polymerization of ϵ -caprolactone, initiated by a di-zinc complex, $[LZn_2(OAc)_2]$, and different diol chain transfer agents. Two types of PCL structures are considered possible, illustrated as Type I and II structures. Reagents and Conditions: (a) Di-zinc pre-catalyst (0.1 mole eq.), in neat cyclohexene oxide (100 mole eq.), and with HO-R-OH (1 mol eq.) as CTA, 353 K, 2.5-3.0 h.

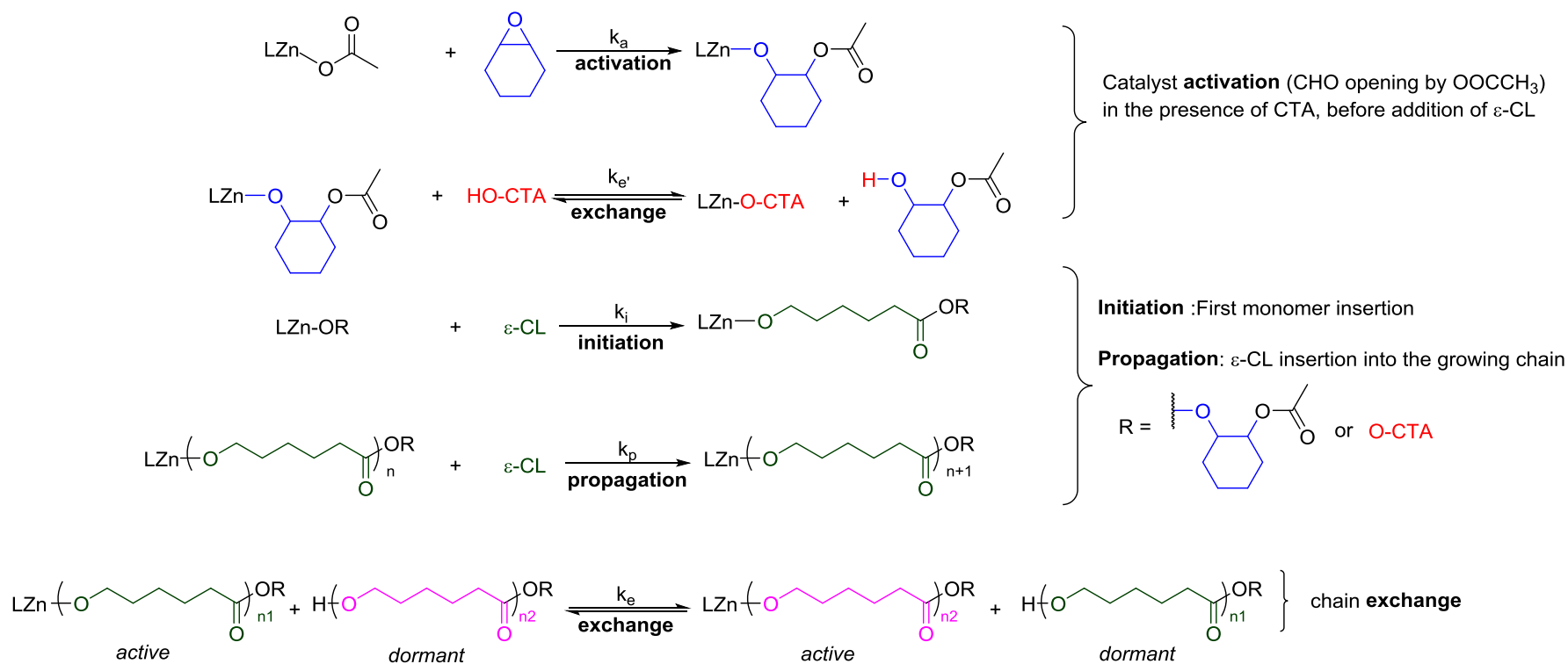


2.2.1 General Mechanism of the Ring-Opening Polymerization Catalyzed by Di-zinc bis(acetate) Complex with the Presence of Chain Transfer Agents

Firstly, a control polymerization was conducted using only the di-zinc *bis*(acetate) complex and *trans*-1,2-cyclohexanediol (CHD) (i.e. without any cyclohexene oxide), this failed to result in any PCL formation even after 18 h. This demonstrates that the diol chain transfer agents are not directly involved in the initiation reaction and cannot by themselves form the active zinc alkoxide species. Rather, the di-zinc *bis*(acetate) pre-catalyst is efficiently transformed into the catalytically active zinc alkoxide complex by reaction with cyclohexene oxide (CHO).³⁶ This occurs *in situ* under the reaction conditions, where cyclohexene oxide is used as the reaction solvent. The insertion of the CHO into the zinc acetate activates the di-zinc catalyst (kinetic constant: k_a , see catalyst activation process in **Scheme 2.2**). After the formation of the zinc alkoxide species, the diol chain transfer agents are thus able to exchange to form new zinc alkoxide species (kinetic constant: k_e , in **Scheme 2.2**). It is also important to point out that it has already been established that there is no homopolymerization of the CHO by either of the zinc species.^{36,63-65} Once the alkoxide complex is generated, it was applied as the active initiator for the immortal ROP of ϵ -CL in the presence of each chain transfer agent (for an illustration of the proposed *in situ* catalyst

formation and initiation, see **Scheme 2.2**). The results of these polymerizations, at different relative loadings of monomer (molar) and CTA, are presented in **Table 2.1**.

Scheme 2.2 The schematic diagram illustrating the process of the *in situ* catalyst formation and the initiation, propagation and exchange reactions.



2.2.2 Ring-Opening Polymerization of ϵ -CL using Di-zinc bis(acetate) Complex with CHD as the Diol Chain Transfer Agent

In a controlled/living polymerization, the molecular weight depends on the concentration of the catalyst ($MW = [\text{monomer}] \times [\text{conversion}] / [\text{catalyst}]$), while in an immortal polymerization the molecular weight depends on the concentration of chain transfer agent (CTA) and the catalyst ($MW = [\text{monomer}] \times [\text{conversion}] / ([\text{catalyst}] + [\text{CTA}])$).⁶⁶ Thus, one of the advantages of the immortal polymerization is that the number of the polymer chains usually exceeds the number of the initiator molecules (catalysts). However, recently it is not recommended to use the term ‘immortal polymerization’. Although ‘immortal polymerization’ is still used in this thesis, ‘controlled ring-opening polymerization’ would be the preferable term to describe the polymerization discussed in this thesis.

Controlled, immortal ring-opening polymerizations were observed in this work with excess chain transfer agent, as evidenced by the PCL number averaged molecular weight (M_n) being predictable and corresponding closely to the values predicted on the basis of monomer conversion and the number of equivalents of chain transfer agent added. This indicates the number of the polymer chains exceeding the number of the initiator molecules ($[\text{LZn}_2(\text{OAc})_2]$), **Figure 2.1** illustrates the number averaged molecular weights (M_n) for the PCL produced using different quantities of the chain transfer agents. In most cases the polydispersities were quite narrow (< 1.30 , see **Table 2.1**), suggesting that the chain transfer reaction occurs reversibly and much faster than the propagation reaction. Also, according to the MALDI-ToF spectrum (**Figure 2.2**), hydroxyl end groups are present on the obtained PCL, suggesting that it is possible to use the obtained PCL as macroinitiator to further initiate the ring-opening polymerization of ϵ -CL.

The addition of 10 equiv. of chain transfer agent in Table 2.1 is also used to suppress the PCL chain terminated by the OAc co-ligand (minor distribution in **Figure 2.2**) present on the $[\text{LZn}_2(\text{OAc})_2]$ catalyst. It is possible to increase the molar ratio of CTA/ $[\text{LZn}_2(\text{OAc})_2]$ to further suppress the amount of PCL chain terminated by OAc co-ligand, however it will decrease the molecular weight of the obtained polymer. Although this can be compensated by

increasing the molar ratio of ϵ -CL/CTA, there is a limitation in the turnover number of the $[\text{LZn}_2(\text{OAc})_2]$ catalyst to polymerize ϵ -CL ($\text{TON} < 5000$). Therefore, the molar ratio of $[\text{LZn}_2(\text{OAc})_2]/\text{CTA}/\epsilon\text{-CL}$ was designed to be 1/10/300-900 in the experiments listed in **Table 2.1**. Since the OAc-terminated PCL population is only suppressed by adding excess CTA rather than eliminated, there should always be a minor PCL population that is initiated by the OAc co-ligand. This explains the small shoulders observed in the SEC traces (**Figure 2.1**) and the minor distribution in MALDI-ToF (**Figure 2.2**).

Table 2.1 The immortal ROP of ϵ -CL, at different molar ratios, using trans cyclohexane diol (CHD), ethylene glycol (EG), 1,2-propanediol (PD), poly(ethylene glycol) (PEG) and 2-methyl-1,3-propanediol (MPD) as the chain transfer agents.

Entry	$[\text{LZn}_2(\text{OAc})_2]/\text{CTA}/\epsilon\text{-CL}/\text{CHO}$	CTA	t (h)	$M_{n,\text{exp}}^a$ (kg/mol)	$M_{n,\text{th}}^b$ (kg/mol)	$\bar{D}$
1	1/10/300/1000	CHD	2.5	4.1	3.4	1.21
2	1/10/500/1000	CHD	2.5	5.7	6.0	1.17
3	1/10/700/1000	CHD	2.5	7.5	7.9	1.26
4	1/10/900/1000	CHD	3.0	9.4	10.3	1.36
6	1/10/300/1000	EG	2.5	3.3	3.4	1.25
7	1/10/300/1000	PD	2.5	3.8	3.4	1.27
8	1/10/300/1000	PEG	2.5	7.8	4.9	1.36
9	1/10/300/1000	MPD	2.5	3.7	3.4	1.32

Polymerization Conditions: All polymerizations were run in neat cyclohexene oxide (CHO) as the reaction solvent at 80 °C, for 2.5-3.0 hours (conversion of ϵ -CL > 95%). The molar ratio of $[\text{LZn}_2(\text{OAc})_2]/[\text{CTA}]/[\text{CHO}]$ was kept constant. ^a $M_{n,\text{exp}}$ was determined by SEC, in THF using polystyrene calibration, with a correction factor (0.56) applied (except for entry 8) as described by Soum *et al.*⁵ ^b $M_{n,\text{th}}$ was determined on the basis of $([\epsilon\text{-CL}] \times \text{conversion})/([\text{LZn}_2(\text{OAc})_2] + [\text{CTA}])$.

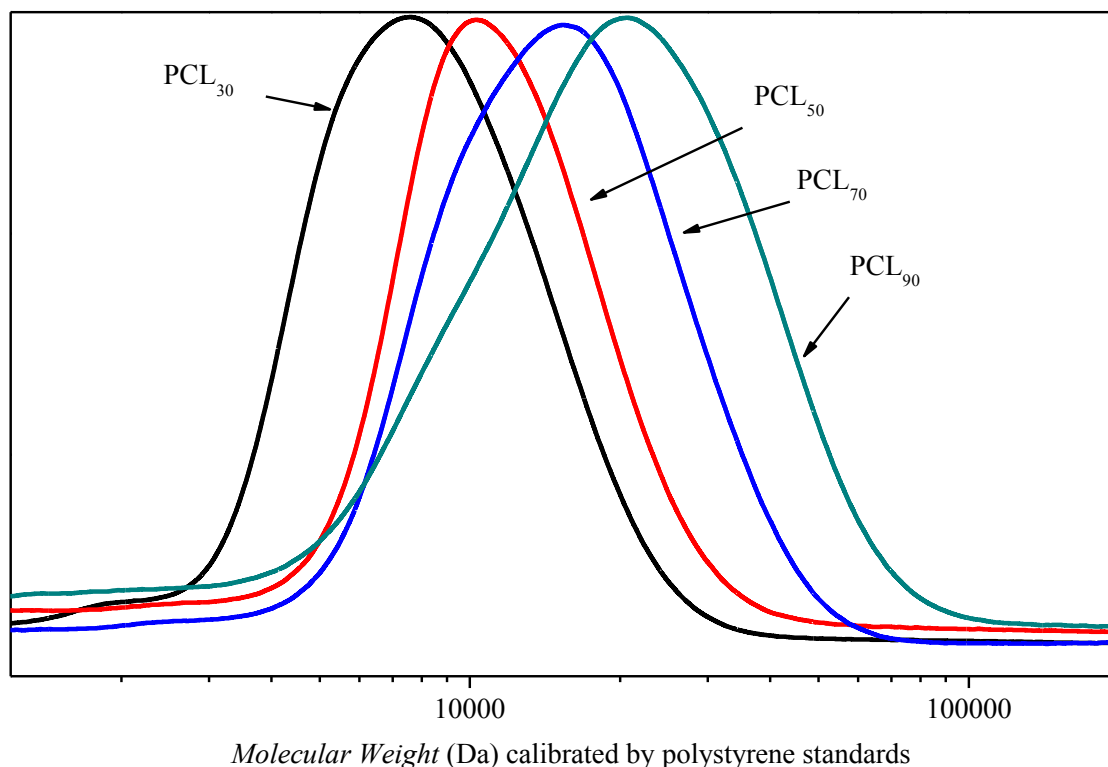


Figure 2.1 Shows the molecular weights (MW) for different PCL samples (Entry 1-4 in **Table 2.1**, obtained by SEC using polystyrene calibration), and the molecular weight can be controlled by tuning the molar ratio of $[\epsilon\text{-CL}]/[\text{CHD}]$. The small shoulder appeared at the low molecular weight side of PCL_{90} is probably contributed by the PCL chain terminated by OAc co-ligand.

2.2.3 Probing into the True Structure of the Obtained PCL with Both Chain Ends Functionalized

The MALDI-ToF spectra (see **Figure 2.2**) displayed two series, indicative of two molecular weight distributions. Each series showed the same separation (ca. 114 m/z), corresponding to the repeated addition of $[\epsilon\text{-CL}]$ units and consistent with the two series resulting from different initiating groups. The major series is assigned to PCL initiated from the added chain transfer agent, showing α,ω -di(hydroxyl) end groups and a single unit of CTA incorporated. The minor series is assigned to PCL prepared from the residual zinc acetate initiator (present

in 1/10 the molar quantity), showing α -acetyl-cyclohexylene ester and ω -hydroxyl end groups.

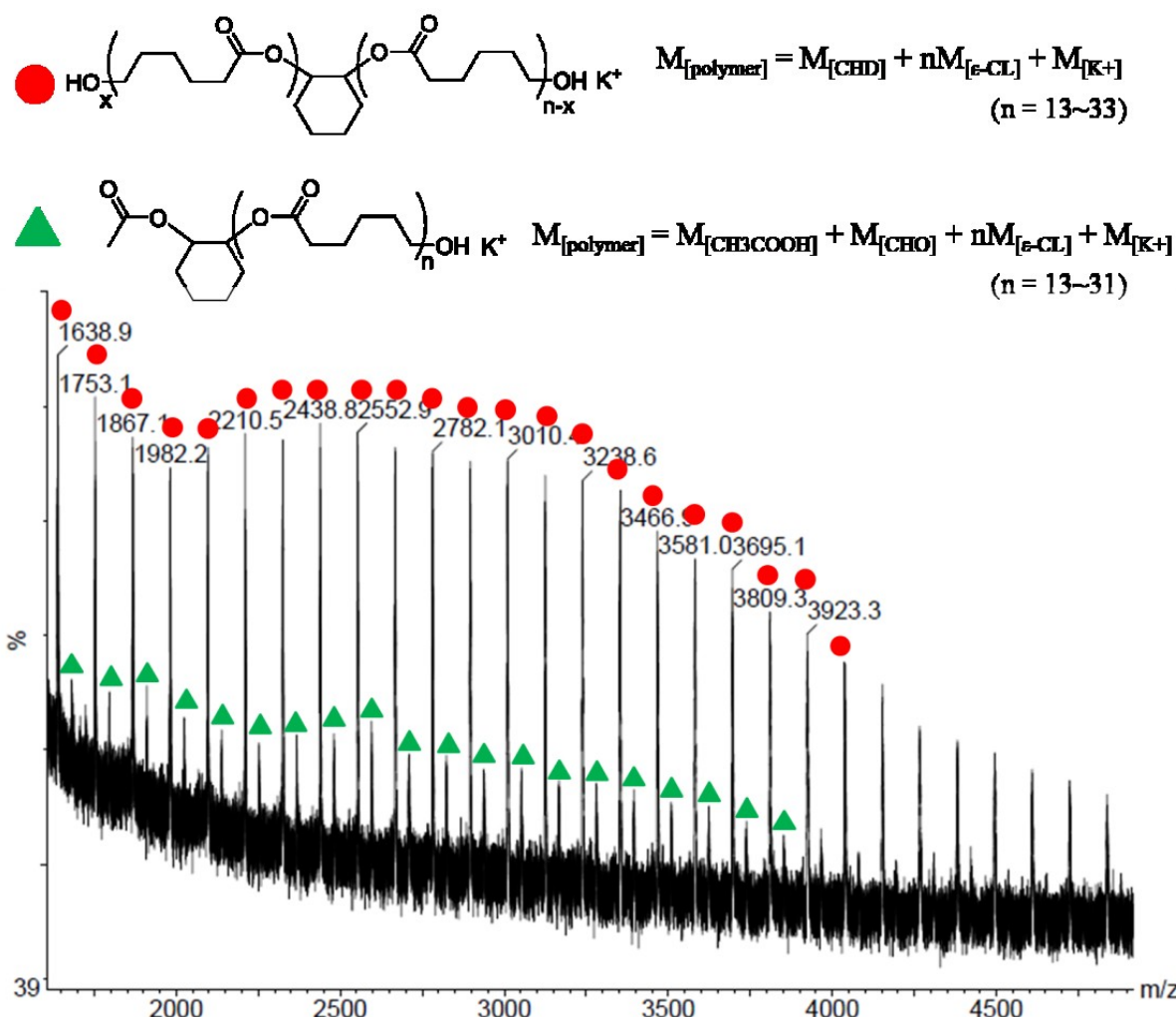


Figure 2.2 A representative MALDI-ToF spectrum of the PCL synthesized with CHD as the CTA (**Table 2.1**, entry 2). The major series (red circles) consists of α , ω -hydroxyl end-groups, which are calculated according to: $(\text{C}_6\text{H}_{10}\text{O}_2)_n\text{C}_6\text{H}_{10}(\text{OH})\cdot\text{K}^+$. The minor series (green triangles) is assigned to chains having α -acetyl-cyclohexyl ester and ω -hydroxyl end-groups, which are calculated according to: $\text{C}_8\text{H}_{13}\text{O}_2(\text{C}_6\text{H}_{10}\text{O}_2)_n\text{OH}\cdot\text{K}^+$.

Even for the major series observed in the MALDI-ToF spectrum, which is initiated from the chain transfer agent, there are two additional different possible structures for the PCL (Types I and II, **Scheme 2.1** and **Figure 2.3**). ^1H - ^{13}C HSQC NMR spectroscopy (**Figure 2.3B** and **Figure 2.3C**) was utilized to distinguish between them, using a sample of the PCL₃₀ (**Table**

2.1, entry 1) which has sufficiently low molecular weight that the end group signals could be clearly examined.

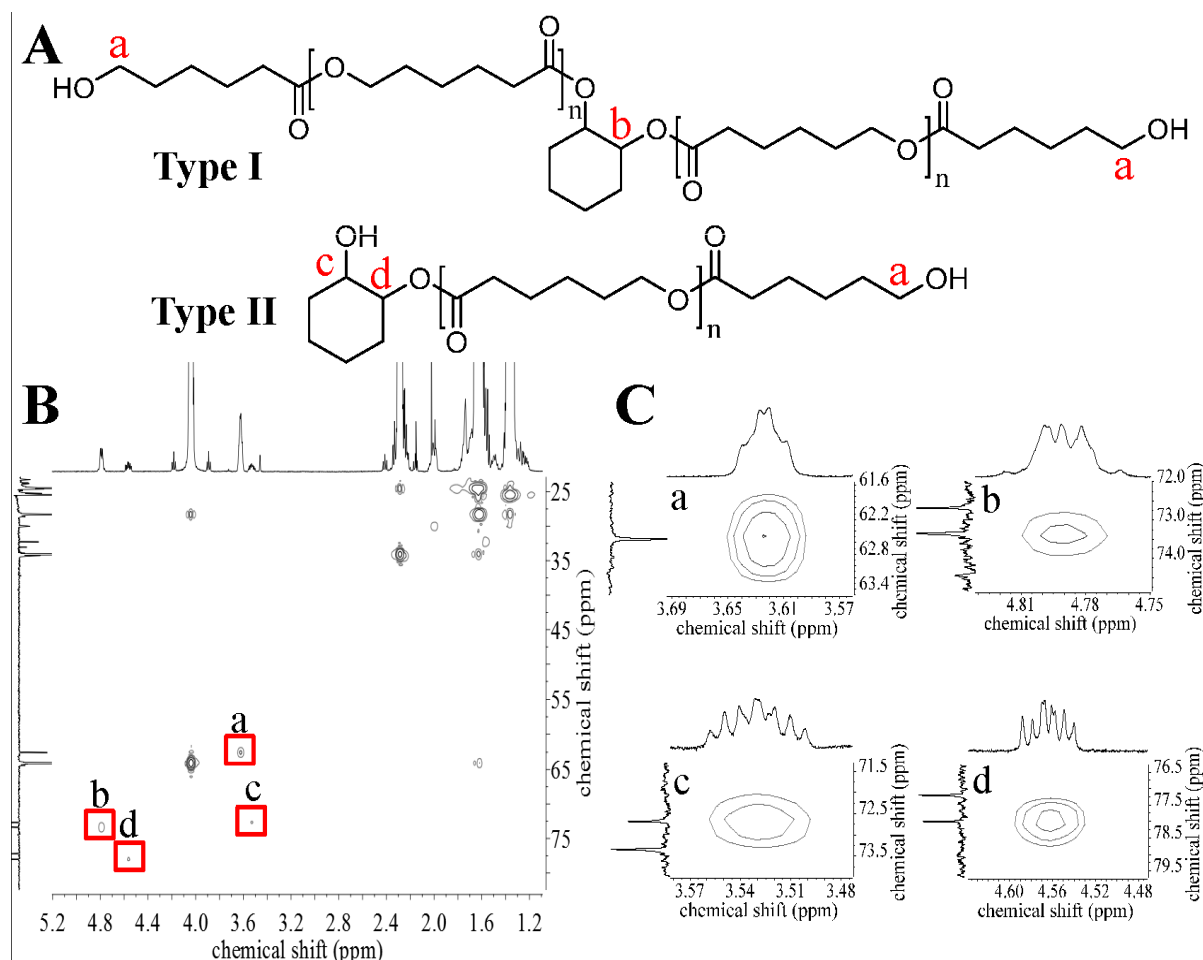


Figure 2.3 (A) Schematic diagram showing the two PCL structures (Type I & II) using cyclohexane diol (CHD) as the CTA; (B) Typical ¹H-¹³C HSQC NMR spectrum of PCL₃₀ (Table 2.1, entry 1) and (C) Enlarged HSQC NMR spectrum (Y axis: ¹³C DEPT 135°) corresponding to the selected area in (B) and showing the correlation between the ¹H and ¹³C{¹H} NMR signals for each of the junction/end groups (A). Peak a (¹H: 3.6 ppm; ¹³C{¹H}: 62.5 ppm) is assigned to the CH₂OH (confirmed by ¹³C NMR DEPT 135°); Peak b (¹H: 4.8 ppm; ¹³C{¹H}: 73.45 ppm) is assigned to the CH 'cyclohexylene junction' group; Peaks c & d [¹H: 3.5 ppm; ¹³C{¹H}: 72.7 ppm) and (¹H: 4.6 ppm; ¹³C{¹H}: 78.0 ppm), respectively] are assigned to the CH 'cyclohexanediol' end groups. Note that the signal at 77.15 ppm in the spectrum illustrating peak d is due to CDCl₃.

The end-groups for PCL chains initiated from acetyl-cyclohexyl ester groups, which were observed as the minor series in the MALDI-ToF, cannot be unambiguously assigned in the ^1H NMR spectrum due to their low signal intensity (<10 mol%). This is exacerbated by signal overlap between methylene groups on cyclohexanediol units and acetyl methyl signal, both of which resonate at ca. 2.0 ppm. On the other hand, the major distribution (>90 mol%) observed in the MALDI spectrum, is clearly defined in the ^1H NMR spectrum. The ^1H - ^{13}C HSQC NMR spectrum indicates that within this series there are two different structures corresponding to chains which are chain extended by the CTA (Type I) and those which are end-capped by it (Type II). As shown in **Figure 2.3**, the methylene protons at the chain end in Type I, peak a (^1H : 3.6 ppm; $^{13}\text{C}\{^1\text{H}\}$: 62.5 ppm), are assigned by their chemical shifts and by the correlation with CH_2 groups in the HSQC NMR spectrum. For this same structure (Type I), the cyclohexylene junction methyne protons, peak b (^1H : 4.8 ppm; $^{13}\text{C}\{^1\text{H}\}$: 73.45 ppm), are assigned based on their chemical shift and correlation with CH signals in the HSQC spectrum. For Type II, peaks c and d [^1H : 3.5 ppm; ^{13}C : 72.7 ppm) and (^1H : 4.6 ppm; ^{13}C : 78.0 ppm), respectively] corresponding to methyne signals on the cyclohexylene end-group are assigned based on their chemical shifts and correlation with the relevant CH groups in the HSQC spectrum. Therefore, both of the structures show signals for protons adjacent to alcohol end groups (a or c) and for protons at cyclohexylene junction groups (b or d). Further support for the assignment of the Type II structure was obtained from the ^1H - ^1H COSY spectrum (**Figure 2.4**) which showed coupling between the signals for H_c and H_d .

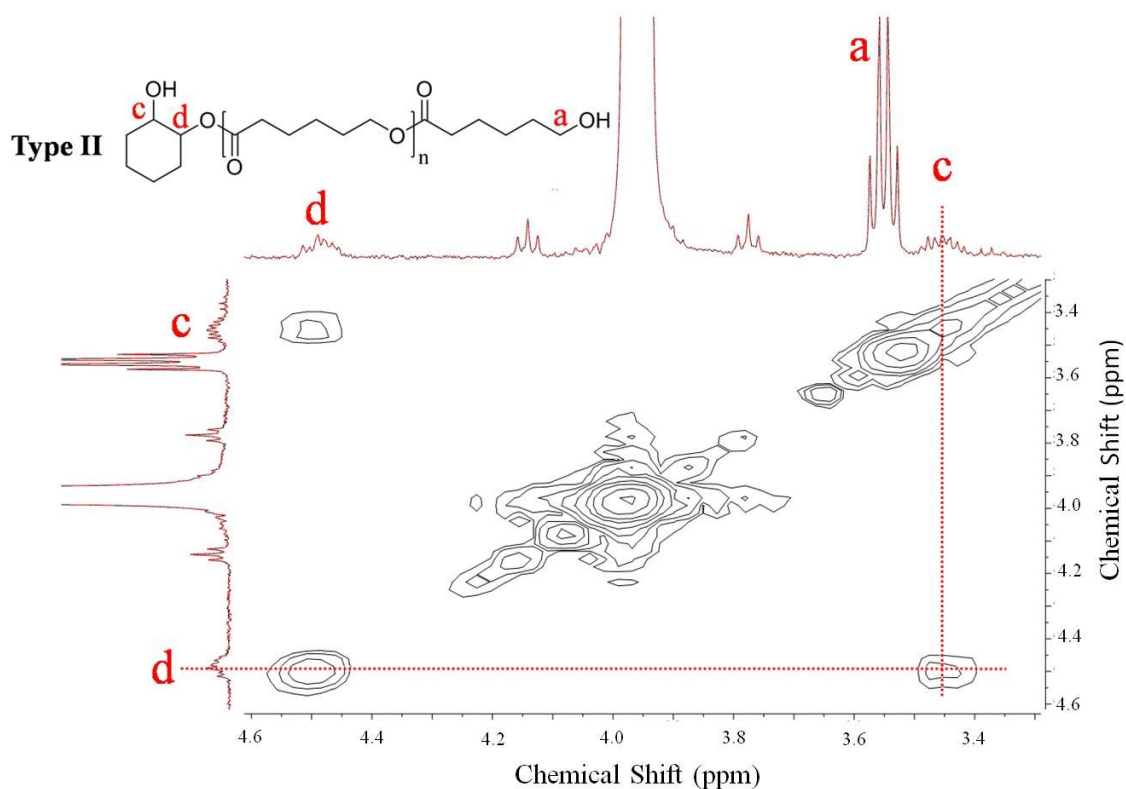


Figure 2.4 ^1H - ^1H COSY spectrum of PCL_{30} (Table 2.1, entry 1) containing chains of Type II (the signal at 3.95 ppm is assigned to methylene protons in the polymer backbone). Since the deuterated solvent is dry, peak a appears to be pseudo-quartet due to the coupling with both the methylene protons and hydroxyl proton. This has been confirmed that after the addition of D_2O , the pseudo-quartet turned back into triplet (see Figure 2.5).

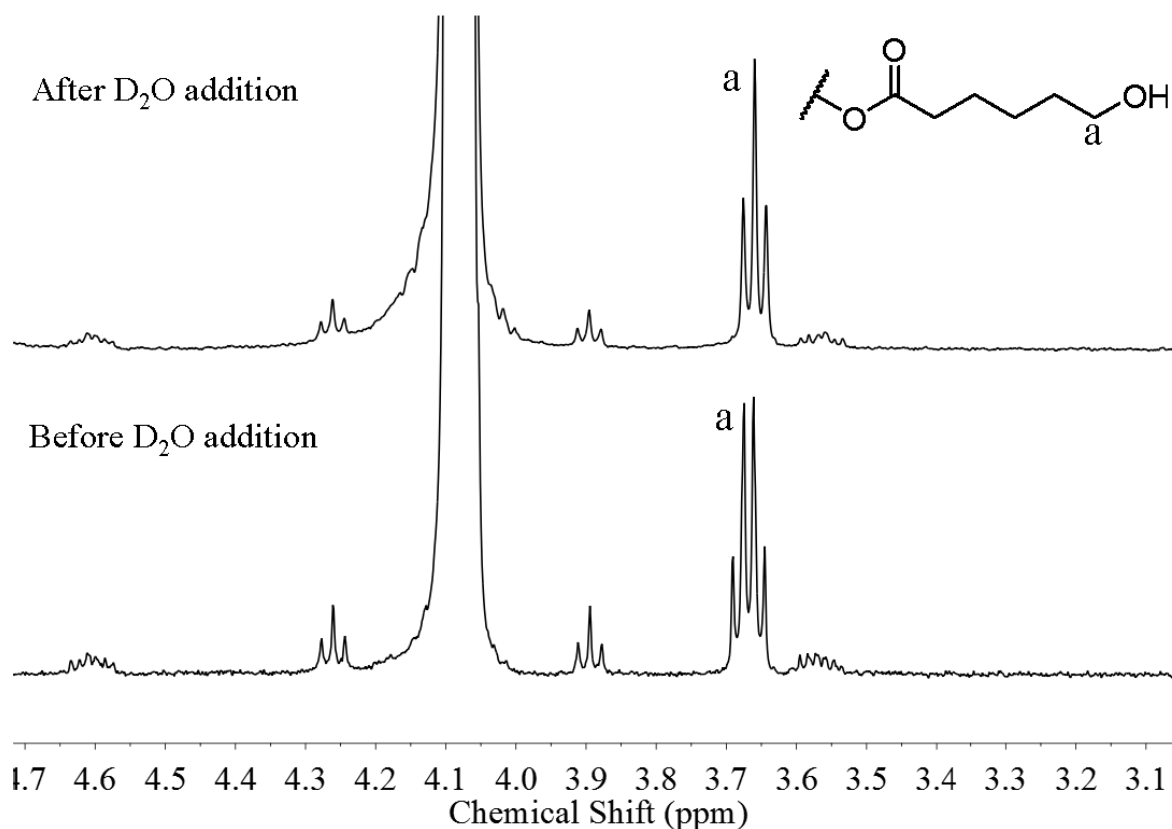


Figure 2.5 ^1H NMR spectra of PCL in CDCl_3 with (upper) or without (below) D_2O addition. After the addition of D_2O , the quartet turned into a triplet. This confirms that the quartet is due to the coupling of H_a with both methylene and hydroxyl protons leading to a pseudo-quartet (in dry solvents) and, more commonly, a triplet (when dynamic exchange of the hydroxyl occurs). Similar phenomenon has been observed in the case of dry/wet ethanol.⁶⁷

$^{31}\text{P}\{^1\text{H}\}$ NMR spectroscopy was utilized to further confirm the presence of both primary and secondary hydroxyl end-groups, consistent with the presence of both Type I and II chain structures.^{68,69} The primary and secondary hydroxyl groups are distinguished on the basis of their chemical shifts after reaction with 2-chloro-4,4,5,5-tetramethyl dioxaphospholane, and using the reaction with bisphenol A (BPA) as an internal reference. Using this method two signals were observed at 146.5 and 147.8 ppm (see **Figure 2.6**) which are assigned to secondary and primary hydroxyl groups, respectively on the basis of the chemical shift assignments in the literature.^{68,69}

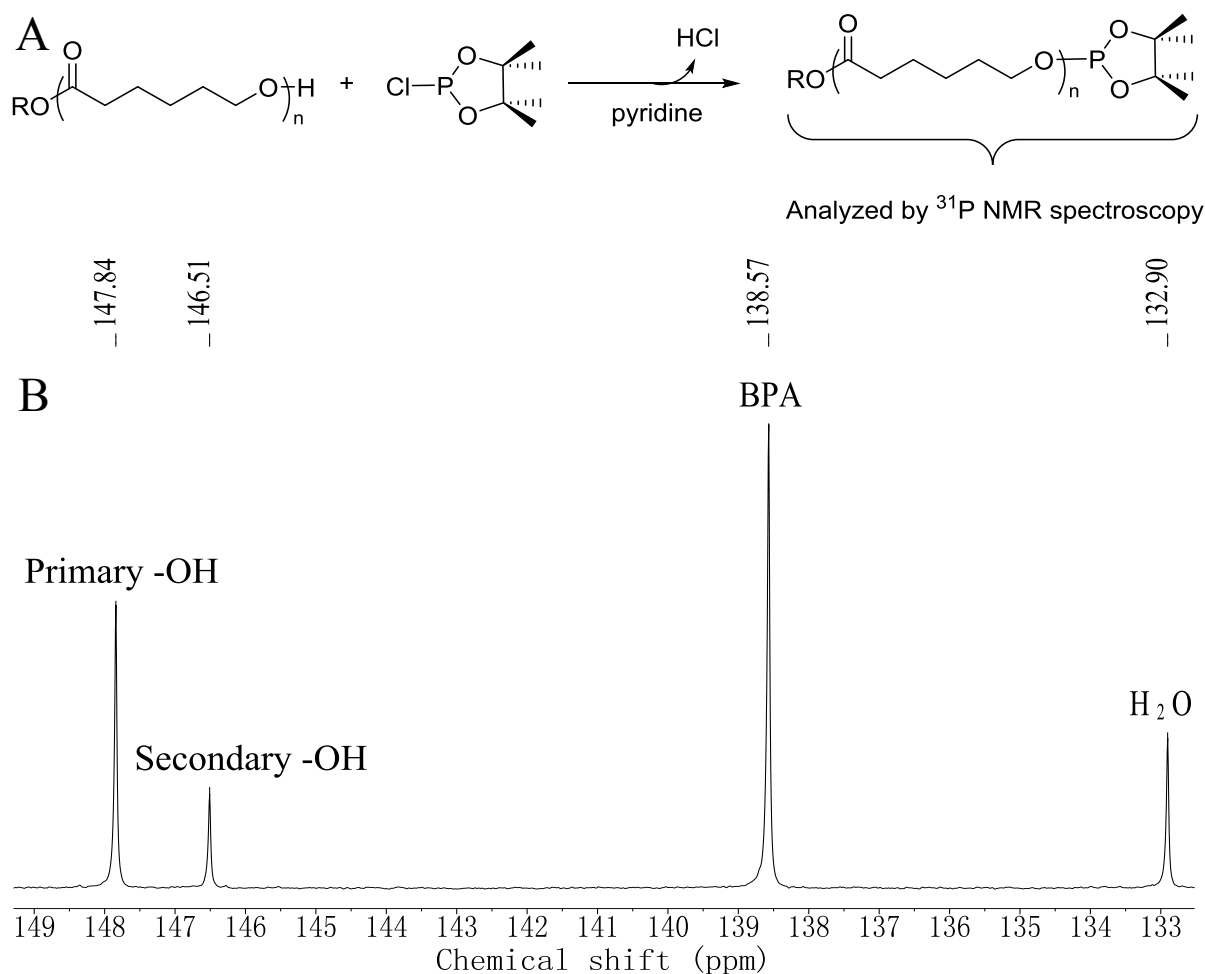


Figure 2.6 (A) Schematic diagram illustrating the reaction between the polymer end groups and 2-chloro-4,4,5,5-tetramethyl dioxaphospholane, used for the determination of the end groups; (B) $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of PCL_{30} (**Table 2.1**, entry 1) after reacted with 2-chloro-4,4,5,5-tetramethyl dioxaphospholane (Bisphenol A was used as an internal standard). The signals at 146.5 and 147.8 ppm are assigned to secondary and primary $-\text{OH}$, respectively.

2.2.4 Calculation of the Relative Content of Type I and Type II in Different PCL Samples

In order to quantify the relative quantities of Type I and II chains, the normalised peak integrals in the ^1H NMR spectra for characteristic signals a and b were compared (see **Figure 2.3** for the assignment and **equation 2.1** for more details of the calculations). During the ^1H NMR data acquisition, the values for t_1 and the relaxation delay ($d_1 = 25$ s) were maximized

so as to ensure the reliability in peak integral values. By calculating the relative integrals of peaks a and b (see **Figure 2.7** & **Table 2.2**), the composition of Type I and II PCL chains was determined (**Table 2.3**). The equation used for the calculation is shown in Equation 1.

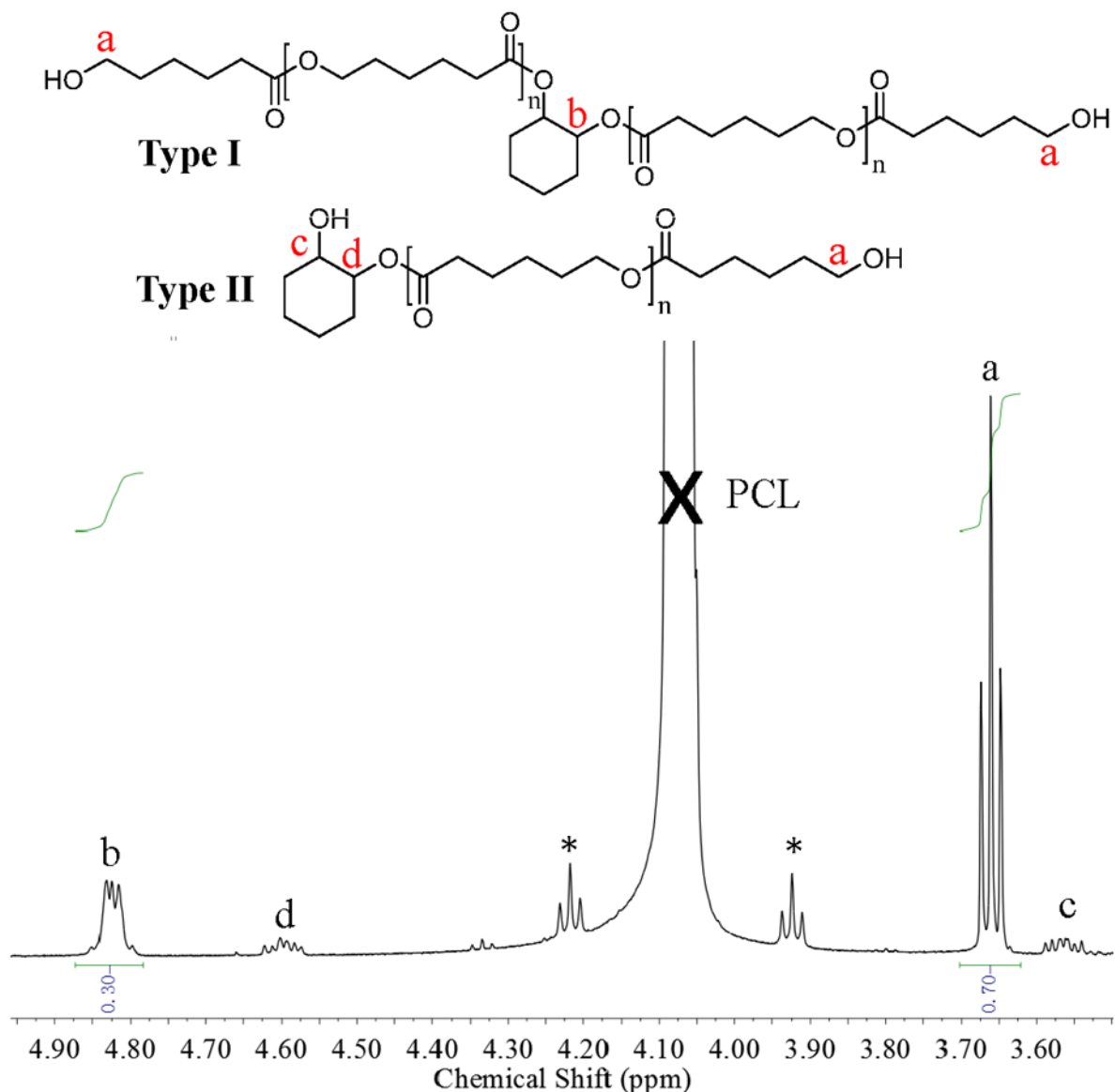


Figure 2.7 ^1H NMR spectrum of PCL_{70} (see **Table 2.3**, entry 3). The composition of Type I/II is calculated using the integrals of peaks a and b. (* are assigned to be satellite peaks)

Table 2.2 The normalized integrals of peaks a and b in PCL_{70} ^a

Polymer	A_a	A_b
PCL_{70}	0.7	0.3

^{a)} A_a and A_b are the integrals of peak a and b in Figure 2.7.

The quantities of Types I and II are determined using the calculations shown below:

$$\begin{aligned} x + y &= 1 \\ \frac{2x + y}{x} &= \frac{A_a}{A_b} \dots\dots\dots \text{Equation 2.1} \end{aligned}$$

Where x represents the amount of Type I; y the quantity of Type II. The relative amounts of Type I and II in PCL₇₀ was calculated to be 75 and 25 mol%, respectively.

Table 2.3 The relative contents of Type I and II in PCL synthesized with various chain transfer agents.^a

Entry	Polymer	CTA	Type I (mol%) ^b	Type II (mol%) ^b
1	PCL ₃₀	CHD	64	36
2	PCL ₅₀	CHD	69	31
3	PCL ₇₀	CHD	75	25
4	PCL ₉₀	CHD	82	18
5	PCL ₃₀	EG	100	0
6	PCL ₃₀	PD	65	26 (a); 9 (b) ^c
7	PCL ₃₀	PEG	100	0
8	PCL ₃₀	MPD	N.A. ^d	N.A. ^d

^{a)} The complete details of the calculations and the relative integrals of peaks used to determine Type I/II for each sample are presented in **Figure 2.7** and **Table 2.2**. ^{b)} Due to signal overlap (peak b in **Figure 2.3**) between Type I and the minor PCL species end-capped by α -acetyl-cyclohexyl ester and ω -hydroxyl groups, the content of Type I might be overestimated by ca. 10 mol%, considering that the molar ratio of [CTA]/[LZn₂(OAc)₂] is 10/1; ^{c)} Two variants of Type II (a and b) co-exist when 1,2-propane diol is used as the CTA depending on the regio-chemistry of initiation; ^{d)} a mixture of Type I and II was observed, but due to the signal overlap between the methyl groups of MPD belonging to both Type I and II, the ratio of Type I and II cannot be quantitatively determined.

When cyclohexanediol is applied as the chain transfer agent, there is a mixture of Type I and II chains in all cases, meaning that the polymer chains are both extended and end-capped by the chain transfer agent. It is important to note that the integral for peak b (present only in Type I chains) may be slightly overestimated due to the expected signal overlap with the minor species (identified in the MALDI-ToF experiments) which is chain end-capped with α -acetyl-cyclohexyl ester and ω -hydroxyl groups. Thus, the quantity of Type I chains may be over-estimated by approximately 10 mol% using this method. In each case, there is a significant proportion of chains which are end-capped with the chain transfer agent (Type II), indicating that the common assumption that all hydroxyl groups initiate chains is not substantiated using cyclohexane diol as the chain transfer agent with this di-zinc initiator. Interestingly, the relative quantity of chain extended PCL (Type I), increases with the molecular weight of the PCL. This implies that greater quantities of monomer (ϵ -CL), and extended times, may enable the complete conversion of Type II chains (end-capped) to Type I (chain extended).

2.2.5 Monitoring the Relative Quantities of Type I and Type II During the ROP of ϵ -CL

In order to investigate this observation further, aliquots were taken during the polymerization to monitor the temporal relationship with the relative quantities of Type I and II chains. As the conversion of ϵ -CL increased from 41 % to 96 %, the relative amount of Type II chains decreased from 37 to 17 mol% (**Table 2.4**, entries 1 and 2), suggesting that as ϵ -CL is polymerized, the quantity of Type II chains present decreases. To rule out the possibility that the decrease of Type II is simply the consequence of transesterification between secondary hydroxyl groups and the PCL chain, the polymer solution was kept at 80 °C, after complete ϵ -CL conversion, for a further 4.5 h. The increase in $\bar{D}$ and the slight decrease in M_n indicate that transesterification, including probable back-biting depolymerization, happened over this extended period (**Table 2.4**, entry 3–5). Despite these transesterification reactions, the relative amount of Type II chains remained constant over this period. However, we are not ruling out the possibility that by further extending the reaction time after the complete conversion of ϵ -CL, more Type II might be converted into Type I due to transesterification.

Table 2.4 Shows the relative contents of Type I and II chains present in a sample of PCL₉₀ over time

Entry	t (min)	conv. of ϵ -CL (%) ^a	M_n (kDa) ^b	$\bar{D}$	Type I (mol%)	Type II (mol%)
1	110	41	8.5	1.15	63	37
2	180	96	16.8	1.36	83	17
3	210	> 98	14.6	1.30	79	21
4	330	> 98	11.7	1.50	85	15
5	450	> 98	11.1	1.52	82	18

^{a)} The conversion of ϵ -CL was determined from the ¹H NMR spectra; ^{b)} M_n was determined by SEC, in THF using polystyrene calibration, with a correction factor (0.56) applied as described by Soum *et al.*⁵ It is noteworthy that this correction factor is examined for PCL with molecular weights ranging from 2500 to 50100 g·mol⁻¹.⁵ Therefore, it may not be accurate to apply this factor to PCL with molecular weights outside this molecular weight range mentioned above.

2.2.6 Investigation of the PCL Structure Using Different Types of Diol Chain Transfer Agent

Meanwhile, both ethylene glycol and polyethylene glycol, PEG, (primary diol) were utilized as the chain transfer agents (**Table 2.1**, entry 6 and 8). Lemaire *et al.* have previously reported that the CH₂ groups of mono-esterified ethylene glycol show ¹H NMR resonances at 4.21 ppm and 3.82 ppm, respectively.⁷⁰ However, as can be seen in **Figure 2.8**, chains initiated from ethylene glycol show only a single resonance at 4.28 ppm. The resonance is assigned to the methylene groups in chain extended PCL. The same result was also observed in PEG-*b*-PCL. No signals of Type II can be observed in both the ¹H NMR (**Figure 2.9A**) and ¹H COSY spectra (see **Figure 2.10**). ³¹P{¹H} NMR spectroscopy was used again to determine the nature of the end group of PEG-*b*-PCL and a single signal solely was observed 147.8 ppm, assigned to the hydroxyl end group of PCL (**Figure 2.9B**). The signal of the

hydroxyl end group of PEG was allocated using commercially available PEG homopolymer. No signal of the hydroxyl end group of PEG can be observed, suggesting an exclusive structure of Type I.

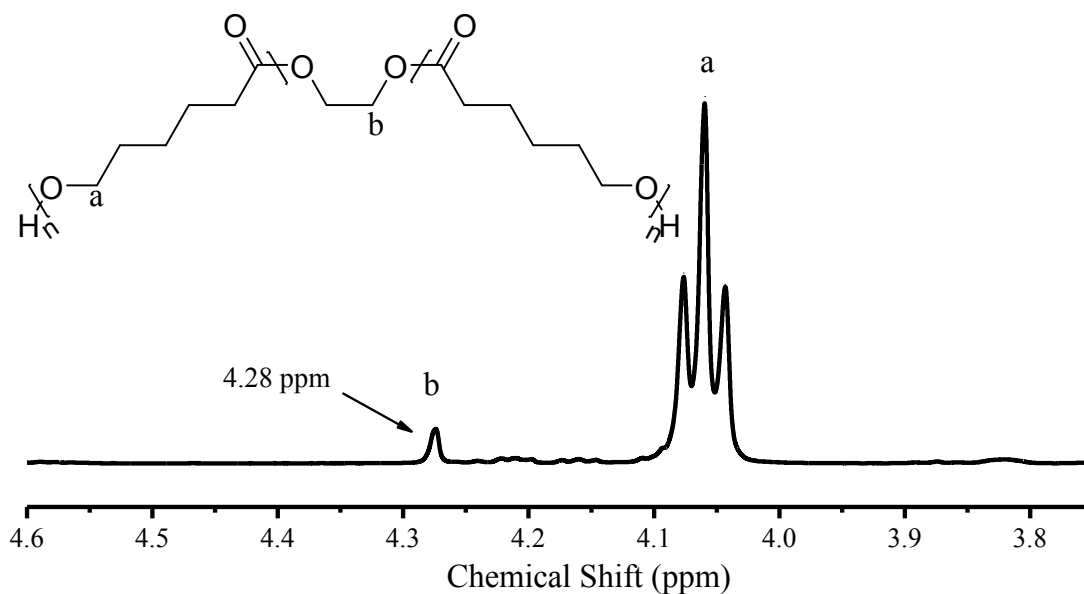


Figure 2.8 ^1H NMR spectrum of PCL polymerized using ethylene glycol (EG) as the chain transfer agent (**Table 2.1**, entry 6). The polymerization was run in neat cyclohexene oxide as the reaction solvent at 80 °C, for 2.5 hours.

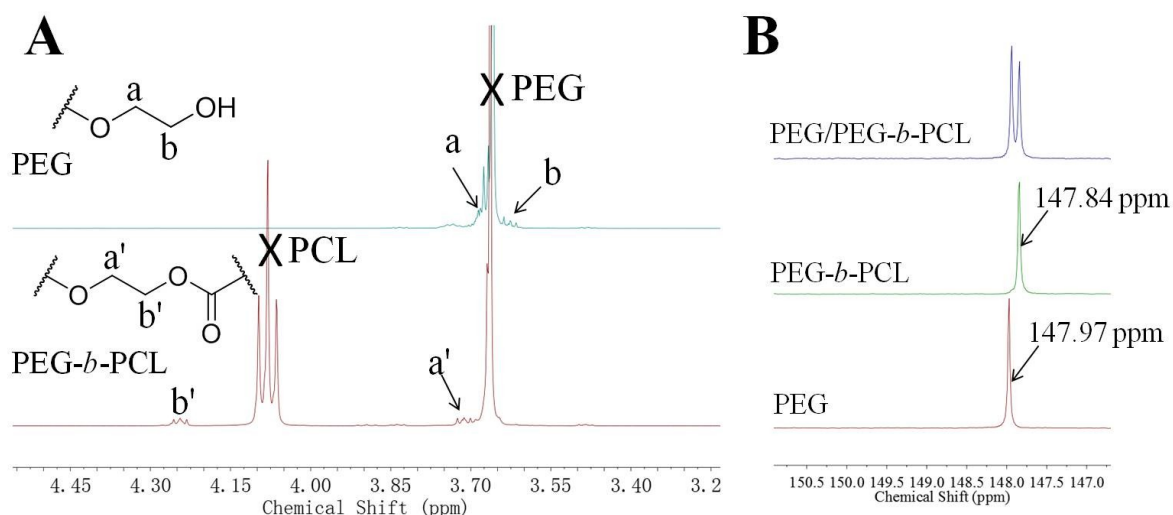


Figure 2.9 (A) ^1H NMR spectra of both PEG and PEG-*b*-PCL (**Table 2.1**, entry 8), the polymerization was run in neat cyclohexene oxide as the reaction solvent at 80 °C, for 2.5 hours; (B) $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of PEG homopolymer, PEG-*b*-PCL (**Table 2.1**, entry 8) and a mixture of PEG/PEG-*b*-PCL after reaction with 2-chloro-4,4,5,5-tetramethyl dioxaphospholane (using bisphenol A as an internal standard). The signals at 147.97 and 147.84 ppm are assigned to the primary –OH end groups of PEG and PCL, respectively.

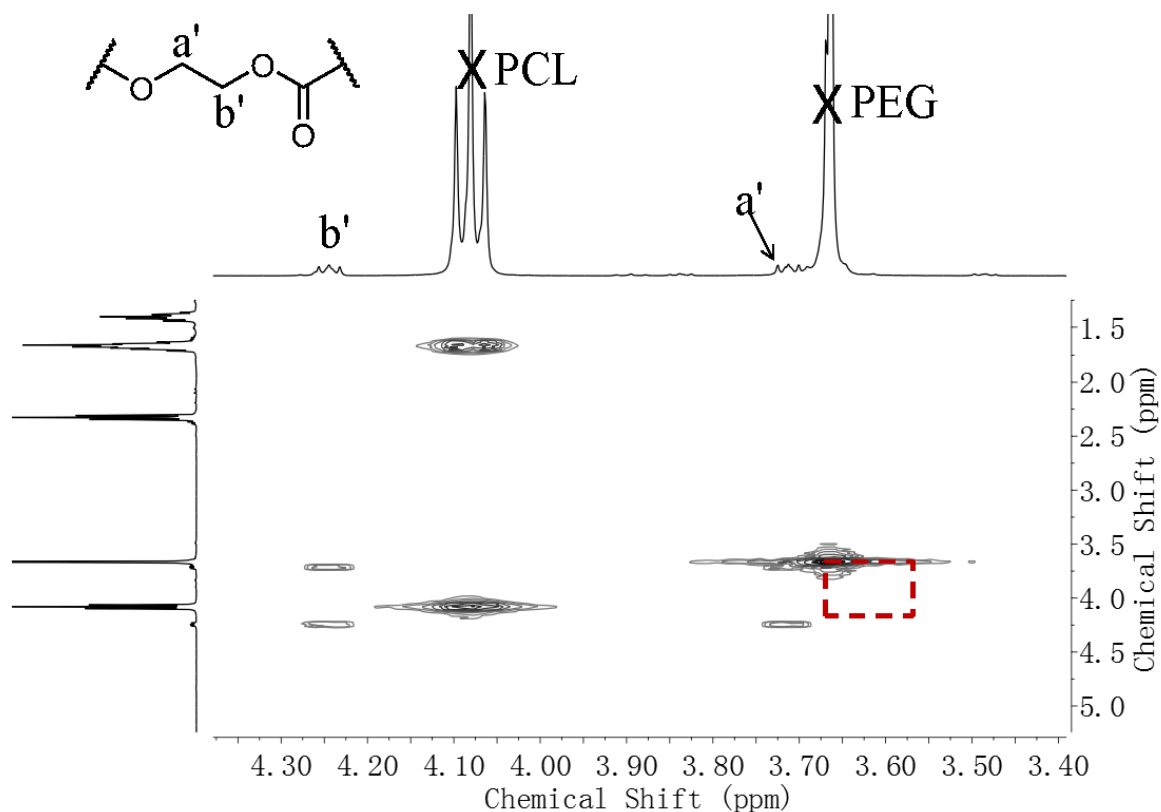


Figure 2.10. ^1H - ^1H COSY spectrum of PEG-*b*-PCL (**Table 2.1**, entry 8). No signals can be

observed in the highlighted area (corresponding to peak b in Figure 2.9A), indicating no remaining free hydroxyl end groups of PEG.

2.2.7 How Kinetics Affect the Nature of the Polymer Chain End Groups

The different PCL structures resulting from primary or secondary hydroxyl groups on the chain transfer agent were proposed to result from different initiation rates (k_i , see initiation process in **Scheme 2.2**), depending on the nature of the hydroxyl group. To verify this hypothesis, three mono-functional alcohols were employed as CTAs: 1-hexanol (primary -OH), 2-hexanol (secondary -OH) and 2-methyl-2-pentanol (tertiary -OH). The polymerization was monitored using *in situ* ATR-IR spectroscopy. In all cases, plots of monomer conversion vs. reaction time exhibited sigmoid shapes (see **Figure 2.11**), indicating that the initiation rate constant, k_i , is lower than the propagation rate constant k_p (see propagation process in **Scheme 2.2**).⁷¹ The plots were fit, for the initiation stages (monomer conversions < 25%, when the monomer concentration can still be considered constant⁷¹), using a kinetic model developed by Wang *et al.* which enables direct determination of the values of k_i and k_p (see **Table 2.5**).⁷² This kinetic model is designed for the immortal polymerization of cyclic esters using organometallic catalysts with excess alcohol chain transfer agent, which is similar to the ϵ -CL polymerization described in this chapter. The advantage of using this kinetic model is that it takes into account the exchange process in the immortal ring-opening polymerization. The ROP of ϵ -CL in the presence of chain transfer agents shows equivalent control to that in the absence of CTAs, indicating fast and reversible chain transfer occurs [$D < 1.3$, suggesting $k_e \gg k_i, k_p$ (see chain exchange process in **Scheme 2.2**)]. Thus, for the kinetic models, the value of chain exchange rate constant (k_e) was set at $100 \text{ L} \cdot \text{mol}^{-1} \cdot \text{s}^{-1}$.⁷² The kinetic models demonstrate that for primary alcohols, k_p is 5 times larger than k_i . Furthermore, the ratio of k_p/k_i depends on the structure of the alcohol. For secondary hydroxyl groups, k_p is ~ 8 times larger and for tertiary groups it is around 10 times larger (**Table 2.5** and **Figure 2.12**).

Therefore, it is reasonable to conclude that the coexistence of two different structures arise from different initiation rates (where initiation refers to the insertion of the first CL monomer

into the zinc alkoxide bond, the nature of which depends on the type of hydroxyl group on the chain transfer agent). The decrease in the quantity of Type II chains with increasing chain length (degree of polymerization) can also be rationalized by the slow initiation from secondary hydroxyl groups compared to propagation from a primary CL alkoxide (**Table 2.4**). It is worth noting that other catalyst systems have also been reported which show faster rates of propagation than initiation, but the impact of these kinetics over telechelic polymer structure was not yet studied.^{71,73,74}

Table 2.5 The immortal ROP of ϵ -CL using mono-functional alcohols as the chain transfer agents.^a

Entry	CTA	Type of -OH	Rates ^b		
			$k_i \times 10^{-3}$ (L·mol ⁻¹ ·s ⁻¹)	$k_p \times 10^{-3}$ (L·mol ⁻¹ ·s ⁻¹)	k_p/k_i
1	1-Hexanol	primary	47.4	226.2	5
2	2-Hexanol	secondary	34.2	265.6	8
3	2-Methyl-2-pentanol	tertiary	27.0	275.2	10

^a) Reaction conditions: [LZn₂(OAc)₂]/[CTA]/[ϵ -CL]/[CHO] = 1/20/500/1000, [LZn₂(OAc)₂] = 10 mM; ^b) Determined from the plots of monomer conversion (< 25 %) vs. reaction time.

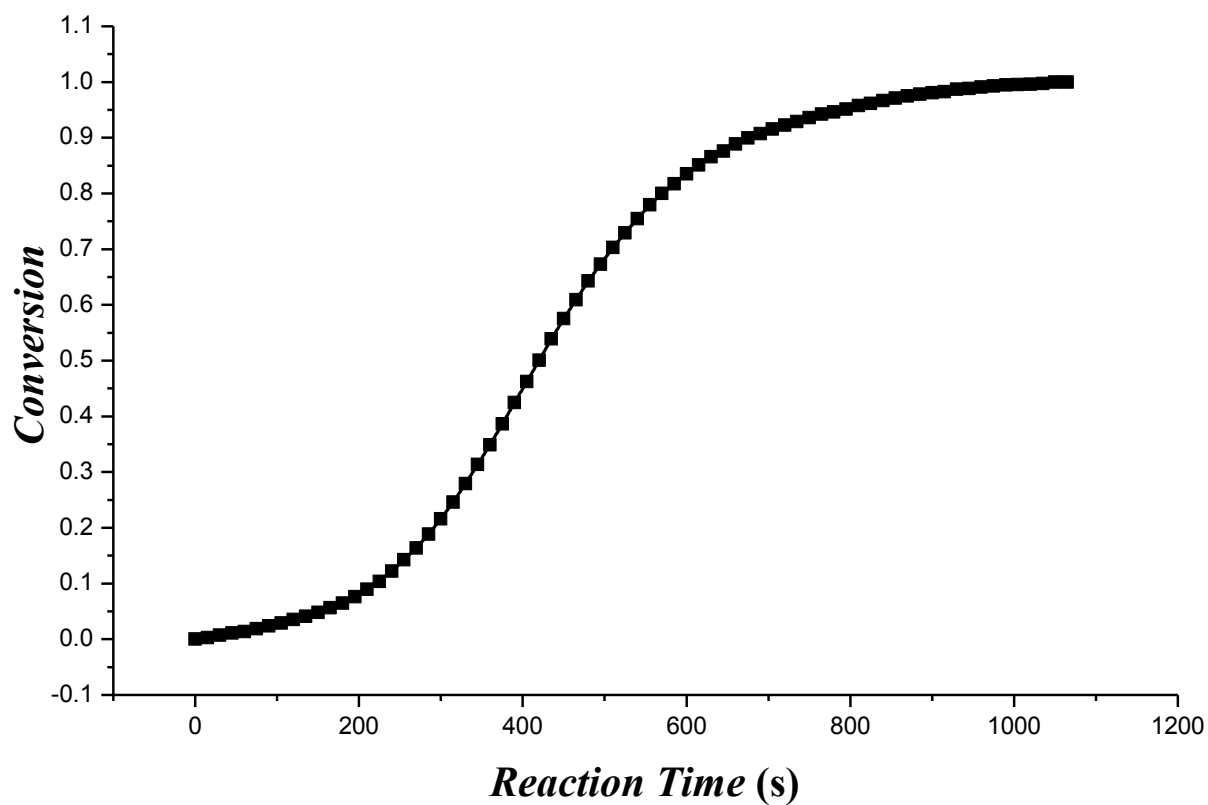
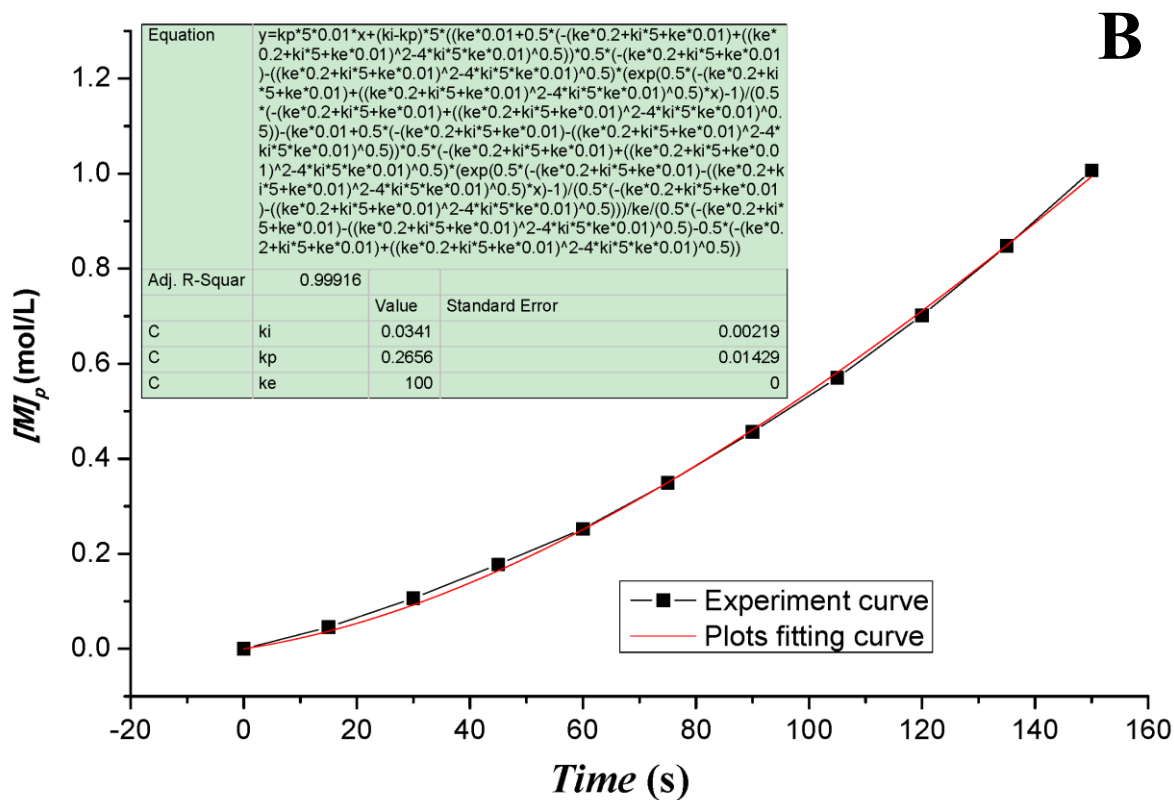
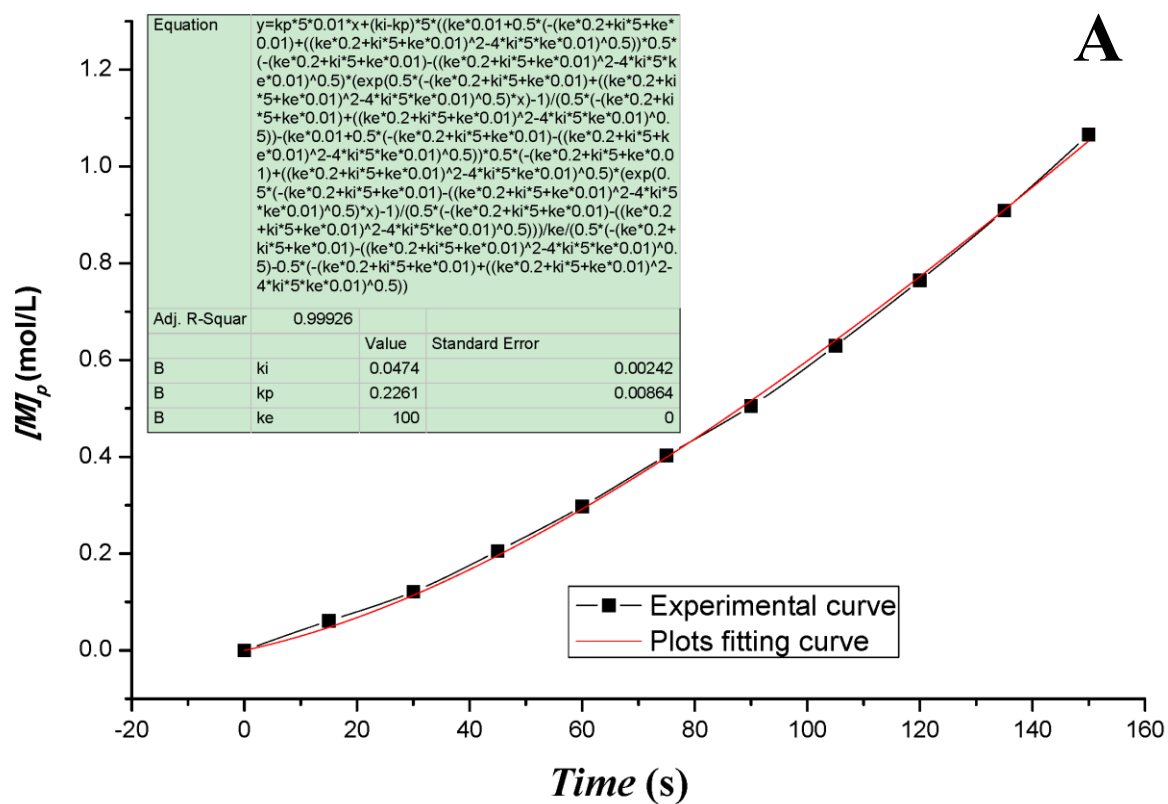


Figure 2.11 Typical plot of monomer conversion vs. time for the ROP of ϵ -CL in neat CHO at 80 °C catalyzed by bimetallic zinc catalyst.



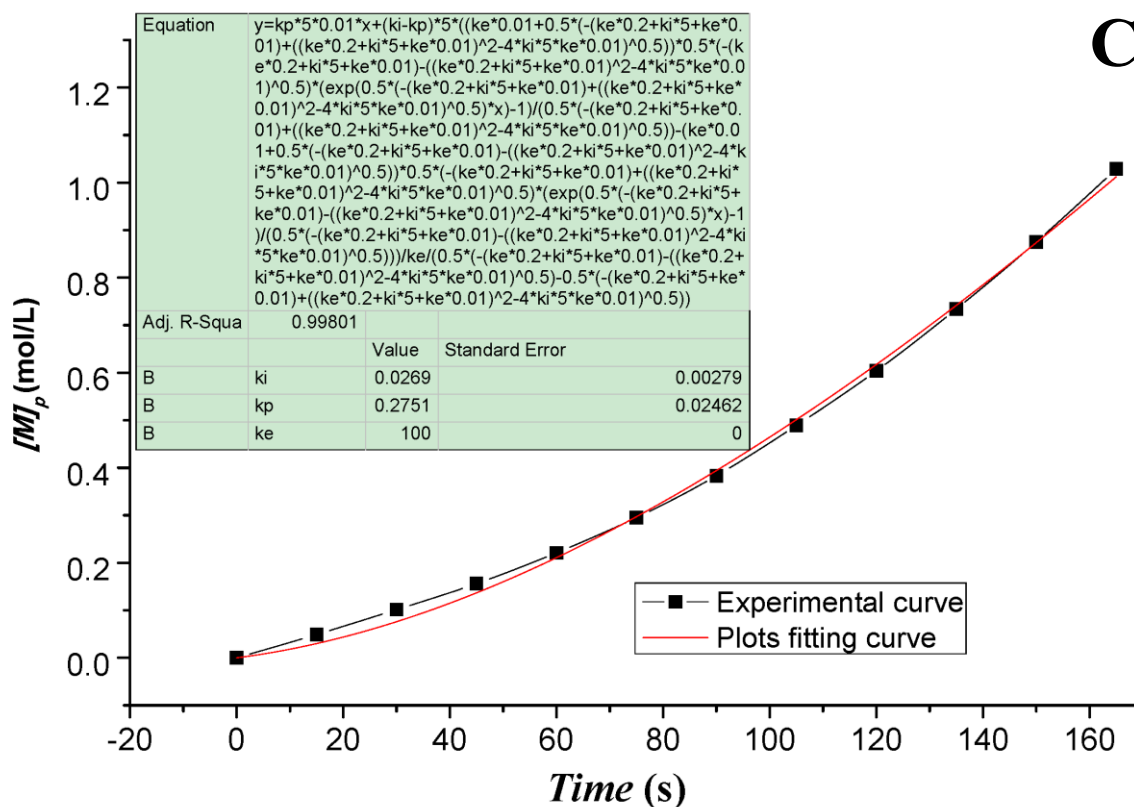


Figure 2.12 Curve-fitting at low monomer conversion (initiation stage, monomer conversion < 25%) catalyzed by bimetallic zinc catalyst using the kinetic model developed by Wang *et al.*⁷² ROP condition: 80 °C, neat CHO, [ε-CL] = 5.0 M, [LZn₂(OAc)₂] = 10 mM, [LZn₂(OAc)₂]/[CTA] = 1/20, using different mono-functional CTA: (A) 1-hexanol; (B) 2-hexanol and (C) 2-methyl-2-pentanol.

In order to compare with other systems from the literature dealing with the synthesis of telechelic PCL,⁶¹ 1,2-propanediol was also employed as the CTA. (**Table 2.3**, entry 6). The ¹H NMR spectrum of the PCL shows peaks at 5.15 and 4.18 ppm (**Figure 2.15B**), which are indicative of Type I PCL.⁶¹ Meanwhile signals at 3.96, 4.14 and 5.03 ppm (H_e and H_g in **Figure 2.15A**, respectively) indicate that two kinds of Type II PCL are also present, in which chains either initiate from the primary or secondary hydroxyl groups of the propane diol. Due to the overlap of the methyne/methylene signals assigned to Type II chains with those from the main chain PCL,⁷⁵ the peaks for H_d (4.06 ppm), H_e (3.96 & 4.14 ppm) and H_h (3.65 ppm) cannot be unambiguously assigned either in the ¹H NMR or ¹H-¹H COSY spectra (**Figure**

2.15B). Fortunately, there is no such signal overlap between the methyl groups on the propane diol units in the different polymer structures (**Figure 2.15**, H_c, H_f and H_i). Three signals were clearly observed in the methyl region of the ¹H-¹H COSY spectrum, each coupling with a different methyne proton, at (1.24 & 4.06 ppm), (1.26 & 5.03 ppm) and (1.27 & 5.15 ppm) (**Figure 2.15C**). This suggests there are three different types of methyl environments and is consistent with methyl groups coupling to H_a (Type I), H_d (Type II a) or H_g (Type II b), confirming that the sample contains a mixture of Type I (chain extended) and II (chain end-capped) chains. The molar ratio of the different PCL structures is calculated to be [Type I]/[Type II a]/[Type II b] = 65/26/9, from the relative integrals of H_c/H_f/H_i (see **Figure 2.13** & **Table 2.6**). However, in addition to the PCL species which are initiated from 1,2-propane diol, a minor distribution initiated from cyclohexanediol was also observed in the MALDI-ToF spectrum (**Figure 2.14**). This latter series is proposed to result from trace contamination of cyclohexene oxide by the diol, which might form by the catalyzed reaction between CHO and any residual water, as has been previously noted by various other groups working with this epoxide.⁷⁶⁻⁸⁰ The minor distribution, initiated from CHD, is not well defined in the ¹H NMR spectrum due to its low content (see **Figure 2.3** for ¹H NMR signals of CHD initiated PCL).

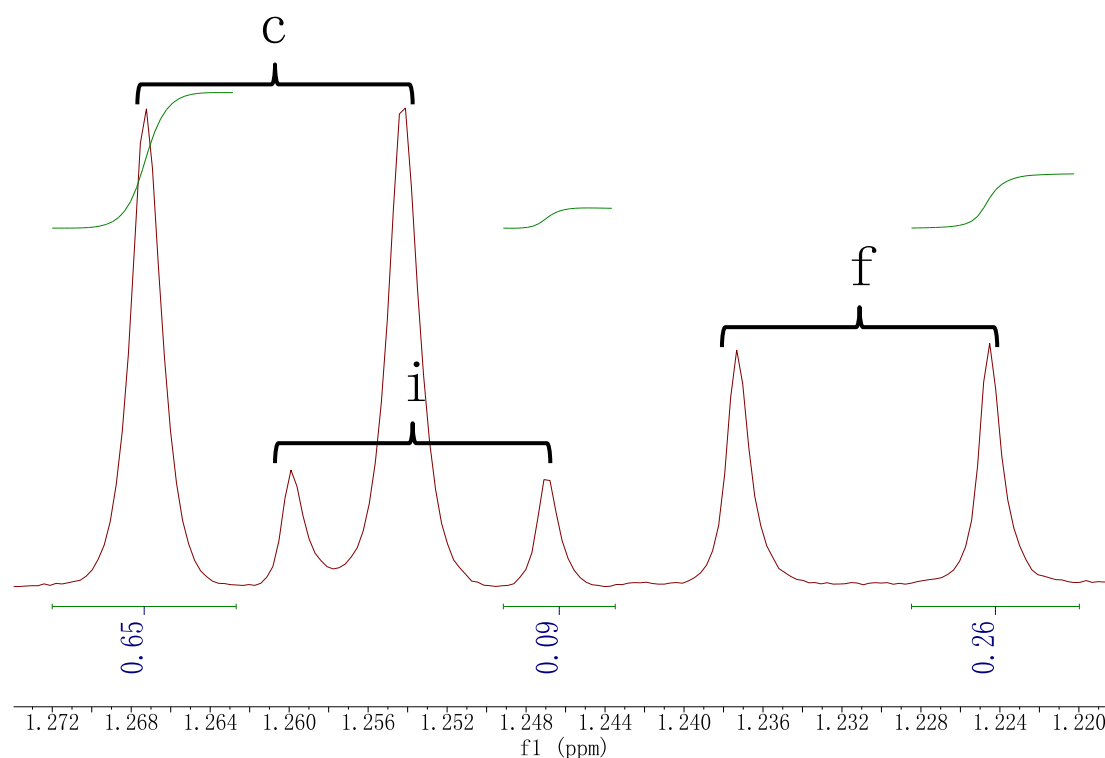


Figure 2.13 ^1H NMR spectrum of PCL_{30} (PD as CTA, see **Table 2.1**, entry 7). The composition of Type I/II is calculated using the integrals of peaks c, f and i.

Table 2.6 The normalized integrals of peaks c, f and i, in PCL_{30} (PD as CTA).^a

Polymer	A_c	A_f	A_i
PCL_{30}	0.65	0.26	0.09

^a) A_c , A_f and A_i are the integrals of peaks c, f and i in Figure 2.13.

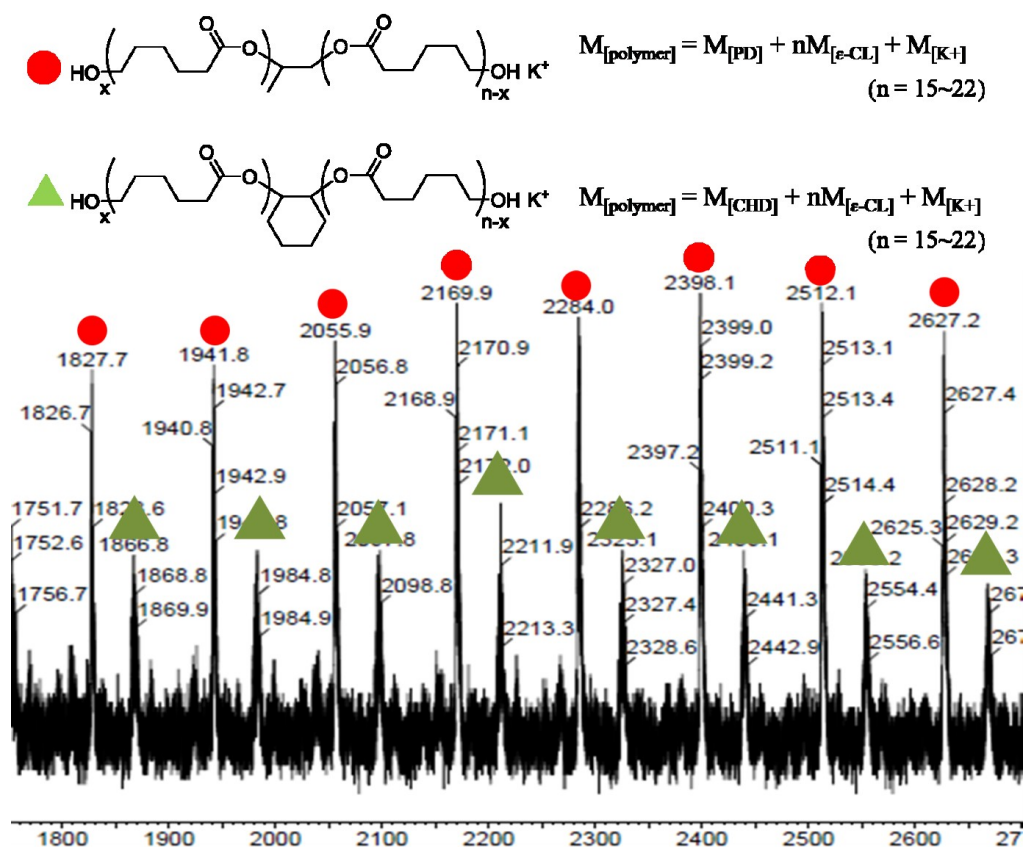


Figure 2.14 MALDI-ToF spectrum of the PCL synthesized with 1,2-propane diol as CTA (Table 2.1, entry 7). The major series (red circles) is assigned to chains initiated by 1,2-propane diol, which are calculated according to: $(\text{C}_6\text{H}_{10}\text{O}_2)_n\text{C}_3\text{H}_6(\text{OH})_2\cdot\text{K}^+$. The minor series (green triangles) consists of α , ω -hydroxyl end-groups, which are calculated according to: $(\text{C}_6\text{H}_{10}\text{O}_2)_n\text{C}_6\text{H}_{10}(\text{OH})_2\cdot\text{K}^+$. The minor series resulted from the trace of cyclohexanediol contained in CHO (might form by the catalyzed reaction between CHO and residual water).

Therefore, using 1,2-propanediol as the CTA results in a mixed structure PCL at comparable molecular weights to those used by Lin and co-workers.⁶¹ In addition, the observation that the molar content of Type IIa is much higher than Type IIb also strongly supports the notion that primary hydroxyl groups show higher initiation rates than secondary groups. Nevertheless, the fact that some primary $-\text{OH}$ groups do not react, i.e. in Type IIb, seems contrary to the kinetic findings. It is proposed that the methyl substituent, on 1,2-propanediol, might lead to sufficient steric hindrance even at the proximal primary hydroxyl to slow initiation from that site.

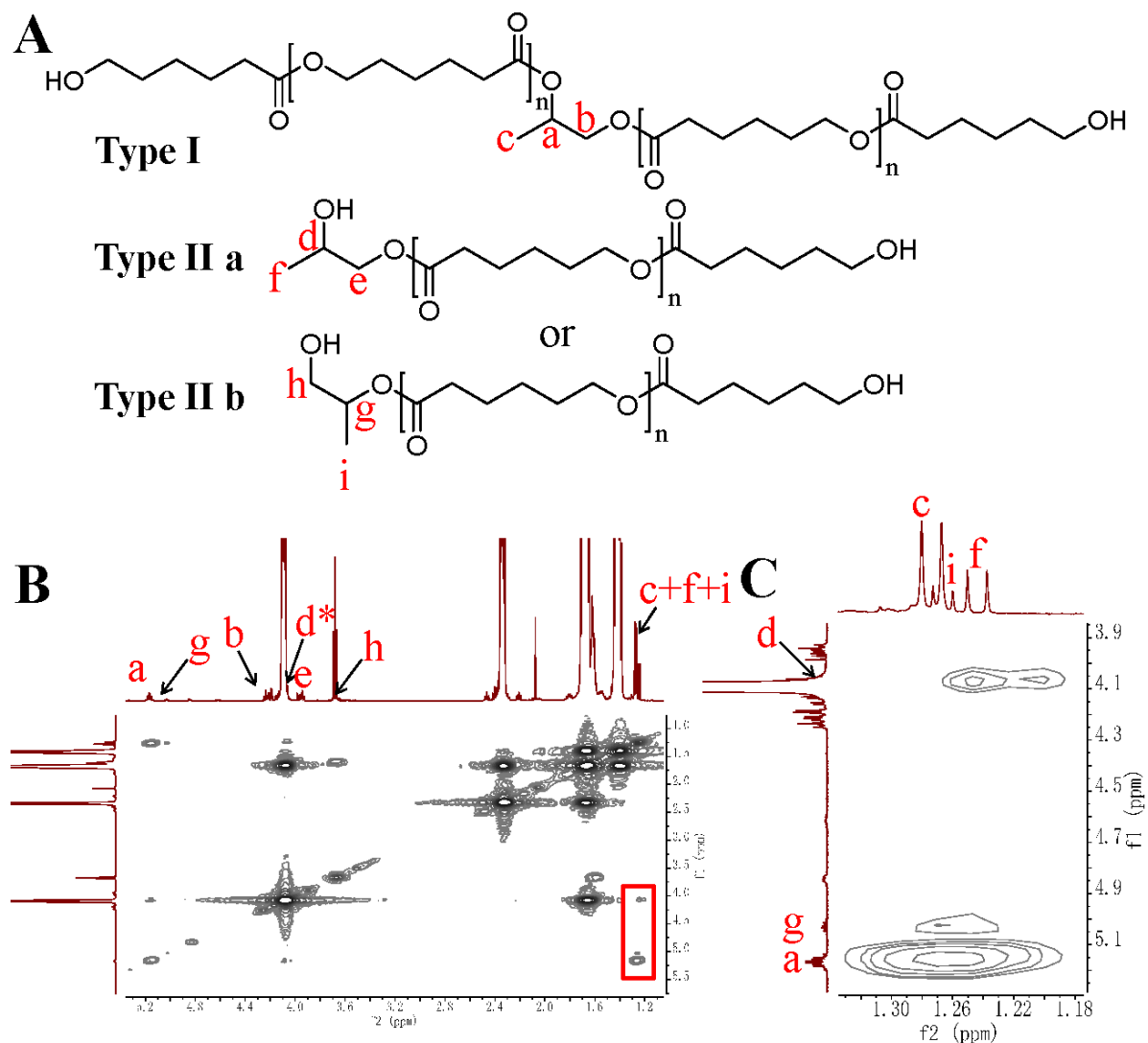


Figure 2.15 (A) A schematic diagram of the two structures (Type I & II) of PCL formed using 1,2-propanediol as the CTA; (B) A typical ^1H - ^1H COSY spectrum of the PCL (PD as CTA) and (C) An enlarged ^1H - ^1H COSY spectrum corresponding to the selected area in (B) and the correlative hydrogens in (A). The signals at (1.24, 4.06) ppm are assigned to the coupling between H_f and H_d resulting from Type II a chains; those at (1.26, 5.03) ppm are assigned to the coupling between H_i and H_g resulting from Type II b chains; whilst the signal at (1.27, 5.15) ppm is assigned to the coupling between H_c and H_a resulting from Type I chains.

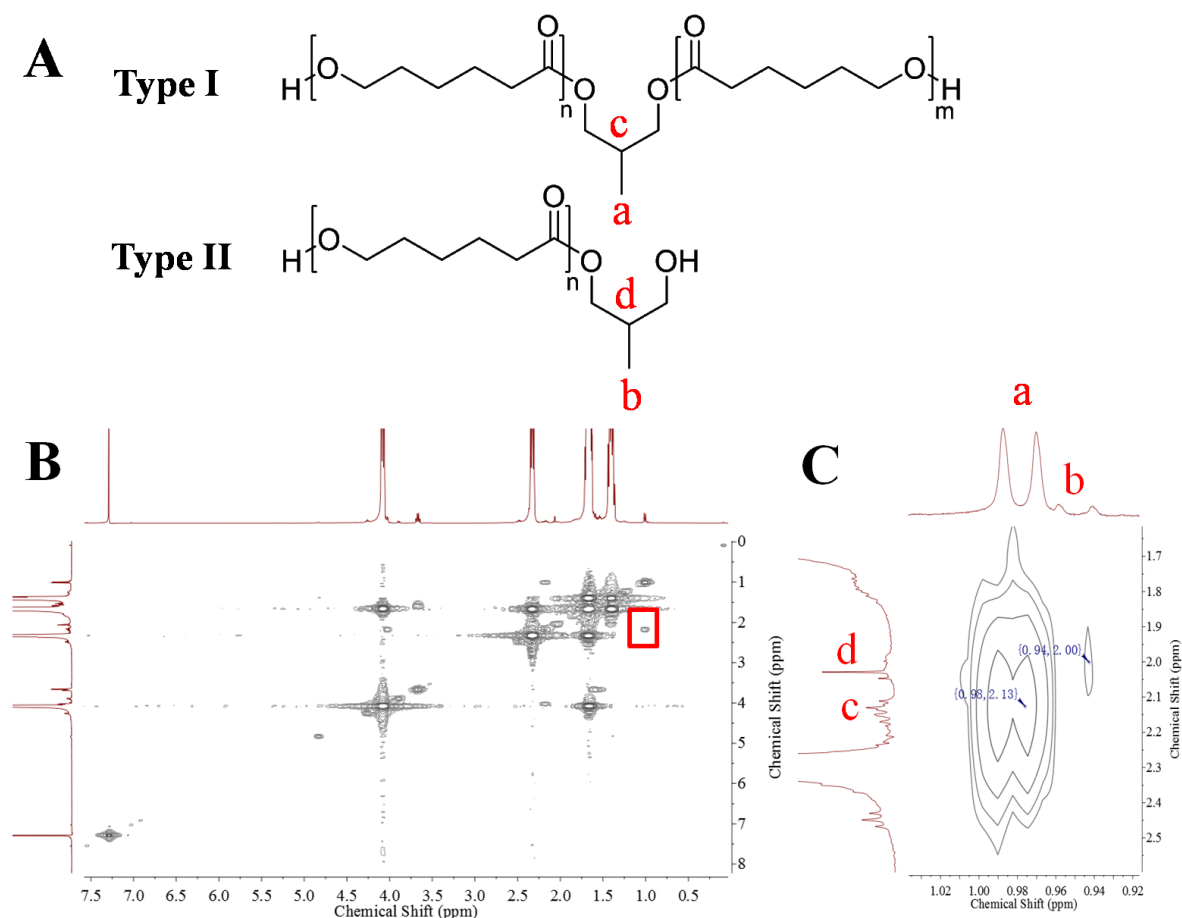


Figure 2.16 (A) A schematic diagram of the two structures (Type I & II) of PCL formed using 2-methyl-1,3-propanediol (MPD) as the CTA (**Table 2.1**, entry 9); (B) A typical ^1H - ^1H COSY spectrum of the PCL (MPD as CTA) and (C) An enlarged ^1H - ^1H COSY spectrum corresponding to the selected area in (B) and the correlative hydrogen in (A). The signal at (0.98, 2.13) ppm is assigned to the coupling between H_a and H_c resulting from Type I; another signal at (0.94, 2.00) ppm is assigned to the coupling between H_b and H_d resulting from Type II.

To test this steric hindrance hypothesis, 2-methyl-1,3-propanediol (MPD), having a similar molecular structure to 1,2-propanediol but with two primary $-\text{OH}$ groups, was used as the CTA (**Table 2.1**, entry 9). In contrast to the results using other bifunctional primary hydroxyl CTAs (i.e. EG and PEG), a mixture of two PCL structures was observed (see **Figure 2.16**). In the ^1H NMR spectra, two different methyl signals (H_a and H_b) were observed, these coupled with the methyne protons, H_c and H_d , respectively. It is, therefore, proposed that both the

steric hindrance and the nature of the –OH group on the chain transfer agent influences the rate of initiation, k_i , a factor which directly affects the structure of the final polymer.

2.3 Conclusions

The ROP of ϵ -CL was investigated using a di-zinc catalyst and various chain transfer agents. This system resulted in the polymerization of ϵ -CL, which fits the description of ‘immortal’. The polymer molecular weight can be predicted from [monomer]/[chain transfer agent]. By using the di-zinc catalyst, an unexpected and unusual result was that the nature of the hydroxyl groups, on the chain transfer agent, influenced the nature of the chain end groups of the PCL chains. Chain transfer agents with primary hydroxyl groups and having limited/no steric hindrance, such as ethylene glycol and PEG, exhibited quantitative initiation from all hydroxyl groups. In contrast, chain transfer agents with secondary hydroxyl groups, such as *trans*-1,2-cyclohexanediol and 1,2-propanediol, resulted in a mixture of different PCL structures. These were polymers chain extended or end-capped by the diol. 2-Methyl-1,3-propanediol, also resulted in the formation of the two different PCL chain structures. The polymerization kinetics revealed that the rate of initiation, k_i , (i.e. the insertion of the first CL monomer into the zinc-O(chain transfer agent)) is significantly slower than the rate constant of propagation (k_p) (i.e. insertion of subsequent CL monomers into the Zn-O(PCL)). Using a series of mono-functional chain transfer agents, the rate of initiation was related to the structure of hydroxyl group, with the rates decreasing in the order: $k_{i,(\text{primary})} > k_{i,(\text{secondary})} > k_{i,(\text{tertiary})}$. Taken as a whole the studies revealed that the structure of PCL formed by the di-zinc complex/CTA system depends on both the nature of the hydroxyl group and on the steric environment(s) proximal to the hydroxyl groups on the chain transfer agent. The studies also highlight the importance of the catalyst system in controlling the relative rates of initiation vs. propagation, and thereby the polymer chain structures. In this case, the di-zinc catalyst shows a clear kinetic selectivity for certain hydroxyl groups/chemical environments compared to others. Such selectivity may be an interesting means to control and target specific polymer chain structures. Further investigation of the generality of these findings using other catalysts is warranted, as are studies to exploit the

catalytic selectivity as a means to target particular chain structures for application. The selectivity for certain hydroxyl groups and the identification of a mixed structure of the obtained polymer lead to the new catalyst design as well as principles of monomer screening. These set the foundation of the studies discussed in the following chapter, focusing on the chemoselective sequential polymerization to prepare well-defined block copolyesters from mixed monomer feedstock.

2.4 References

- (1) Ropson, N.; Dubois, P.; Jerome, R.; Teyssie, P. *Macromolecules* **1995**, *28*, 7589-7598.
- (2) Stevels, W. M.; Ankone, M. J. K.; Dijkstra, P. L.; Feijen, J. *Macromol. Chem. Phys.* **1995**, *196*, 1153-1161.
- (3) Dubois, P.; Ropson, N.; Jérôme, R.; Teyssié, P. *Macromolecules* **1996**, *29*, 1965-1975.
- (4) Stevels, W. M.; Ankoné, M. J. K.; Dijkstra, P. J.; Feijen, J. *Macromolecules* **1996**, *29*, 8296-8303.
- (5) Save, M.; Schappacher, M.; Soum, A. *Macromol. Chem. Phys.* **2002**, *203*, 889-899.
- (6) Chen, H.-Y.; Huang, B.-H.; Lin, C.-C. *Macromolecules* **2005**, *38*, 5400-5405.
- (7) Zhang, D.; Hillmyer, M. A.; Tolman, W. B. *Biomacromolecules* **2005**, *6*, 2091-2095.
- (8) Nomura, N.; Taira, A.; Nakase, A.; Tomioka, T.; Okada, M. *Tetrahedron* **2007**, *63*, 8478-8484.
- (9) Woodruff, M. A.; Hutmacher, D. W. *Prog. Polym. Sci.* **2010**, *35*, 1217-1256.
- (10) Chen, S.; Zhang, X. Z.; Cheng, S. X.; Zhuo, R. X.; Gu, Z. W. *Biomacromolecules* **2008**, *9*, 2578-2585.
- (11) Zhang, Y. Z.; Wang, X.; Feng, Y.; Li, J.; Lim, C. T.; Ramakrishna, S. *Biomacromolecules* **2006**, *7*, 1049-1057.
- (12) Gan, Z. H.; Jim, T. F.; Li, M.; Yuer, Z.; Wang, S. G.; Wu, C. *Macromolecules* **1999**, *32*, 590-594.
- (13) Calandrelli, L.; Calarco, A.; Laurienzo, P.; Malinconico, M.; Petillo, O.; Peluso, G. *Biomacromolecules* **2008**, *9*, 1527-1534.
- (14) Kwon, I. K.; Kidoaki, S.; Matsuda, T. *Biomaterials* **2005**, *26*, 3929-3939.
- (15) Tang, M.; Purcell, M.; Steele, J. A. M.; Lee, K.-Y.; McCullen, S.; Shakesheff, K. M.; Bismarck, A.; Stevens, M. M.; Howdle, S. M.; Williams, C. K. *Macromolecules* **2013**, *46*, 8136-8143.
- (16) Allard, D.; Prudhomme, R. E. *J. Appl. Polym. Sci.* **1982**, *27*, 559-568.
- (17) Cheung, Y. W.; Stein, R. S. *Macromolecules* **1994**, *27*, 2512-2519.
- (18) Yang, J. M.; Chen, H. L.; You, J. W.; Hwang, J. C. *Polym. J.* **1997**, *29*, 657-662.
- (19) Kowalski, A.; Duda, A.; Penczek, S. *Macromolecules* **2000**, *33*, 7359-7370.
- (20) Lohmeijer, B. G. G.; Pratt, R. C.; Leibfarth, F.; Logan, J. W.; Long, D. A.; Dove, A. P.; Nederberg, F.; Choi, J.; Wade, C.; Waymouth, R. M.; Hedrick, J. L. *Macromolecules* **2006**, *39*, 8574-8583.
- (21) Shen, Y. Q.; Shen, Z. Q.; Zhang, Y. F.; Yao, K. M. *Macromolecules* **1996**, *29*, 8289-8295.

- (22) Nomura, N.; Taira, A.; Tomioka, T.; Okada, M. *Macromolecules* **2000**, *33*, 1497-1499.
- (23) Sanda, F.; Sanada, H.; Shibasaki, Y.; Endo, T. *Macromolecules* **2002**, *35*, 680-683.
- (24) Mecerreyes, D.; Jerome, R.; Dubois, P. *Adv. Polym. Sci.* **1999**, *147*, 1-59.
- (25) Vanhoorne, P.; Dubois, P.; Jerome, R.; Teyssie, P. *Macromolecules* **1992**, *25*, 37-44.
- (26) Zhong, Z. Y.; Dijkstra, P. J.; Birg, C.; Westerhausen, M.; Feijen, J. *Macromolecules* **2001**, *34*, 3863-3868.
- (27) Bailey, W. J.; Ni, Z.; Wu, S. R. *Macromolecules* **1982**, *15*, 711-714.
- (28) Jin, S.; Gonsalves, K. E. *Macromolecules* **1997**, *30*, 3104-3106.
- (29) Yuan, J. Y.; Pan, C. Y.; Tang, B. Z. *Macromolecules* **2001**, *34*, 211-214.
- (30) Darensbourg, D. J.; Karroonnirun, O. *Macromolecules* **2010**, *43*, 8880-8886.
- (31) Sanchez-Barba, L. F.; Garces, A.; Fajardo, M.; Alonso-Moreno, C.; Fernandez-Baeza, J.; Otero, A.; Antinolo, A.; Tejeda, J.; Lara-Sanchez, A.; Lopez-Solera, M. I. *Organometallics* **2007**, *26*, 6403-6411.
- (32) Tsai, Y. H.; Lin, C. H.; Lin, C. C.; Ko, B. T. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 4927-4936.
- (33) Darensbourg, D. J.; Karroonnirun, O.; Wilson, S. J. *Inorg. Chem.* **2011**, *50*, 6775-6787.
- (34) Pepels, M. P. F.; Bouyahyi, M.; Heise, A.; Duchateau, R. *Macromolecules* **2013**, *46*, 4324-4334.
- (35) Darensbourg, D. J.; Choi, W.; Karroonnirun, O.; Bhuvanesh, N. *Macromolecules* **2008**, *41*, 3493-3502.
- (36) Romain, C.; Williams, C. K. *Angew. Chem., Int. Ed.* **2014**, *53*, 1607-1610.
- (37) Martello, M. T.; Hillmyer, M. A. *Macromolecules* **2011**, *44*, 8537-8545.
- (38) Lin, J.-O.; Chen, W.; Shen, Z.; Ling, J. *Macromolecules* **2013**, *46*, 7769-7776.
- (39) Kaszas, G.; Puskas, J. E.; Kennedy, J. P.; Hager, W. G. *J. Polym. Sci., Part A: Polym. Chem.* **1991**, *29*, 427-435.
- (40) Shin, J.; Martello, M. T.; Shrestha, M.; Wissinger, J. E.; Tolman, W. B.; Hillmyer, M. A. *Macromolecules* **2011**, *44*, 87-94.
- (41) Storey, R. F.; Chisholm, B. J. *Macromolecules* **1993**, *26*, 6727-6733.
- (42) Wanamaker, C. L.; O'Leary, L. E.; Lynd, N. A.; Hillmyer, M. A.; Tolman, W. B. *Biomacromolecules* **2007**, *8*, 3634-3640.
- (43) Baez, J. E.; Marcos-Fernandez, A.; Lebron-Aguilar, R.; Martinez-Richa, A. *Polymer* **2006**, *47*, 8420-8429.
- (44) Barqawi, H.; Ostas, E.; Liu, B.; Carpentier, J. F.; Binder, W. H. *Macromolecules* **2012**, *45*, 9779-9790.
- (45) Guillaume, S. M. *Eur. Polym. J.* **2013**, *49*, 768-779.
- (46) Duda, A. *Macromolecules* **1994**, *27*, 576-582.
- (47) Duda, A. *Macromolecules* **1996**, *29*, 1399-1406.
- (48) Tasdelen, M. A.; Kahveci, M. U.; Yagci, Y. *Prog. Polym. Sci.* **2011**, *36*, 455-567.
- (49) Sisson, A. L.; Ekinci, D.; Lendlein, A. *Polymer* **2013**, *54*, 4333-4350.
- (50) Lendlein, A.; Neuenchwander, P.; Suter, U. W. *Macromol. Chem. Phys.* **2000**, *201*, 1067-1076.
- (51) Kricheldorf, H. R.; Rost, S. *Polymer* **2005**, *46*, 3248-3256.
- (52) Kricheldorf, H. R.; Behnken, G.; Schwarz, G. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 3175-3183.

- (53) Nakayama, Y.; Okuda, S.; Yasuda, H.; Shiono, T. *React. Funct. Polym.* **2007**, *67*, 798-806.
- (54) Guillaume, S. M.; Schappacher, M.; Soum, A. *Macromolecules* **2003**, *36*, 54-60.
- (55) Dove, A. P. *Chem. Commun.* **2008**, 6446-6470.
- (56) Magbitang, T.; Lee, V. Y.; Connor, E. F.; Sundberg, L. K.; Kim, H. C.; Volksen, W.; Hawker, C. J.; Miller, R. D.; Hedrick, J. L. *Macromol. Symp.* **2004**, *215*, 295-306.
- (57) Magbitang, T.; Lee, V. Y.; Miller, R. D.; Toney, M. F.; Lin, Z.; Briber, R. M.; Kim, H. C.; Hedrick, J. L. *Adv. Mater.* **2005**, *17*, 1031-1035.
- (58) Lee, H.-i.; Jakubowski, W.; Matyjaszewski, K.; Yu, S.; Sheiko, S. S. *Macromolecules* **2006**, *39*, 4983-4989.
- (59) Han, D.-H.; Pan, C.-Y. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 789-799.
- (60) Chen, W.; Ling, J.; Shen, Z. Q. *Sci. China, Ser. B: Chem.* **2005**, *48*, 334-342.
- (61) Ling, J.; Liu, J.; Shen, Z.; Hogen-Esch, T. E. *J. Polym. Sci., Part A: Polym. Chem.* **2011**, *49*, 2081-2089.
- (62) Zhu, Y.; Romain, C.; Poirier, V.; Williams, C. K. *Macromolecules* **2015**, *48*, 2407-2416.
- (63) Kember, M. R.; Knight, P. D.; Reung, P. T. R.; Williams, C. K. *Angew. Chem., Int. Ed.* **2009**, *48*, 931-933.
- (64) Buchard, A.; Jutz, F.; Kember, M. R.; White, A. J. P.; Rzepa, H. S.; Williams, C. K. *Macromolecules* **2012**, *45*, 6781-6795.
- (65) Saini, P. K.; Romain, C.; Zhu, Y.; Williams, C. K. *Polym. Chem.* **2014**, *5*, 6068-6075.
- (66) Aida, T.; Inoue, S. *Accounts. Chem. Res.* **1996**, *29*, 39-48.
- (67) Chaloner, P. *Organic Chemistry: A Mechanistic Approach*; CRC Press, 2014.
- (68) Hatzakis, E.; Archavlis, E.; Dais, P. *J. Am. Oil Chem. Soc.* **2007**, *84*, 615-619.
- (69) Spyros, A.; Argyropoulos, D. S.; Marchessault, R. H. *Macromolecules* **1997**, *30*, 327-329.
- (70) Sutter, M.; Dayoub, W.; Méta, E.; Raoul, Y.; Lemaire, M. *ChemSusChem* **2012**, *5*, 2397-2409.
- (71) Wang, L.; Bochmann, M.; Cannon, R. D.; Carpentier, J.-F.; Roisnel, T.; Sarazin, Y. *Eur. J. Inorg. Chem.* **2013**, *2013*, 5896-5905.
- (72) Wang, L.; Poirier, V.; Ghiotto, F.; Bochmann, M.; Cannon, R. D.; Carpentier, J.-F.; Sarazin, Y. *Macromolecules* **2014**, *47*, 2574-2584.
- (73) Kowalski, A.; Duda, A.; Penczek, S. *Macromolecules* **1998**, *31*, 2114-2122.
- (74) Puaux, J.-P.; Banu, I.; Nagy, I.; Bozga, G. *Macromol. Symp.* **2007**, *259*, 318-326.
- (75) Fevrier, P.; Guégan, P.; Yvergnaux, F.; Pierre Callegari, J.; Dufossé, L.; Binet, A. *J. Mol. Catal. B-Enzym.* **2001**, *11*, 445-453.
- (76) van Meerendonk, W. J.; Duchateau, R.; Koning, C. E.; Gruter, G.-J. M. *Macromolecules* **2005**, *38*, 7306-7313.
- (77) Sugimoto, H.; Ohtsuka, H.; Inoue, S. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 4172-4186.
- (78) Sugimoto, H.; Kuroda, K. *Macromolecules* **2007**, *41*, 312-317.
- (79) Nakano, K.; Nakamura, M.; Nozaki, K. *Macromolecules* **2009**, *42*, 6972-6980.
- (80) Cyriac, A.; Lee, S. H.; Lee, B. Y. *Polym. Chem.* **2011**, *2*, 950-956.

Chapter 3

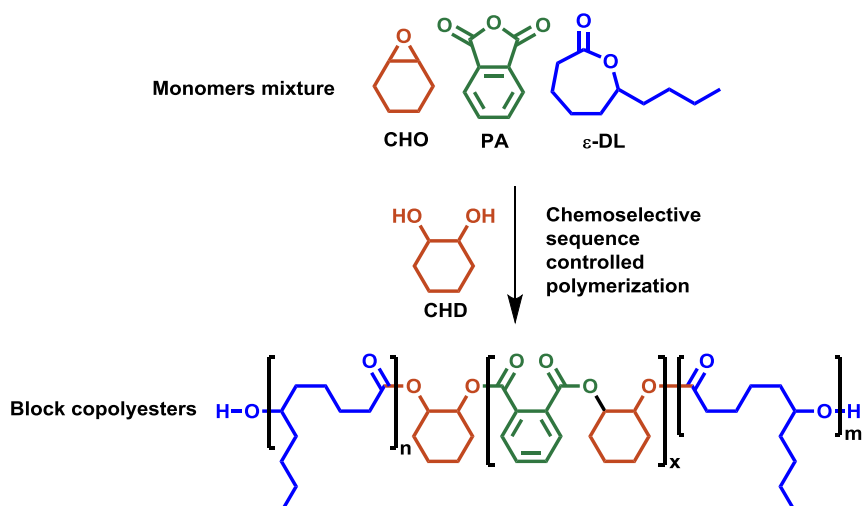
Selective Polymerization Catalysis:
Controlling the Metal Chain End Group to
Prepare Block Copolyesters

3.1 Background and Aims

A central challenge in polymer synthesis is to develop methods which enable complex architectures to be prepared, particularly if this can be achieved using mixtures of monomers.¹ Generally, using two or more monomers, the copolymer composition or sequence is determined by empirical monomer ‘reactivity ratios’.² Recently, controlled radical polymerization methods have enabled sequence control.³⁻⁶ Using catalysis to control monomer enchainment from mixtures would be highly attractive, but there are not yet many such options for oxygenated copolymers. Some of the best routes to such oxygenated polymers are by catalyzed ring-opening polymerization (ROP) of lactones or the ring-opening copolymerizations of (ROCOP) of epoxides and anhydrides/CO₂.⁷⁻¹⁰ Previously, Coates and Thomas developed a selective yttrium catalyst for stereocontrolled ROP from mixtures of two lactones.¹¹ Recently, my colleague reported dinuclear catalysts able to switch between two different polymerization cycles: ROP and ROCOP and to control block sequences from mixtures of epoxide, CO₂ and ϵ -CL.¹² By controlling the zinc-chain end group chemistry, the polymerization pathways were directed: zinc alkoxide groups catalyze ROP, whilst zinc carbonate groups catalyze epoxide/CO₂ ROCOP.¹³

Multi-block copolymers have the potential for significantly enhanced properties and functionality.¹⁴ Block regulation provides a means to differentiate macroscopic thermal/mechanical performances and, of particular relevance for oxygenated polymers, degradation rates.¹⁵⁻¹⁷ Directing the block compositions in conventional polyester synthesis is extremely difficult and more often impossible, due to step-growth synthetic methods. In contrast, the ROP of lactones¹⁸ or ROCOP of epoxides/anhydrides^{13,19-25} allow controlled syntheses.²⁶ Currently, the catalysts used for these two processes have been reported separately, there is just one report, from 1985, of a homogeneous aluminium porphyrin complex active for both ROP and ROCOP.²⁷ It is yet unexplored whether these catalysts are active for both ROP and ROCOP. To address the issues mentioned above, it is both timely and novel to explore the possibility of combining the ROCOP and ROP methods to prepare polyesters with controlled block sequence in ‘one step; one pot’ (**Scheme 3.1**). In this chapter,

the unique ‘chemoselective polymerization’ behaviour of the di-zinc catalysts are studied. Since the alternating polymerization of phthalic anhydride (PA) and cyclohexene oxide (CHO) has already been studied using di-zinc catalysts,¹³ these monomers are used as the examples in the following investigation.



Scheme 3.1 Overview of the chemoselective sequence controlled polymerization method and typical block copolyesters investigated in this chapter

3.2 Results and Discussion

3.2.1 The ROCOP of epoxide and anhydride

It is important to investigate the production of polyesters by ROCOP before any greater complexity is introduced. Using the di-zinc acetate catalyst, $[LZn_2(OAc)_2]$ (described in Chapter 2), alternating polyester, poly(cyclohexylene phthalate) (PCHPE), can be prepared from PA and CHO (see **Figure 3.1**).¹³ However, ether linkages may also form between two epoxide monomers during the reaction.²⁸ Normally, the content of ether linkages was determined by comparing the integral in the ^1H NMR spectrum (in $CDCl_3$) between 3.4~3.6 ppm (ether linkage) and between 4.8~5.3 ppm (ester linkage). As pointed out in **Figure 3.2**, multiple peaks were also observed in the PCHPE sample. These multiple peaks were considered to be ether linkages at first, however no ether linkage signals were observed in the

2D HSQC NMR (ether linkages are supposed to appear within the area as circled in **Figure 3.3**).¹³

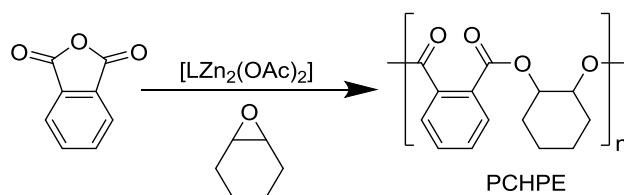


Figure 3.1 Scheme of the ring-opening copolymerization (ROCOP) of the PCHPE catalyzed by di-zinc acetate catalyst.

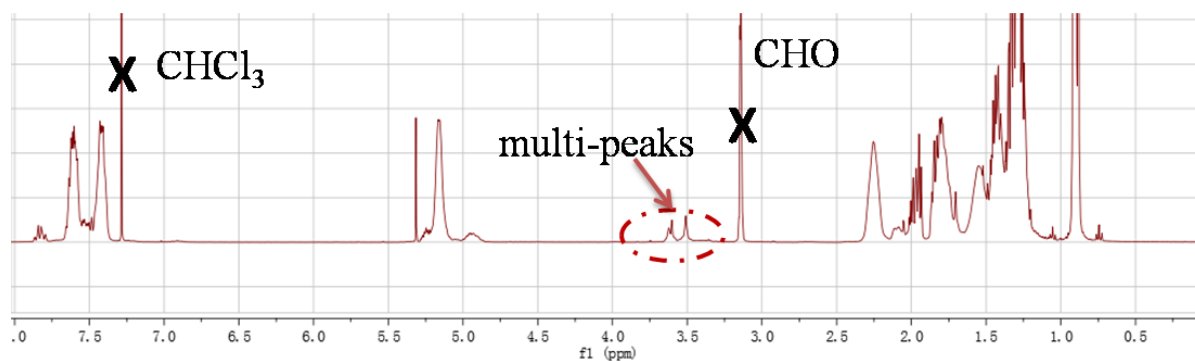


Figure 3.2 ^1H NMR spectrum of PCHPE in CDCl_3 . Multiple peaks were observed at the chemical shift between 3.4~3.6 ppm.

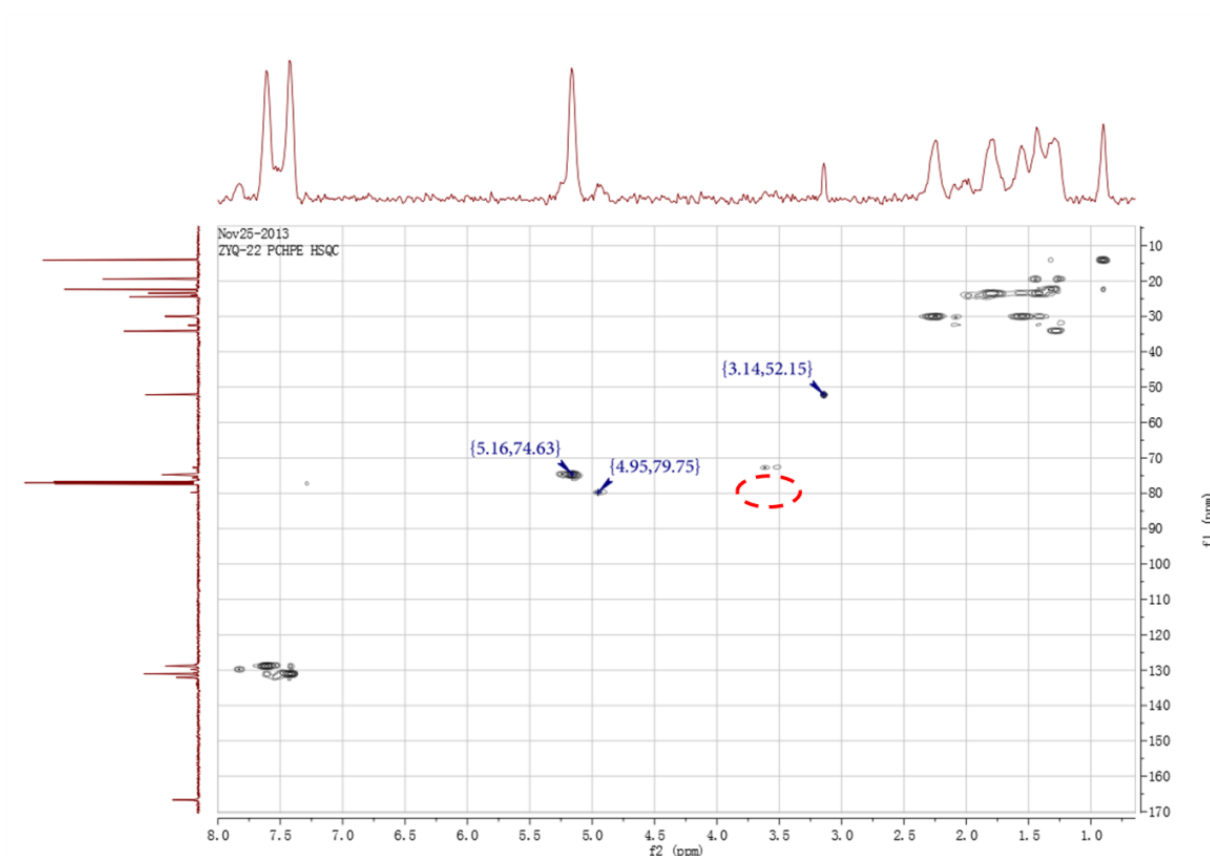


Figure 3.3 2D HSQC NMR spectrum of PCHPE in CDCl_3 . No signals can be observed within the circle where ether linkages expected to appear.

To verify the content of ether linkages in the polyester chain, PCHPE was characterized *via* ^1H NMR spectroscopy in another solvent, $\text{DMSO}-d_6$. As displayed in **Figure 3.4C**, the multi-peaks converted to a single peak at 3.48 ppm which could be assigned to the polymer end group signals. Also, no evidence of ether linkages was found in the HSQC spectrum of PCHPE. To further investigate the lack of ether linkages, the ^1H NMR spectrum of poly(cyclohexene oxide) was conducted as a reference to show the actual chemical shift of ether linkages in $\text{DMSO}-d_6$ (at 3.61 ppm, see **Figure 3.4B**). Meanwhile, in order to rule out the possibility that the difference between 3.48 and 3.61 ppm might be due to some artefact, the ^1H NMR spectrum of a mixture of PCHPE and poly(cyclohexene oxide) was also recorded. It is quite clear that two peaks appear at 3.48 and 3.61, respectively, indicating that the purported ether linkages in the polyether were in fact mis-assigned end group signals.¹³

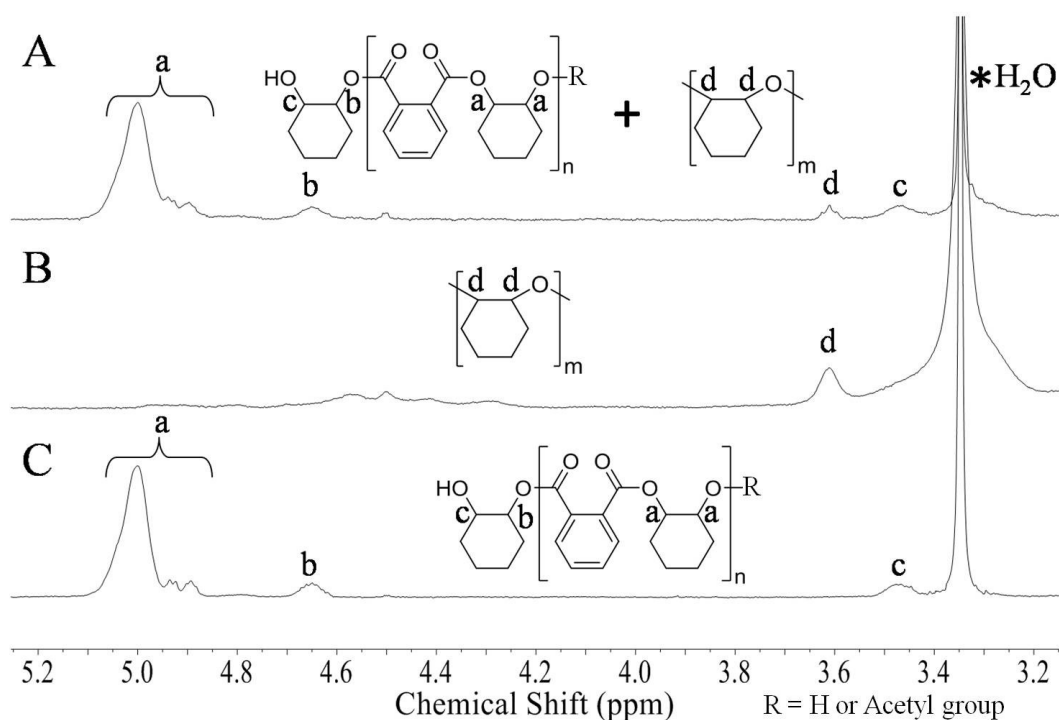


Figure 3.4 ^1H NMR spectra of (A) a mixture of PCHPE and poly(cyclohexene oxide), (B) poly(cyclohexene oxide) and (C) PCHPE in $\text{DMSO-}d_6$. The peaks at 3.48 and 4.65 ppm represent the end group of PCHPE shown in (A), and the peak at 3.61 ppm stands for the ether linkage of poly(cyclohexene oxide) illustrated in (B). The small peaks at 4.88 and 4.93 in (A) and (C) might arise from the second cyclohexene unit at the polymer chain end, which requires further investigation.

Although the lack of ether linkages indicates that the polymer has a perfectly alternating microstructure of $[\text{PA} + \text{CHO}]$, the Size Exclusion Chromatography (SEC) traces of PCHPE remain complex. The molecular weights (MWs), obtained by THF SEC, were always 6 to 8 times smaller than the theoretical ones (**Table 3.1**). The small molecular weights might arise from the different hydrodynamic radius of PCHPE and the PS standards or by some issue associated with non-covalent interactions between PCHPE and the SEC column. However, the molecular weights determined by NMR calculation (using $-\text{OH}$ end groups as the internal reference) [M_{th} (kDa) column in **Table 3.1**] also suggest a large deviation from the theoretical molecular weights [$M_{\text{n,NMR}}$ (kDa) column in **Table 3.1**]. Therefore, it is reasonable to believe that the low molecular weights are due to residual chain transfer agents such as water,

cyclohexanediol or phthalic acid. To address this, a completely new purification procedure was developed for PA. Prior to sublimation, the crude PA was treated with benzene and recrystallized from CHCl_3 (see experimental chapter for details). After the purification, the molecular weights of PCHPE significantly increased under the same polymerization conditions (**Table 3.1**, entry 3). Though the molecular weights given by SEC are still smaller than theoretical values, this is attributed to both the different hydrodynamic radius of PCHPE and the PS standards (discussed in Section 3.2.3.1) and the presence of cyclohexanediol which might arise from the catalyzed reaction between CHO and any residual water. This has been previously reported by other groups using this epoxide.²⁹⁻³³ For example, Darensbourg and co-workers reported the formation of diol *via* a hydrolysis process between the epoxide and the residual water happens before the ring-opening copolymerization. The diol then acts as the chain transfer agent during the ROCOP.³⁴ The polymer MWs can be more accurately determined using a multi angle light scattering detector, which will be discussed in section 3.2.3. Using this method a very good agreement between calculated and experimental MW values is obtained.

During the investigation using $[\text{LZn}_2(\text{OAc})_2]$ complex, SEC traces featuring bimodal distributions were observed by my colleagues and I (entry 3, Table 3.1).^{13,25} This is proposed to be due to the initiation from both the acetate co-ligand (OAc, monofunctional initiator) and the trace of residual chain transfer agent (usually diols derived from epoxides, bifunctional initiator).

Table 3.1 The MW of various PCHPE samples.

#	[cat]/[CHO]/[PA]	M_{th} (kDa) ^a	$M_{\text{n,SEC-PS}}$ (kDa) ^b	$M_{\text{n,NMR}}$ (kDa) ^c	$\bar{D}$
1	1/800/100	24.6	3.1	3.5	1.22
2	1/500/100	24.6	3.7	3.8	1.31
3 ^d	1/800/100	24.6	20.4; 9.8 ^f	18.5 ^e	1.04; 1.05 ^f

*Polymerization conditions: all polymerizations were run in neat CHO as the reaction solvent at 100 °C for 3.0-4.0 h. ^{a)}theoretical molecular weight was calculated based on the molar ratio of $[LZn_2(OAc)_2]/[PA]$, assuming > 95 % conversion of PA; ^{b)} the M_n was acquired using THF SEC with near monodispersed polystyrene standards for calibration; ^{c)} the M_n was calculated using the integrals of the PCHPE end groups (peak b in **Figure 3.4C**) in the ^1H NMR spectrum; ^{d)} using PA purified via a completely new procedure; ^{e)} may not be accurate due to the weak signal of PCHPE end group; ^{f)} bimodal distribution*

3.2.2 Synthesis of PCHPE-*b*-PCL

3.2.2.1 Sequential addition method

A sequential method (see experimental section) was used first to carry out block copolyester preparation. Basically, PA and CHO were polymerized to form PCHPE block first. After the complete conversion of PA (monitored by ^1H NMR), ϵ -CL was added to the reaction mixture to sequentially grow the PCL block. By using the sequential method, the reaction temperature can be easily tailored for certain monomers, for instance, the temperature was 100 °C for the ROCOP of PA/CHO and then reduced to 80 °C for the ROP of ϵ -CL. Using the two temperatures optimized the high turnover frequency and maintained narrow molecular weight distributions. Additionally, monomers used to make different blocks were added sequentially in this case, which avoids the potential competition between monomers.

A series of PCHPE-*b*-PCL with different molar ratios of $[PA]/[\epsilon\text{-CL}]$ were prepared (listed in **Table 3.2**). Although the increases in molecular weight (entry 1-4 in **Table 3.2** and **Figure A1**) suggests the initiation of ϵ -CL from the –OH end groups of PCHPE, slight shoulders can be seen in the SEC traces of all samples. The lower MW ‘shoulders’ can be assigned to residual PCHPE chains that did not initiate ϵ -CL polymerization. Meanwhile, in the ^1H DOSY spectrum the signals of PCHPE chain (e.g. 7.58, 7.40 & 5.14 ppm) are not perfectly in line with the signals of PCL chain (e.g. 4.04 & 3.32 ppm) (see **Figure 3.5**), suggesting the contamination of the block material by free PCHPE chains.

Table 3.2 The sequential addition synthesis of PCHPE-*b*-PCL using different monomer ratio.

#	[LZn ₂ (OAc) ₂]/[CHO]/[PA]/[ε-CL] ^a	<i>M_n</i> ^b (kDa)	<i>Đ</i>
1	1/400/20/100	9.8	1.33
2	1/400/20/150	12.2	1.42
3	1/400/20/200	20.3	1.47
4	1/400/20/0	1.8	1.14
5 ^c	1/400/20/150	11.3	1.53

^a) the polymerization of PCHPE block is conducted at 100 °C for 2.0 h before the addition of ε-CL at 80 °C. The ROP of ε-CL is conducted at 80 °C for another 2.0 h, with the conversion of monomers > 95%.; ^b) molecular weights are acquired by SEC; ^c) both the polymerization of PCHPE block and PCL block are conducted at 100 °C.

The intensity of the residual PCHPE signal in SEC decreased with the increase in the number of ε-CL equivalents (from 100 to 200 equiv.). This observation is probably due to the relatively low initiation rate of the secondary –OH discussed in Chapter 2. Due to secondary hydroxyl groups being the end groups of the first block, PCHPE (confirmed by MALDI-TOF spectrometry),¹³ some of the PCHPE chains might fail to initiate a PCL block before the full consumption of ε-CL. Therefore, by increasing the number of ε-CL equivalents, more PCHPE chain end groups are likely to participate in the initiation of the second block, PCL, leading to less residual PCHPE chains (**Figure A1**).

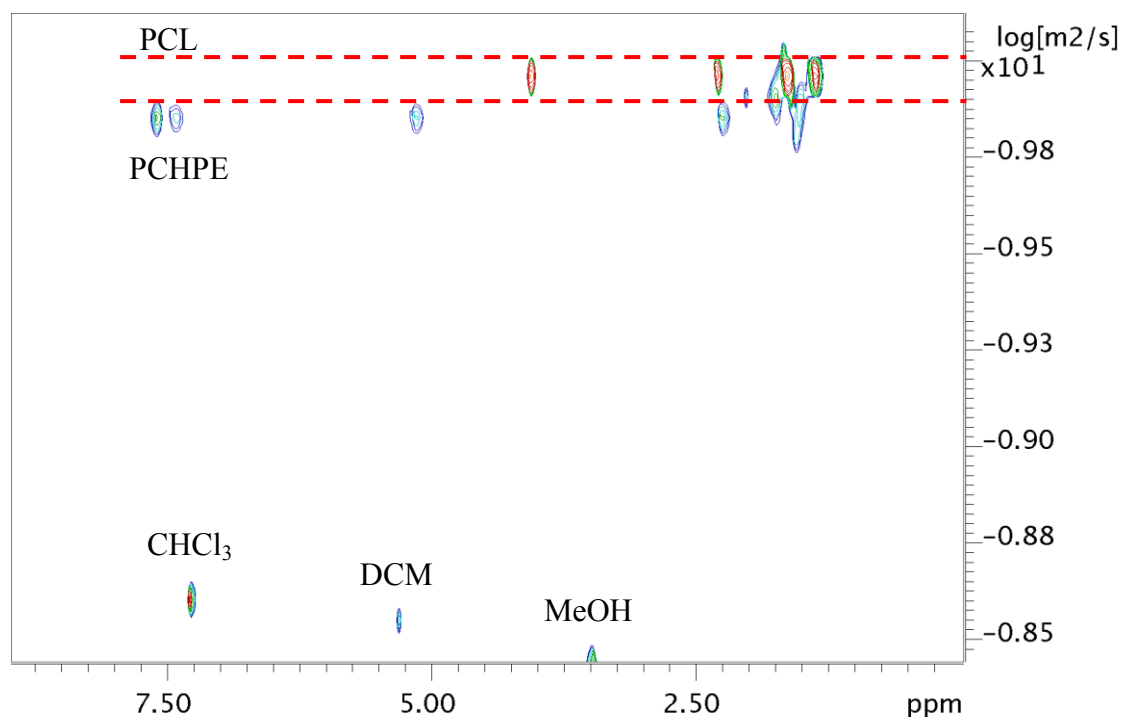


Figure 3.5 Typical ^1H NMR DOSY spectrum of PCHPE-*b*-PCL prepared using the sequential method. The diffusion coefficient overlapping between 1.0 to 2.0 ppm is probably due to this sample being a mixture of PCHPE-*b*-PCL and PCHPE homopolymer. Also, signals between 0.0 ppm to 2.5 ppm may not be suitable for the comparison of diffusion coefficients as explained in section 3.2.2.2.

3.2.2.2 Synthesis of PCHPE-*b*-PCL: from mixed feedstock

Alternatively, the synthesis of PCHPE-*b*-PCL block copolyesters from mixed monomer feedstocks was studied using the same di-zinc catalyst with acetate co-ligand (see **Figure A6** for catalyst structure). The catalyst has already proved to be active for both ring-opening copolymerization of anhydrides/epoxides and ring-opening polymerization of lactones separately. It is now relevant to investigate how the catalyst behaves when exposed to mixtures of all three monomers. The reaction was monitored by *in situ* ATR-IR spectroscopy (**Figure 3.6**) and an unexpected chemoselective polymerization was observed. When PA, CHO and ϵ -CL were added together at the beginning of polymerization, no consumption of ϵ -CL was seen (0~154 min) until the full consumption of PA has occurred. The selectivity is

proposed to derive from a combination of the metal-chain end group effect and the monomer insertion kinetics. As mentioned in the previous Chapter, the zinc acetate species are unable to initiate the ROP of ϵ -CL. Meanwhile, the insertion rate of PA into zinc alkoxide bond is proposed to be much faster than ϵ -CL on the basis of the selectivity. This hypothesis is supported by a DFT study, revealing that the anhydride insertion has lower barrier than the ϵ -CL ROP and that there is a greater stability to the PCHPE ester linkage than that of PCL.³⁵ Therefore, PA and ϵ -CL can be sequentially consumed even from a mixed monomer feedstock. Moreover, the lack of ether linkage signals in the ^1H NMR indicates no homopolymerization of CHO. Another advantage of this method lies in its ‘one-pot; one step’ nature. This avoids the introduction of protic impurities (such as traces of water) during the sequential addition, preventing the formation of free PCL.

Thus, PCHPE-*b*-PCL samples with different molecular weights and compositions were prepared (see **Table 3.3**) using the chemoselective polymerization method. After the propagation of the PCL block, no free PCHPE chains were observed in the SEC traces indicating that complete initiation of PCHPE end groups (**Figure 3.9**). The block copolymer was characterized by ^1H DOSY, the signals of the PCHPE chain (e.g. 7.58, 7.40 & 5.14 ppm) are in line with the signals of PCL chain (e.g. 4.04 & 3.32 ppm) (see **Figure 3.7**), suggesting the formation of PCHPE-*b*-PCL block copolyesters. Signals between 0.0 ppm to 2.5 ppm are not suitable for the comparison of diffusion coefficients because the ^1H NMR signals of PCHPE and PCL in this region slightly overlap with each other. In DOSY, when different molecules have overlapping NMR signals, it is hard to identify the different contributions to the overall decay of signal strength made by individual signals.³⁶ This observation is further confirmed by monitoring the end groups, using ^1H NMR spectroscopy (**Figure 3.10**). The block copolymer has no signals at 4.65 & 3.46 ppm (end groups of PCHPE). Meanwhile, $^{13}\text{C}\{^1\text{H}\}$ NMR spectroscopy was conducted to evaluate the extent of transesterification. Usually, new carbonyl signal forms in the $^{13}\text{C}\{^1\text{H}\}$ NMR when transesterification occurs. However, in the case of PCHPE-*b*-PCL, only signals at ca. 173.6 ppm (carbonyl from PCL) and 166.8 ppm (carbonyl from PCHPE) were observed (**Figure 3.8**), ruling out any

significant extent of transesterification between these two blocks. However, this method cannot rule out the possibility of transesterification between PCHPE blocks or PCL blocks.

Table 3.3 The synthesis of PCHPE-*b*-PCL from a mixed monomer feedstock of PA, CHO and ϵ -CL.

Entry	[cat]/[CHO]/[PA]/[ϵ -CL] ^a	TOF of PA (h ⁻¹)	$M_{n,SEC-PS}$ (kDa) ^b	$\bar{D}^b$
1	1/400/20/100	~ 13	12.2	1.42
2	1/400/20/150	~ 13	15.8	1.43
3	1/400/20/200	~ 13	18.7	1.57
4	1/400/10/150	~ 10	22.5	1.46
5	1/400/40/150	~ 14	28.0	1.52
			3.9	1.03

^a) All polymerizations are conducted at 100 °C, in neat CHO as the reaction solvent at 100 °C for 1.5-3.5 h, with the conversion of monomers > 95%.; ^b) molecular weights are acquired by SEC.

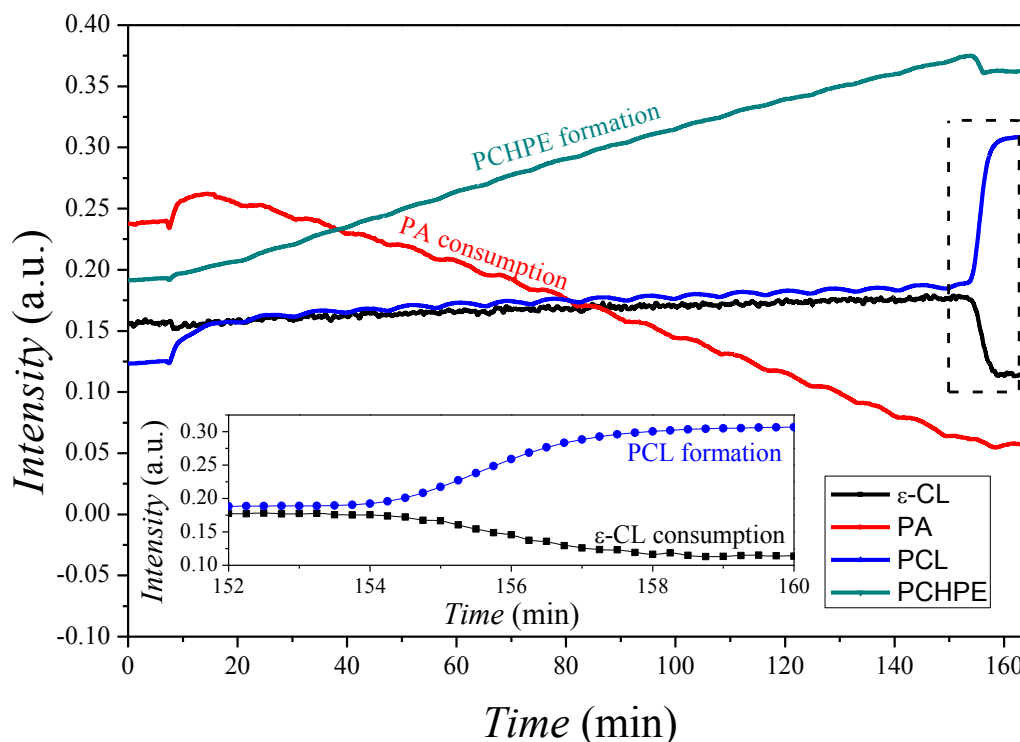


Figure 3.6 Time-resolved ATR-IR spectra showing the formation of polymer (PCHPE & PCL) and the consumption of monomers (PA & ϵ -CL). Inset: enlarged spectra of the PCL polymerization. The polymerization was conducted at 100 °C.

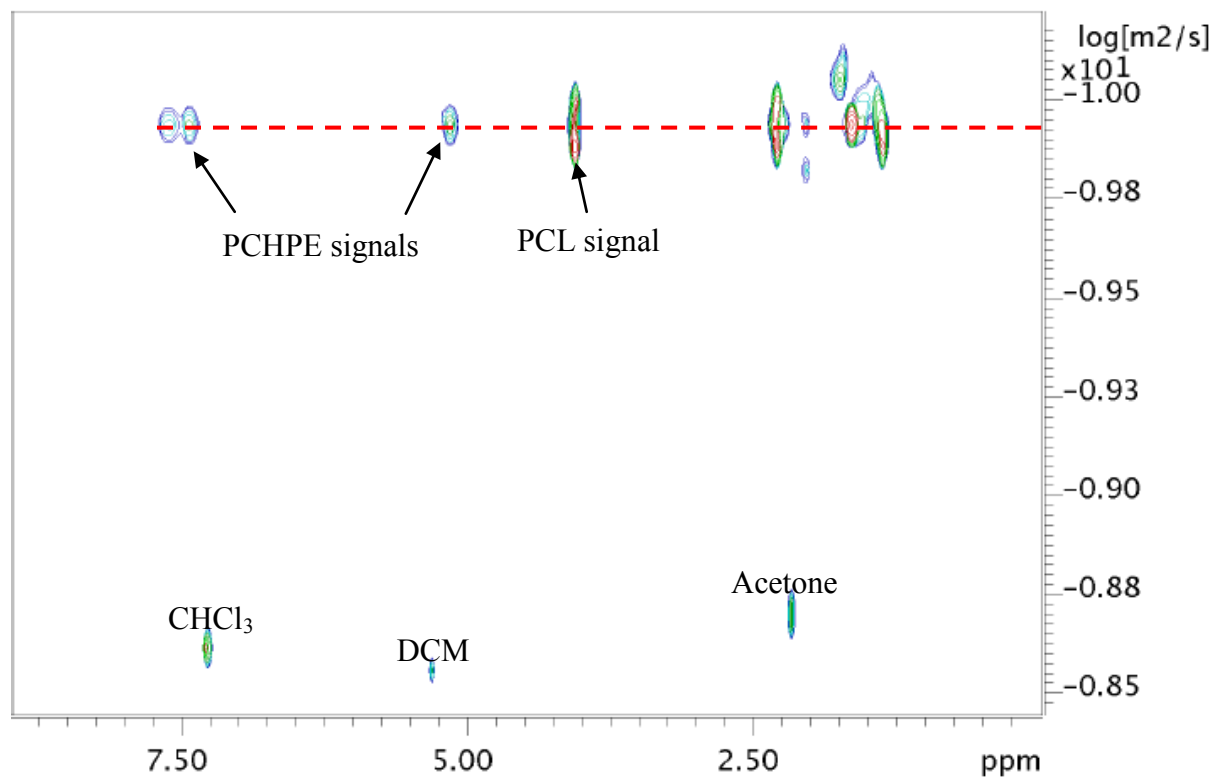


Figure 3.7 Typical ¹H NMR DOSY spectrum of PCHPE-*b*-PCL prepared from the mixed monomer feedstock method.

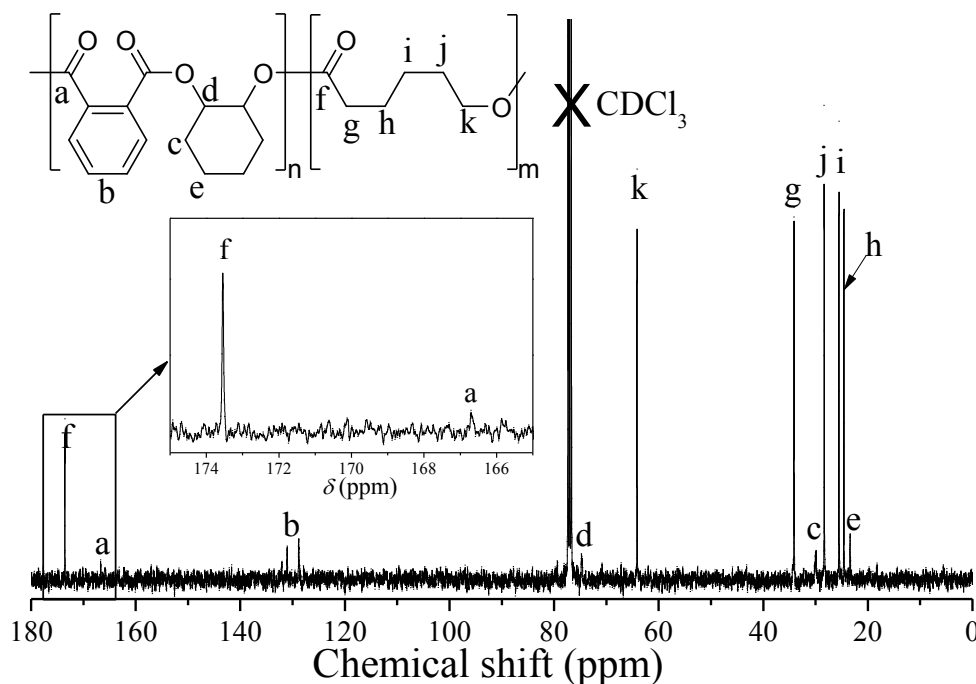


Figure 3.8 The $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the PCHPE-*b*-PCL copolyester. Inset: magnified region of the carbonyl signals from either PCHPE or PCL.

The complete initiation from the PCHPE chain ends (entry 1-4, **Table 3.3**) is aided by the higher reaction temperature (from 80 to 100 °C) of ϵ -CL ROP, which might be due to the increased initiation rate of ϵ -CL from the secondary $-\text{OH}$. However, it cannot be ruled out that the complete initiation might result from the enhanced transesterification at higher temperature. Monomodal MW distribution was also observed when ϵ -CL was sequentially added into preformed PCHPE reaction mixture at 100 °C (entry 5, **Table 3.2**), suggesting higher reaction temperature facilitates the formation of block polymer. However, incomplete initiation from PCHPE chains occurred again, when increasing the PCHPE chain length (from 20 equiv. to 40 equiv., entry 5, **Table 3.3**). One possible explanation is due to the increase in molecular weight, the secondary $-\text{OH}$ end groups of PCHPE might be ‘buried’ within the polymers’ random coil, which hinders the coordination of PCHPE chain end to the zinc centre. However, whether this hypothesis is true or not requires further investigation. As already demonstrated in chapter 2, the coordination of $-\text{OH}$ groups to the zinc centre can be strongly impacted by any steric hindrance. In short, increasing temperature can facilitate the

formation of block polymer to some extent, but the issue cannot be truly solved as long as lactones with high propagation rates are used, at least with the di-zinc catalysts, $[\text{LZn}_2(\text{OAc})_2]$. Therefore, lactones with lower propagation rate and/or secondary zinc-alkoxide propagating species (such as ϵ -decalactone) were selected for investigations of block selectivity.

Also, using the di-zinc acetate catalyst, it was already reported that epoxide/ CO_2 /lactone copolymerization¹² and lactone homopolymerization³⁷ afforded polymers featuring different chain end groups (**Table 3.4**). Both α -acetyl- ω -hydroxyl (initiated from the acetate co-ligand) and α,ω -dihydroxyl polymer end groups (initiated from cyclohexanediol) were observed.^{13,37} Although an encouraging result, the limitation is that both AB and ABA type copolymers formed concurrently in the case of terpolymerization, causing potential bimodal molecular weight distributions (MW). Most importantly, the coexistence of α -acetyl- ω -hydroxyl (monofunctional) and α,ω -dihydroxyl (bifunctional) polymer end groups might affect the post-polymerization modification, for example the chain extension reaction using diisocyanate compounds to form multi-block polymers with higher molecular weight. The presence of monofunctional α -acetyl- ω -hydroxyl species will terminate the chain extension reaction.^{38,39} In order to solve this problem, a new di-zinc complex with phenyl co-ligand was prepared, $[\text{LZn}_2(\text{Ph})_2]$. In contrast to $[\text{LZn}_2(\text{OAc})_2]$, the phenyl co-ligands on $[\text{LZn}_2(\text{Ph})_2]$ do not initiate the ring-opening copolymerization of anhydride/epoxide and the ring-opening polymerization of lactones with the presence of protic initiators, for example cyclohexanediol. $[\text{LZn}_2(\text{Ph})_2]$ complex is a pre-catalyst. The true catalytic species is the zinc alkoxide formed *in situ* from the reaction between $[\text{LZn}_2(\text{Ph})_2]$ and alcohol (**Figure 3.12**).

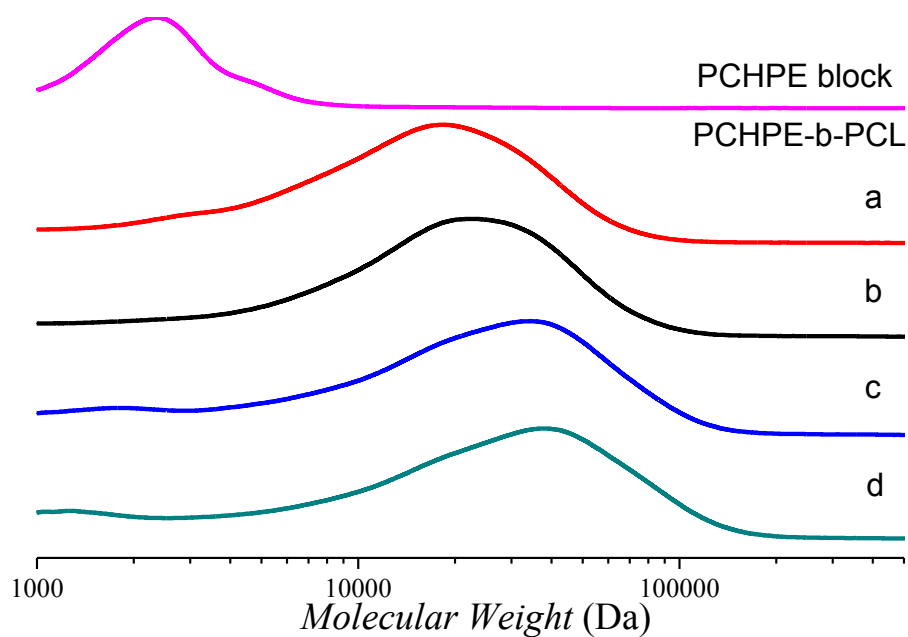


Figure 3.9 SEC traces of PCHPE-*b*-PCL and PCHPE block. Curve a~d are corresponding to entry 1-4 in **Table 3.3**, respectively.

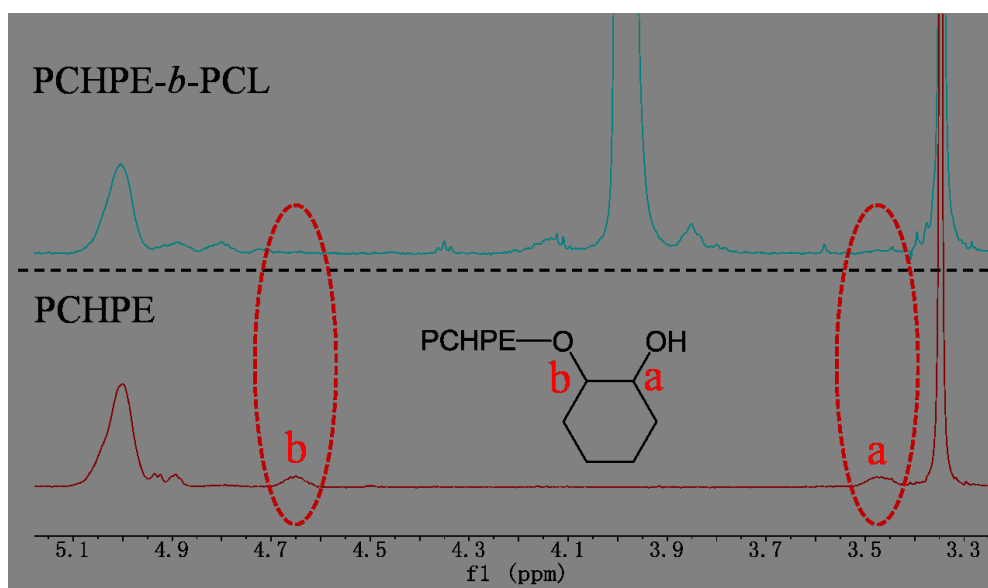


Figure 3.10 ^1H NMR spectra of PCHPE homopolymer and PCHPE-*b*-PCL block copolyesters.

Table 3.4 Preparation of PDL-*b*-PCHPE-*b*-PDL using the di-zinc acetate complex, $[\text{LZn}_2(\text{OAc})_2]$.

Entry	[PA]/[ϵ -DL]	t (h)	$M_{n,SEC-PS}$ (Đ) ^a	$\bar{D}$ ^b
1	20/0	1.0	1.9	1.18
2	20/100	2.0	23.4; 9.2	1.06; 1.05
3	20/150	2.0	25.6; 11.2	1.10; 1.03
4	20/200	2.5	27.6; 12.3	1.08; 1.04

Polymerization Conditions: All polymerizations were run in neat cyclohexene oxide as the reaction solvent at 100 °C for predetermined reaction time with the conversion of monomers > 95%. ^a M_n of the crude polymer was determined by SEC, in THF using polystyrene calibrates, with units of $\text{kg}\cdot\text{mol}^{-1}$; bimodal distribution appears in entry 2-4; ^ball block copolymers exhibit bimodal distribution

3.2.3 Synthesis of PCHPE-*b*-PDL block copolymers⁴⁰

Before studying the selective catalysis, it was important to investigate the two reactions, ROCOP and ROP, independently.

3.2.3.1 Ring-opening copolymerization of PA/CHO and ring-opening polymerization of ϵ -DL

A new di-zinc phenyl complex was prepared: $[\text{LZn}_2(\text{Ph})_2]$ (**Figure 3.11** and **Figure A7-A9**). $[\text{LZn}_2(\text{Ph})_2]$ is activated by reaction with a diol to form, *in situ*, the catalyst system (**Figure 3.12-3.13**). It showed a good performance in epoxide/anhydride ROCOP (**Figure 3.13**, **Table 3.5**).

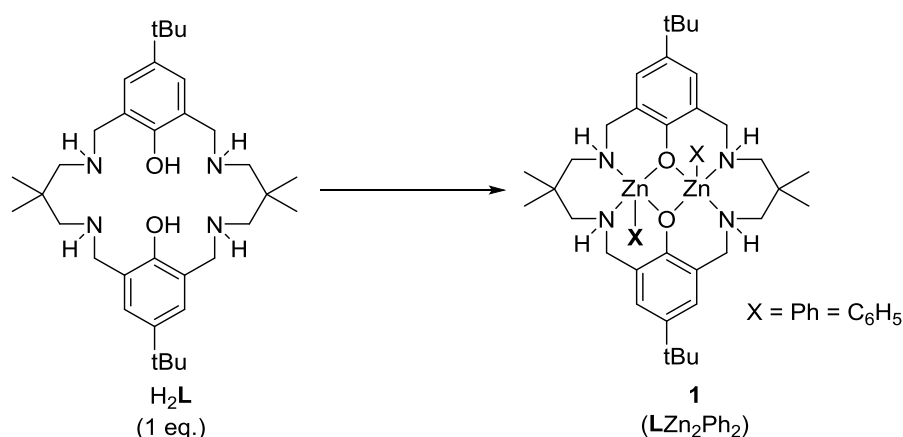


Figure 3.11 Preparation of di-zinc phenyl complex, $[\text{LZn}_2(\text{Ph})_2]$, in THF using ZnPh_2 as the precursor.

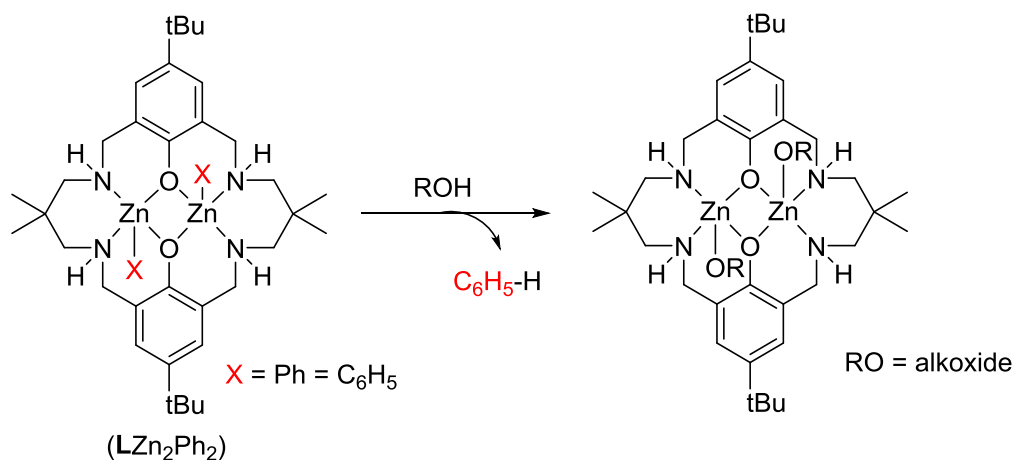


Figure 3.12 The *in situ* catalyst forming reaction between $[\text{LZn}_2(\text{Ph})_2]$ and cyclohexanediol (used as CTAs).

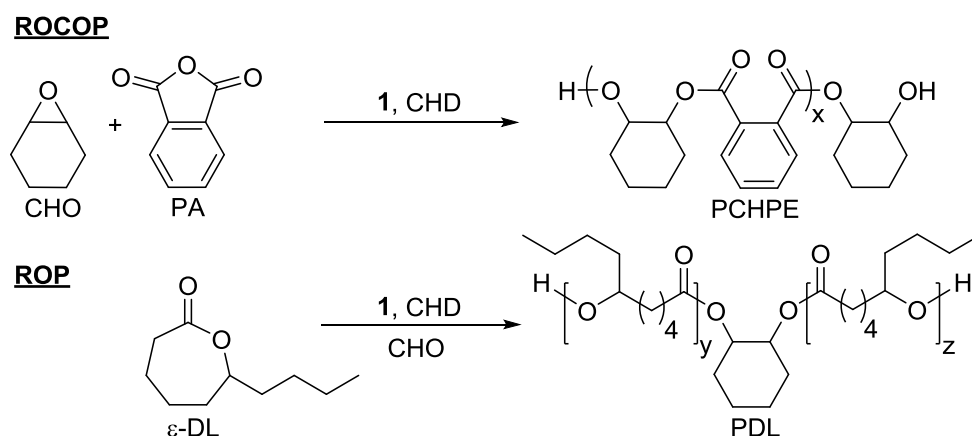


Figure 3.13 The ROCOP and ROP reactions catalyzed by $[\text{LZn}_2(\text{Ph})_2]$, where CHD is 1,2-cyclohexanediol.

Table 3.5 The ROCOP of phthalic anhydride and cyclohexene oxide, using $[\text{LZn}_2(\text{Ph})_2]$ and cyclohexane diol.

entry	$[\text{LZn}_2(\text{Ph})_2]: \text{diol}^a$	$M_{n,\text{theo}}^b$	$M_{n,\text{SEC-PS}}^c$	M_w/M_n^c	$M_{n,\text{SEC-MALLS}}^d$	$\bar{D}^d$
1	1:2	12.3	5.3	1.33	9.3	1.03
2	1:4	6.2	2.9	1.29	5.2	1.02

3	1:6	4.1	2.3	1.33	3.6	1.10
4	1:8	3.1	1.8	1.27	2.9	1.06
5	1:10	2.5	1.6	1.32	2.5	1.07

^{a)} $[LZn_2(Ph)_2]:[PA]:[CHO] = 1:100:800$, 100 °C, 3-4 h, PA conversion >99%. Diol refers to 1,2-cyclohexane diol (CHD); ^{b)} Determined on the basis of $\{([PA] + [CHO]) \times (\text{conversion of PA})\} / [CHD]$, with units of $\text{kg} \cdot \text{mol}^{-1}$; ^{c)} Determined by SEC calibrated using narrow MW polystyrene (PS) standards, with units of $\text{kg} \cdot \text{mol}^{-1}$; ^{d)} Determined by SEC-MALLS in THF ($dn/dc = 0.133 \pm 0.001 \text{ mL} \cdot \text{g}^{-1}$), with units of $\text{kg} \cdot \text{mol}^{-1}$.

The diphenyl zinc complex system showed moderate activity, with TOF values of 25 h^{-1} and an excellent selectivity for polyester (>99%, **Figure 3.14**), which is comparable to some catalysts reported by other groups in this field.¹⁰ It also showed high degrees of polymerization control, with predictable molecular weights and narrow dispersities (≤ 1.30). The MWs of the polymers are determined using SEC, calibrated with polystyrene standards and using multiple-angle-laser light scattering (SEC-MALLS) (see **Table 3.5** below and **Figure A2**). Previously, the MW of poly(cyclohexylene phthalate) (PCHPE) was only determined by PS calibrated SEC; there was a poor correlation between theoretical and experimental MW.^{13,21} In contrast, using SEC-MALLS, excellent agreement between MW values is observed, confirming that the ROCOP is very well-controlled. Although the MWs given by MALLS detector are still smaller than the predicted values (**Table 3.5**), it is due to the presence of cyclohexanediol (discussed in Section 3.2.1) which functions as the chain transfer agent. However, the experimental MW reported in this field is usually 1.5~6.0 times smaller than the theoretical MW.^{28,41-43} Therefore, the MW values of the alternating polyesters presented in this work can certainly be considered as well-controlled. The polymerization control is further demonstrated by the linear fits of M_n vs. [CHD] (**Figure 3.15**). The MALDI spectrum shows a single series of perfectly alternating polyester chains, end-capped by α, ω -dihydroxyl groups (**Figure 3.16**).

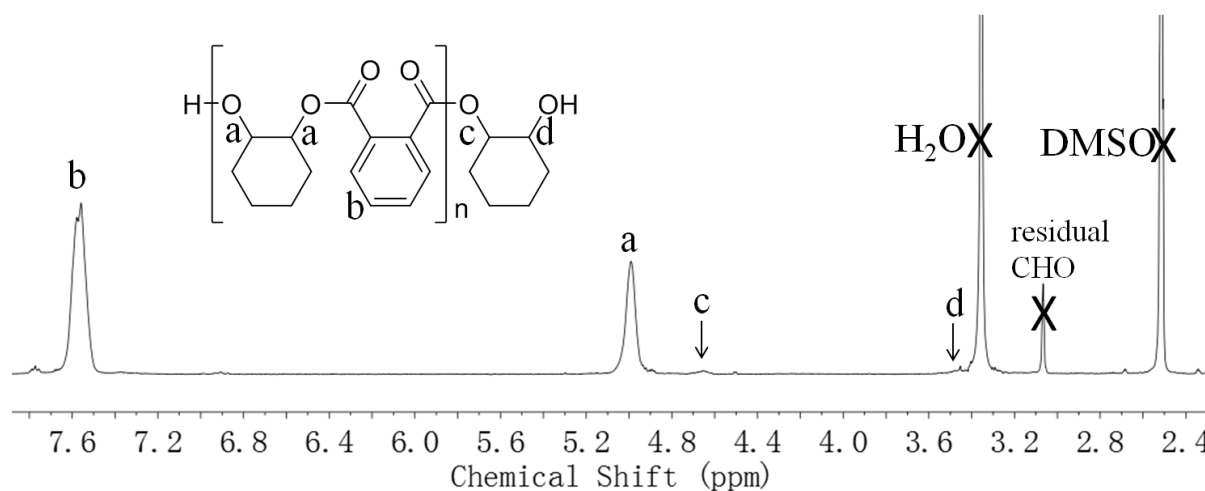


Figure 3.14. ^1H NMR spectrum of PCHPE homopolymer. No signal appears at 3.6 ppm, indicating no ether linkages.¹³

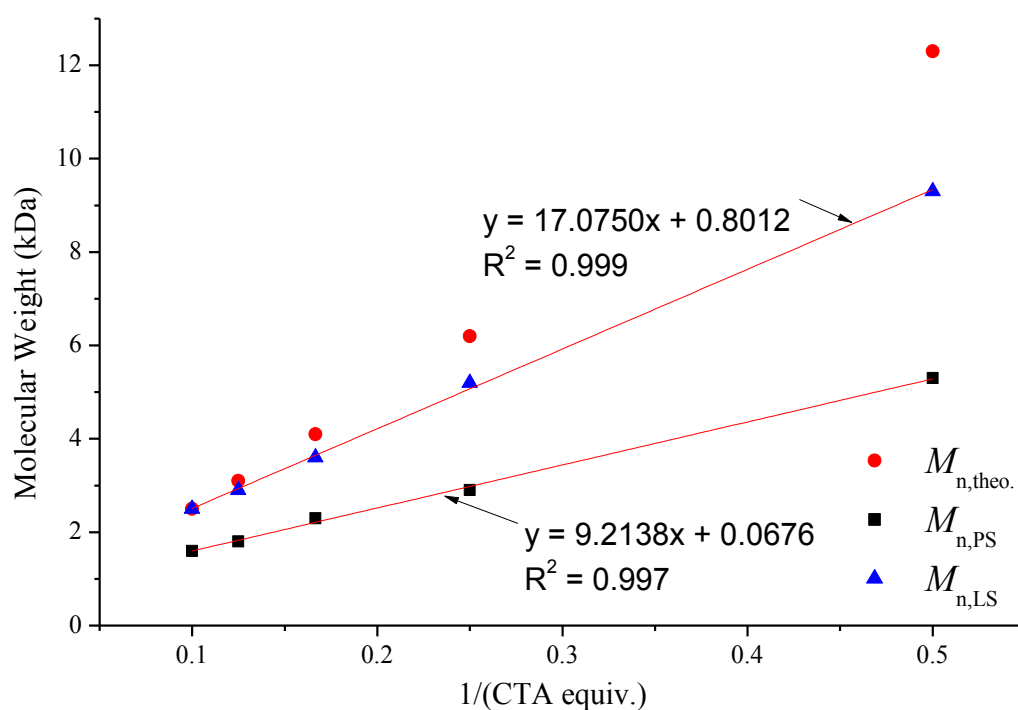


Figure 3.15. Plots showing the molecular weight of PCHPE (red dots: theoretical M_n ; black squares: experimental M_n given by SEC RI detector; and blue triangles: experimental M_n given by SEC LS detector, see **Table 3.5**) and the number of equivalents of cyclohexanediol

used during the ring-opening copolymerization. (Red lines: linear fittings of the experimental M_n).

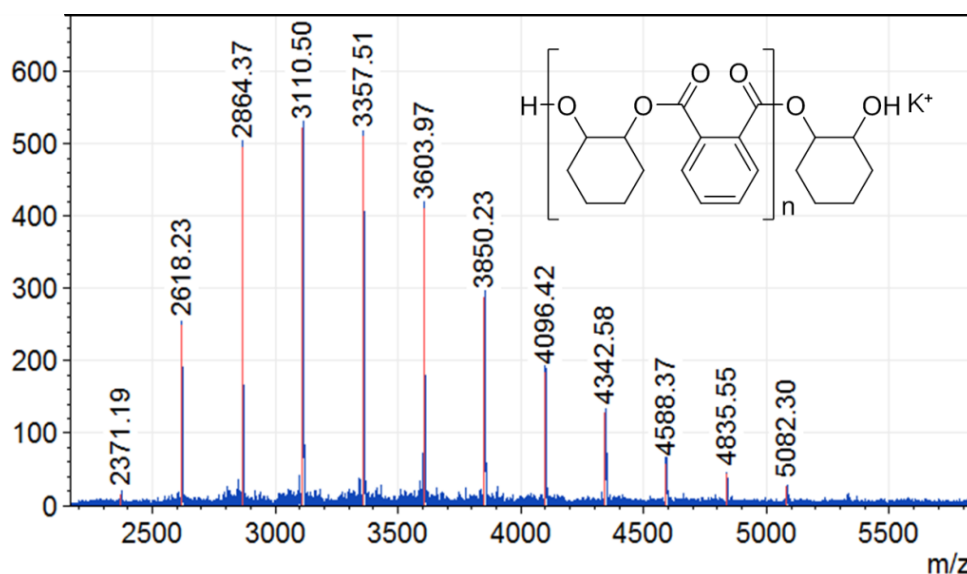


Figure 3.16. The MALDI-ToF spectrum of the polyester (Table 3.5, entry 2). The series show $m/z = [116.1 \text{ (cyclohexanediol)} + (246.1 \times n) \text{ (PA-}i\text{alt-CHO)} + 39.0 \text{ (K}^+)]$ ($n = 9\sim 20$).

$[\text{LZn}_2(\text{Ph})_2]$, with 1,2-cyclohexanediol (CHD), was also tested, as a catalyst for the ROP of ϵ -DL, using cyclohexene oxide as the solvent (Table 3.6, Figure 3.13). It showed good activity, with TOF values of 160 h^{-1} and no evidence for any epoxide homopolymerization or insertion into the PDL chain (see Figure 3.16 below and Figure A3). The polymers' MWs are in close agreement with the theoretical values and show narrow dispersities. Immortal polymerization is also feasible and the amount of CHD used controls the molecular weights, whilst maintaining narrow dispersities (see Figure 3.18 below and Figure A4).

Table 3.6 The ROP of ϵ -decalactone, using $[\text{LZn}_2(\text{Ph})_2]$ and cyclohexanediol.

entry	$[\text{LZn}_2(\text{Ph})_2]: \text{diol}^a$	$M_{n,\text{theo}}^b$	$M_{n,\text{SEC-PS}}^c$	M_w/M_n^c	$M_{n,\text{SEC-MALLS}}^d$	$\bar{D}^d$
1	1:2	17.0	14.0	1.16	13.4	1.07
2	1:4	8.5	7.8	1.10	6.8	1.06
3	1:6	5.7	6.7	1.12	4.7	1.05
4	1:8	4.3	5.3	1.11	3.5	1.11
5	1:10	3.4	4.3	1.12	3.0	1.05

^{a)} $[LZn_2(Ph)_2]:[\epsilon\text{-DL}]:[CHO] = 1:200:800$, 100 °C, 1.25 h, $\epsilon\text{-DL}$ conversion >95%. Diol refers to 1,2-cyclohexane diol (CHD); ^{b)} Determined on the basis of $\{[\epsilon\text{-DL}] \times (\text{conversion of } \epsilon\text{-DL})\} / [CHD]$, with units of $\text{kg}\cdot\text{mol}^{-1}$; ^{c)} Determined by SEC calibrated using narrow MW polystyrene (PS) standards, with units of $\text{kg}\cdot\text{mol}^{-1}$; ^{d)} Determined by SEC-MALLS, in THF, ($dn/dc = 0.054 \pm 0.001 \text{ mL}\cdot\text{g}^{-1}$ for entry 1, $0.067 \pm 0.001 \text{ mL}\cdot\text{g}^{-1}$ for entry 2 and $0.072 \pm 0.002 \text{ mL}\cdot\text{g}^{-1}$ for entry 3-5), with units of $\text{kg}\cdot\text{mol}^{-1}$.

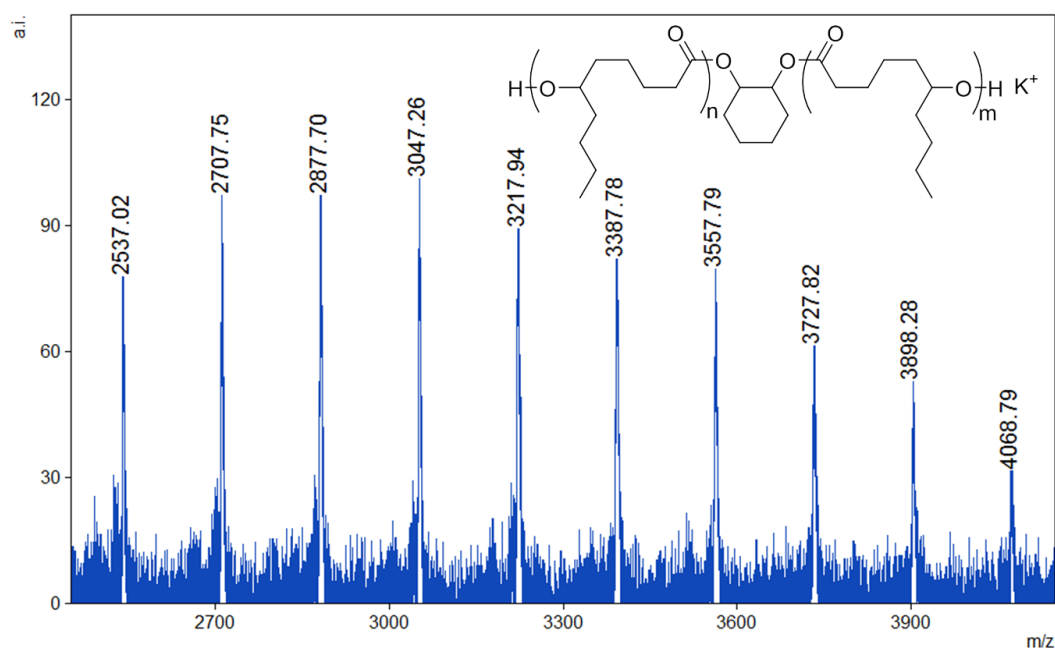


Figure 3.17 Shows the MALDI-ToF spectrum of the polyester (**Table 3.6**, entry 5). The series show $m/z = [116.1 \text{ (cyclohexanediol)} + (170.1 \times n) \text{ (}\epsilon\text{-decalactone)} + 39.0 \text{ (K}^+)]$ ($n = 14\sim 23$).

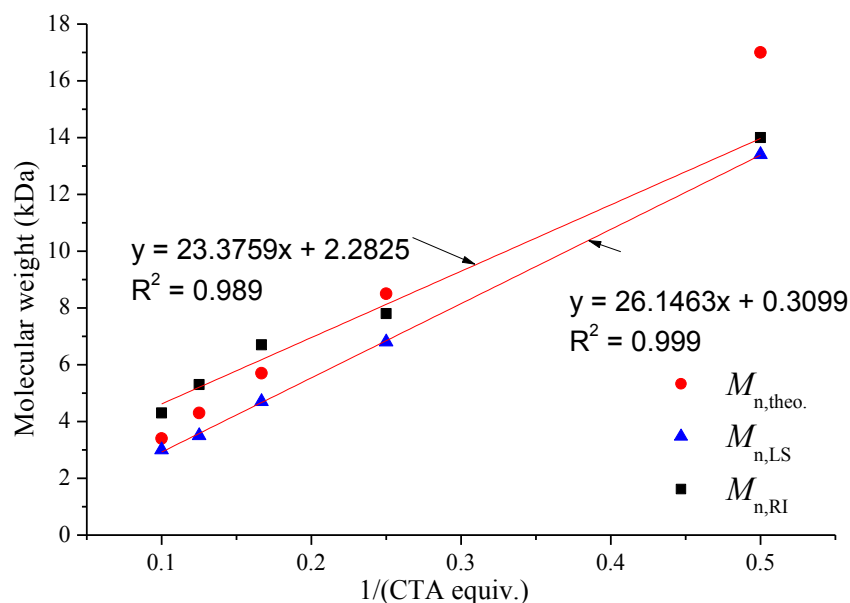


Figure 3.18 Plots showing the fit between molecular weight of PDL (red dots: theoretical M_n ; black squares: experimental M_n given by SEC RI detector; and blue triangles: experimental M_n given by SEC LS detector, see **Table 3.6**) and the number of equivalent of cyclohexanediol used during the ring-opening polymerization. (Red lines: linear fittings of the experimental M_n).

3.2.3.2 Chemoselective sequence controlled polymerization of PA, CHO and ϵ -DL

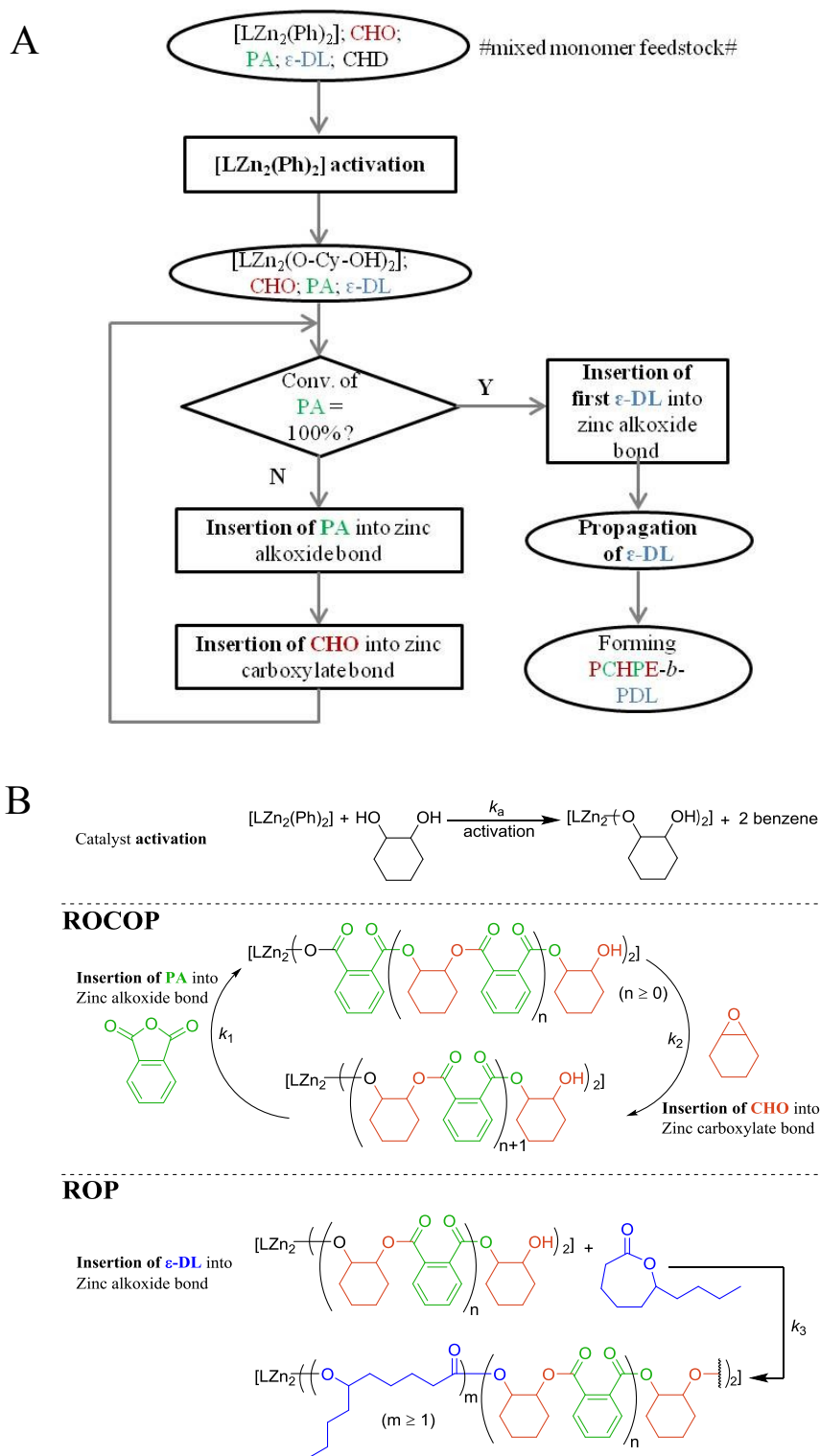
Given that both ROP and ROCOP are catalyzed independently, it was of high interest to establish whether concurrent reactions could be achieved using $[LZn_2(Ph)_2]$. Thus, mixtures of lactone (ϵ -DL), epoxide (CHO) and anhydride (PA) monomers were reacted with the catalyst system comprising $[LZn_2(Ph)_2]$ and diol (**Table 3.3**, **Scheme 3.2**). The terpolymerizations were all successful and unexpected monomer selectivity was observed, resulting in the controlled formation of ABA type block copolyesters. Such selectivity behaviour is very unusual, yet is potentially useful given the importance of block copolymers. The terpolymerizations were monitored by ATR-IR spectroscopy (**Figure 3.19**) which showed that initially epoxide/anhydride ROCOP occurred, as shown by the disappearance of the diagnostic PA resonance at 1790 cm^{-1} and the growth of the characteristic polyester (PCHPE) resonance ($1065\text{--}1068\text{ cm}^{-1}$). During this time, there was no change to any

resonances associated with the lactone (ϵ -DL), a finding confirmed by aliquot analysis using ^1H NMR spectroscopy which only showed signals for perfectly alternating polyester (PCHPE) and residual ϵ -DL (**Figure 3.20**). Once the PA was consumed, in the presence of excess CHO, the reaction entered the second phase whereby ϵ -DL ROP occurred, leading to block polyester formation. During this stage, the ATR-IR monitoring showed the decrease of the ϵ -DL resonance, at 1735 cm^{-1} , accompanied by the growth of the block of poly(ϵ -decalactone) as signalled by its resonance at 1190 cm^{-1} . The IR absorptions were all independently confirmed in control experiments using pure, isolated monomers/polymers (**Figure A10**).

Table 3.7 Sequence controlled block copolyester syntheses.

<i>entry</i>	<i>[PA]:[ϵ-DL]^a</i>	<i>Time</i> <i>(h)</i>	<i>% PCHPE^b</i>	<i>M_{n,theo}^c</i>	<i>M_{n,SEC-PS}^d</i>	<i>$\bar{D}$^d</i>	<i>T_g (°C)^e</i>
1	0:100	1.0	0	8.5	6.9	1.20	-58
2	50:100	3.0	33	18.9	12.3	1.25	-49
3	100:200	5.5	42	28.0	15.9	1.21	-49;57
4	100:100	5.0	59	22.4	12.0	1.15	-47; 61
5	150:50	6.5	81	22.7	11.9	1.29	55
6	100:0	4.5	100	12.3	5.3	1.33	97

^a) $[\text{LZn}_2(\text{Ph})_2]:[\text{CHD}]:[\text{CHO}] = 1:2:800$, $100\text{ }^\circ\text{C}$, PA and ϵ -DL conversion $>95\%$; ^b) Weight content of PCHPE block in the polyester (PDL-*b*-PCHPE-*b*-PDL); ^c) Determined by $\{([\text{PA}] + [\text{CHO}]) \times (\text{conversion of PA}) + [\epsilon\text{-DL}] \times (\text{conversion of } \epsilon\text{-DL})\}/[\text{CHD}]$ with units of $\text{kg}\cdot\text{mol}^{-1}$; ^d) Determined by SEC using polystyrene calibration, with units of $\text{kg}\cdot\text{mol}^{-1}$. MALLS is not suitable for such block copolymer analysis.⁴⁴ ^e) Determined after three heating–cooling cycles, on the third cycle.



Scheme 3.2 (A) Diagram illustrating the chemoselective sequence controlled polymerization; (B) Reactions corresponding to the steps illustrated in (A). The typical reaction conditions are in the footnotes to **Table 3.7**.

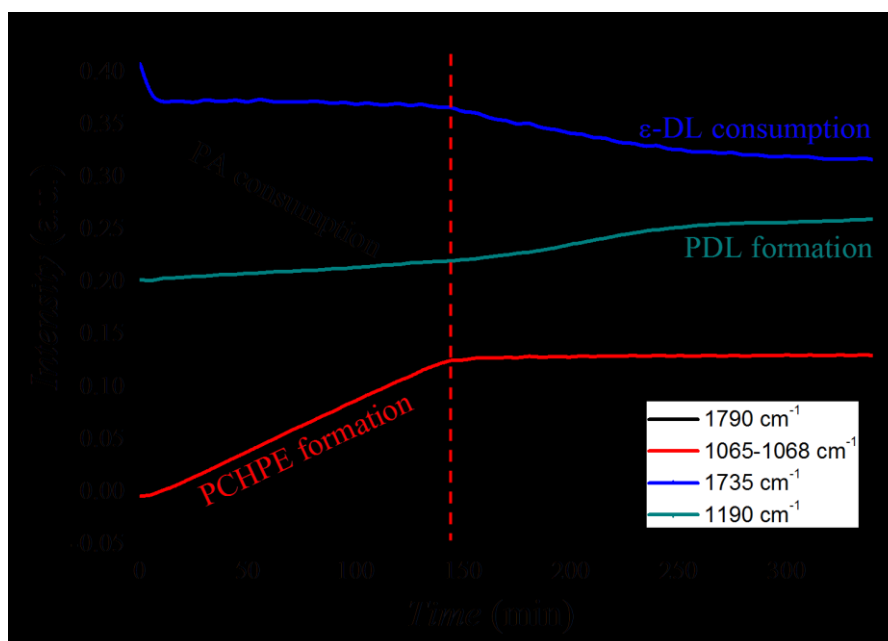


Figure 3.19 Representative ATR-IR spectrum acquired during (PDL-*b*-PCHPE-*b*-PDL) formation (**Table 3.7**, entry 2).

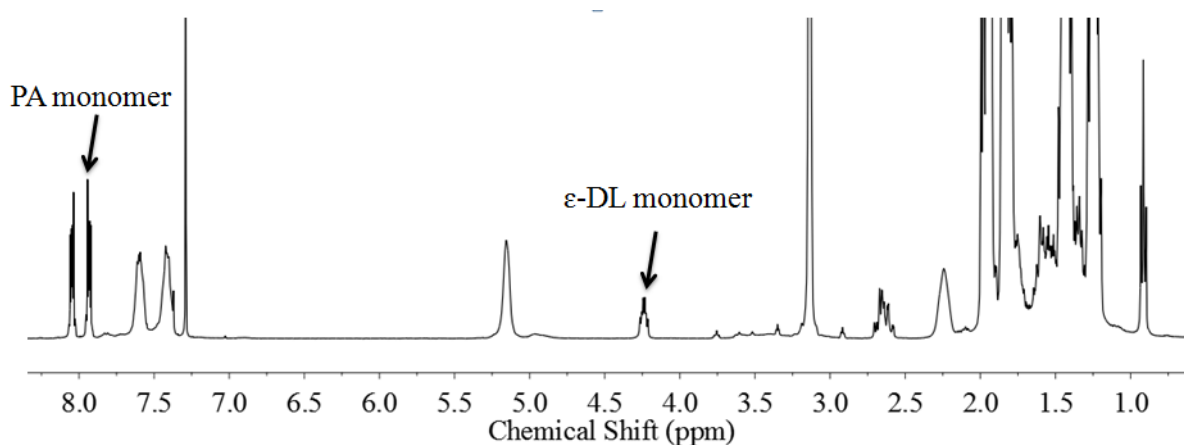


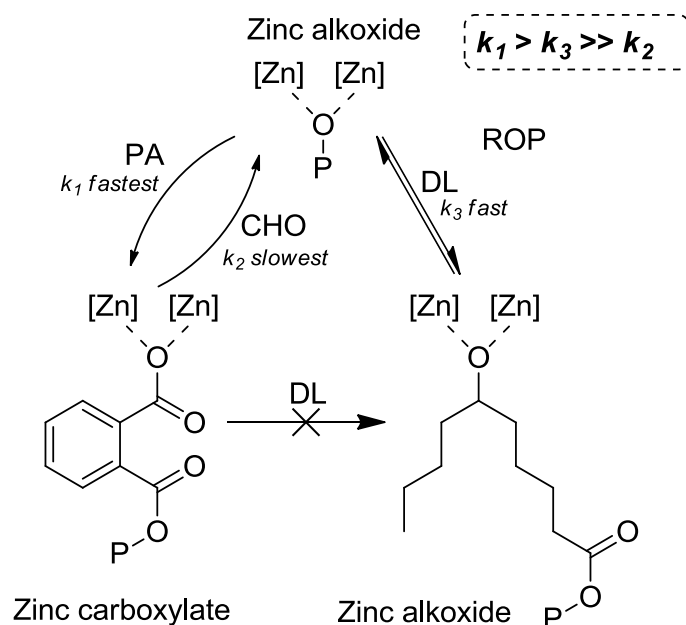
Figure 3.20 ^1H NMR spectrum of the aliquot taken before the complete conversion of phthalic anhydride (ca. 73 mol%). No consumption of ϵ -decalactone can be observed (aromatic signals as the internal reference), suggesting the formation of the perfectly alternating polyester (PCHPE).

The monomer sequence selectivity would not be expected on the basis of the activities, where the TOF values are ROP: 160 h^{-1} and ROCOP: 25 h^{-1} , respectively. **Scheme 3.3** illustrates the key intermediates present during polymerization. The different rate of insertion of monomers

into the zinc alkoxide intermediate, which is common to both catalytic cycles, must be responsible for the selectivity. Accordingly, the rate of PA insertion into the Zn-alkoxide bond is significantly faster than the insertion of ϵ -DL (i.e. $k_1 \gg k_3$). It is also relevant that the zinc-carboxylate intermediate, formed by PA insertion, does not react with lactones, a finding supported by the failure of $[\text{LZn}_2(\text{OAc})_2]$ to catalyze ϵ -DL ROP (**Table 3.8**) and also the DFT studies mentioned in section 3.2.2.2, showing there is a lower barrier to anhydride insertion, compared to the ROP of lactones, and a greater stability to the product ester linkage formed, thereby also providing a thermodynamic rationale for the observed selectivity.⁴⁵ The further reaction of the zinc-alkoxide intermediate with epoxide (CHO) has been calculated to have a significantly higher barrier and thus ether linkages are not observed experimentally.⁴⁵ To confirm the ABA type triblock copolyester structure with no presence of free block materials, aliquots were analyzed by SEC just before the complete conversion of PA (ca. 95%) and after the propagation of PDL block (ca. 96% conv. of ϵ -DL) (**Figure 3.21**). It is quite clear that after ϵ -DL ROP the polymer has a higher MW and that in both cases distributions are monomodal, with narrow dispersities. Since the block formed by ROCOP (PCHPE) has an aromatic repeat unit, analysis using SEC with a UV-detector can be used to confirm block attachment.

Although the length of the PCHPE block ($[\text{PA}]/[\text{cat.}] = (50\sim 150)/1$) in **Table 3.7** is much longer than that in **Table 3.3**, entry 5 ($[\text{PA}]/[\text{cat.}] = 40/1$), no PCHPE residual peak was observed in SEC after the propagation of ϵ -DL. This is probably due to the secondary zinc alkoxide being the active species during the ROP of ϵ -DL rather than changing from secondary to primary zinc alkoxide in the case of PA/CHO/ ϵ -CL terpolymerization, which might suffer the unmatched initiation and propagation rates. Although it is much less likely due to the similar TOF of the $[\text{LZn}_2(\text{OAc})_2]$ and $[\text{LZn}_2(\text{Ph})_2]$, this improvement might also result from the better initiation rate using $[\text{LZn}_2(\text{Ph})_2]$. However, this hypothesis requires further investigation.

$^{31}\text{P}\{^1\text{H}\}$ NMR spectroscopy was also used to distinguish the two different hydroxyl end-groups (from PCHPE and PDL, respectively), on the basis of their chemical shifts after reaction with excess 2-chloro-4,4,5,5-tetramethyl dioxaphospholane. This is to check whether all the PCHPE block chains formed in the first stage (the ROCOP) participate in the initiation of the second block, PDL, during ROP. Before the initiation of PDL block, only one signal at 147.1 ppm can be observed, which can be assigned to the secondary hydroxyl groups of PCHPE. After the initiation of the second block (PDL), the signal at 147.1 ppm completely disappears, while a new signal appears at 149.2 ppm, which can be assigned to the secondary hydroxyl end groups of PDL block from the ABA triblock (**Figure 3.22**). The assignment of different secondary hydroxyl groups of PCHPE and PDL block was confirmed by applying the same technique to pure PCHPE and PDL polyesters. It is noteworthy that the same result can be observed even if only one ϵ -DL is ring-opened by the -OH end group of PCHPE. However, it is unlikely due to the narrow distributions and controlled molecular weights observed in the ROP of ϵ -DL (**Table 3.6**) and terpolymerization of PA/CHO/ ϵ -DL (**Table 3.7**). In the ROP of ϵ -DL using cyclohexanediol as the CTA, both predictable MW and narrow polydispersity were observed (**Table 3.6**). Therefore, it is reasonable to hypothesise that the chain growth rate of PDL from each of the secondary -OH (bifunctional initiators) is similar and the PDL blocks at both sides of the PCHPE block are symmetric. To further investigate the block structure, ^1H DOSY NMR spectroscopy was employed. In the case of block copolyesters, ^1H NMR signals that belong to different blocks have the same diffusion coefficient (signals a, b, c in **Figure 3.23A**). To rule out the possibility of this being an artefact, control experiments were also conducted. In the control experiment, using pure PCHPE and PDL polyesters of near equivalent MW, showed that the ^1H NMR signals of different polyesters exhibit different diffusion coefficients (signals a, b, c in **Figure 3.23B**). Therefore, the exclusive block structure of the polyesters is confirmed by the DOSY experiments.



Scheme 3.3 Reactions proposed to occur during sequence-selective polymerizations. Where ‘[Zn] [Zn]’ is the active site of $[\text{LZn}_2(\text{Ph})_2]$ and ‘P’ is a propagating polymer chain.

Table 3.8 Ring-opening polymerization of ϵ -DL using $[\text{LZn}_2(\text{OAc})_2]$.

$[\text{LZn}_2(\text{OAc})_2]/[\text{cyclohexanediol}]/[\epsilon\text{-DL}]$	Solvent	Temp. ($^{\circ}\text{C}$)	t (h)	Conv. (%)
1/2/200	Toluene ^a	100	6.0	0

^a the initial concentration of ϵ -DL in toluene is 5M.

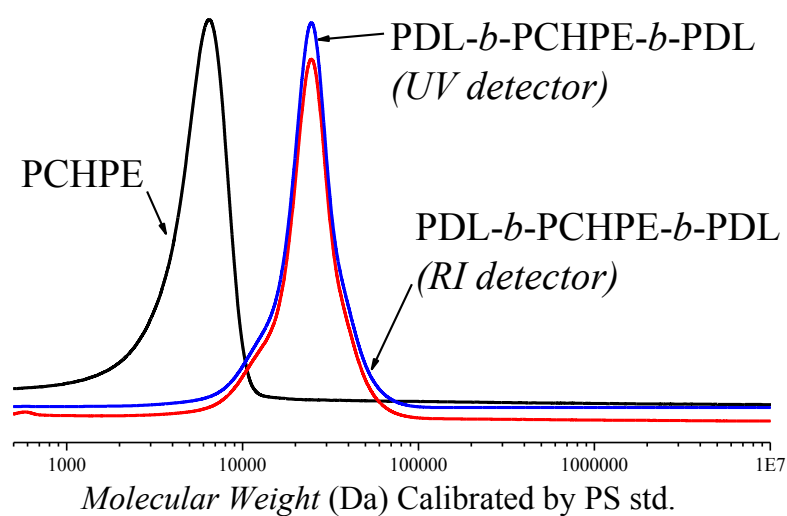


Figure 3.21 SEC traces of the polymer aliquots before and after propagation of the PDL block (**Table 3.7**, entry 3), inter-detector delay was corrected using toluene as internal standard.

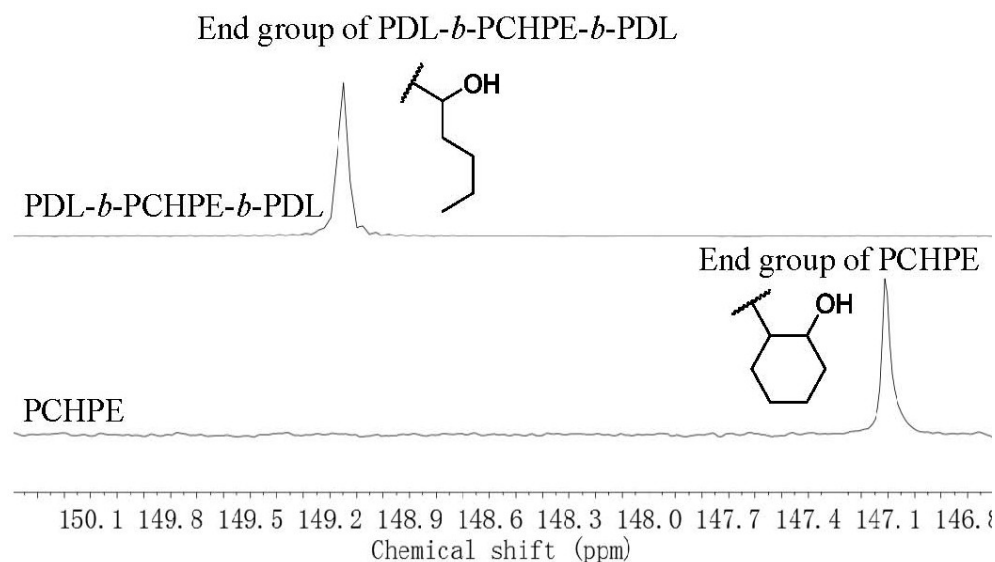


Figure 3.22 $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of PCHPE, PDL-*b*-PCHPE-*b*-PDL (**Table 3.7**, entry 4) after reaction with 2-chloro-4,4,5,5-tetramethyl dioxaphospholane (using bisphenol A as an internal standard), in CDCl_3 . The signals at 147.1 ppm and 149.2 ppm are assigned to the secondary $-\text{OH}$ end groups of the PCHPE homopolymer and the PDL-*b*-PCHPE-*b*-PDL triblock copolyester, respectively.

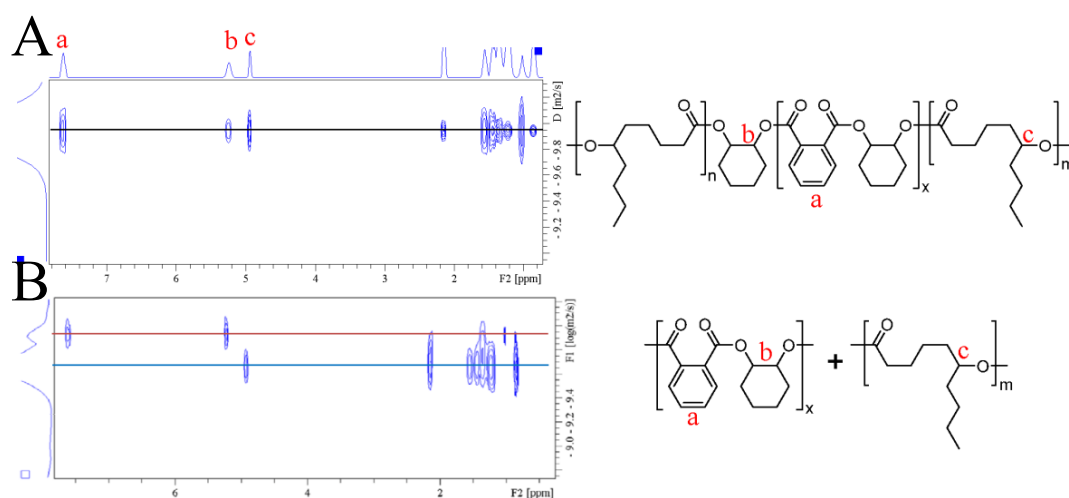


Figure 3.23 ^1H NMR DOSY spectra of (A) PDL-*b*-PCHPE-*b*-PDL (**Table 3.7**, entry 3) and (B) a blend of PCHPE/PDL homopolymers with the similar chain length as the blocks in PDL-*b*-PCHPE-*b*-PDL, respectively, in toluene- d_8 .

If transesterification reactions occur, these would scramble the block structure, especially the block number. Therefore, it is important to check the extent of transesterification reactions when preparing block polyesters or poly(ester-*b*-carbonate)s.^{28,46-49} The $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the copolymer shows only two carbonyl resonances, at 172.4 ppm and 166.5 ppm, assigned to the carbonyl groups of the PDL and PCHPE blocks, respectively (**Figure 3.24**). In contrast, the $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the copolymer after reaction with a well-known transesterification catalyst [1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD), at 60 °C for 48 h] shows new signals at 168.1 and 164.2 ppm (**Figure A11**). The signals are assigned to scrambled [CHO-DL] and [PA-DL] diads.⁴⁶ Thus, there is no significant inter- or intra-chain transesterification, a finding previously observed for other Zn lactone ROP catalysts.^{50,51}

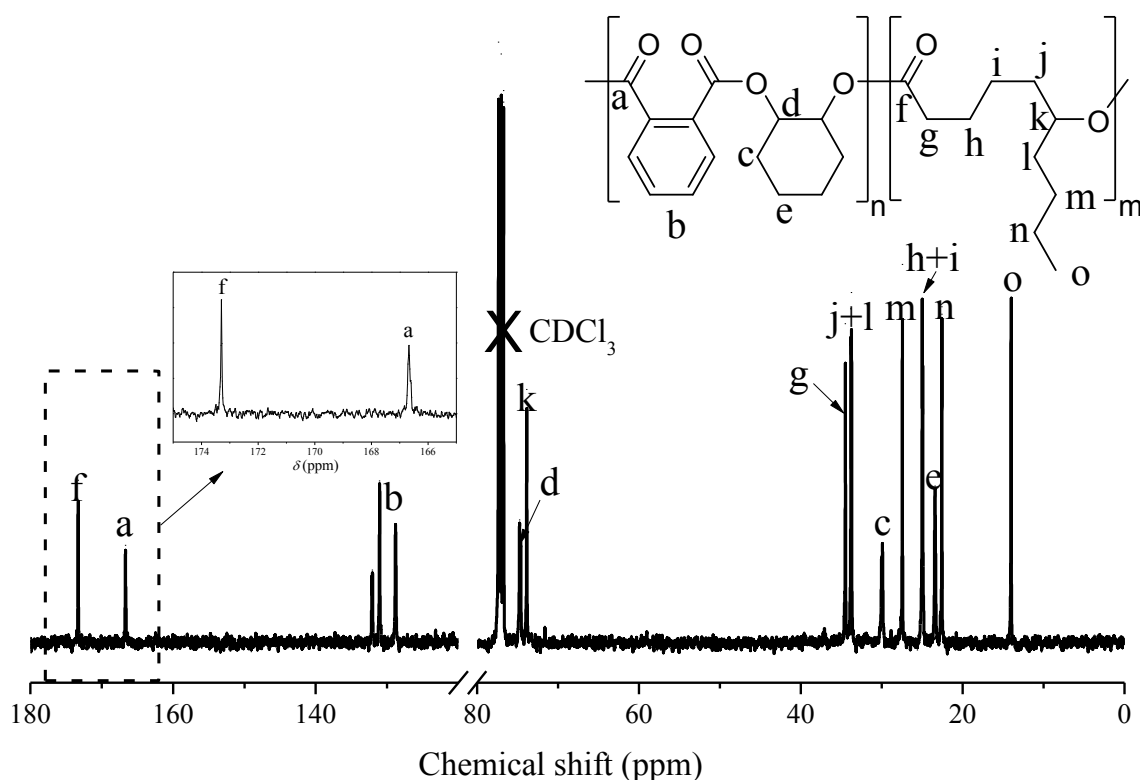


Figure 3.24 The typical $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the PDL-*b*-PCHPE-*b*-PDL copolyester. Inset: magnified region of the carbonyl signals from both the PCHPE and PDL blocks.

3.2.3.3 PCHPE-*b*-PDL Multi-block formation

The selective catalysis was extended, by addition of further equivalents of monomers, to prepare a multi-block copolymer (**Table 3.9**). Thus, a PDL-*b*-PCHPE-*b*-PDL triblock was synthesized and, after complete consumption of the ϵ -DL, a multiblock copolymer can be prepared by adding more PA and ϵ -DL. The block selectivity followed the same selectivity already established (**Figure 3.25-3.27**). Although it is tempting to compare the predicted MW with the experimental MW to further confirm the formation of heptablock, the MW of PCHPE block given by SEC usually deviates significantly from the theoretical value, as discussed in **Table 3.5**. Therefore, the MW of the multiblock polymer given by SEC does not represent the true MW. Furthermore, it should be done with extra cautiousness when comparing the predicted MW of a multiblock copolymer with its experimental MW (given by RI) because the experimental MW (given by RI) of a multiblock copolymer might not simply

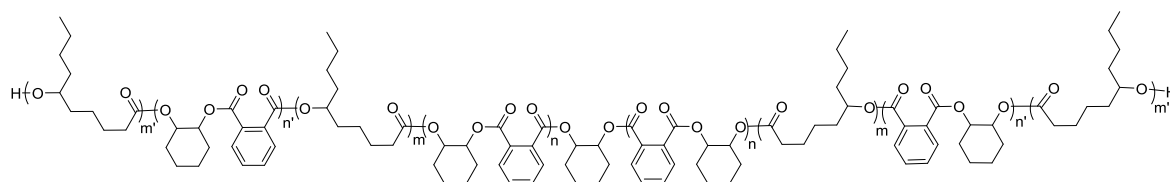
be the sum of the molecular weight of each blocks, especially when the RI experimental MW of the either one of the blocks already deviates significantly from its predicted MW (e.g. PCHPE block, discussed in section 3.2.3.1). The ideal comparison could be done by comparing the absolute MW (given by MALLS detector) with the predicted MW. However, light scattering is not the right technique for characterizing the absolute MW of a block copolymer because the dn/dc value may change across the MW distribution. Considering that both the ROCOP of PA/CHO and the ROP of ϵ -DL afford polymers with controlled MWs and narrow distributions, it is reasonable to presume that the chain growth rates from each chain ends of a bifunctional initiator are similar, leading to the formation of the heptablock polymer. It has been reported by Perrier and co-workers that in a controlled radical polymerization the block number can be jeopardised by the block length distribution and polymers having many short blocks usually containing large amount of defective chains (block number not controlled).⁵² For example, the growth of a short block of average 3 repeat units will fail in ca. 5% of chains, but the proportion of missing blocks can be exponentially decreased by increasing the average block length to 6 repeat units.⁵² This finding may also be applied to other polymerization methods. In this work, the shortest block should still have approximately 25 repeat units (entry 3, **Table 3.9**) to prevent missing blocks from happening. Therefore, it is reasonable to believe that the obtained multiblock polymer primarily consists of seven blocks.

It is noteworthy that slight shoulders can be observed on the SEC traces of the block polymers (**Figure 3.25**). There are several possibilities which might give rise to the shoulders, for example, the increasing viscosity over the polymerization period. Moreover, although the transesterification between different types of blocks (PCHPE and PDL) cannot be observed in $^{13}\text{C}\{^1\text{H}\}$ NMR, the possibility of transesterification occurring within one type of block (either PCHPE or PDL) cannot be ruled out. As this type of transesterification cannot be identified in $^{13}\text{C}\{^1\text{H}\}$ NMR, further investigation is required to evaluate this possibility.

Table 3.9 Molecular weight of block copolyesters with different block numbers.

#	conv. of PA (%) ^a	conv. of ε-DL (%) ^a	Number of Blocks	$M_{n,theo}^b$ (kDa)	$M_{n,SEC-PS}^c$ (kDa)	$\bar{D}^c$
1	>95	0	1	12.3	5.6	1.29
2	100	>96	3	29.3	22.2	1.26
After 2 nd monomer addition						
3	ca. 90	0	5	34.9	25.4	1.23
4	100	>96	7	52.5	40.0	1.31

Polymerization conditions are described in the experimental section, the relative loadings of monomers during the first and second additions were: $[LZn_2(Ph)_2]/[CHD]/[CHO]/[PA]/[\epsilon-DL]/[PA(2^{nd} \text{ addition})]/[\epsilon-DL(2^{nd} \text{ addition})]$ was 1/2/800/100/200/50/200. ^a)calculated by ¹H NMR spectroscopy via aliquoting, the data in entries 3 and 4 corresponds to the conversion of those monomers during the second polymerization phase; ^b) Determined by $\{([PA] + [CHO]) \times (\text{conversion of PA}) + [\epsilon-DL] \times (\text{conversion of } \epsilon-DL)\}/[CHD]$ with units of $kg \cdot mol^{-1}$; ^c)Determined by SEC, calibrated using narrow molecular weight polystyrene standards, with units of $kg \cdot mol^{-1}$. The structure of the heptablock copolyester is illustrated below, where $n = 50$, $m=100$, $n'=25$, $m'=100$.



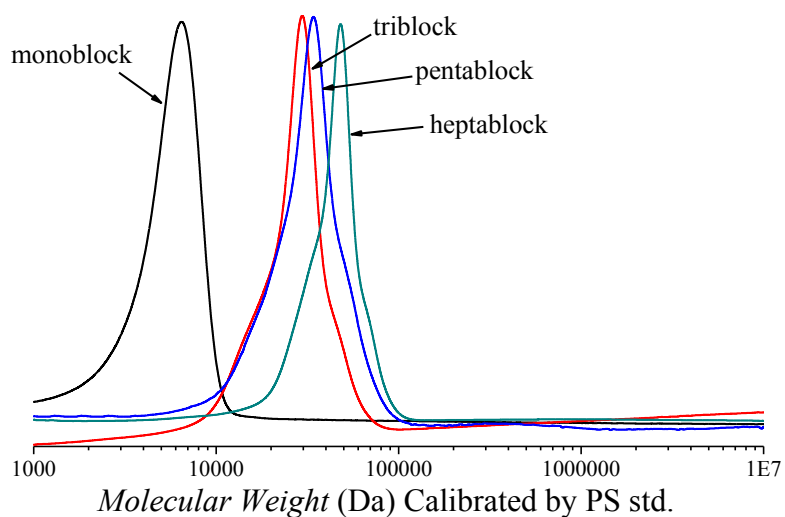


Figure 3.25 The SEC traces of the polymer aliquots of multi-block polyesters (**Table 3.9**).

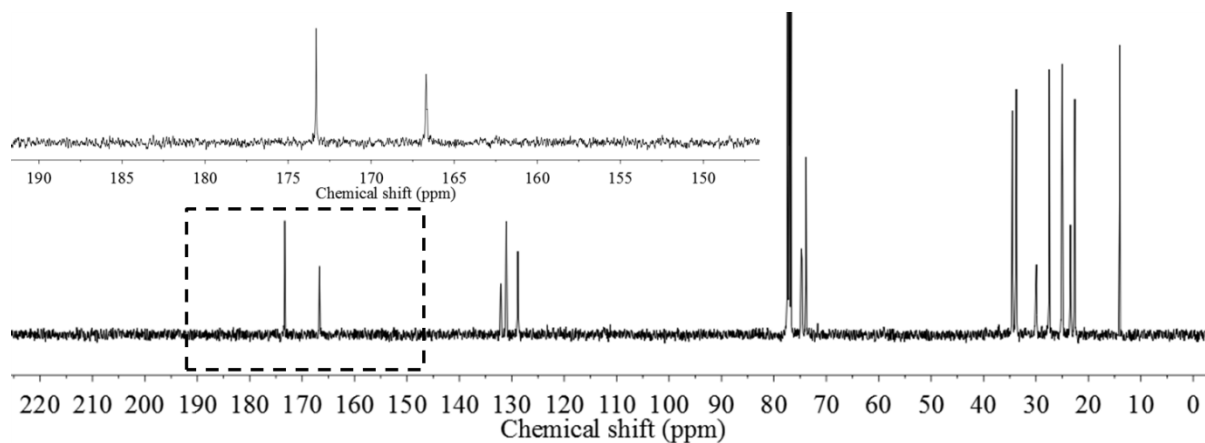


Figure 3.26 The $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the (A) PCHPE-*b*-PDL heptablock copolyester (**Table 3.9**, entry 4).

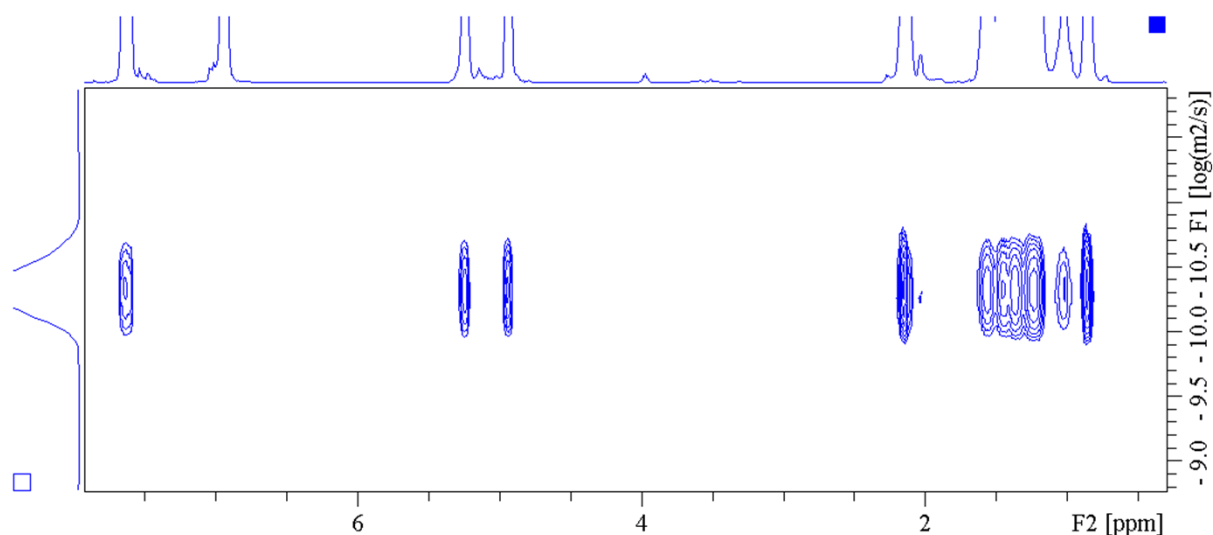


Figure 3.27 ^1H NMR DOSY spectrum of PCHPE-*b*-PDL heptablock copolyester (**Table 3.9**, entry 4) in toluene- d_8 .

3.2.3.4 Thermal properties of the PDL-*b*-PCHPE-*b*-PDL triblock copolyesters

Triblock copolyesters with different MW values and compositions were prepared and analysed as already described (**Table 3.7**). In terms of thermal properties, the copolymers showed T_g values tuneable over the range -59 to 61 °C. The homopolymers are both amorphous (no melting peaks can be observed within the experimental temperature range), with T_g values of -58 °C (PDL) and 97 °C (PCHPE), respectively. A blend of them showed identical T_g values to the homopolymers, indicating likely block immiscibility. Copolyesters with low (33 wt%) or high (81 wt%) PCHPE compositions showed only a single T_g , close to that of the dominant block material (PDL or PCHPE). Where the block composition was more evenly balanced (42-59 wt% PCHPE), two T_g values were observed, suggesting microphase separation of the soft/hard blocks (**Figure 3.28**). However, the glass transition of the PCHPE block is rather weak, comparing to that of the PDL block. It is inappropriate to conclude on the microphase separation merely based on the DSC curves in **Figure 3.28**. Further investigation regarding the phase separation between PDL and PCHPE blocks is discussed in the following chapter.

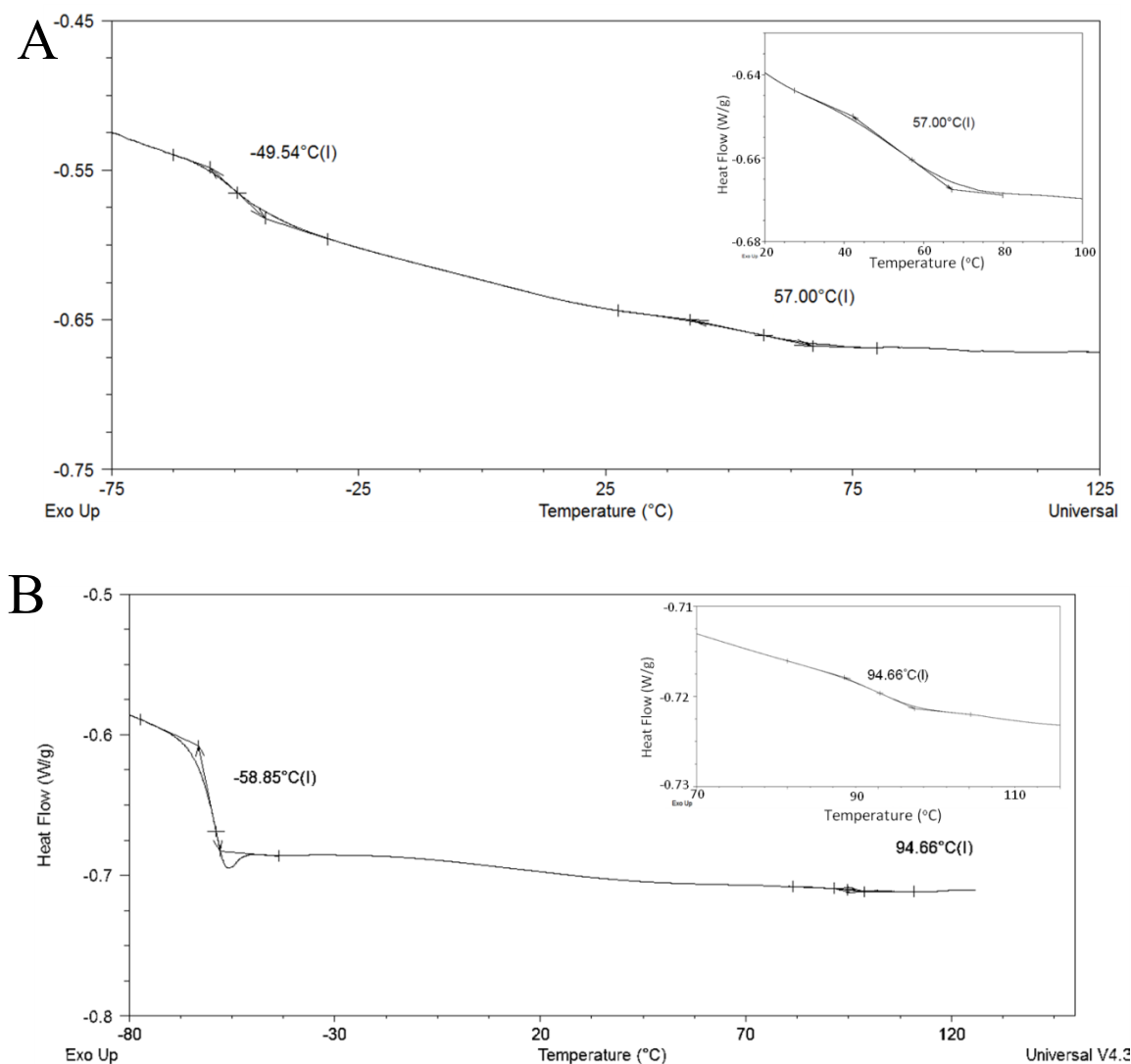


Figure 3.28 DSC thermograms (*exothermal up*) of (A) PDL-*b*-PCHPE-*b*-PDL (**Table 3.7**, entry 3 with 42 wt% of PCHPE) and (B) PCHPE/PDL blend (**Table 3.7**, entry 1 and 6, composition: 1/1, m/m).

3.2.3.5 Can the chemoselective method be generalized to other monomer combinations?

As part of a preliminary evaluation of the generality of the selective synthesis, this method was evaluated using other epoxides and lactones (see **Table 3.10**). The other monomers were selected by the following rationale: vCHO was selected for its C=C double bond which can allow post-polymerization modification; δ -VL for the high crystallinity of PVL and *rac*-LA for its renewability. Typically, during the chemoselective polymerization of PA/CHO/ δ -VL, PA was consumed first with no consumption of δ -VL during the PA/CHO ROCOP (**Figure**

3.30), which means the polymerization of this other mixture show the same sequence selectivity. The obtained polymers (Table 3.10) were examined using SEC, ^1H DOSY NMR and $^{13}\text{C}\{^1\text{H}\}$ NMR spectroscopy (see **Figure 3.31-3.34**). For the chemoselective polymerization of PA/vCHO/ ϵ -DL (**Figure 3.31**), a clear increase in molecular weight was observed in SEC traces. ^1H DOSY NMR spectrum shows that all the signals have the same diffusion coefficient, suggesting a block copolymer structure. Also, no observable transesterification occurred as indicated by two well-defined signals being observed in the carbonyl region in the $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum, which can be assigned to PvCHPE and PDL blocks, respectively. The same characterization procedure was used to determine the polymer structure of PLA-*b*-PCHPE-*b*-PLA (**Figure 3.32**), PVL-*b*-PCHPE-*b*-PVL (**Figure 3.33**) and PVL-*b*-PvCHPE-*b*-PVL (**Figure 3.34**). In all cases, block structures were successfully achieved. It is noteworthy that only one peak appears in the $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of PLA-*b*-PCHPE-*b*-PLA. This is due to the fact that carbonyl signal of PCHPE has the same chemical shift as that of PLA.

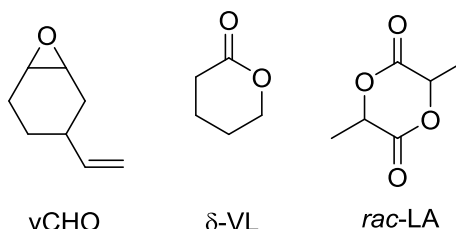


Figure 3.29 Epoxide and cyclic esters used in this section.

Table 3.10 Block copolyesters prepared using other epoxides and cyclic esters: 4-vinyl-1-cyclohexene 1,2-epoxide (vCHO), *rac*-lactide (*rac*-LA) and δ -valerolactone (δ -VL). (see **Figure 3.31-3.34** for SEC traces)

#	Monomers ^a	t	$M_{n,SEC-PS}^b$ of the first $\bar{D}^b$	$M_{n,SEC-PS}^c$ of the $\bar{D}^c$
		(h)	aliquot (just before the full conversion of PA)	block copolyester

1	PA/vCHO/ ϵ -DL	5.0	4.2	1.32	12.8	1.34
2	PA/CHO/rac-LA	5.0	2.5	1.16	6.0	1.53
3	PA/CHO/ δ -VL	6.0	5.5	1.34	11.6	1.59
4	PA/vCHO/ δ -VL	6.0	3.9	1.33	12.0	1.60

a) $[LZn_2(Ph)_2]:[CHD]:[anhydride]:[epoxide]:[cyclic\ ester] = 1:2:100:800:200$, 100 °C; b) Determined by SEC using polystyrene calibration, with units of $kg \cdot mol^{-1}$ (PA conversion > 90%); c) Determined by SEC using polystyrene calibration, with units of $kg \cdot mol^{-1}$ (cyclic ester conversion > 80%).

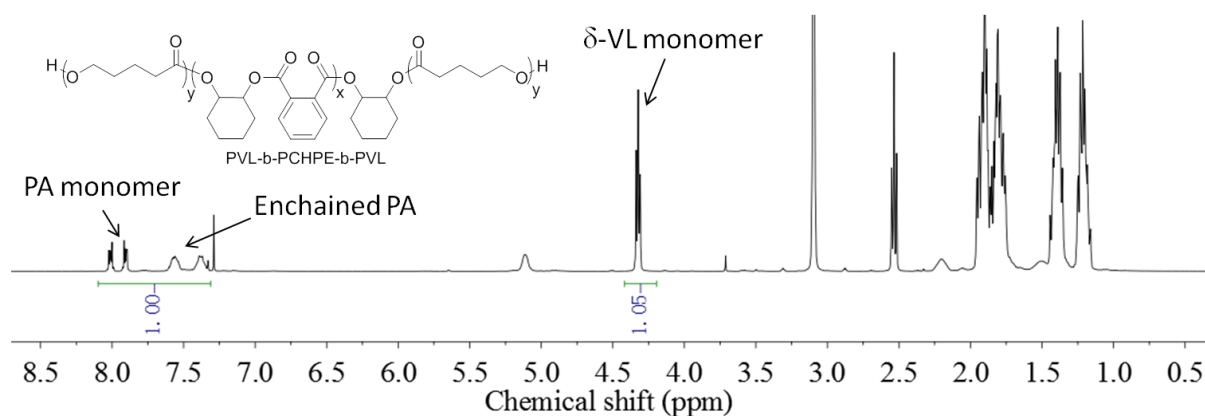
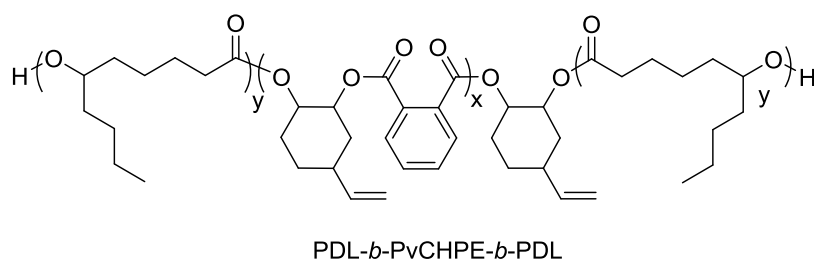


Figure 3.30 ^1H NMR spectrum of the aliquot taken before the complete conversion of phthalic anhydride (ca. 66 mol%) during the polymerization of PA/CHO/ δ -VL. No consumption of δ -valerolactone can be observed (aromatic signals as the internal reference).



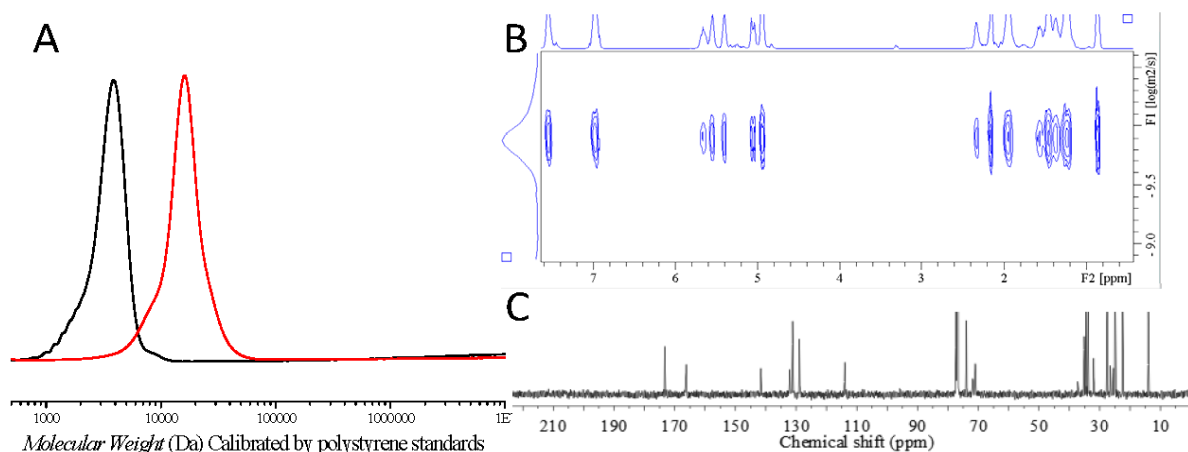


Figure 3.31 (A) SEC traces of the copolyesters prepared from PA/vCHO/ ϵ -DL, before and after the polymerization of the cyclic ester, ϵ -DL (Table 3.10, entry 1). (B) The corresponding ^1H NMR DOSY spectrum of the PA/vCHO/ ϵ -DL block copolyester, in toluene- d_8 . (C) The corresponding $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the PA/vCHO/ ϵ -DL block copolyester, in CDCl_3 .

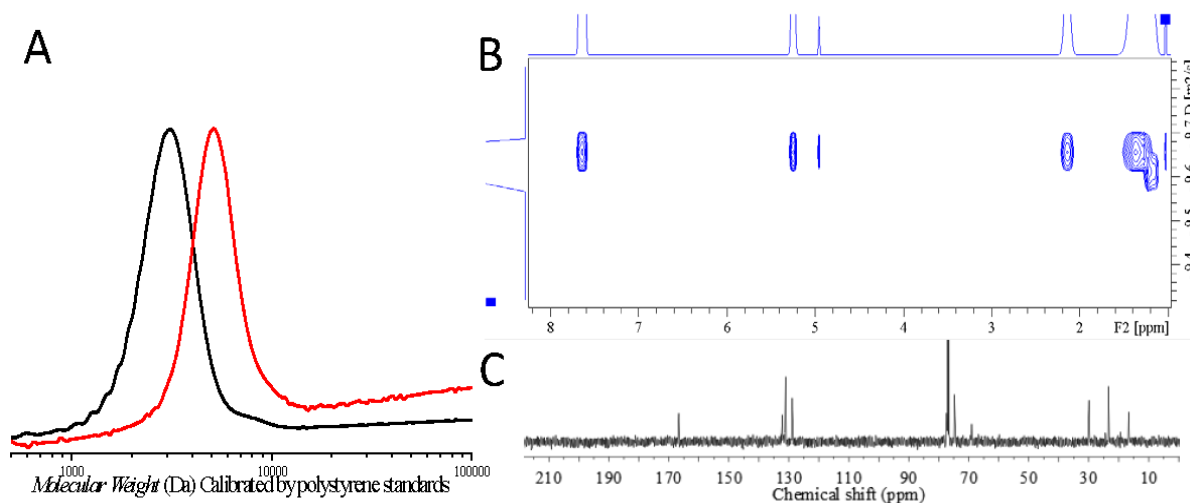
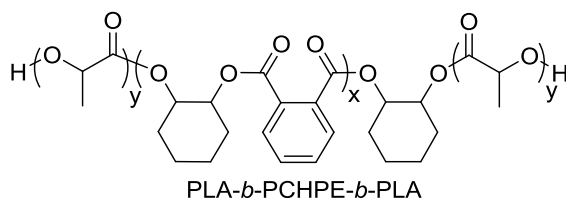


Figure 3.32 (A) SEC traces of the copolyester prepared from PA/CHO/*rac*-LA, before and after the polymerization of the cyclic ester, *rac*-LA (Table 3.10, entry 2). (B) The

corresponding ^1H NMR DOSY spectrum of the PA/CHO/*rac*-LA block copolyester, in toluene- d_8 . (C) The corresponding $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the PA/CHO/*rac*-LA block copolyester, in CDCl_3 .

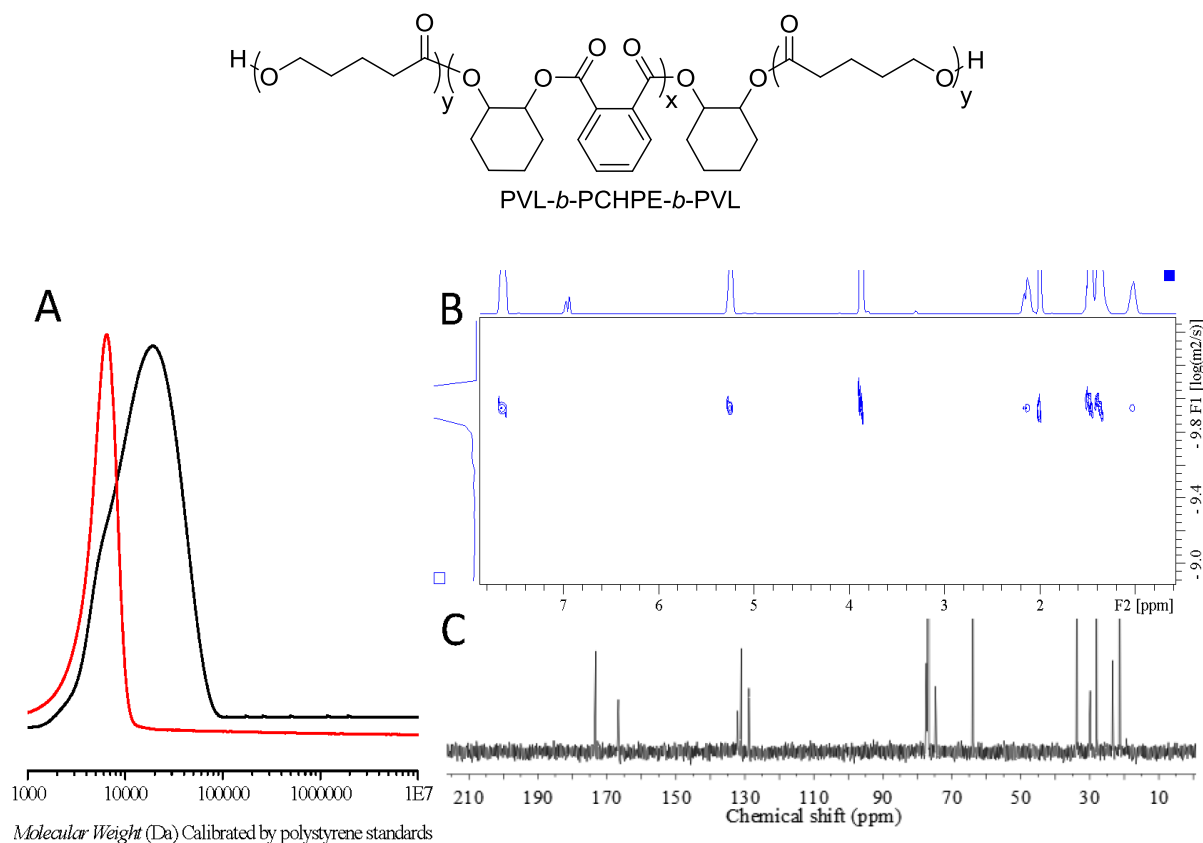
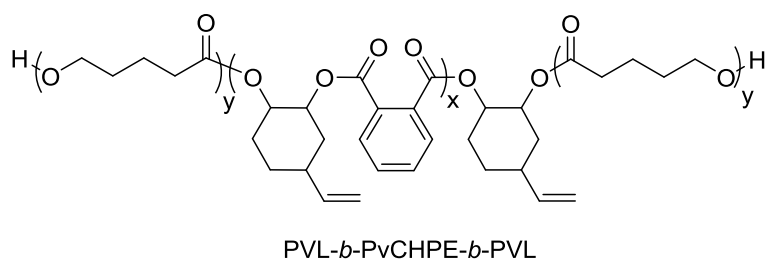


Figure 3.33 (A) The SEC traces of the copolyester prepared from PA/CHO/ δ -VL, before and after the polymerization of the cyclic ester, δ -VL (**Table 3.10**, entry 3). (B) The corresponding ^1H NMR DOSY spectrum of the PA/CHO/ δ -VL block copolyester, in toluene- d_8 . (C) The corresponding $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the PA/CHO/ δ -VL block copolyester, in CDCl_3 .



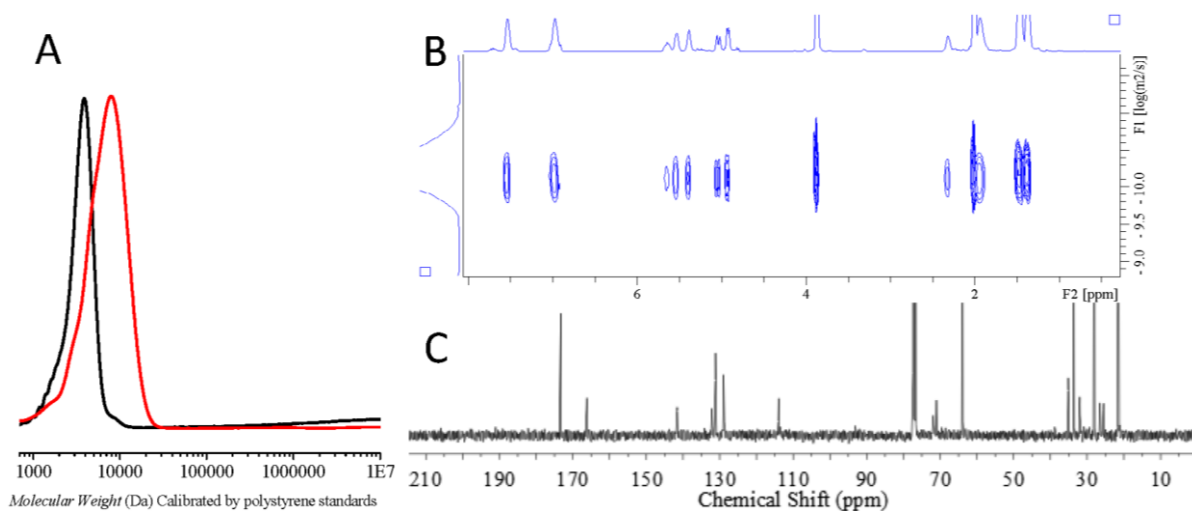


Figure 3.34 (A) SEC traces of copolyester prepared from PA/vCHO/ δ -VL, before and after the polymerization of the cyclic ester, δ -VL (Table 3.10, entry 4). (B) The corresponding ^1H NMR DOSY spectrum of the PA/vCHO/ δ -VL block copolyester, in toluene- d_8 . (C) The corresponding $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the PA/vCHO/ δ -VL block copolyester, in CDCl_3 .

Hence, the chemoselective method using $[\text{LZn}_2(\text{Ph})_2]$ complex can be applied to other monomer combinations, suggesting the possibility of tuning the thermal/mechanical properties of the block polymer by simply changing monomer combination in feedstock. Further investigation is needed to evaluate the properties (e.g. glass transition temperature, melting temperature, crystallinity and microphase separation) of the obtained block polymer. In particular, it is might be possible to further tuning the property by introducing functional groups to PVL-*b*-PvCHPE-*b*-PVL *via* post-polymerization modification, such as thiol-ene chemistry or hydroboration.

3.3 Conclusions

The di-zinc catalyst, $[\text{LZn}_2(\text{OAc})_2]$, can catalyze the ring-opening polymerization of lactones and the ring-opening copolymerization of epoxides/anhydrides to afford polyesters with good control. Additionally, it exhibits a very unusual switchable catalysis whereby the catalyst selectively polymerizes epoxides/anhydrides first, followed by the propagation of lactones. However, using this catalyst, the molecular weight, molecular weight distribution and polymer chain architecture cannot be well controlled. The limitation is associated with the

incomplete initiation of ϵ -caprolactone from the secondary –OH groups of PCHPE block as discussed in the previous Chapter. The phenomenon results in slow initiation *versus* fast propagation of ϵ -CL from secondary or primary hydroxyl groups, respectively. Practically, it is observed that despite the high degree of selectivity exerted, both α -acetyl- ω -hydroxyl (initiated from the acetate co-ligand) and α , ω -dihydroxyl polymer end-groups (initiated from the cyclohexanediol) were observed. Therefore, though it is encouraging to observe the chemoselectivity, the reaction is limited by simultaneously production of both AB and ABA type copolymers, leading to a mixture of chain structures. This mixed chain structure is not ideal, especially for post-polymerization modifications (e.g. chain extension with diisocyanate) due to the partly acetate-capped ‘dead’ chain end.

To address these two major limitations, another lactone monomer (ϵ -DL) having secondary alkoxide propagating species was selected and a new di-zinc complex, $[LZn_2(Ph)_2]$, with phenyl co-ligands was developed. The new di-zinc complex is established to catalyze the ring-opening copolymerization of anhydrides/epoxides and ring-opening polymerization of lactones. Most importantly, $[LZn_2(Ph)_2]$ complex affords well-defined telechelic polymer structure when applied with a bifunctional chain transfer agent (e.g. cyclohexene diol). Furthermore, it catalyzes the sequence controlled polymerization of anhydrides/epoxides/lactones. ABA type triblock copolyesters are prepared, in one-pot from monomer mixtures. It is interesting to observe that at balanced block compositions, PDL-*b*-PCHPE-*b*-PDL triblocks show two separate T_g values, which suggests the existence of microphase separation between PCHPE and PDL domains, though further investigation is needed to confirm this observation.

Furthermore, multi-block copolyesters can be synthesized by the same sequence controlled polymerization method. The ground rules for implementing the selective process are uncovered and the ability to apply it to other monomers is demonstrated; it is expected that broader classes of catalysts and monomers will also be successful. The method simplifies the preparation of block copolyesters and is expected to be of value for the preparation of

materials with tailored properties, such as new types of thermoplastic elastomer. In the next chapter, the mechanical properties of PDL-*b*-PCHPE-*b*-PDL as either the thermoplastic elastomer or shape memory materials will be discussed.

3.4 References

- (1) Lutz, J. F.; Ouchi, M.; Liu, D. R.; Sawamoto, M. *Science* **2013**, *341*, 628-636.
- (2) Fineman, M.; Ross, S. D. *J. Polym. Sci.* **1950**, *5*, 259-262.
- (3) Badi, N.; Lutz, J. F. *Chem. Soc. Rev.* **2009**, *38*, 3383-3390.
- (4) Lutz, J. F. *Nat. Chem.* **2010**, *2*, 84-85.
- (5) Anastasaki, A.; Nikolaou, V.; Pappas, G. S.; Zhang, Q.; Wan, C.; Wilson, P.; Davis, T. P.; Whittaker, M. R.; Haddleton, D. M. *Chem. Sci.* **2014**, *5*, 3536-3542.
- (6) Gody, G.; Maschmeyer, T.; Zetterlund, P. B.; Perrier, S. *Nat. Commun.* **2013**, *4*, doi:10.1038/ncomms3505.
- (7) Ajellal, N.; Carpentier, J. F.; Guillaume, C.; Guillaume, S. M.; Helou, M.; Poirier, V.; Sarazin, Y.; Trifonov, A. *Dalton Trans.* **2010**, *39*, 8363-8376.
- (8) Childers, M. I.; Longo, J. M.; Van Zee, N. J.; LaPointe, A. M.; Coates, G. W. *Chem. Rev.* **2014**, *114*, 8129-8152.
- (9) Lu, X.-B.; Darensbourg, D. J. *Chem. Soc. Rev.* **2012**, *41*, 1462-1484.
- (10) Paul, S.; Zhu, Y.; Romain, C.; Brooks, R.; Saini, P. K.; Williams, C. K. *Chem. Commun.* **2015**, *51*, 6459-6479.
- (11) Kramer, J. W.; Treitler, D. S.; Dunn, E. W.; Castro, P. M.; Roisnel, T.; Thomas, C. M.; Coates, G. W. *J. Am. Chem. Soc.* **2009**, *131*, 16042-16044.
- (12) Romain, C.; Williams, C. K. *Angew. Chem., Int. Ed.* **2014**, *53*, 1607-1610.
- (13) Saini, P. K.; Romain, C.; Zhu, Y.; Williams, C. K. *Polym. Chem.* **2014**, *5*, 6068-6075.
- (14) Bates, F. S.; Hillmyer, M. A.; Lodge, T. P.; Bates, C. M.; Delaney, K. T.; Fredrickson, G. H. *Science* **2012**, *336*, 434-440.
- (15) Takizawa, K.; Tang, C.; Hawker, C. J. *J. Am. Chem. Soc.* **2008**, *130*, 1718-1726.
- (16) Lee, H. S.; Roy, A.; Lane, O.; Lee, M.; McGrath, J. E. *J. Polym. Sci., Part A: Polym. Chem.* **2010**, *48*, 214-222.
- (17) Lendlein, A.; Neuenchwander, P.; Suter, U. W. *Macromol. Chem. Phys.* **1998**, *199*, 2785-2796.
- (18) Platel, R. H.; Hodgson, L. M.; Williams, C. K. *Polym. Rev.* **2008**, *48*, 11-63.
- (19) Jeske, R. C.; DiCiccio, A. M.; Coates, G. W. *J. Am. Chem. Soc.* **2007**, *129*, 11330-11331.
- (20) Jeske, R. C.; Rowley, J. M.; Coates, G. W. *Angew. Chem., Int. Ed.* **2008**, *47*, 6041-6044.
- (21) Hosseini Nejad, E.; van Melis, C. G. W.; Vermeer, T. J.; Koning, C. E.; Duchateau, R. *Macromolecules* **2012**, *45*, 1770-1776.
- (22) Nejad, E. H.; Paoniasari, A.; Koning, C. E.; Duchateau, R. *Polym. Chem.* **2012**, *3*, 1308-1313.
- (23) Harrold, N. D.; Li, Y.; Chisholm, M. H. *Macromolecules* **2013**, *46*, 692-698.
- (24) Darensbourg, D. J.; Poland, R. R.; Escobedo, C. *Macromolecules* **2012**, *45*, 2242-2248.

- (25) Winkler, M.; Romain, C.; Meier, M. A. R.; Williams, C. K. *Green Chem.* **2015**, *17*, 300-306.
- (26) Brule, E.; Guo, J.; Coates, G. W.; Thomas, C. M. *Macromol. Rapid Commun.* **2011**, *32*, 169-185.
- (27) Aida, T.; Sanuki, K.; Inoue, S. *Macromolecules* **1985**, *18*, 1049-1055.
- (28) Huijser, S.; HosseiniNejad, E.; Sablong, R.; de Jong, C.; Koning, C. E.; Duchateau, R. *Macromolecules* **2011**, *44*, 1132-1139.
- (29) van Meerendonk, W. J.; Duchateau, R.; Koning, C. E.; Gruter, G.-J. M. *Macromolecules* **2005**, *38*, 7306-7313.
- (30) Sugimoto, H.; Ohtsuka, H.; Inoue, S. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 4172-4186.
- (31) Sugimoto, H.; Kuroda, K. *Macromolecules* **2007**, *41*, 312-317.
- (32) Nakano, K.; Nakamura, M.; Nozaki, K. *Macromolecules* **2009**, *42*, 6972-6980.
- (33) Cyriac, A.; Lee, S. H.; Lee, B. Y. *Polym. Chem.* **2011**, *2*, 950-956.
- (34) Wu, G.-P.; Darensbourg, D. J. *Macromolecules* **2016**, *49*, 807-814.
- (35) Romain, C.; Zhu, Y.; Dingwall, P.; Paul, S.; Rzepa, H. S.; Buchard, A.; Williams, C. K. *J. Am. Chem. Soc.* **2016**, *138*, 4120-4131.
- (36) Morris, G. A. In *eMagRes*; John Wiley & Sons, Ltd: 2007.
- (37) Zhu, Y.; Romain, C.; Poirier, V.; Williams, C. K. *Macromolecules* **2015**, *48*, 2407-2416.
- (38) Lyman, D. J. *J. Polym. Sci.* **1960**, *45*, 49-59.
- (39) Lee, S. H.; Cyriac, A.; Jeon, J. Y.; Lee, B. Y. *Polym. Chem.* **2012**, *3*, 1215-1220.
- (40) Zhu, Y.; Romain, C.; Williams, C. K. *J Am Chem Soc* **2015**, *137*, 12179-12182.
- (41) Nejad, E. H.; Paoniasari, A.; van Melis, C. G. W.; Koning, C. E.; Duchateau, R. *Macromolecules* **2013**, *46*, 631-637.
- (42) Darensbourg, D. J.; Poland, R. R.; Escobedo, C. *Macromolecules* **2012**, *45*, 2242-2248.
- (43) DiCiccio, A. M.; Coates, G. W. *J. Am. Chem. Soc.* **2011**, *133*, 10724-10727.
- (44) Gores, F.; Kilz, P. In *Chromatography of Polymers*; American Chemical Society: 1993; Vol. 521, p 122-148.
- (45) Buchard, A.; Jutz, F.; Kember, M. R.; White, A. J. P.; Rzepa, H. S.; Williams, C. K. *Macromolecules* **2012**, *45*, 6781-6795.
- (46) Wu, G. P.; Darensbourg, D. J.; Lu, X. B. *J. Am. Chem. Soc.* **2012**, *134*, 17739-17745.
- (47) Darensbourg, D. J.; Wu, G. P. *Angew. Chem., Int. Ed.* **2013**, *52*, 10602-10606.
- (48) Zhao, J.; Pahovnik, D.; Gnanou, Y.; Hadjichristidis, N. *Macromolecules* **2014**, *47*, 3814-3822.
- (49) Wilson, J. A.; Hopkins, S. A.; Wright, P. M.; Dove, A. P. *Biomacromolecules* **2015**, *16*, 3191-3200.
- (50) Jasinska-Walc, L.; Bouyahyi, M.; Rozanski, A.; Graf, R.; Hansen, M. R.; Duchateau, R. *Macromolecules* **2015**, *48*, 502-510.
- (51) Jasinska-Walc, L.; Hansen, M. R.; Dudenko, D.; Rozanski, A.; Bouyahyi, M.; Wagner, M.; Graf, R.; Duchateau, R. *Polym. Chem.* **2014**, *5*, 3306-3310.
- (52) Gody, G.; Zetterlund, P. B.; Perrier, S.; Harrisson, S. *Nat. Commun.* **2016**, *7*, doi:10.1038/ncomms10514.

Chapter 4
Renewable and Degradable Multiblock
Polyesters with Tunable Elasticity or as
Shape Memory Materials

4.1 Background and Aims

Concerns associated with the sustainability, cost and adverse environmental impacts of petrochemicals have spurred the development polymers sourced from renewable resources, such as plants, and of degradable materials.^{1,2} Nonetheless, it is still important to improve upon the thermal/mechanical properties of these renewable polyesters so as to broaden application and access higher value products such as thermoplastic elastomers (TPEs) and shape-memory polymers.³ Although the market size of either the TPEs or the shape-memory polymers is rather small compared to other commodity plastics, these two types of polymers feature high-value markets with high cost tolerance, which are the ideal markets to start deploying renewable plastics.

There are two important types TPEs: microphase separated block (including graft) copolymers and segmented polyurethanes, which are essentially linear multiblock copolymers.⁴ A block copolymer formed using immiscible polymers featuring ‘soft’ and ‘hard’ domains undergo phase separation on the nano- or micro-scale. For TPE, the separated domains of hard blocks act as network crosslinking points, while the soft domains act as the matrix. In contrast to covalently crosslinked structures like natural rubber, the crosslinking points in TPEs are kinetically trapped polymer phases, thus TPEs can be thermally transformed and processed, such as by injection molding, pressure molding and extrusion.⁴ Due to the attractive thermal properties, many TPEs are made from (multi)block copolymers.⁵⁻¹⁴ Alternatively, TPEs can also be prepared using vitrimers. Vitrimers are polymers that show reversible temperature-induced thermoset to thermoplastic transitions. This means they behave like covalently crosslinked rubbers at ambient temperature, but can be processed as thermoplastics at evaluated temperature.^{15,16}

Current thermoplastic elastomers (TPEs) are almost entirely sourced from petrochemicals and produced on a significant scale (>3.5 Mt/year).¹⁷ It is possible to replace, or partly replace, some of the petrochemical raw materials with renewable resources, for example monomers derived from terpenes, vegetable oils, sugars or CO₂ have all been reported in the academic

literature.^{8,11,18-23} As one of the key parameters of a thermoplastic elastomer, the elongation at break describes how far the material can be stretched before it breaks. So far, the most commercially successful TPE, poly(styrene-*b*-butadiene-*b*-styrene), can reach elongation at break values ranging from 800% to 1100%.²⁴ Sustainable or partly sustainable materials with high elongation at break values (500-1800%) can also be found in literature.^{6-8,11,22,23,25,26} Castor oil-derived decalactones are particularly attractive soft-block-forming monomers due to the low T_g value (-60 °C) and lack of crystallinity. Using ϵ -DL to make elastomers afforded high elongation at break values (ca. 800%).^{27,28} However, elongation at break values exceeding 2000% are rarely observed in either academic or industrial.^{5-14,24,25} One example, featuring such a high elongation at break value (2500%) was observed using a biocomposite consisting of cellulose, rosin and fatty acids, but the material suffered from low tensile stress (0.5 MPa).²⁹ The soft block is also a key component in a TPE as it delivers the stretchability. However, the hard block prevents the TPEs from undergoing creep. Polymers with high thermal resistance (high T_g or T_m), high Young's modulus and strength are suitable candidates for the hard blocks. Currently sustainable polyesters/polycarbonates which fit these requirements are rare because most are not designed to show rigidity.³⁰ The most commonly used polyester hard block is polylactide.^{6,22,31} Although, it is possible to reach a high melting temperature (120 °C) by controlling the stereochemistry, PLA suffers from low tensile strength (50-70 MPa) as well as inherent brittleness.³² Therefore, it is to develop new polyesters or polycarbonates showing high thermal resistance (high T_g or T_m), Young's modulus and strength to make sustainable and degradable TPEs.

During the past decades, shape memory polymers have attracted significant attention both in academia and industry due to the facility of such materials to reversibly change shape upon the application of an external stimulus, such as heat or light.³³⁻⁴² Various potential applications have been proposed, including as biomedical devices,³⁴ electronic devices^{43,44} or smart textiles.⁴⁵ Given the advantage of implanting bulky devices through small apertures or of triggering a knotting of a suture only at a specific location, major efforts have been paid to the development of shape memory materials for biomedicine. Biodegradable shape memory

polymers with drug-releasing capability also have potential as multifunctional bioengineering scaffolds.^{35,37} Recently, Meijer and co-workers presented a shape memory hydrogel, made from 2-ureido-4[1H]-pyrimidinone (UPy) hydrogen-bonding units within the backbone of segmented poly(ethylene glycol) (PEG). The material showed a high strength (> 30 MPa) and impressive strain fixation (200% upon uniaxial stretching).⁴⁶ The design of shape-memory polymers is underpinned by the programming cycle whereby the polymer is initially formed into a permanent shape, *via* conventional processing methods, and is subsequently deformed into a fixed but temporary shape. The programming is often accomplished by heating above a glass/melting temperature but can also be achieved by ‘cold drawing’ processes.³³ After being fixed in the temporary structure, shape memory materials can revert to the permanent shape once the stimulus is applied. Commonly, this stimulus is thermal and may involve heating the sample above particular transition temperatures. Examples which are degradable and/or which are sourced from renewable sources are now quite well known,³⁴⁻³⁷ but combinations of both properties remain more unusual.^{41,47,48}

The goal is to develop simultaneously sustainable and degradable polyesters suitable for high value applications. The approach is to target a series of new multiblock copolyesters comprising rigid, but amorphous, hard blocks and soft, amorphous blocks. The materials will be prepared using switchable polymerization catalysis, although chain extension, e.g. with a di-isocyanate, is likely to be necessary to overcome the low molecular weight achieved by ring-opening copolymerizations. The triblock copolymers comprise hard blocks from the ring-opening copolymerization of phthalic anhydride (PA) and cyclohexene oxide (CHO) and soft blocks from the ring-opening polymerization of ϵ -decalactone (ϵ -DL).⁴⁹ Today these monomers are petrochemicals but routes from renewable sources have been pioneered: ϵ -decalactone from castor oil, phthalic anhydride from carbohydrates and cyclohexene oxide from fatty acids.^{50,51}

4.2 Results and Discussion

4.2.1 Chain extension reaction of PDL-*b*-PCHPE-*b*-PDL triblock copolyesters

Using the switchable polymerization catalysis method described in chapter 3, the preparation of block copolyesters from mixtures of epoxides, anhydrides and lactones was carried out. A series of ABA type copolyesters comprising poly(cyclohexylene phthalate) (PCHPE) (B block) and poly(ϵ -decalactone) (PDL) (A block) blocks were prepared in high yield.⁴⁹ The polymers were purified by precipitation in cold MeOH and were dried under vacuum. Some of the characterization data, including the MW values, is presented in **Table 4.1**.



Figure 4.1 Synthetic route of {PDL_m-*b*-PCHPE_n-*b*-PDL_m}_y multiblock copolyesters. In the sample with 26 wt% of PCHPE block (entry 1, Table 4.1), $n = 36$; $2m = 150$.

One limitation of the synthesis is that rather medium/low molecular weight (MW) polymers are produced, this arises from relatively higher catalyst loadings required and the fact that immortal polymerization occurs as chain transfer agents are present. Therefore, the triblock copolyesters were chain extended to reach higher molecular weights (MW). The chain extension reactions were catalyzed by Sn(Oct)₂, using 4,4'-methylenebis(phenyl isocyanate) (MDI) as the chain extension agent. As shown in **Table 4.1**, the MWs were approximately doubled in all four samples, while the molecular weight distribution remained narrow (<1.50), all indicative of at least one successful coupling between triblock copolyesters.

Table 4.1 Characterization data for the block copolyester materials.

#	{PDL _m - <i>b</i> -PCHPE _n - <i>b</i> -PDL	wt%	$M_{n,exp} (\text{Ð})^b$	$M_{n,exp} (\text{Ð})^{b,c}$ of the	T_g1	T_g2
---	--	-----	--------------------------	-------------------------------------	--------	--------

m/y^a	PCHPE	triblock precursor	(°C) ^d	(°C) ^d
1 n = 36; 2m = 150; y = 1.6	26	56.6 (1.32) 34.6 (1.19)	-49	N.A.
2 n = 38; 2m = 76; y = 2.0	42	44.8 (1.47) 22.3 (1.22)	-47	98
3 n = 43; 2m = 64; y = 2.2	49	47.4 (1.38) 21.5 (1.16)	-43	103
4 n = 46; 2m = 47; y = 2.5	59	48.1 (1.50) 19.4 (1.21)	-42	107
5 n = 0; 2m = 93; y = 1.9	0	29.8 (1.67) 15.9 (1.19)	-49	N.A.

^{a)} *n* and *m* represent the repeat units of [PA/CHO] and [DL] in each triblock precursor; *y* stands for the coupling number of the multiblocks; ^{b)} Determined by SEC equipped with RI detector, calibrated using narrow MW polystyrene standards; ^{c)} Chain coupling reaction was catalyzed by Sn(Oct)₂ with MDI as the chain extension agent at 60 °C for 2.0 h ; ^{d)} acquired from the second heating cycles in DSC curves, using chain coupled samples. *T_{g1}* is the glass transition temperature of the PDL block, while *T_{g2}* is the glass transition temperature of the PCHPE block.

4.2.2 Microphase separation of the PDL-*b*-PCHPE-*b*-PDL multiblocks

The polymers comprised of two amorphous polymer blocks and there was no evidence of any crystallization of either the ABA or multiblock materials. A wide-angle X-ray scattering (WAXS) technique has been widely applied to determine the crystallinity of a polymers.^{33,46,52} The multiblock copolymers display no scattering peaks associated with crystallinity in the WAXS spectrum (**Figure 14**). To confirm this observation, both the triblock and multiblock copolymers were characterized by DSC and no melting/crystalline peaks can be observed.⁴⁹ The triblock copolymers exhibited two *T_g* values during DSC characterization.⁴⁹ The chain extended multiblock materials also showed two *T_g* values, in the DSC thermograms, apart from the sample with the lowest content of PCHPE where only a single value was observed (**Table 4.1**). For reference, the *T_g* values were also determined for the constituent polymers, PDL and PCHPE, and were -58 °C and 97 °C, respectively. Therefore, for most of the multiblock materials the lower *T_g* value (~ -45 °C) is attributed to

the PDL portions and the higher value (~ 100 °C) to the hard PCHPE portions. Furthermore, the materials likely form microphase-separated structures. To confirm the microphase separation, multiblock films were analyzed by small-angle X-ray scattering (SAXS), at ambient temperature (see **Figure 4.2**). SAXS analysis in this thesis was conducted in collaborations with Prof. Marc Hillmyer and was performed by Dr Madalyn Radlauer. Principal scattering peaks corresponding to microphase separation were observed, however, the absence of well-defined secondary peaks indicated poor long-range order.⁸ The exception was the 59 wt% sample which showed a secondary scattering peak. The domain spacing values (D) were calculated to be 14.3 nm (#1 in **Table 4.1**), 12.1 nm (#2 in **Table 4.1**) and 11.9 nm (#4 in **Table 4.1**), suggesting microphase separation occurred even in the case of the lowest PCHPE content (#1 in **Table 4.1**). Thermally annealed multiblock samples were also characterized by SAXS. After annealed at 130 °C for 48.0 h, secondary peaks were observed in the 49 wt% and 59 wt% samples. This suggests that it is possible to access long range order at certain composition values *via* thermal annealing. Similar principle scattering peaks corresponding to microphase separation were also observed in solvent-cast triblock samples. This observation rules out the possibility that the microphase separation in the multiblock samples is induced by the chain coupling using MDI.

To confirm the microphase separation and the domain spacing, bulk samples of the multiblock copolymers were also analyzed by TEM. The samples were first sectioned by ultra-microtome and stained with RuO_4 (which preferably stains the aromatic moiety) (**Figure 4.3**). The TEM analysis confirmed the proposed microphase separation and showed distinct changes in morphology with increasing hard (PCHPE) block content (**Figure 4.3**). Similar domain spacing values were also measured to be 10.2 nm (#1 in **Table 4.1**), 8.6 nm (#2 in **Table 4.1**) and 7.9 nm (#4 in **Table 4.1**), respectively, from the TEM image using a FFT method. It should be noted that due to the broad ring size (**Figure 4.3D**) and the weak signal-to-noise ratio, the domain spacing values were determined from the frequency domain images (**Figure 4.3D**) and so may not be as accurate as value determined by SAXS. Furthermore, in agreement with the SAXS results, there was no evidence in TEM of

well-defined long-range order, even in the case of 59 wt% PCHPE (#4 in **Table 4.1**). The analysis of the TEM images leads to the hypothesis that at the lowest PCHPE content (26 wt%) a morphology consistent with cylinders/worm-like PCHPE domains separated by a PDL matrix is observed (**Figure 4.3A**). In contrast, at the highest PCHPE content (59 wt%), the opposite morphology is observed: PDL cylinders/worm domains in a PCHPE matrix (**Figure 4.3C**). Meanwhile, at moderate PCHPE contents (42 wt%) there seems to be a transition to a bicontinuous morphology (**Figure 4.3B**). However, such proposals are tentative as a complete investigation of the phase diagram for the materials is outside the scope of this thesis. The goal of this chapter is to make better materials, so the mechanical properties of the series of PDL-*b*-PCHPE-*b*-PDL multiblock copolyesters were examined by tensile measurements which are discussed hereinafter (**Table 4.2**).

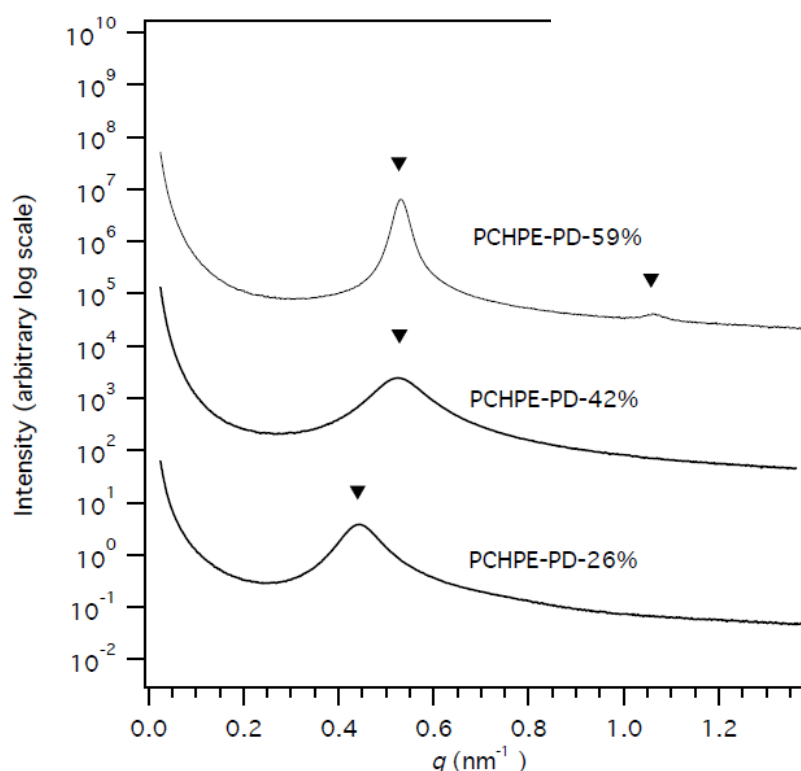


Figure 4.2 SAXS profiles of PDL-*b*-PCHPE-*b*-PDL multiblock copolyesters. Domain spacing (D) values are calculated ($D = 2\pi/q$) to be 14.3 nm, 12.1 nm and 11.9 nm, corresponding to #1, #2 and #4 in **Table 4.1**, respectively.

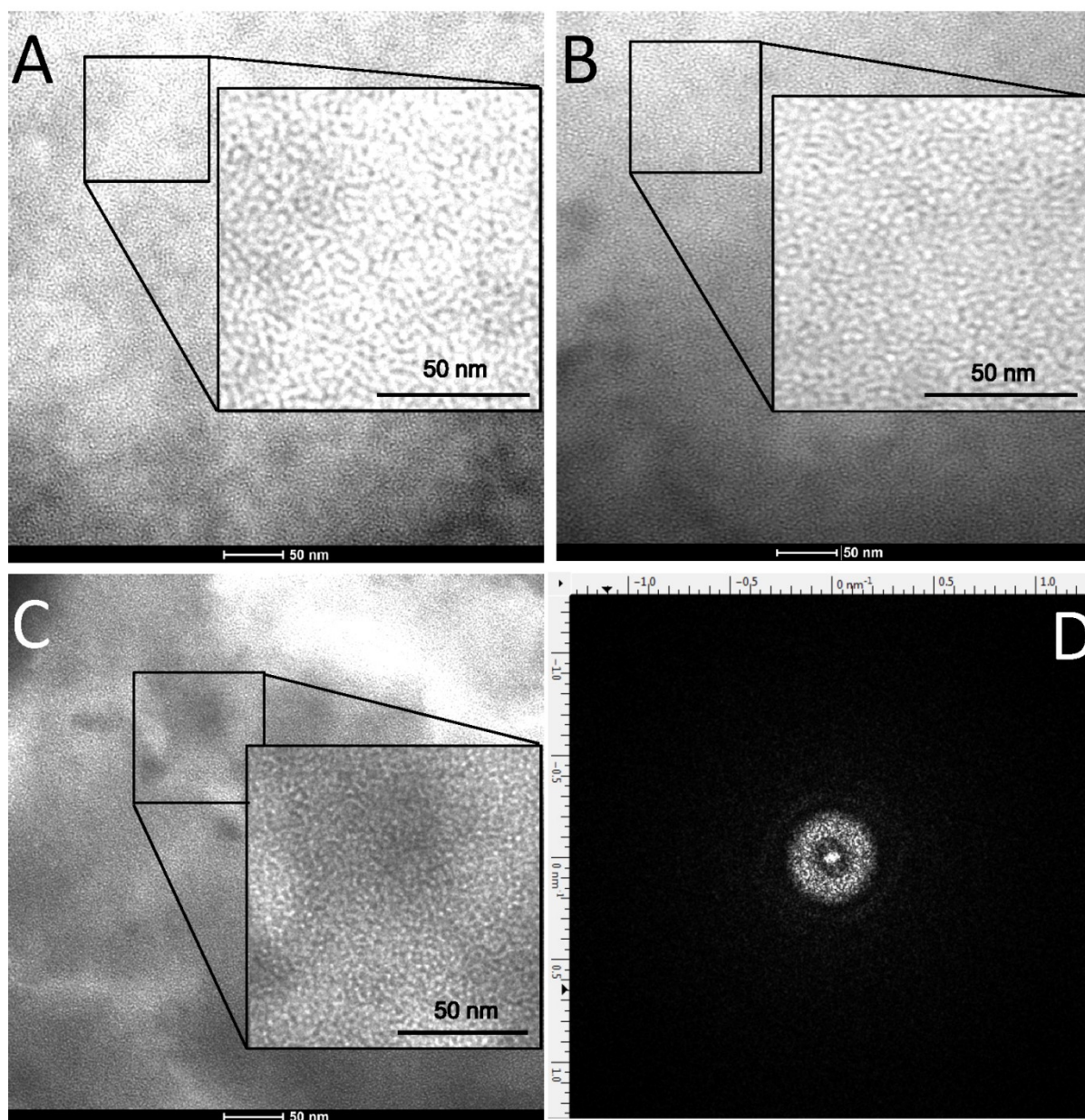


Figure 4.3 TEM images of PCHPE-*b*-PDL multiblock samples sectioned by ultra-microtome and stained with RuO_4 . These images show different types of microphase separation of PCHPE (gray) and PDL (white). (A) Multiblock polyester with 26 wt% of PCHPE (#1 in **Table 4.1**), cylinder/worm-like PCHPE domains in the PDL matrix; (B) Multiblock polyester with 42 wt% of PCHPE (#2 in **Table 4.1**), proposed bicontinuous phase separation of PCHPE and PDL; (C) Multiblock polyester with 59 wt% of PCHPE (#4 in **Table 4.1**), cylinder/worm-like PDL domains in the PCHPE matrix, similar to multiblock polyester with 49 wt% of PCHPE. ***Inset in each image: enlarged image corresponding to the selected

region. (D) Typical frequency domain image acquired from (A) using the Fast Fourier Transform (FFT) method. [It is noteworthy that morphology proposals are tentative as a complete investigation of the phase diagram for the materials is outside the scope of this thesis]

4.2.3 Multiblocks exhibiting thermoplastic elastomeric properties

The tensile mechanical results for the multiblock copolymers showed stress at break values from 11.5 MPa to 17.1 MPa (the testing procedure is described in chapter 7). The elongations at break ranged from 420% to 2450%, depending on the composition of hard/soft blocks (**Figure 4.4**). The results demonstrate the facility to control the macroscopic properties of the materials over quite a significant range of values by control of block ratio, and underscore the utility of the selective catalysis to furnish materials with such distinct differences in thermal properties. In the case with the lowest proportion of the rigid plastic block (26 wt%, #1 in **Table 4.1**), the polymer clearly exhibited elastomeric behaviour with no yield point being observed and the value for the elongation at break was very high at 2450%. Indeed, such a high elongation at break is competitive with leading TPEs reported in the literature^{7,22,25,26,29} and exceeds values reported for other commercialized (biorenewable) aliphatic polyesters which are usually less than 900%.²⁴ The elastic recovery (hysteresis) of the sample was also evaluated by repeated cycles (6 times) of strain-stress tests, conducted from 0% to 200% strain at a constant velocity of displacement (10 mm/min). A rather low residual strain value of $\epsilon_r = 4 \pm 0.6\%$ was observed after retraction which demonstrates the polymer's excellent elasticity and potential as a thermoplastic elastomer, TPE (**Table 4.2** and **Figure 4.4**). As mentioned in the introduction, sustainable polymers showing high thermal resistance (high T_g or T_m), high Young's modulus and strength are excellent candidates for hard blocks but remain rare.³⁰ It is worth noticing that the PCHPE hard block has a T_g value $\sim 100^\circ\text{C}$ (see **Table 4.1**) which is higher than most of the sustainable polyesters and polycarbonates in the literature.⁵³⁻⁵⁶ The high elongation at break value and the low residual stain value indicate that the material can retain its physically crosslinked network even upon repetitive high

deformation ($> 200\%$ in **Figure 4.4B**). The properties are attributed to the high strength and rigidity of the hard region. Indeed, PCHPE itself shows a Young's modulus: 6.6 GPa and hardness: 0.5 GPa as observed in nano-indentation tests, and a high thermal resistance ($T_g \geq 100\text{ }^\circ\text{C}$). The observation of thermoplastic elastomeric behaviour (**Figure 4.4B**) is also consistent with the proposed morphology of microphase separated PCHPE domains in a PDL matrix (**Figure 4.3A**). As a control experiment, the PDL homopolymer was chain extended by exactly the same method using MDI (**Table 4.1**, entry 5). The resulting material could not retain its shape outside the mould and exhibited no elastomeric behaviour at all. Furthermore, the DSC analysis of the sample showed only the glass transition temperature for the PDL material, with no evidence of any MDI crystallization likely due to its very low content (ca. $<1.0\text{ wt}\%$). These findings suggest that the elastomeric behaviour of the new multiblock material (#1) really does result from the phase separated domains of rigid PCHPE blocks in the elastomeric PDL matrix and is not due to any observable crystallization of the MDI moiety. Also, after being kept under ambient conditions, the DSC results of the 26 wt% sample did not change over 8 months.

In contrast to the good TPE properties of polymer #1, the other multiblocks which contain progressively greater quantities of PCHPE showed plastic behaviours (#2, #3 and #4 in **Table 4.1**, yield points observed in **Figure 4.4**). The characterization data suggested that at higher PCHPE contents ($\geq 42\text{ wt}\%$), the multiblocks form continuous PCHPE morphologies as demonstrated in the TEM analyses (**Figure 4.3B and 4.3C**) which explains the observation of yield points in these three samples.

Interestingly, a well-defined strain-induced plastic-to-rubber transition⁵⁷ was observed for the sample containing 42 wt% PCHPE (**Figure 4.5**). The transition was observed when the polymer was first extended to 350% strain, at the rate of 10 mm/min, and allowed to retract, at the same rate, until reaching 0 MPa stress. Then, a second extension was applied to the similar strain value. The second stress-strain curve shows elastomeric behaviour and the yield point disappeared. The data could be consistent with the PCHPE continuous phase being

disrupted to generate a new structure with isolated domains of PCHPE in a continuous matrix of PDL. It is proposed that the rigid isolated PCHPE domains may be able to act as network points in the PDL matrix and thereby deliver a structure able to exhibit elastomeric behaviour (see the schematic illustration in **Figure 4.5**). The results are also consistent with a continuous phase forming before stretching, in line with the bicontinuous morphology hypothesis from the characterization data. Thus, the strain-induced plastic-to-rubber transition for the 42 wt% sample (#2 in **Table 4.1**) is distinct from that of polymers with higher PCHPE values (#3 and #4 in **Table 4.1**) and it may be rationalized by the distinct nanoscopic morphologies observed, with the former showing a bicontinuous structure whilst the latter two both show domains of separated PDL in a PCHPE matrix.

Table 4.2 Mechanical properties of the multiblock copolyesters as a function of the different block compositions.^a

#	wt% PCHPE	Young's modulus (MPa)	Stress at break (MPa)	ϵ at yield (%)	ϵ at break (%)
1	26	1.7 ± 0.2	11.5 ± 1.0	N.A. ^b	2450 ± 150
2	42	78.7 ± 3.2	13.3 ± 1.7	19.2 ± 1.5	1200 ± 120
3	49	178.9 ± 6.3	15.7 ± 2.2	11.7 ± 0.9	570 ± 55
4	59	390.0 ± 2.5	17.1 ± 2.1	9.2 ± 1.9	420 ± 60

^a) All tensile tests were conducted according to ISO 527 standard, see experimental section for details; ^b) no yield point was observed in this sample.

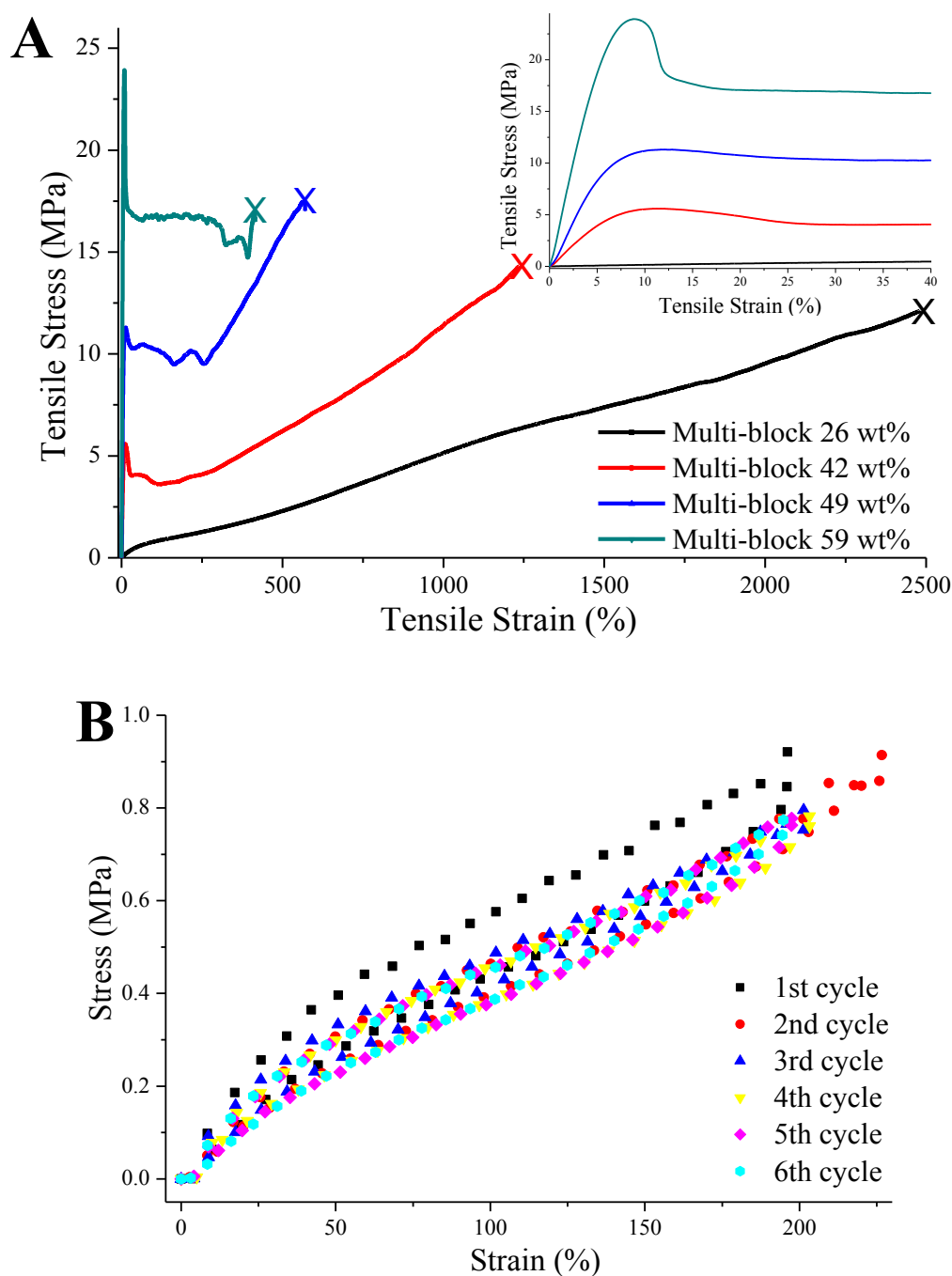


Figure 4.4 (A) Stress-strain curves of the multiblock copolyesters (#1~4 in **Table 4.1**). The failure points are marked by 'X'. Inset: enlarged stress-strain curves of the multiblocks in the low strain region (0~40%); (B) hysteresis study on the multiblock polyester with 26 wt% of PCHPE (6 cycles from 0% to 200% strain at the velocity of 10 mm/min, showing excellent elasticity. The average residual strain of the 6 cycles is $4 \pm 0.6\%$).

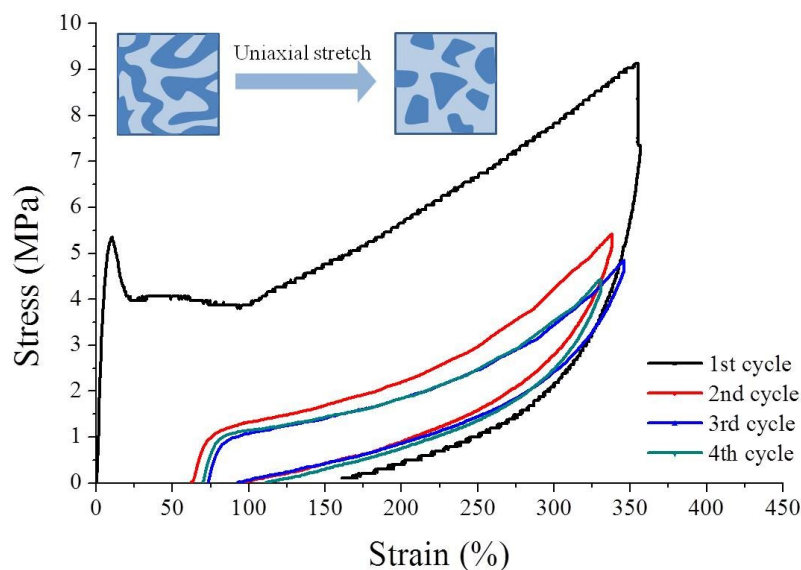


Figure 4.5 Strain stress curves and schematic illustration of the plastic-to-rubber transition observed in the 42 wt% sample, confirming the bicontinuous phase separation morphology.

4.2.4 Multiblocks exhibiting shape memory effects

The tensile test using the 59 wt% sample (#4) revealed a rather broad plateau over the range 20% to 300% strain (**Figure 4.4**). This plateau is attributed to a cold-draw process.^{58,59} Cold drawing is a process whereby polymer segments undergo forced orientation to non-equilibrium conformations along the direction of the external force, when the material is stretched at a temperature below the T_g value. The deformation is retained even after the external force is removed. Fundamentally, cold drawing is a type of elastic deformation: a forced high elastic deformation.^{58,59} Therefore, the stretched sample can recover from the deformation after being heated above the transition temperature.^{60,61} Initially, cold draw effects were considered as defects in the field of shape memory polymers since they do not cause true plastic deformation.⁶² However, more recently cold-drawing has become a popular programming method and has been adopted by many groups to temporarily fix shape because of its convenience: it only involves a one-step stretching without any heating.^{40,46,52,63-66} Cold draw programming has also been used in shape memory materials consisting of degradable polyesters which have potential in biomedical applications.^{64,65} Given the tensile mechanical

performance of the 59 wt% sample, it was considered relevant to be investigated for shape memory effects. A range of different temperatures were investigated first to identify the optimum transition temperature, T_{trans} (35 °C, 55 °C, 75 °C and 95 °C). Even at a $T_{\text{trans}} = 55$ °C, which is well below the glass transition temperature of the hard block (ca. 100 °C), near complete recovery of the original shape was achieved, with the residual strain being < 5% (1st cycle in **Figure 4.6**). Similar observations that other cold-drawn polymers can retract at temperatures (T_{trans}) significantly lower than the glass transition temperature have been reported.^{67,68} The phenomenon may be due to the shrinkage stress in oriented polymer segments [e.g. polycarbonate and poly(ethylene glycol terephthalate)],⁶⁹ also known as the enthalpy of relaxation in terms of thermal mechanics.⁶⁸ This sub T_g transition offers great advantage in designing shape memory polymers with accessible transition temperatures for medicine as the high T_g value is retained under operational conditions. However, such sub T_g transitions have rarely been observed in shape memory polymers.^{33,62,66,70} DSC was used to further characterize the enthalpy of relaxation transition of the pre-stretched multiblock (**Figure 4.7**). Comparing the second heating cycle (**Figure 4.7B**) with the first heating cycle (**Figure 4.7A**) shows an additional endothermic peak (at 50 °C) below the PCHPE glass transition temperature, assigned to its enthalpy of relaxation. The low experimental transition temperature (55 °C) is remarkably close to the enthalpy of relaxation of oriented PCHPE segments, suggesting it is indeed the transition responsible for mechanical retraction.

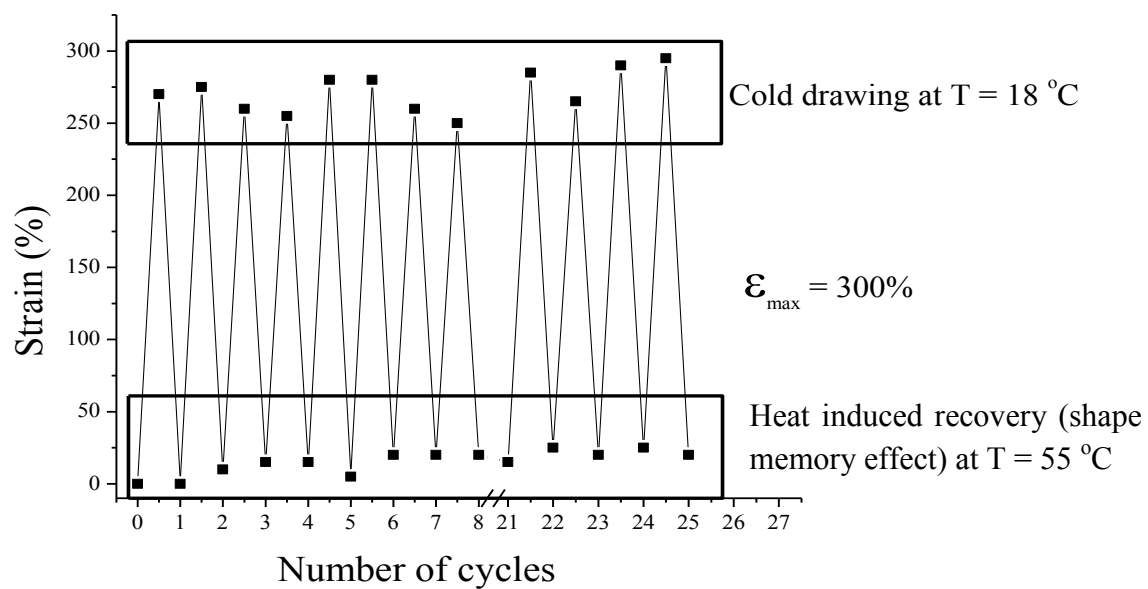
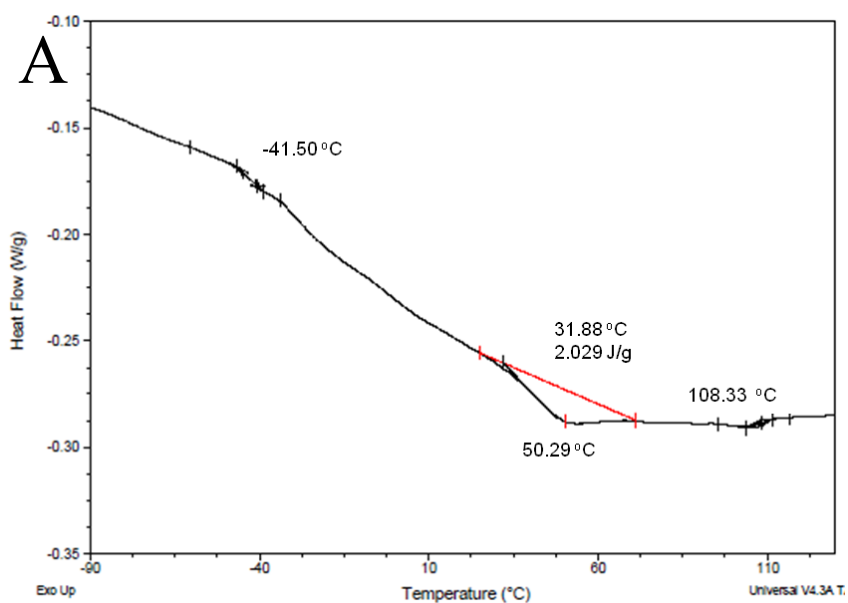


Figure 4.6 Thermal induced shape memory effect of PCHPE-*b*-PDL 59 wt% multiblock (#4 in Table 4.1).



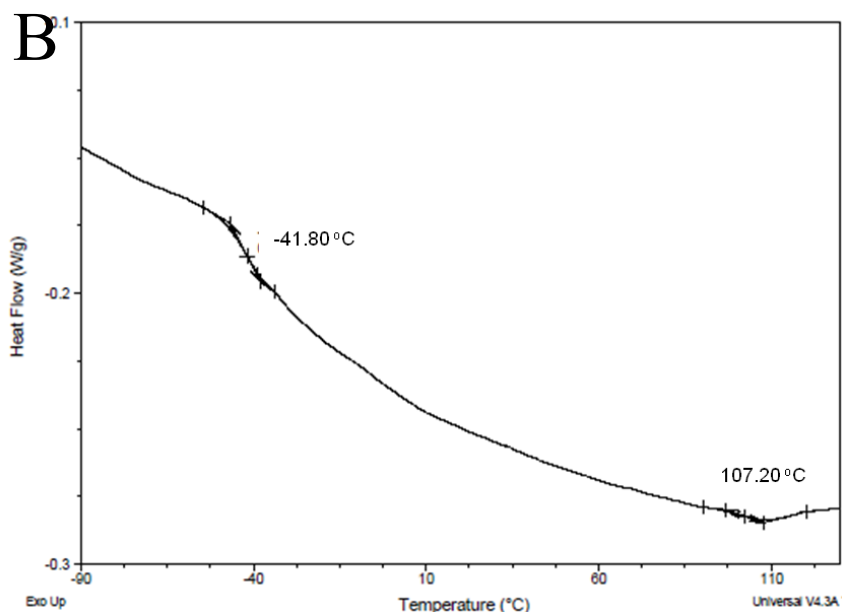


Figure 4.7 DSC analysis of pre-stretched PCHPE-*b*-PDL multiblock with 59 wt% of PCHPE (#4 in **Table 4.1**): (A) first cycle heating; (B) second cycle heating.

The shape memory effect of the sample was tested by repeatedly stretching it to strains of 300%, at ambient temperature (18 °C), which is well below the T_{trans} . Then, the sample was allowed to relax freely, at ambient temperature, for 30 min to achieve a fixed strain (ϵ_f). Subsequently, the sample was heated to T_{trans} (55 °C) for 30 s which allowed the recovery from the deformation, followed by immediate cooling to ambient temperature. **Figure 4.6** demonstrates the results of 25 consecutive thermo-mechanical cycles and illustrates the promising shape-memory properties of the multiblock copolymer. Generally, high strain fixity ratios (ca. 100%) are achieved by stretching samples at temperatures above the transition temperature, followed by cooling to the temperatures below T_g/T_m to fix the chain movement.^{34,37,62,71} In contrast, using cold-draw programming usually affords strain fixity ratios below < 100% and only approaches 100% when chemical crosslinking is applied.^{40,52} The strain fixity ratio (ca. 91%) observed in this work is competitive with the best values in the literature.^{33,46,62} Strain fixation is another key value and it demonstrates the extent to which the material can be deformed. As such it is critical to areas like medical implants which need to be added using only a small incision.^{33,62,70} However, the high strain fixation

(250-290%, see **Figure 6**, and equation 1 in the experiments chapter) is amongst the highest values reported in the field (usually below 200%).^{34,35,39,46,72} Furthermore, the sample exhibited a high strain recovery ratio of $\sim 96\%$ (see equation 2 in the experiments chapter) after being heated at just $55\text{ }^{\circ}\text{C}$, which is a considerably higher than typical for non-covalently crosslinked samples.^{34,65} Photographs illustrating the shape memory processing and effects of the sample are shown in **Figure 4.8**. The shape memory effect was also investigated on the microscopic scale using TEM. Cross sections of the samples (vertical to the extension direction) were acquired at each stage (original, stretched, recovered) and were sectioned, stained with RuO_4 and analyzed by TEM imaging. As shown in **Figure 4.8**, after being stretched, the network formed by the PCHPE phase (grey) became more compact (**Figure 4.8B**) compared to the starting morphology (**Figure 4.8A**) and this was attributed to the Poisson effect. The phenomenon occurs when a material is stretched in one direction and it tends to contract in the other two directions (perpendicular to the axis of stretching).⁶¹ After the recovery of the original shape, the morphology was observed to return to its original state (**Figure 4.8C**). Meanwhile, a series of samples that had been allowed to recover to various different extents were also characterized by SAXS (see **Figure 4.9** and experimental chapter for sample preparation details). It was observed that the domain spacing decreased from 11.9 nm to 10.5 nm after the sample was stretched to 280%. At the same time, the scattering curve shows a broadening and intensity change. It is notable that similar broadening and intensity changing effects in SAXS were also observed for other cold-draw shape-memory polymers (styrene-butadiene-styrene or styrene-isoprene-styrene).^{57,73,74} During the recovery process, which corresponded to a decrease in strain from 280% to ca. 0%, the domain spacing increases and reverts to the original value which is consistent with the recovery of the original morphology (**Figure 4.9**). A reduced shape memory effect was also observed for polymer samples with 42 and 49 wt% PCHPE, but in these cases there was less strain fixation. The 42 and 49 wt% PCHPE multiblocks only demonstrate the cold draw effect over a limited region of strain (**Figure 4.4**) and due to the lower content of the rigid block, the continuous PCHPE phase appears to be easily disrupted to separate domains at high strain values (**Figure**

4.5). Therefore, high strain fixation, which is one of the key parameters of shape memory material, is only achievable in the sample with the highest PCHPE content.

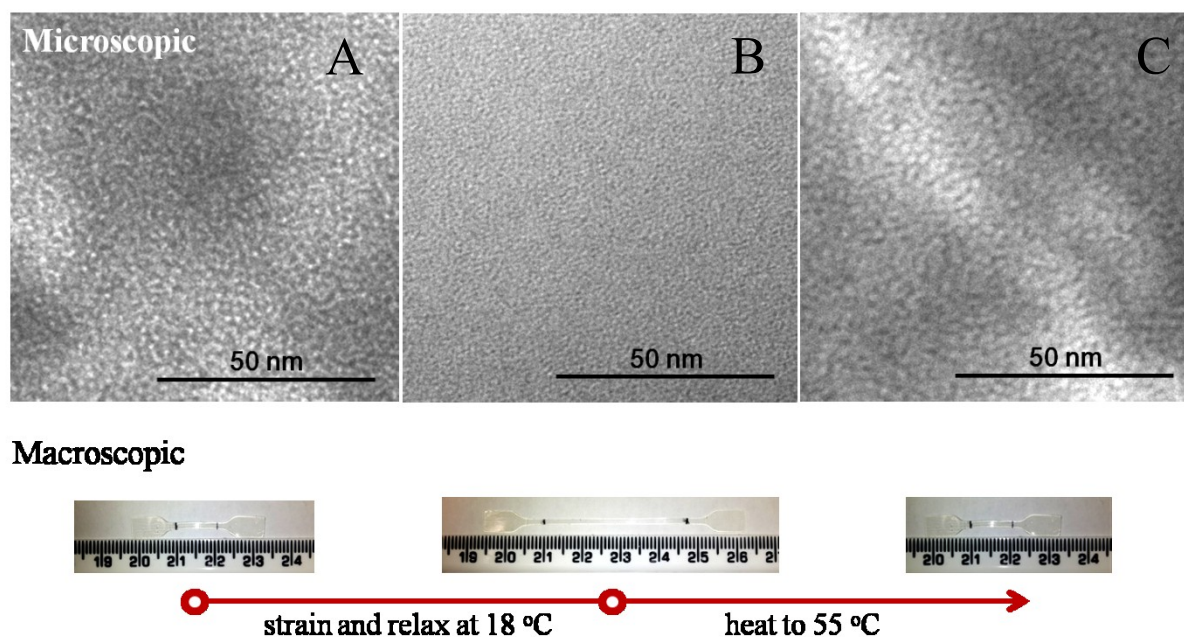


Figure 4.8 Images of the uniaxial reversible shape memory effect of PCHPE-*b*-PDL 59 wt% multiblock (#4 in **Table 4.1**). Microscopic: the cross section (vertical to the extension direction) TEM images of each stage (sectioned by ultra-microtome and stained with RuO₄). Macroscopic: optical images of each stage.

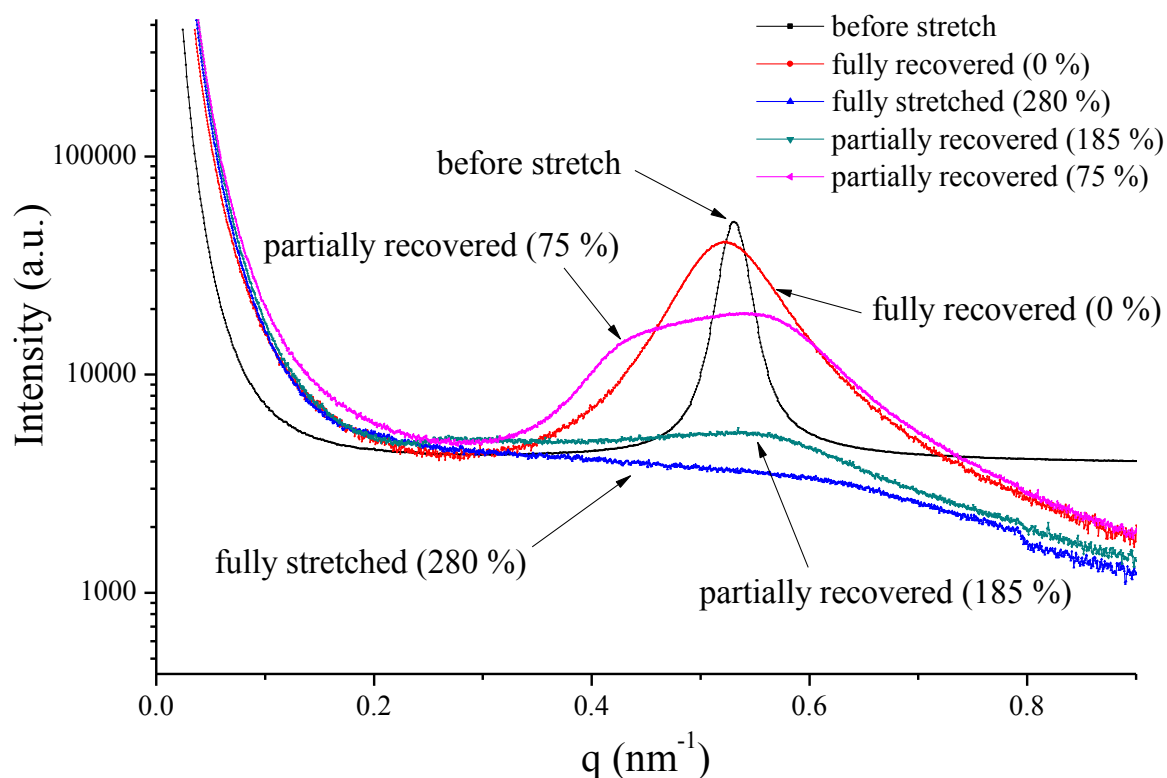


Figure 4.9 SAXS profiles of PCHPE-*b*-PDL 59 wt% multiblock (#4 in **Table 4.1**) with different fixed strain value. Domain spacing (*D*) values are calculated, using $D = 2\pi/q^*$.

4.2.5 Thermal stability and thermo mechanical properties of the multiblocks

The thermal stability of a polymer is critical for any industrial application because it sets the boundary for the processing temperature. The thermal stability of all the multiblocks was assessed by TGA characterization, under an inert atmosphere (N_2). The TGA thermograms in **Figure 4.10** indicate that all the multiblocks have similar degradation temperatures of ~ 270 °C. Given the absence of crystallinity and moderate T_g value (ca. 100 °C), PCHPE containing multiblocks might have a wide processing window ($\Delta T = 170$ °C).

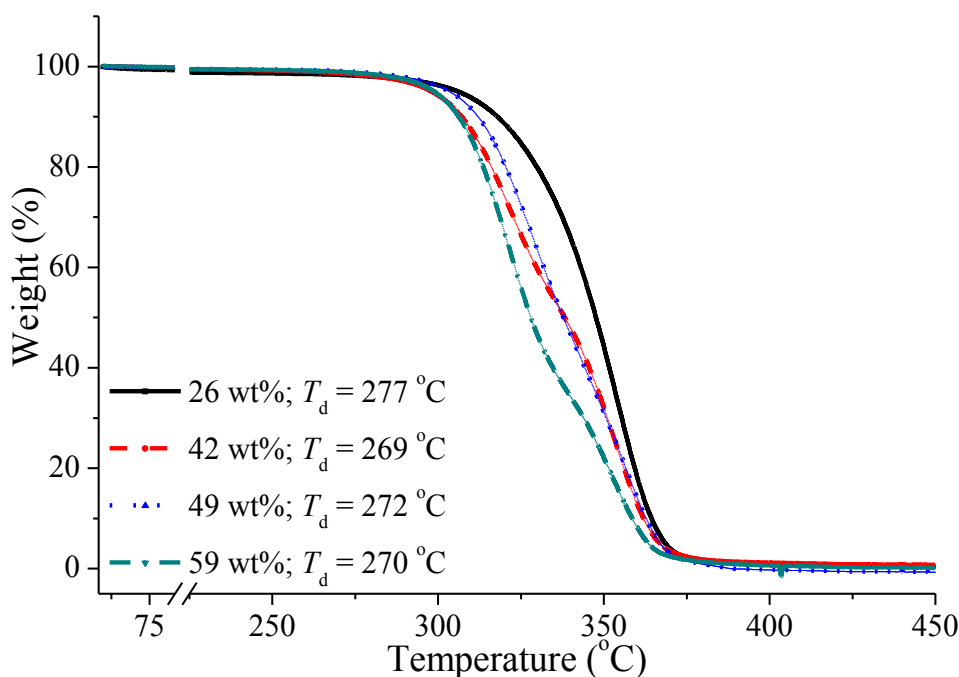


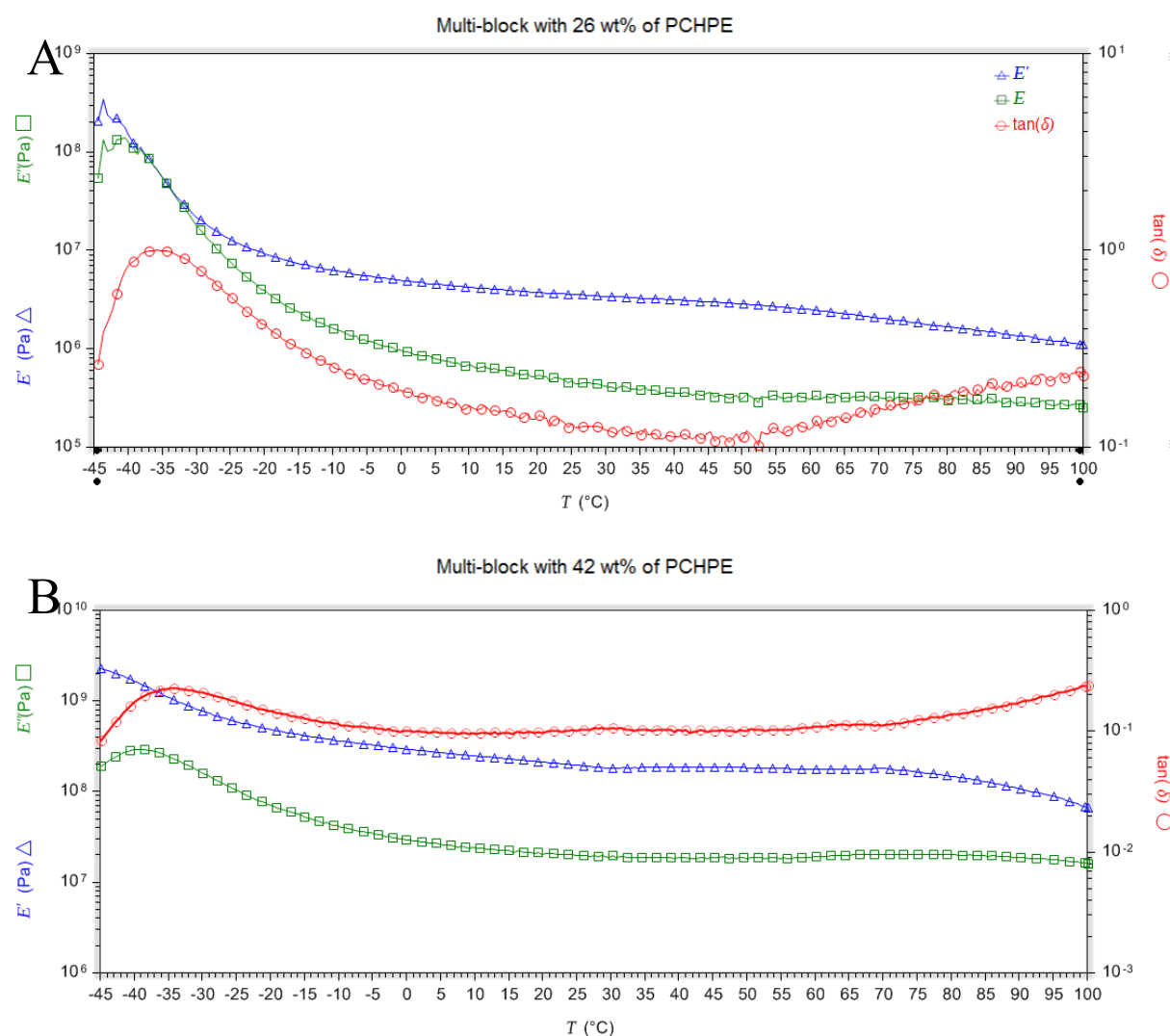
Figure 4.10 TGA profiles of the multiblocks with different PCHPE content. Heating rate: $10\text{ }^{\circ}\text{C}\cdot\text{min}^{-1}$, under N_2 .

The thermo-mechanical properties of the multiblock copolyesters were also investigated using dynamic mechanical analysis (**Figure 4.11**). **Table 4.3** summarizes the mechanical properties recorded at ambient temperature ($22\text{ }^{\circ}\text{C}$). The change in dynamic storage modulus E' as a function of temperature shows the same trends for all the multiblocks (**Figure 4.11**). It drops rapidly between $-45\text{ }^{\circ}\text{C}$ and $-10\text{ }^{\circ}\text{C}$, which corresponds to the softening of the PDL phase. Then, it reaches a plateau over the temperature range $-10\text{ }^{\circ}\text{C}$ to ca. $55\text{ }^{\circ}\text{C}$, due to the high T_g value of the PCHPE phase. Although the storage moduli of the multiblocks begin to decrease slowly above $55\text{ }^{\circ}\text{C}$, it is only a minimal effect and the values of the storage modulus remain high even at $100\text{ }^{\circ}\text{C}$ ($> 1.0\text{ MPa}$) in all cases. Additionally, no cross points between storage and loss moduli are observed. This finding indicates that the materials retain solid forms below $100\text{ }^{\circ}\text{C}$,⁷⁵ which is in-line with the high T_g values measured by DSC (**Table 4.1**). In particular, the findings are relevant for the thermoplastic elastomer sample (26 wt% sample) as the usable temperature range meets that for many commodity applications.

Table 4.3 Mechanical properties of the multiblock copolyesters with different compositions, at ambient temperature (22 °C) measured *via* DMTA.

#	wt% PCHPE	Storage Modulus E' (MPa) ^a	Loss Modulus E'' (MPa) ^a
1	26	3.8	0.5
2	42	204.5	20.5
3	49	491.0	30.4
4	59	869.8	44.3

^a) Storage and loss modulus at ambient temperature (22 °C)



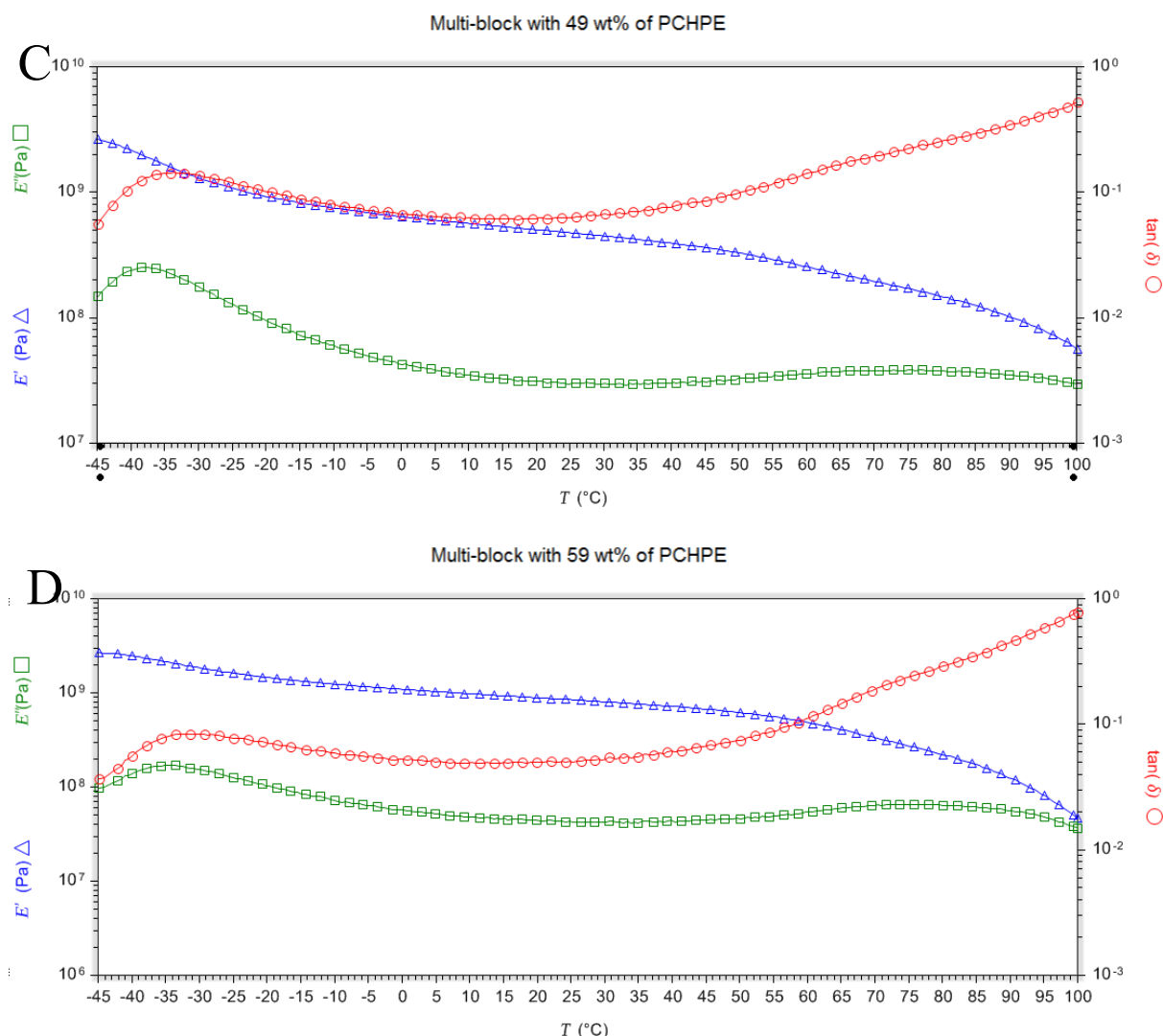


Figure 4.11 Overlay of the storage modulus E' , loss modulus E'' and $\tan(\delta)$ of the multiblock copolyesters with (A) 26 wt% of PCHPE, (B) 42 wt% of PCHPE, (C) 49 wt% of PCHPE and (D) 59 wt% of PCHPE; $\omega = 1$ Hz with 1% of strain and a 3 °C/min temperature ramp rate.

4.3 Conclusions

A series of multiblock copolyesters comprising hard and soft polyester blocks prepared from the alternating copolymerization of phthalic anhydride and cyclohexene oxide (PCHPE) and ϵ -decalactone (PDL) have been investigated. Depending on the block compositions, a range of PCHPE-*b*-PDL multiblocks showed distinctive and interesting properties relevant for higher value applications, such as thermoplastic elastomers and shape memory polymers. In the case of the lowest incorporation of hard block (26 wt% PCHPE) the polymers were excellent thermoplastic elastomers showing impressive elongation at break (ca. 2450%) with

comparable stress at break (11.5 MPa) to many existing industrial materials. In the case of the highest proportion of the hard block (59 wt% PCHPE), shape memory properties were achieved over repeated cycles comprising cold-draw at ambient temperature, and heating to 55 °C allowed near complete recovery from the deformation. The material showed a high strain fixity (> 250%) and excellent recovery ratio (> 96%), both of which are important criterion for any use of the material. The polymers' microscopic morphologies were also characterized by TEM and SAXS. It was observed that the diverse mechanical properties are in line with quite distinct nanostructures. The range of structures spans hard domains in the soft matrix, a bicontinuous phase to soft domains in the hard matrix, depending on the relative block ratios. In the case of the TPE, cylinders/worm like domains of PCHPE were observed in a continuous matrix of PDL – the morphology clearly rationalizes the observed mechanical properties. For the shape memory material (59 wt% PCHPE), changes in morphology during a shape memory cycle were also characterized by TEM and SAXS. The shape memory effect arose from a cold draw process at ambient temperature which was reversible when the sample was heated allowing recovery of its original shape and morphology. Instead of the transition temperature corresponding to the T_g of PCHPE blocks, a rather rare transition temperature consistent with the enthalpy of relaxation was applied to trigger the recovery. The low temperature recovery offers a particular advantage as a low transition temperature combined with a high T_g should allow access to materials useful for medicine. It is notable that thermoplastic elastomers showing 'strain-induced plastic-to-rubber transitions' are not well documented yet except for the SBS type elastomers.⁵⁷ It is also relevant that the new multiblock copolyesters are all expected to be degradable, although the rigid blocks are likely more slowly biodegraded. Furthermore, there are literature precedents for preparing and sourcing all the monomers from renewable raw materials.^{27,50,51} Thus, the new materials merit further development and investigation as renewable and degradable alternatives to the widely applied SBS elastomers and related materials. So far, block copolyesters prepared *via* the combination of ring-opening copolymerization and ring-opening polymerization are hardly reported for biomedical

applications, especially in drug delivery. Considering the huge monomer pool and tuneable cyclic anhydrides/epoxides, it should be possible to make block copolyesters with tailored amphiphilicity, stimuli-responsive behaviour and biocompatibility. As a first step to demonstrate the bio-application potential of such block copolyesters, a proof-of-concept study of their self-assembly, drug delivery and biodegradation behaviour is discussed in the following chapter.

4.4 References

- (1) van der Ploeg, F. J. *Econ. Lit.* **2011**, *49*, 366-420.
- (2) Jambeck, J. R.; Geyer, R.; Wilcox, C.; Siegler, T. R.; Perryman, M.; Andrady, A.; Narayan, R.; Law, K. L. *Science* **2015**, *347*, 768-771.
- (3) Zhu, Y.; Romain, C.; Williams, C. K. *Nature* **2016**, Accepted.
- (4) Spontak, R. J.; Patel, N. P. *Curr. Opin. Colloid Interface Sci.* **2000**, *5*, 334-341.
- (5) Cohn, D.; Hotovely Salomon, A. *Biomaterials* **2005**, *26*, 2297-2305.
- (6) Wanamaker, C. L.; O'Leary, L. E.; Lynd, N. A.; Hillmyer, M. A.; Tolman, W. B. *Biomacromolecules* **2007**, *8*, 3634-3640.
- (7) Martello, M. T.; Hillmyer, M. A. *Macromolecules* **2011**, *44*, 8537-8545.
- (8) Shin, J.; Lee, Y.; Tolman, W. B.; Hillmyer, M. A. *Biomacromolecules* **2012**, *13*, 3833-3840.
- (9) Guerin, W.; Helou, M.; Carpentier, J. F.; Slawinski, M.; Brusson, J. M.; Guillaume, S. M. *Polym. Chem.* **2013**, *4*, 1095-1106.
- (10) Wang, S.; Kesava, S. V.; Gomez, E. D.; Robertson, M. L. *Macromolecules* **2013**, *46*, 7202-7212.
- (11) Bolton, J. M.; Hillmyer, M. A.; Hoyer, T. R. *ACS Macro Lett.* **2014**, *3*, 717-720.
- (12) Martello, M. T.; Schneiderman, D. K.; Hillmyer, M. A. *ACS Sustainable Chem. Eng.* **2014**, *2*, 2519-2526.
- (13) Crawford, K. E.; Sita, L. R. *ACS Macro Lett.* **2015**, *4*, 921-925.
- (14) Wang, Z.; Yuan, L.; Trenor, N. M.; Vlaminc, L.; Billiet, S.; Sarkar, A.; Du Prez, F. E.; Stefik, M.; Tang, C. *Green Chem.* **2015**, *17*, 3806-3818.
- (15) Montarnal, D.; Capelot, M.; Tournilhac, F.; Leibler, L. *Science* **2011**, *334*, 965-968.
- (16) Altuna, F. I.; Pettarin, V.; Williams, R. J. J. *Green Chem.* **2013**, *15*, 3360-3366.
- (17) Albertsson, A.-C.; Voepel, J.; Edlund, U.; Dahlman, O.; Soderqvist-Lindblad, M. *Biomacromolecules* **2010**, *11*, 1406-1411.
- (18) Du, Y. Z.; Yu, M.; Ge, J.; Ma, P. X.; Chen, X. F.; Lei, B. *Adv. Funct. Mater.* **2015**, *25*, 5016-5029.
- (19) Tran, C. D.; Chen, J.; Keum, J. K.; Naskar, A. K. *Adv. Funct. Mater.* **2016**, *26*, 2677-2685.
- (20) Lee, S. H.; Cyriac, A.; Jeon, J. Y.; Lee, B. Y. *Polym. Chem.* **2012**, *3*, 1215-1220.
- (21) Bates, F. S.; Hillmyer, M. A.; Lodge, T. P.; Bates, C. M.; Delaney, K. T.; Fredrickson, G.

H. *Science* **2012**, *336*, 434-440.

- (22) Xiong, M. Y.; Schneiderman, D. K.; Bates, F. S.; Hillmyer, M. A.; Zhang, K. C. *Proc. Natl. Acad. Sci. U. S. A.* **2014**, *111*, 8357-8362.
- (23) Cordier, P.; Tournilhac, F.; Soulie-Ziakovic, C.; Leibler, L. *Nature* **2008**, *451*, 977-980.
- (24) Fakirov, S. *Handbook of Condensation Thermoplastic Elastomers*; WILEY-VCH Verlag GmbH & Co. KGaA: Weinheim, 2005.
- (25) Martello, M. T.; Hillmyer, M. A. *Macromolecules* **2011**, *44*, 8537-8545.
- (26) Schneiderman, D. K.; Vanderlaan, M. E.; Mannion, A. M.; Panthani, T. R.; Batiste, D. C.; Wang, J. Z.; Bates, F. S.; Macosko, C. W.; Hillmyer, M. A. *ACS Macro Lett.* **2016**, *5*, 515-518.
- (27) Lin, J.-O.; Chen, W.; Shen, Z.; Ling, J. *Macromolecules* **2013**, *46*, 7769-7776.
- (28) Tang, D.; Macosko, C. W.; Hillmyer, M. A. *Polym. Chem.* **2014**, *5*, 3231-3237.
- (29) Liu, Y.; Yao, K.; Chen, X.; Wang, J.; Wang, Z.; Ploehn, H. J.; Wang, C.; Chu, F.; Tang, C. *Polym. Chem.* **2014**, *5*, 3170-3181.
- (30) Hauenstein, O.; Reiter, M.; Agarwal, S.; Rieger, B.; Greiner, A. *Green Chem.* **2016**, *18*, 760-770.
- (31) Hillmyer, M. A.; Tolman, W. B. *Acc. Chem. Res.* **2014**, *47*, 2390-2396.
- (32) Madhavan Nampoothiri, K.; Nair, N. R.; John, R. P. *Bioresour. Technol.* **2010**, *101*, 8493-8501.
- (33) Lendlein, A.; Kelch, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 2034-2057.
- (34) Lendlein, A.; Langer, R. *Science* **2002**, *296*, 1673-1676.
- (35) Neffe, A. T.; Hanh, B. D.; Steuer, S.; Lendlein, A. *Adv. Mater.* **2009**, *21*, 3394-3398.
- (36) Xue, L. A.; Dai, S. Y.; Li, Z. *Biomaterials* **2010**, *31*, 8132-8140.
- (37) Serrano, M. C.; Carbajal, L.; Ameer, G. A. *Adv Mater* **2011**, *23*, 2211-2215.
- (38) Yao, X.; Dunn, S. S.; Kim, P.; Duffy, M.; Alvarenga, J.; Aizenberg, J. *Angew. Chem., Int. Ed.* **2014**, *53*, 4418-4422.
- (39) Zhou, J.; Turner, S. A.; Brosnan, S. M.; Li, Q.; Carrillo, J.-M. Y.; Nykypanchuk, D.; Gang, O.; Ashby, V. S.; Dobrynin, A. V.; Sheiko, S. S. *Macromolecules* **2014**, *47*, 1768-1776.
- (40) Lewis, C. L.; Meng, Y.; Anthamatten, M. *Macromolecules* **2015**, *48*, 4918-4926.
- (41) Wang, Z.; Zhang, Y.; Yuan, L.; Hayat, J.; Trenor, N. M.; Lamm, M. E.; Vlaminck, L.; Billiet, S.; Du Prez, F. E.; Wang, Z.; Tang, C. *ACS Macro Lett.* **2016**, 602-606.
- (42) Lendlein, A.; Jiang, H.; Junger, O.; Langer, R. *Nature* **2005**, *434*, 879-882.
- (43) Yu, Z.; Zhang, Q.; Li, L.; Chen, Q.; Niu, X.; Liu, J.; Pei, Q. *Adv Mater* **2011**, *23*, 664-668.
- (44) Deng, J. E.; Zhang, Y.; Zhao, Y.; Chen, P. N.; Cheng, X. L.; Peng, H. S. *Angew. Chem., Int. Ed.* **2015**, *54*, 15419-15423.
- (45) Hu, J. L.; Meng, H. P.; Li, G. Q.; Ibekwe, S. I. *Smart Mater. Struct.* **2012**, *21*, 1-23.
- (46) Guo, M.; Pitet, L. M.; Wyss, H. M.; Vos, M.; Dankers, P. Y. W.; Meijer, E. W. *J. Am. Chem. Soc.* **2014**, *136*, 6969-6977.
- (47) Lowe, J. R.; Tolman, W. B.; Hillmyer, M. A. *Biomacromolecules* **2009**, *10*, 2003-2008.
- (48) Wu, T. F.; Frydrych, M.; O'Kelly, K.; Chen, B. Q. *Biomacromolecules* **2014**, *15*, 2663-2671.

- (49) Zhu, Y.; Romain, C.; Williams, C. K. *J Am Chem Soc* **2015**, *137*, 12179-12182.
- (50) Mahmoud, E.; Watson, D. A.; Lobo, R. F. *Green Chem.* **2014**, *16*, 167-175.
- (51) Winkler, M.; Romain, C.; Meier, M. A. R.; Williams, C. K. *Green Chem.* **2015**, *17*, 300-306.
- (52) Zotzmann, J.; Behl, M.; Feng, Y.; Lendlein, A. *Adv. Funct. Mater.* **2010**, *20*, 3583-3594.
- (53) Van Zee, N. J.; Coates, G. W. *Chem. Commun.* **2014**, *50*, 6322-6325.
- (54) Nejad, E. H.; Paoniasari, A.; van Melis, C. G. W.; Koning, C. E.; Duchateau, R. *Macromolecules* **2013**, *46*, 631-637.
- (55) DiCiccio, A. M.; Coates, G. W. *J. Am. Chem. Soc.* **2011**, *133*, 10724-10727.
- (56) Jeske, R. C.; DiCiccio, A. M.; Coates, G. W. *J. Am. Chem. Soc.* **2007**, *129*, 11330-11331.
- (57) Hashimoto, T.; Fujimura, M.; Saijo, K.; Kawai, H.; Diamant, J.; Shen, M. In *Multiphase Polymers*; American Chemical Society: 1979; Vol. 176, p 257-275.
- (58) Vinogradov, G. V.; Ya. Malkin, A.; Volosevitch, V. V.; Shatalov, V. P.; Yudin, V. P. *J. Polym. Sci., Part B: Polym. Phys.* **1975**, *13*, 1721-1735.
- (59) Pokrovskii, V. N. *Polym. Mech.* **1968**, *4*, 189-195.
- (60) Vincent, P. I. *Polymer* **1960**, *1*, 7-19.
- (61) Bower, D. *An Introduction to Polymer Physics*; Cambridge University Press, 2002.
- (62) Hu, J. L.; Zhu, Y.; Huang, H. H.; Lu, J. *Prog. Polym. Sci.* **2012**, *37*, 1720-1763.
- (63) Katzenberg, F.; Heuwers, B.; Tiller, J. C. *Adv. Mater.* **2011**, *23*, 1909-1911.
- (64) Wang, W.; Jin, Y.; Ping, P.; Chen, X. S.; Jing, X. B.; Su, Z. H. *Macromolecules* **2010**, *43*, 2942-2947.
- (65) Mohr, R.; Kratz, K.; Weigel, T.; Lucka-Gabor, M.; Moneke, M.; Lendlein, A. *Proc. Natl. Acad. Sci. U. S. A.* **2006**, *103*, 3540-3545.
- (66) Xie, T. *Polymer* **2011**, *52*, 4985-5000.
- (67) Yianakopoulos, G.; Vanderschueren, J.; Niezette, J. *IEEE Trans. Electr. Insul.* **1989**, *24*, 429-438.
- (68) Berens, A. R.; Hodge, I. M. *Macromolecules* **1982**, *15*, 756-761.
- (69) Pakula, T.; Trznadel, M. *Polymer* **1985**, *26*, 1011-1018.
- (70) Meng, H.; Li, G. Q. *Polymer* **2013**, *54*, 2199-2221.
- (71) Fritzsche, N.; Pretsch, T. *Macromolecules* **2014**, *47*, 5952-5959.
- (72) Li, Y.; Pruitt, C.; Rios, O.; Wei, L.; Rock, M.; Keum, J. K.; McDonald, A. G.; Kessler, M. R. *Macromolecules* **2015**, *48*, 2864-2874.
- (73) Honeker, C. C.; Thomas, E. L.; Albalak, R. J.; Hajduk, D. A.; Gruner, S. M.; Capel, M. C. *Macromolecules* **2000**, *33*, 9395-9406.
- (74) Prasman, E.; Thomas, E. L. *J. Polym. Sci., Part B: Polym. Phys.* **1998**, *36*, 1625-1636.
- (75) Mezger, T. G. *The Rheology Handbook*; Vincentz Network: Hannover, 2011.

Chapter 5

Non-toxic and degradable amphiphilic polyesters for drug delivery applications

5.1 Background and Aims

As one of the most interesting classes of biomaterials, polymers, either natural or synthetic, have long been tailored to interact with biological systems for biomedical applications. Degradable polymers are of high interest because they break down, *via* hydrolytic or enzymatic process, into small molecules which can be excreted or absorbed by the body rather than accumulating *in vivo* or requiring removal by surgery.¹ Although collagen and other natural polymers have been applied in biomedicine since the very beginning of human history, comparable research into degradable synthetic polymers is still at an early stage, in terms of clinic application.¹ In the design of degradable polymers for bio-applications, especially drug delivery, some key criteria should be met: (1) the polymer should be non-toxic; (2) the polymer backbone should be both hydrolytically and/or enzymatically degradable;^{1,2} (3) the degradation products should be non-toxic and readily absorbed or excreted;^{1,2} (4) the polymer should contain amphiphilic or stimuli-responsive moieties to enable formation of colloidal nanostructures in aqueous solutions in the field of self-assembly; (5) the degradation time scale should be tuneable or suitable for the target application. Over the past fifty years, a range of degradable synthetic polymers with different backbone structure have been developed, including successful uses of polypeptides,³⁻⁵ polysaccharides,⁶⁻⁸ poly(α -esters),^{9,10} polyanhydrides,^{11,12} polycarbonates¹³⁻¹⁷ and polyphosphesters.¹⁸⁻²⁰ Unfortunately, most of these synthetic degradable polymers can meet only a few of the criteria listed above. Aliphatic polyesters are particularly effective as they are biodegradable and biocompatible and polymers such as PCL and PLA may even be suitable as hydrophobic components of polymer self-assemblies.²¹⁻²⁷

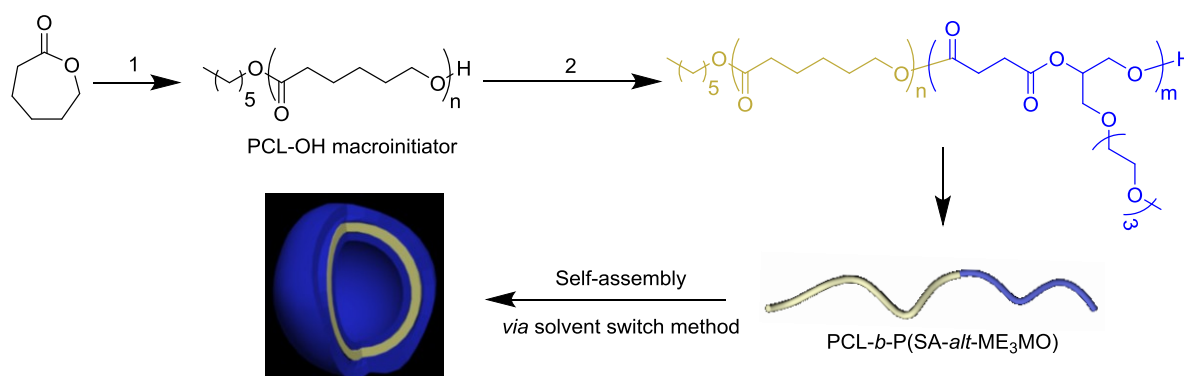
To date, most of the aliphatic polyesters are prepared *via* the ring-opening polymerization (ROP) of cyclic esters, such as ϵ -caprolactone and lactide. Although a wide range of functionalized cyclic esters have been reported in literature, polymerization can be limited by issues of ring-strain and side reactions, and is usually less well controlled.²⁸ Only few cyclic esters have really been applied to make biomaterials and in most cases these polymers are hydrophobic (e.g. PCL and PLA). Such commonly used aliphatic polyesters need to

incorporate other hydrophilic polymer blocks, e.g. PEG, to achieve amphiphilicity and water solubility.^{21-23,25,26} So far, there are some reports of amphiphilic and aliphatic block copolyesters.²⁹ However, the functional lactones are usually hard to synthesis, and most importantly, there is very little exploration of their biomedical applications.

An alternative controlled synthetic method is the ring-opening copolymerization (ROCOP) of cyclic anhydrides and epoxides to produce alternating polyesters. Whilst the range of polymerizable lactones is quite narrow, there is a much larger pool of epoxides and cyclic anhydrides, indeed many are commercial products.³⁰ Furthermore, the properties, including the amphiphilicity, stimuli-responsive behaviour, biodegradability and biocompatibility of the alternating polyesters can be more easily controlled by changing either the cyclic anhydride or epoxide monomer. However, research into amphiphilic or hydrophilic alternating polyesters produced by ROCOP is rather limited.^{2,31,32} In the related area of CO₂/epoxide ROCOP various amphiphilic poly(carbonate-*b*-phosphoester)s and hydrophilic polycarbonates have been reported.³³⁻³⁵ The potential for bio-medical applications for these alternating polycarbonates was also demonstrated.³³⁻³⁵ However, the biocompatibility and biodegradability of the polymers was not yet reported. Considering the similarity between ROCOP to make polyesters and polycarbonates and the potential to introduce two different functional groups in an alternating manner along the polyester chains, it is interesting to develop amphiphilic or hydrophilic ROCOP polyesters for biomedical applications. Another key issue is the toxicity of the polyester degradation products. Usually, the toxicity of the polymers is well characterized, but so far many studies ignore or make assumptions regarding toxicity of the degradation products.^{34,36,37}

To address these challenges, amphiphilic block copolyesters able to be both biodegradable and biocompatible were targeted. In this work, the synthetic route to them applied a combination of ROP and ROCOP (**Scheme 5.1**). Amphiphilic block copolyesters of the type, PCL-*b*-P(SA-*alt*-ME₃MO), with different hydrophilic/hydrophobic ratios were targeted for self-assembly behaviour, biodegradability and drug release profile studies. The monomer

ME₃MO has already been reported in a poly(ether-co-ester) system which showed potential thermal-responsive behaviour, and specifically showed the lower critical solution temperature (LCST).^{31,32,38} Depending on the number of the pendent ethylene glycol units, the LCST was tuned from 15 °C to 70 °C. To improve the thermal stability of the polymer self-assembly in this study, an epoxide monomer with 3 ethylene glycol units was selected as the co-monomer. It is notable that two other monomers, MEMO and ME₂MO, also have great potential in the preparation of stimuli-responsive self-assemblies, and will certainly be good candidates for future investigations. **Scheme 5.1** illustrates the target copolymers and possible route to self-assembly.



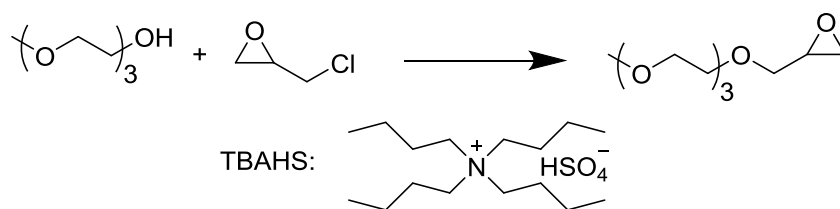
Scheme 5.1 Schematic illustration of the proposed preparation of amphiphilic block copolyesters, PCL-*b*-P(SA-*alt*-ME₃MO), and the self-assembly procedure. Reaction conditions: (1) ring-opening polymerization of ε-caprolactone in toluene initiated from n-hexanol, using TBD as the catalyst at 25 °C; (2) ring-opening copolymerization of succinic anhydride and ME₃MO in toluene initiated from PCL-OH macroinitiator, using [salenCrCl/PPNCl] catalyst system at 80 °C.

5.2 Results and Discussion

5.2.1 Synthesis of the hydrophilic epoxide monomer

The hydrophilic epoxide monomer (ME₃MO) was synthesized according to a previously reported method (see **Scheme 5.2** for synthetic route and **Figure 5.1** for ¹H NMR details, the

detailed procedure is described in the experimental chapter).³⁹ The yield (65%) is also comparable with the value (70%) reported in the literature.



Scheme 5.2 Synthetic route of the hydrophilic epoxide monomer.³⁹ Reaction conditions: in NaOH aqueous solution (50 wt%) with the presence of tetrabutylammonium hydrogen sulphate (TBAHS) at 25 °C for 5.0 h.

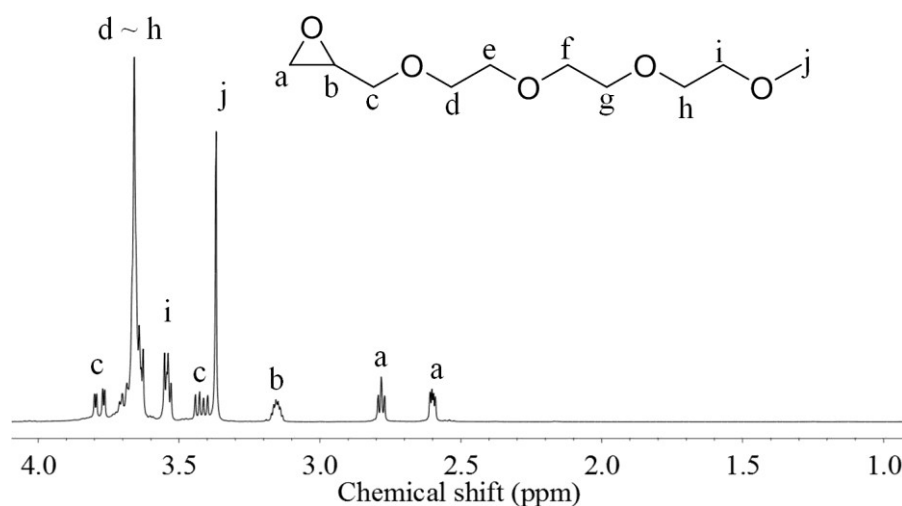


Figure 5.1 ^1H NMR data of the hydrophilic epoxide monomer, ME_3MO .

5.2.2 Preparation of the amphiphilic block copolyesters with different block ratios

The aliphatic block copolyesters were synthesized *via* a combination of ring-opening polymerization and ring-opening copolymerization. Two monofunctional PCL-OH macroinitiators, $\text{PCL}_{38}\text{-OH}$ and $\text{PCL}_{54}\text{-OH}$, were prepared by the ring-opening polymerization of $\epsilon\text{-CL}$ initiated from *n*-hexanol, using an organo-catalyst (1,5,7-Triazabicyclo[4.4.0]dec-5-ene, TBD) at 25 °C in toluene. The catalyst system afforded PCL-OH macroinitiators with predictable molecular weight and narrow dispersities (see **Table 5.1**). The $\overline{\text{DP}}$ values of the macroinitiators were calculated from ^1H NMR spectra, by

analysis of the integrals assigned to the methyl end groups and the repeat units (peaks a and c in **Figure 5.2A**). The values were in close agreement with the molecular weight determined by SEC, after applying the correction factor (0.56 as discussed in Table 2.1).

Since the morphology of polymeric self-assemblies are determined by the ratio of the hydrophobic/hydrophilic blocks, two amphiphilic block copolyesters were prepared with different block ratios. The weight contents of the hydrophobic block (PCL) were 66 wt% and 73 wt%, respectively, which is expected to afford different morphologies during self-assembly (**Table 5.1**).

The block copolyesters, PCL-*b*-P(SA-*alt*-ME₃MO), were synthesized by the ROCOP approach catalyzed by a [salenCrCl/PPNCl] catalyst system, using PCL-OH as the macroinitiator. The ¹H NMR spectrum of a representative polymer is shown in **Figure 5.2**. The amphiphilic block copolyesters all showed moderate MW and narrow molecular weight dispersity values (< 1.2) (entry 3-5, **Table 5.1**). There was some contamination of the block copolyesters by poly(SA-*alt*-ME₃MO). The formation of poly(SA-*alt*-ME₃MO) occurred due to the initiation of chains by Cl⁻ anions, from the catalyst system [salenCr(Cl)/PPNCl]. Although the free P(SA-*alt*-ME₃MO) polyester can be easily separated from PCL-*b*-P(SA-*alt*-ME₃MO) block copolyesters, by simple precipitation using MeOH, its presence makes the prediction of molecular weight of the block copolyesters very difficult. The molar percentage of each of the monomers (cyclic anhydride and epoxide) enchainned to the PCL macroinitiator was usually ~40%, calculated based on the ratio of converted monomers and monomers enchainned to PCL-OH as determined by NMR spectroscopy (**Table 5.1**). The removal of free P(SA-*alt*-ME₃MO) polyesters was monitored using SEC and ¹H DOSY NMR (see **Figure 5.4** for representative ¹H DOSY NMR spectrum of isolated diblock copolyester) to ensure the complete removal of the free polyesters. Using this approach, it was still possible to control the molecular weight empirically and the experiments afforded various PCL-*b*-P(SA-*alt*-ME₃MO) block copolyesters with different block compositions (**Table 5.1**, see **Figure 5.3** for the corresponding SEC traces).

There are many factors that control the morphology of the self-assembled nanostructures, such as the hydrophilic/hydrophobic ratio, the polymer concentration, salt concentration, pH value, temperature and the nature of the solvent. The hydrophilic/hydrophobic ratio is considered as the most important factor.⁴⁰ Empirically, block copolymers with the hydrophilic/hydrophobic ratio higher than 1:1 afford micelles; block copolymers with the ratio lower than 1:2 tend to form vesicles.⁴⁰ However, these values are empirical and thus may not be true for a certain block copolymer.⁴⁰ Therefore, a range of block copolymers with different hydrophilic/hydrophobic ratios were prepared to afford different morphologies. The weight contents of the hydrophobic block (PCL) were targeted to be 66 wt%, 73 wt% and 79 wt%, respectively (**Table 5.1**, entry 3-5). In control experiments, pure PCL precipitated during the self-assembly process (**Table 5.1**, entry 1 and 2), while pure P(SA-*alt*-ME₃MO) polyester was completely hydrophilic at 25 °C.

Table 5.1 Synthesis of the amphiphilic block copolyesters with different compositions. The polymer data were acquired from purified polymers.

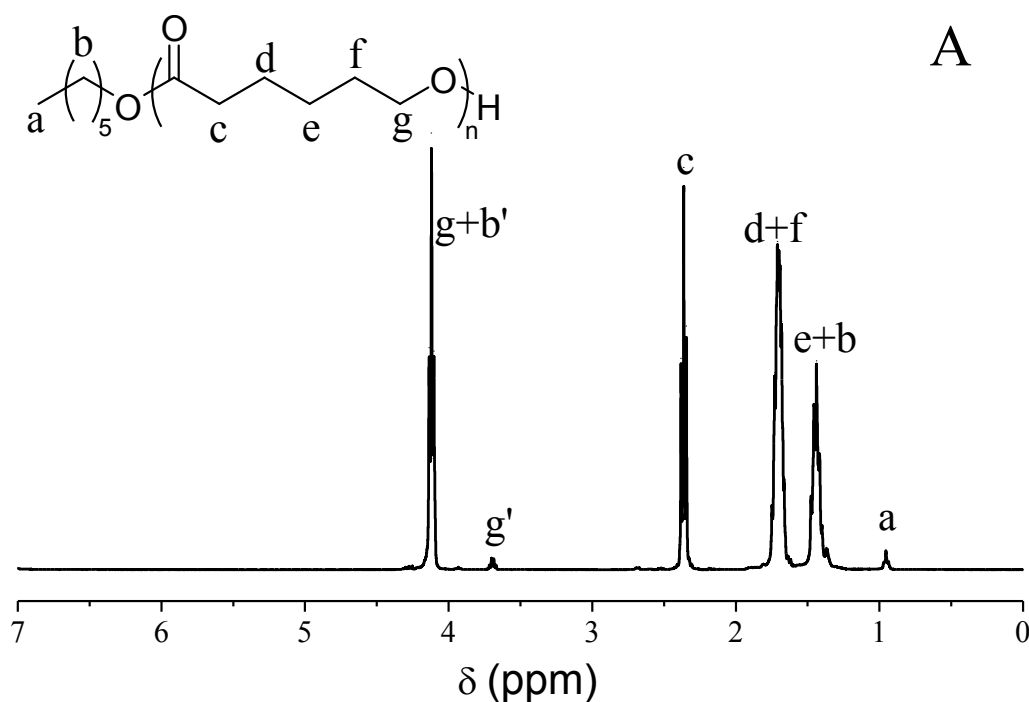
#	Polymer	wt% of PCL	$M_{n,theo}$ (kDa) ^c	$M_{n,NMR}$ (kDa) ^d	$M_{n,SEC}$ (kDa) ^e	$\bar{D}$
1	PCL ₃₈ -OH ^a	100	4.6	4.3	4.4 ^f	1.15
2	PCL ₅₄ -OH ^a	100	5.7	6.2	6.4 ^f	1.20
3	PCL ₃₈ - <i>b</i> -P(SA- <i>alt</i> -ME ₃ MO) ₇ ^b	66	9.1	6.6	11.0	1.13
4	PCL ₅₄ - <i>b</i> -P(SA- <i>alt</i> -ME ₃ MO) ₇ ^b	73	11.0	8.4	16.5	1.18
5	PCL ₅₄ - <i>b</i> -P(SA- <i>alt</i> -ME ₃ MO) ₅ ^b	79	9.8	7.7	14.3	1.20

^a) Polymerization Conditions for #1-2: All polymerizations were run in toluene with the initial concentration of ϵ -CL at 5.0 M using *n*-hexanol as the CTA at 25 °C for 6.5-10.0 h. See supporting information for details. ^b) Polymerization Conditions for #3-5:

$[SalenCrCl]/[PPNCl]/[PCL-OH]/[SA]/[ME_3MO] = 1/1/10/(150-200)/(170-220)$. All polymerizations were run in toluene as the reaction solvent, at 80 °C for 6.0-9.0 h, with an initial concentration of SA at 1.0 M. Reactions were terminated at close to full conversion of SA (conv. of SA = ca. 90%). ^c) Theoretical molecular weight of #1-2 was determined on the basis of $([\epsilon-CL] \times \text{conversion} \times M_{[\epsilon-CL]})/[CTA]$, while the theoretical molecular weight of

#3-5 was determined on the basis of $([SA] \times \text{conversion} \times M_{[SA+ME3MO]})/([PCL-OH] + [Cl])$.

^{d)} Calculated on the basis of the ^1H NMR integrals, the methyl end group was used as the internal reference for #1-2 (comparing the integrals of peaks a and c in **Figure 5.2A**), while PCL-OH was used as internal reference for #3-5 (comparing the integrals of peak c and peak h in **Figure 5.2B**). ^{e)} Determined by THF SEC at 30 °C calibrated using narrow MW polystyrene standards. ^{j)} Corrected M_n with a correction factor (0.56) applied as described by Soum et al.⁴¹



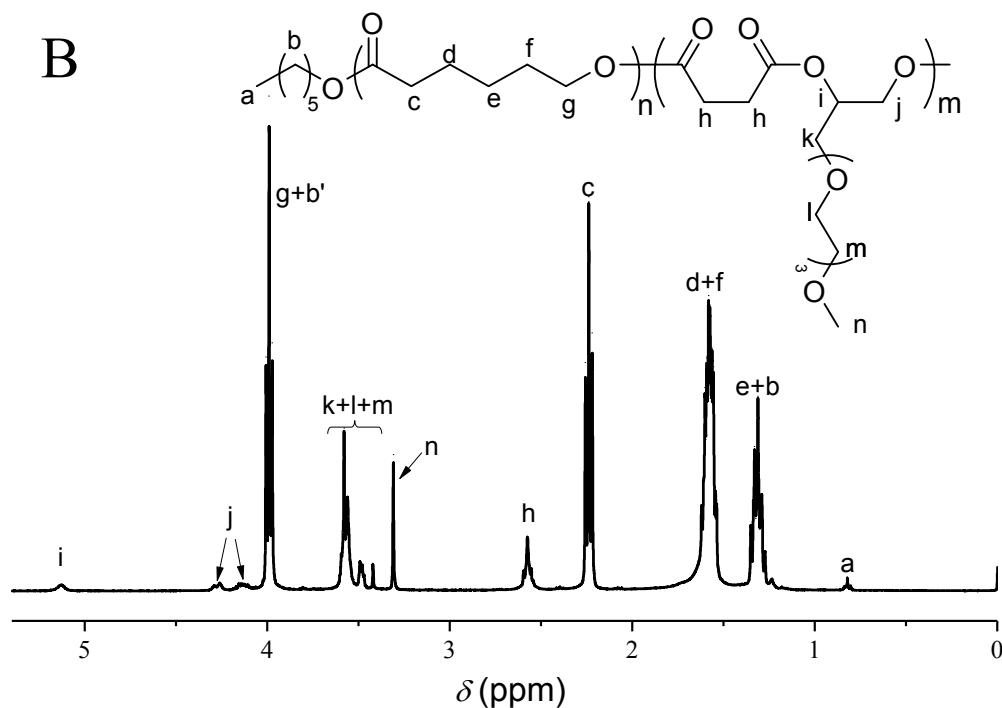


Figure 5.2 Typical ¹H NMR spectrum of (A) PCL-OH macroinitiator (**Table 5.1**, entry 1) and (B) PCL-*b*-P(SA-*alt*-ME₃MO) (**Table 5.1**, entry 3).

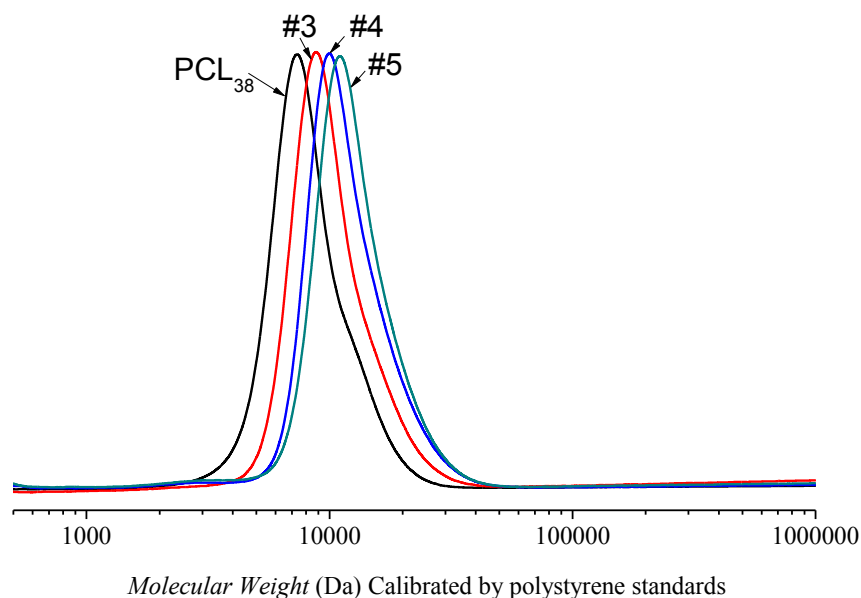


Figure 5.3 SEC traces of PCL-*b*-P(SA-*alt*-ME₃MO), corresponding to polymers listed in **Table 5.1**.

5.2.3 Characterization of the block copolymer architecture

To evaluate the block copolymer architecture, ^1H DOSY spectroscopy was employed. A typical spectrum is displayed in **Figure 5.4**, the diffusion coefficients attributed to both the PCL block and P(SA-*alt*-ME₃MO) block are very close to each other, indicating that these two blocks are most likely covalently attached to each other and implying the successful removal of free hydrophilic polyester. However, it is noteworthy that the diffusion coefficients of the PCL block and P(SA-*alt*-ME₃MO) block are not exactly the same (**Figure 5.4**). Therefore, further investigation is required to confirm the ^1H DOSY result and compare the block copolymer with the blend of two homopolymers (with similar block length). This observation was confirmed by $^{31}\text{P}\{^1\text{H}\}$ NMR spectroscopy. The ^{31}P NMR method allows the end groups of PCL-OH and P(SA-*alt*-ME₃MO) to be distinguished.⁴² It is based on different shifts chemical shifts being observed after reacting the -OH groups with excess 2-chloro-4,4,5,5-tetramethyl dioxaphospholane and using bisphenol A (BPA) as an internal standard.^{42,43} The end groups of the polymers before and after the propagation of P(SA-*alt*-ME₃MO) block were characterized (see **Figure 5.5**). After propagation of the P(SA-*alt*-ME₃MO) block, the signal assigned to the -OH end group of PCL (147.85 ppm) completely disappeared, while new signals at 147.05 ppm and 135.50 ppm appeared, which are assigned to the -OH and -COOH end groups of PCL-*b*-P(SA-*alt*-ME₃MO). In previous research, it was observed that steric effects of the bulky organometallic catalyst and the nature of -OH groups resulted in ring-opening polymerization being initiated from one or two of the -OH end groups of diols.⁴⁴ In the case of the macroinitiator PCL-OH, the end groups analysis suggested that all chains initiate the second block.

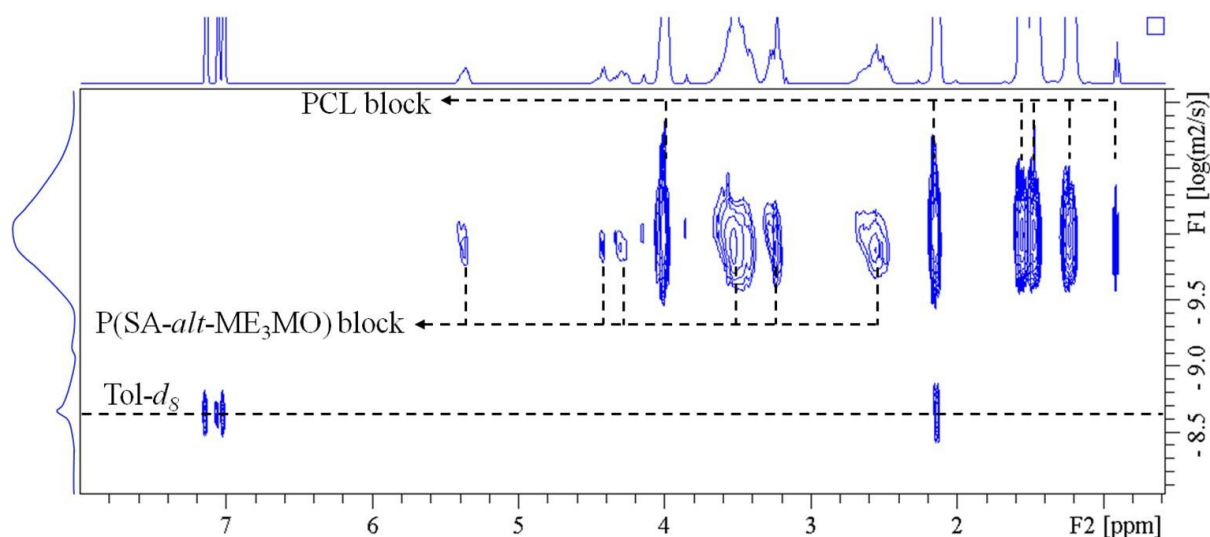


Figure 5.4 A representative ^1H NMR DOSY spectrum of PCL-*b*-P(SA-*alt*-ME₃MO) in toluene-*d*₈. (Table 5.1, entry 5).

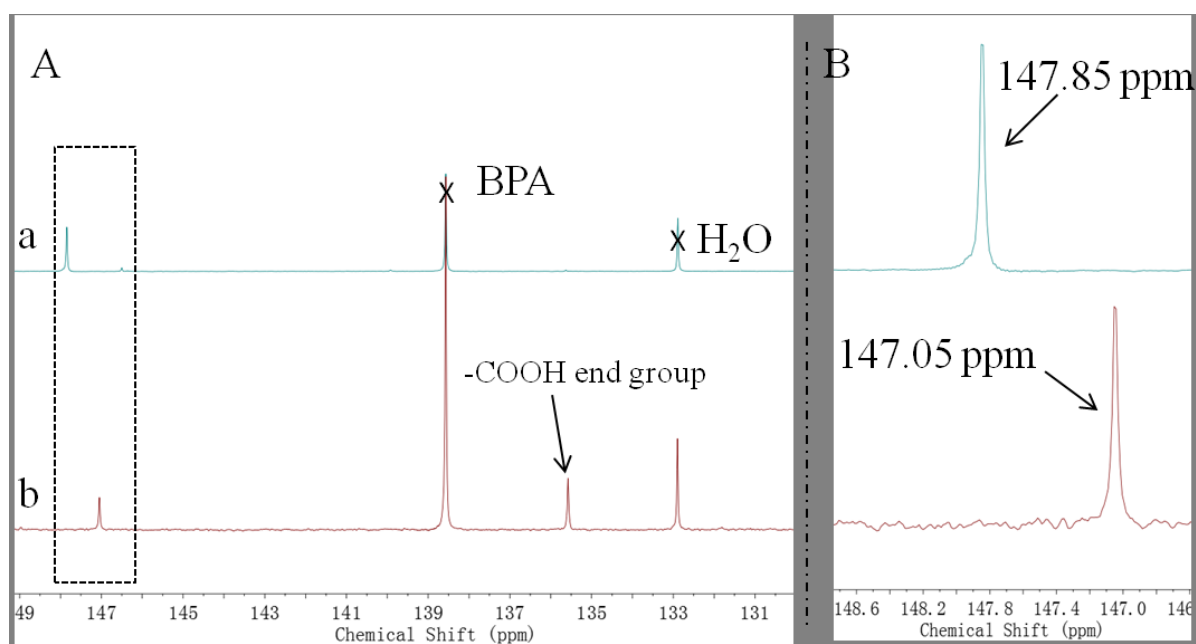


Figure 5.5 (A) A typical $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum in CDCl_3 of (a) PCL-OH (Table 5.1, entry 1) and (b) PCL-*b*-P(SA-*alt*-ME₃MO) (Table 5.1, entry 5) after being reacted with 2-chloro-4,4,5,5-tetramethyl dioxaphospholane (using bisphenol A as internal reference); (B) the enlarged $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum corresponding to the highlighted area in (A). The signals at 147.85 ppm and 147.05 ppm are assigned to the primary $-\text{OH}$ end groups of the PCL-OH macroinitiator and the $-\text{OH}$ end group of PCL-*b*-P(SA-*alt*-ME₃MO) block

copolyester, respectively. The carboxylate acid signal in (b) is also assigned to the PCL-*b*-P(SA-*alt*-ME₃MO) block copolyester (end capped by the succinic acid unit).

5.2.4 Investigation of the self-assembly of the amphiphilic block copolyesters

Self-assembled nanostructures were formed *via* the commonly used ‘Solvent Switch’ method.³⁶ The amphiphilic block copolyesters were first dissolved in THF at a concentration of ~1.25 mg/mL, followed by the dropwise addition of excess DI water at 25 °C. As shown in **Table 5.2** and **Figure 5.6**, DLS was used to determine that the amphiphilic block copolyesters formed self-assemblies with low polydispersities (PDI). The hydrodynamic diameter of #1, #2 and #3 were determined to be 53 nm (PDI 0.38), 398 nm (PDI 0.17) and 277 nm (PDI 0.25), respectively, indicating the formation of micelles in #1 and vesicles in #2 and #3. The proposed structures were also confirmed by TEM analysis (*vide infra*). To verify the reliability of the DLS results, both the raw correlation data and the cumulant fit curves were examined (**Figure 5.7**). It was observed that there were very low cumulant fit errors (< 0.005) and the flat baselines observed in the raw correlation data indicate that the corresponding DLS results (D_h and PDI) listed in **Table 5.2** are reliable.

Table 5.2 DLS analysis of the self-assemblies of the block copolyesters, prepared as per Table 5.1.^a

#	Block copolymer	D_h (nm)	PDI	Proposed morphology
1	PCL ₃₈ - <i>b</i> -P(SA- <i>alt</i> -ME ₃ MO) ₇	53	0.38	micelles
2	PCL ₅₄ - <i>b</i> -P(SA- <i>alt</i> -ME ₃ MO) ₇	398	0.17	vesicles
3	PCL ₅₄ - <i>b</i> -P(SA- <i>alt</i> -ME ₃ MO) ₅	277	0.25	vesicles

^{a)} All self-assemblies were prepared using the ‘solvent-switch’ method (see the experiments chapter for details)

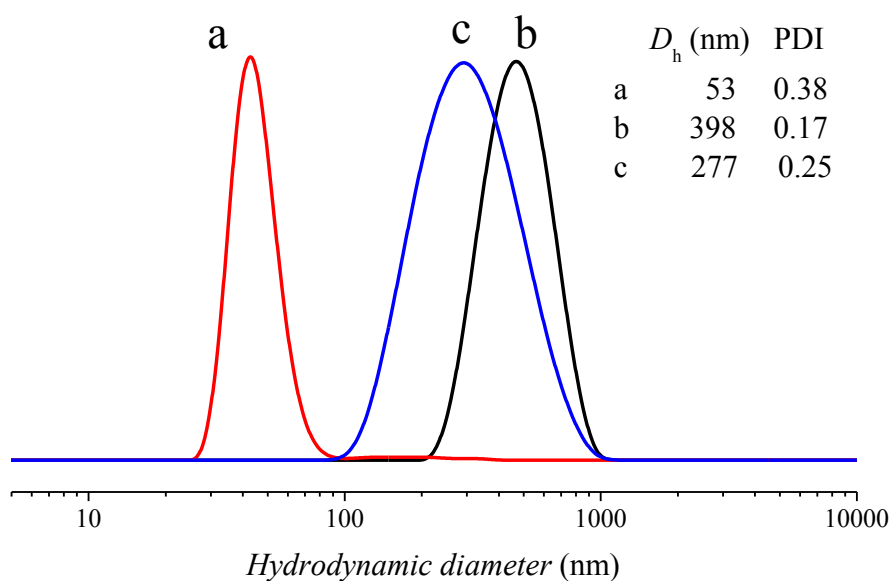


Figure 5.6 Dynamic light scattering analyses of nanostructures self-assembled from PCL-*b*-P(SA-*alt*-ME₃MO). Hydrodynamic diameter (D_h) and polydispersity index (PDI) of the self-assembled nanostructure formed from (a) PCL₃₈-*b*-P(SA-*alt*-ME₃MO)₇ (**Table 5.2**, entry 1), (b) PCL₅₄-*b*-P(SA-*alt*-ME₃MO)₇ (**Table 5.2**, entry 2) and (c) PCL₅₄-*b*-P(SA-*alt*-ME₃MO)₅ (**Table 5.2**, entry 3)

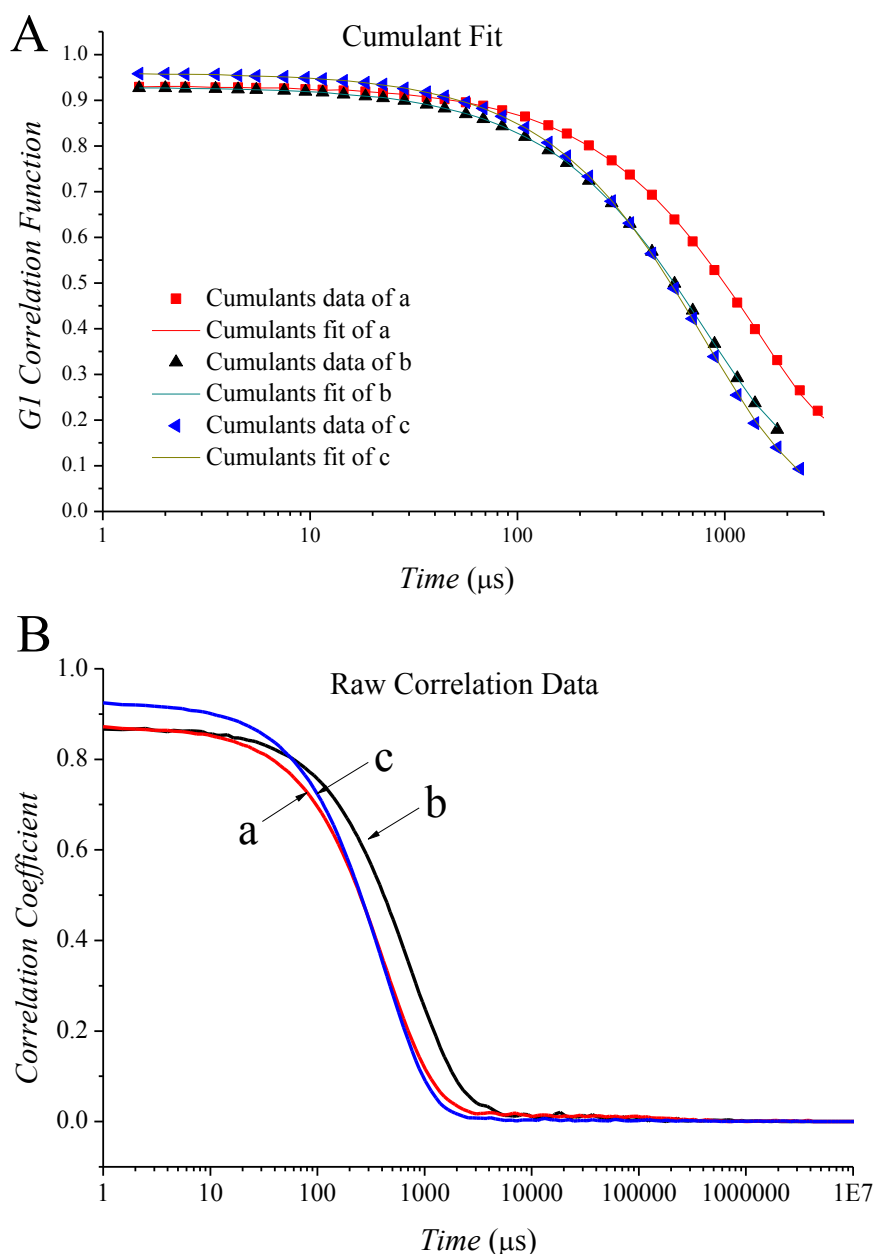


Figure 5.7 (A) Cumulant fit and (B) Correlation functions of DLS studies of the self-assemblies (a, b and c correspond to entry 1-3 in **Table 5.2**, respectively)

5.2.5 TEM characterization of the self-assembled block copolyesters

Transmission electron microscopy (TEM) was used to examine the morphology of the self-assemblies listed in **Table 5.2**. All TEM samples were stained with uranium acetate to increase the contrast. The sample preparation procedure is described in chapter 8 and the characterization was conducted by Dr. Jens Gaitzsch from Prof. Giuseppe Battaglia's group

at UCL. As illustrated in **Figure 5.8** and in line with the DLS results, the copolyester with the lowest hydrophobic weight content (66 wt% in entry 3, **Table 5.1**) forms micelles (see **Figure 5.8C & D**), while those with higher hydrophobic weight contents (79 wt% in entry 5, **Table 5.1**) form vesicles with membrane thickness value of ca. 30 nm (see **Figure 5.8A & B**). Furthermore the average diameters observed for the nanostructures, shown in **Figure 5.8**, are in close accordance with the hydrodynamic diameters measured by DLS (see **Table 5.2**). However, it is worth pointing out that TEM images only provide the representative morphology of a small part of the sample. SAXS or SANS would be the better techniques to evaluate the true morphologies of the self-assembled nanostructures.^{24,45} Also, during the conventional TEM characterization, high vacuum is applied, which might change the morphology of the nanostructures. Nonetheless, this can be prevented by using the cryo-TEM in the future. The TEM and DLS results demonstrate the feasibility to tune the particle morphology by changing the quantity of the hydrophilic block in the block copolyesters. The concept is already well-known for other amphiphilic copolymers⁴⁰ but has yet to be demonstrated for such fully degradable block copolyesters.

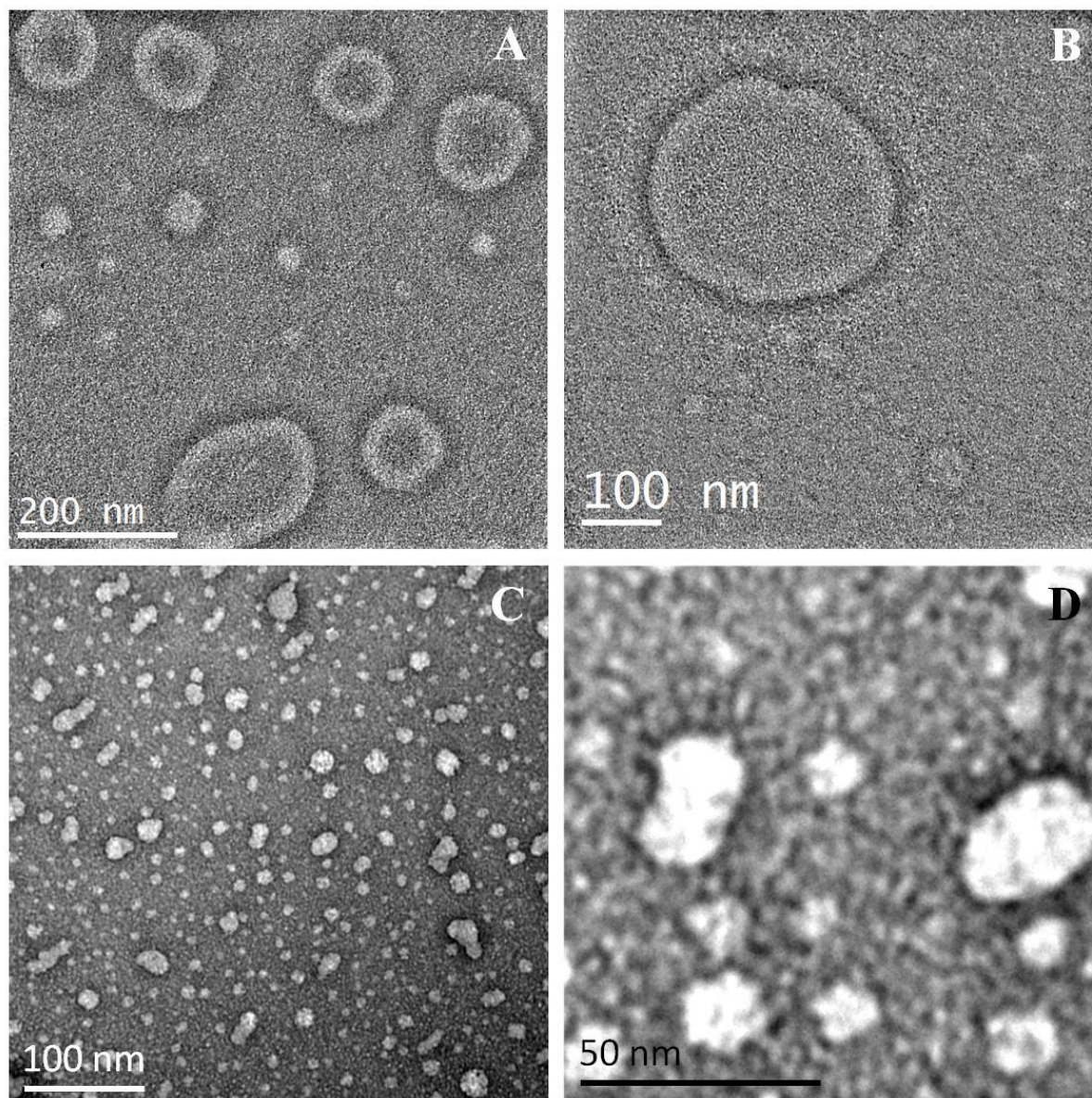


Figure 5.8. TEM images of representative block copolymer self-assemblies: (A) & (B) vesicles formed from $\text{PCL}_{54}\text{-}b\text{-P}(\text{SA-}alt\text{-ME}_3\text{MO})_5$ (Table 5.2, entry 3); (C) & (D) micelles formed from $\text{PCL}_{38}\text{-}b\text{-P}(\text{SA-}alt\text{-ME}_3\text{MO})_7$ (Table 5.2, entry 1)

5.2.6 Thermal stability of the vesicles

The triethylene glycol side chains in the $\text{P}(\text{SA-}alt\text{-ME}_3\text{MO})$ block are known to undergo a hydrophilic to hydrophobic transition when the polymer is heated above the LCST temperature.^{46,47} The thermoresponsive behaviour of the block copolyester vesicle was monitored *via* a temperature-dependent determination of zeta potential. The zeta potential

monitoring revealed that the LCST occurred at ca. 75 °C, based on the sharp decrease in the absolute value of the zeta potential ($|\zeta|$) observed at temperatures above this value (see **Figure A5**). This LCST temperature is similar with the value (73.3 °C) reported in literature.³¹ Meanwhile, the zeta potential is also widely applied to evaluate the stability of the colloidal systems.^{2,40,48} The absolute value of the zeta potential suggests the extent of the electrostatic repulsion between neighbouring colloidal nanoparticles.⁴⁸ Therefore, higher zeta potential (negative or positive) means higher colloidal stability, as the high electrostatic repulsion prevents the colloidal nanoparticles from aggregation. Usually, colloidal systems having zeta potentials ranging from ± 40 to ± 60 is considered as the ‘good stability’.⁴⁸ In this work, the rather high ζ (< -42 mV) at temperatures below the LCST indicates a good colloidal stability of the PCL₅₄-*b*-P(SA-*alt*-ME₃MO)₇ self-assembled structures at physiological temperature, relevant to any use in biomedicine.

5.2.7 *In vitro* lipase catalyzed biodegradation of the polyester vesicles

To demonstrate the polymers’ biodegradability, *Pseudomonas cepacia* lipase was added to the polyester vesicle solutions, which were placed in a shaker at a rate of 600 rpm at 37 °C. Since the mean count rate given by DLS is proportional to both the size and the number of self-assemblies, as long as the attenuator is fixed,⁴⁹⁻⁵¹ the biodegradation process could thus be monitored by DLS. As shown in **Figure 5.9A** (curve b), after the addition of the lipase solution, the mean count rate decreased rapidly from 151 kcps to 24 kcps in merely 90 min (the attenuator was set at 6, and is a non-dimensional parameter). In contrast, the mean count rate of the control enzyme-free polyester vesicle solution remained constant over the entire time period (curve a). Additionally, photos were taken ‘before’ and ‘after’ the enzymatic degradation (see **Figure 5.9A** inset). After lipase catalyzed degradation, the solution transparency increases (in accordance to the mean count rate given by DLS), indicating the disassociation of the self-assemblies, caused by polyester hydrolysis. The change in size distribution (see **Figure 5.9B**), from monomodal narrow distributions to bimodal broad distributions, confirms the disruption of the ordered structure (vesicle morphology). The

decrease in molecular weight during biodegradation was also monitored by SEC (**Figure 5.10**). After 2.0 h, the molecular weight of the block copolyesters decreased from 16.5 kDa to 1.4 kDa (**Table 5.3**, entry 1 and 2) along with an increase in dispersity from 1.18 to 3.14. After 4.0 h, the polymer signal was no longer detectable by the SEC, indicating the complete degradation of polymers into small molecules (**Table 5.3**, entry 3).

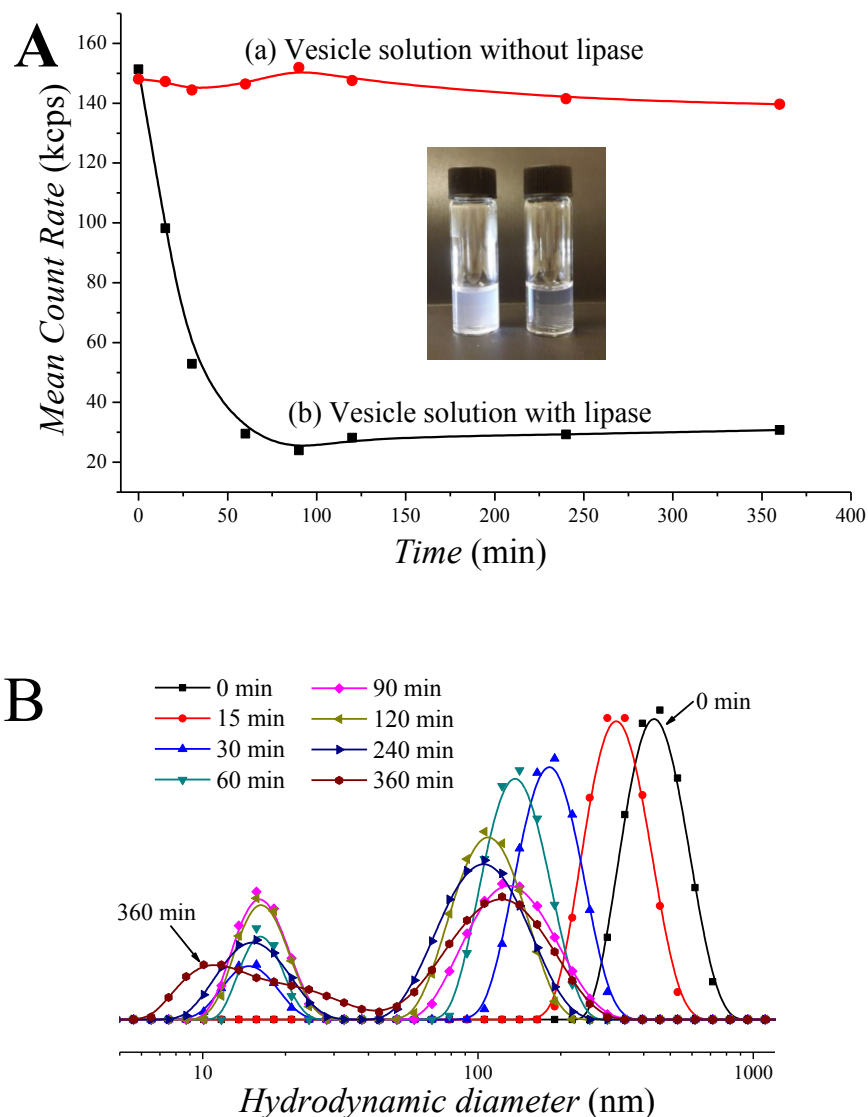


Figure 5.9 Lipase catalyzed biodegradation of polyester vesicles monitored by DLS. Conditions: *Pseudomonas cepacia* lipase at 37 °C, the concentration of vesicles and lipase were 0.21 mg/mL and 100 unit/mL, respectively. (A) Mean count rate (measured also by DLS) variation of polyester vesicle solutions during the experimental period with (b) or

without (a) the presence of lipase. Inset: photos of the polyester vesicle solution before (left) and after (right) enzymatic degradation. (B) Hydrodynamic diameter variation of polyester vesicle solutions during the experimental period.

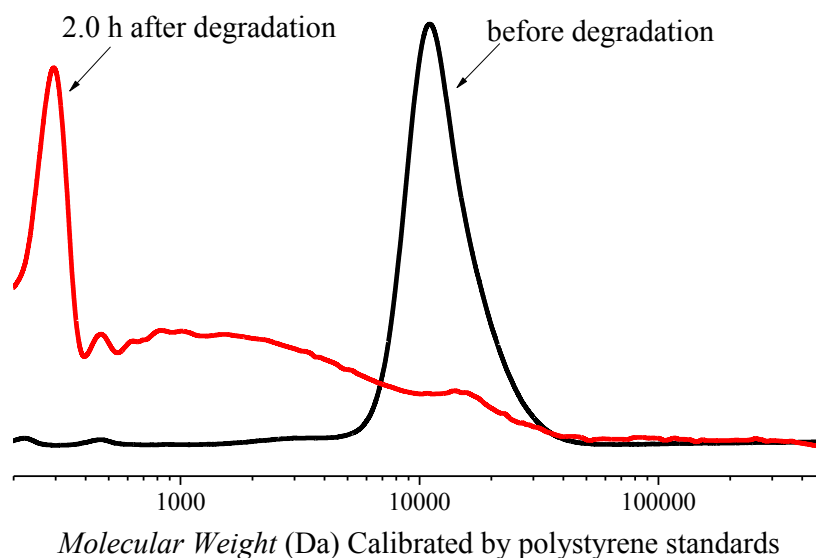


Figure 5.10 SEC traces of the biodegradation products during block copolyester reacting with lipase.

Table 5.3 Molecular weights and dispersities of the block copolyesters during biodegradation experiments.

#	Block copolymer	Lipase conc. (unit/mL)	t (h)	M_n (kDa), M_w/M_n
1	PCL ₅₄ - <i>b</i> -P(SA- <i>alt</i> -ME ₃ MO) ₇	7.7	0.0	16.5, 1.18
2	conc. of the self-assembly solution (0.23 mg/mL)		2.0	1.4, 3.14
3			4.0	N.A. (low signal-to-noise ratio)

5.2.8 Model drug release experiments

Since the copolyester vesicles were found to be biodegradable and were targeted as biocompatible, it was of interest to study their potential in drug delivery. The drug loading efficiency was evaluated using doxorubicin hydrochloride (DOX•HCl) which is commonly used as a model drug.^{45,52-54} Before beginning any drug delivery experiments, a fluorescence calibration was conducted using known concentrations of DOX in PBS buffer (the PO_4^{3-} concentration of the PBS buffer = 10 mM; and the pH value = 7.4). Next, the vesicles' drug loading efficiency (DLE) was determined by $\text{DLE (\%)} = \frac{M_e}{M_f} \times 100\%$, where M_e represents the weight of drug encapsulated in vesicles, M_f stands for the weight of drug used in total. The DLE was found to be 20.5% (see equation 3 in chapter 7). The value is moderate compared to those reported in the literature⁵⁵⁻⁵⁸ but could perhaps be improved with experimental condition optimization. The *in vitro* release profiles of DOX-loaded polyester vesicles were conducted in 10.0 mM PBS buffer, at 37 °C and pH 7.4. The detailed experimental procedure is described in chapter 7. As shown in **Figure 5.12**, the release of the encapsulated DOX (**Figure 5.12**, curve b) was much slower than that of the free DOX control solution (**Figure 5.12**, curve a), though the initial burst release behaviors were similar. After ca. 20 h, the DOX in the control experiment was almost completely released (**Figure 5.12**, curve a). However, at the same time, only ca. 60% of DOX was released when it was encapsulated by the vesicles, indicating the controlled release of DOX. Lipases are over-expressed in certain aggressive cancer cells.⁵⁹ To demonstrate the passive targeting capability of the polyester vesicles, the *in vitro* release profiles of DOX-loaded polyester vesicles in the presence of lipase were also recorded (**Figure 5.12**, curve c). Due to the disruption of the hollow sphere structure by the lipase, the DOX was not fully encapsulated by the self-assembly. Therefore, the corresponding cumulative release profile demonstrated yet faster release, compared to the one without any enzyme presence. Despite there being no active targeting mechanism, the potential for 'burst' release behaviour inside an aggressive cancer cell may be a potential strength of using this type of block copolyesters. The work also sets the foundation for an indepth study focussed on attaching cell targeting groups to the self-assemblies, which could be investigated in the future.

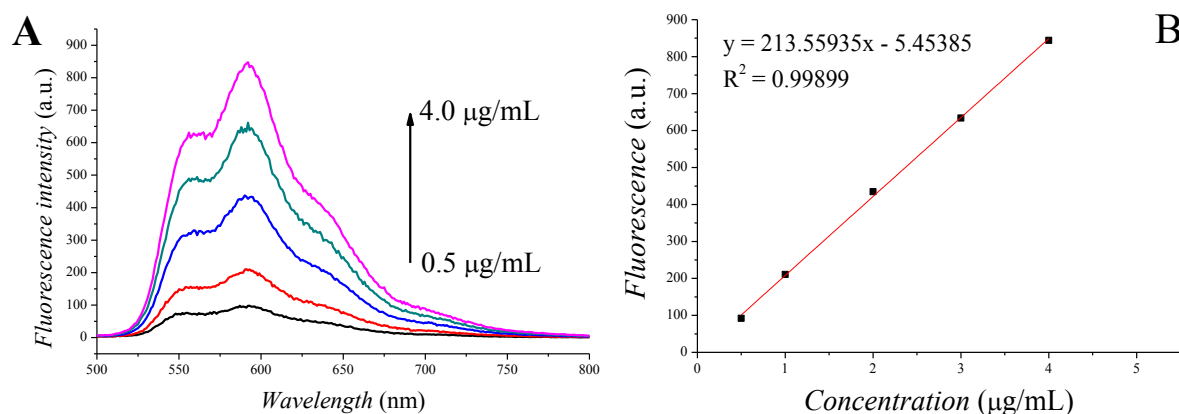


Figure 5.11 The fluorescence spectrum (A) and calibration curve (B) of DOX•HCl in PBS solution (10.0 mM, pH 7.4). ($\lambda_{\text{ex}} = 461 \text{ nm}$)

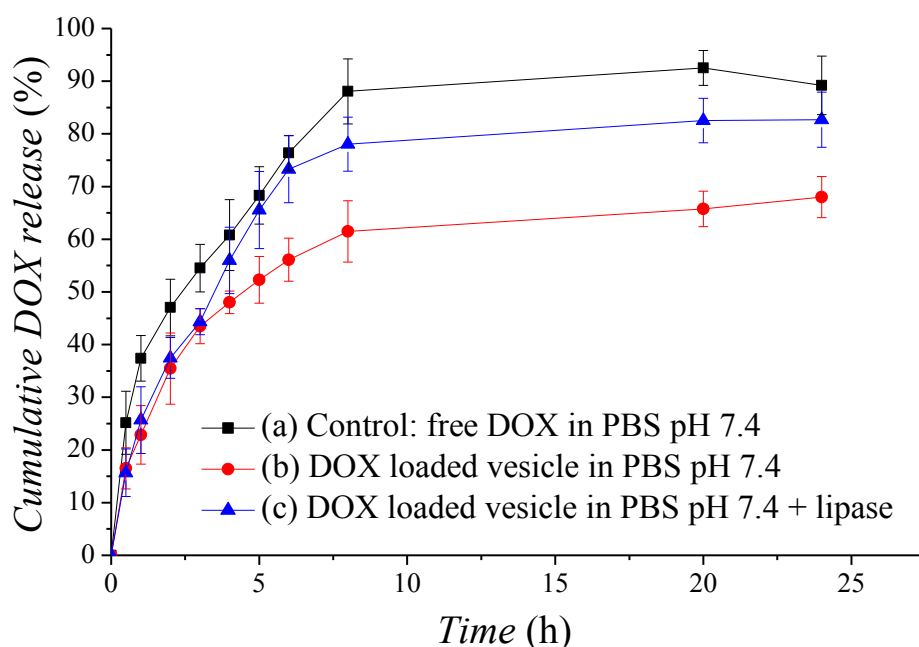


Figure 5.12 Cumulative drug release profiles of DOX-loaded copolyester vesicles at 37 °C in PBS buffer (10.0 mM, pH 7.4).

5.2.9 Cytotoxicity Tests

To investigate the biocompatibility of the micelles, vesicles (polymersomes) and the corresponding degradation products, cytotoxicity tests were conducted using three different cell lines, including cancer cells, FaDu (a hypopharyngeal carcinoma cell line) and HeLa (a cervical carcinoma cell line), and the normal cells, HDF (*human dermal fibroblasts*). These

experiments are conducted by Dr Alessandro Poma and Dr Loris Rizzello as part of the collaboration with Prof. Giuseppe Battaglia at UCL. The cell viability was quantified in each case by a 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide (MTT) assay. Each cell line was treated with micelles, vesicles (polymersomes) and the corresponding degradation products, at three different concentrations for 48 hours. Compared to the negative control (cells treated with DMSO which is known to be toxic), none of the samples exhibited cytotoxicity (**Figure 5.13**) as observed by the cell viability remaining high ($> 80\%$). However, some unexpected cell behavior was observed in the case of FaDu and HDF cells. Instead of a decrease in cell viability, the cell viability values of these two cell lines increased significantly. For FaDu cells, the value increased to ca. 150% after being treated with the degradation products for 24 h, and with micelles and polymersomes the same increase was observed after 48 h. For HDF cells, the cell viability values also increased to $> 150\%$ in certain cases. The MTT assay reflects the general cell metabolic activity which relates to both cell number and the rate of metabolism, thus, the increase in cell viability value could either be due to the proliferation of cells or an inflammation response, during which the metabolic rate increases. To evaluate the true cause of the increase in the ‘viability’, a cell counting method was also used (**Figure 5.14**). Again, the HDF cells were treated with micelles, vesicles (polymersomes) and the corresponding degradation products for 48 h (see the experiment section for details). Instead of cell proliferation, a slight decrease in cell number was observed in all three cases from ca. 1.2×10^5 cells/mL to ca. 1.0×10^5 cells/mL. However, it is noteworthy that all these decreases were in the margin of error. Also, the significance of the values requires further evaluation. The cell counting results suggest that the apparent increase in cell viability, measured by MTT assay, is likely caused by an inflammation response.⁶⁰ Nonetheless, the ‘slight’ decrease (described above) in cell number also confirms that the micelles, vesicles (polymersomes) and the corresponding degradation products are generally non-toxic, in accordance to the results given by the MTT assay. The inflammation response was studied using the nuclear translocation of Nf-kB. Nf-kB is a protein complex which controls the transcription of DNA and cytokine production; it regulates the cell immune

response to infection.⁶¹ In short, Nf-kB usually locates evenly in both the cell cytoplasm and nucleus.⁶¹ However, during inflammation Nf-kB present in the cytoplasm translocates into the nucleus.⁶² Therefore, the translocation of Nf-kB can be used as an indication of inflammation.⁶² Fluorescence agents (nuclear: blue; Nf-kB: red) were used to image the translocation of Nf-kB using confocal microscopy (**Figure 5.15**). After 48 hours, the translocation of Nf-kB from cytoplasm to nucleus was observed (near complete overlapping between blue and red signals) in all three HDF samples. The amount of signal overlap was measured and is listed in **Table 5.4**. The signal overlap in cells treated by the degradation products and micelles are broadly similar. However, the value for cells treated by polymersomes decreases from 98.9% to 82.5%. The slower translocation is probably due to a slower endocytosis rate of large polymersomes compared to small micelles or degradation products, leading to cells exhibiting less inflammation response over time in the former sample.

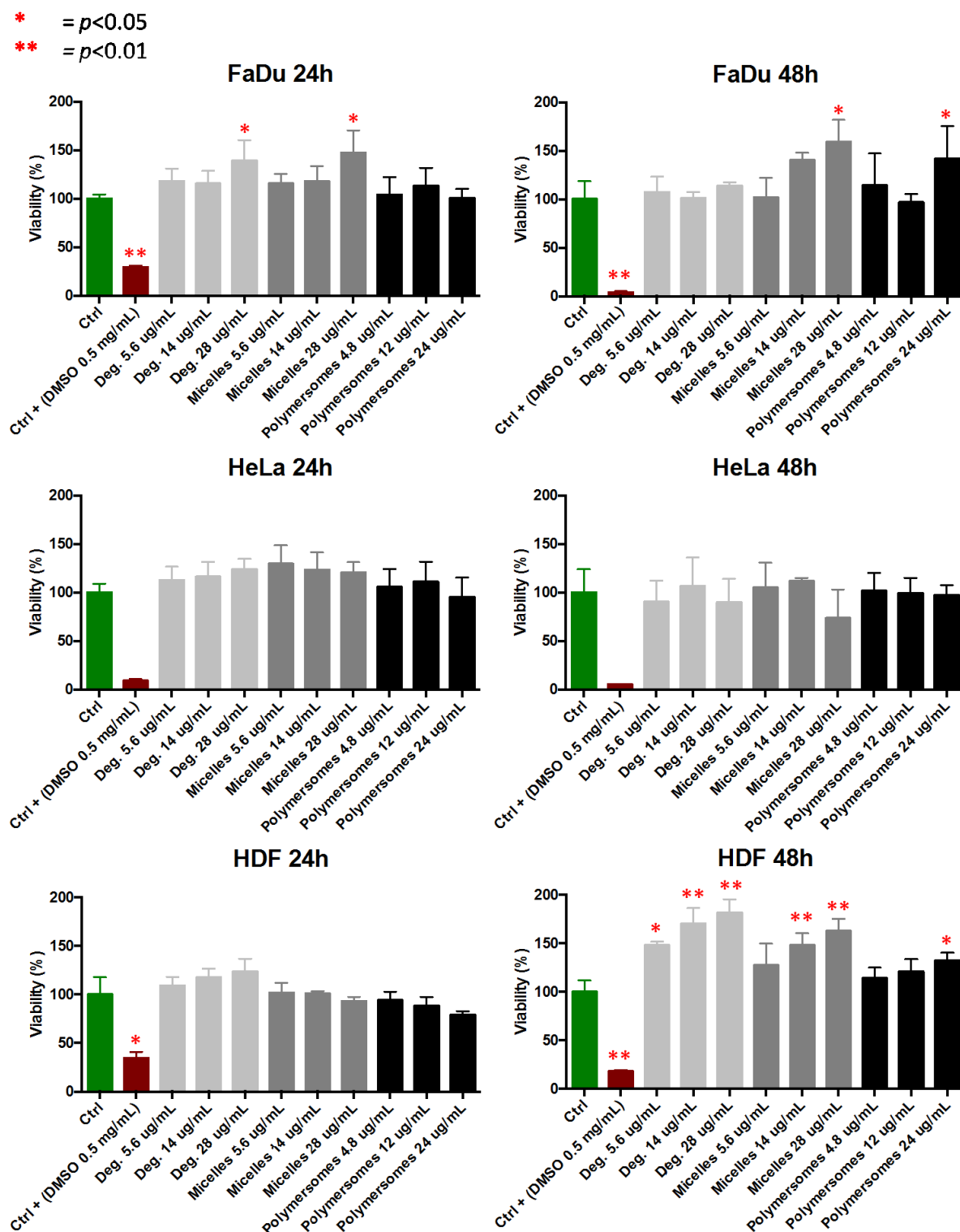


Figure 5.13 Cell viability tests using 3 different cell lines, including cancer cells, FaDu and HeLa, and normal cells, HDF and quantified by an MTT assay. Each cell line was treated with micelles, vesicles (polymersomes) and the corresponding degradation products at three different concentrations for 48 hours.

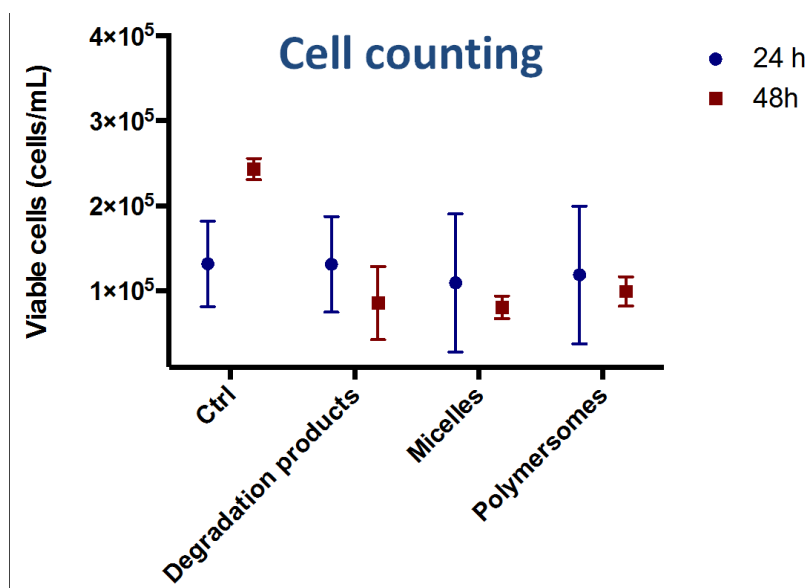
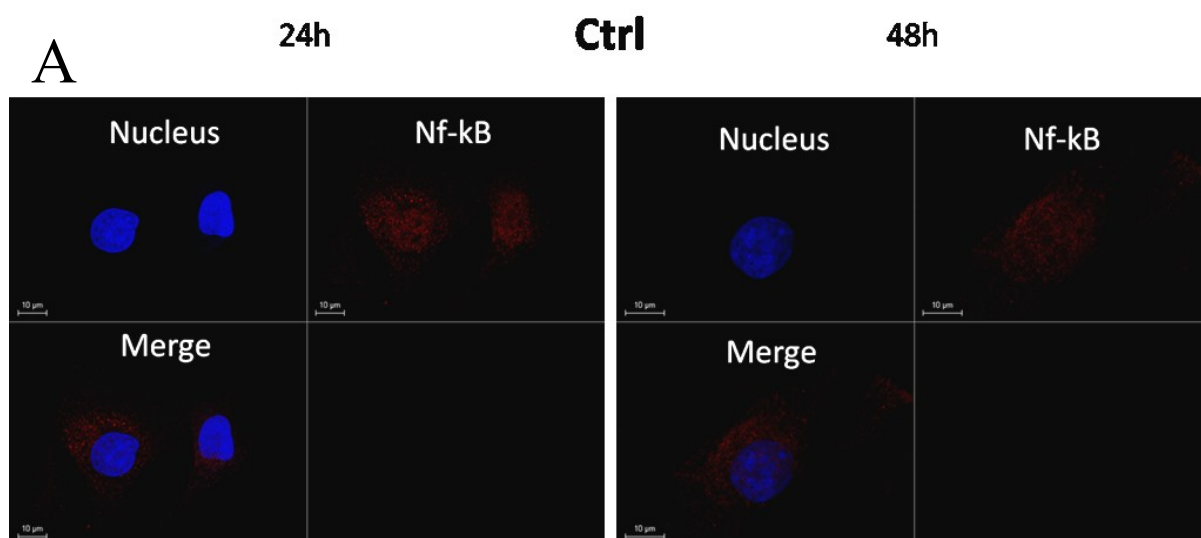


Figure 5.14 Cytotoxicity tests quantified by the cell counting method, using HDF cells treated with the degradation products, micelles, and polymersomes, respectively.



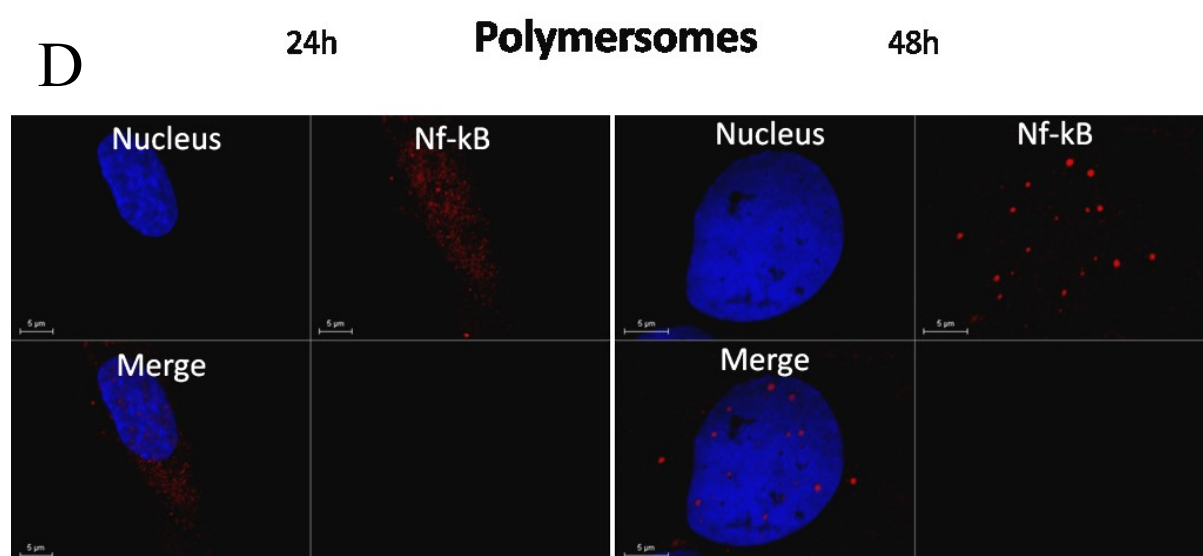
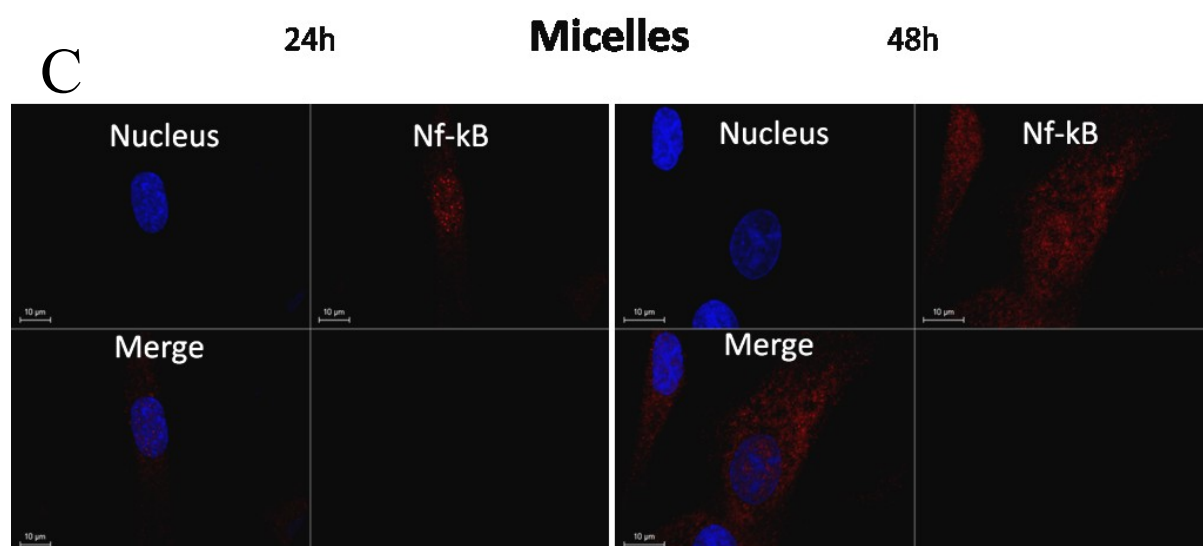
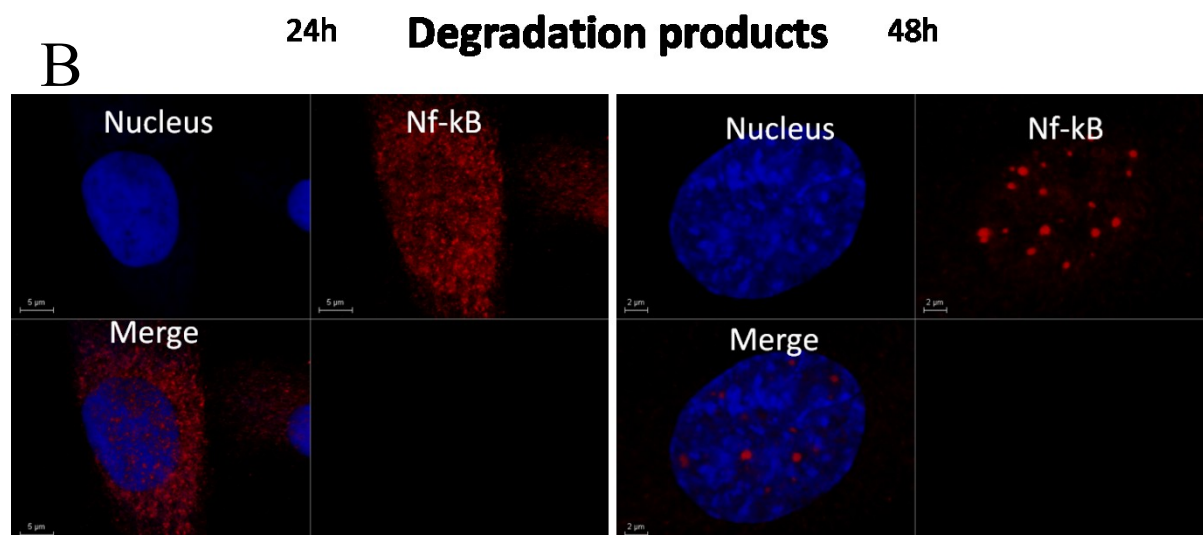


Figure 5.15 Confocal microscopy images of the nuclear translocation process observed for Nf-kB in HDF cells treated with degradation products, micelles, and polymersomes, respectively for 48 hours. Both the nucleus and Nf-kB were marked with fluorescent agents (nucleus: blue; Nf-kB: red). The signal overlap values were measured and are listed in **Table 5.4**.

Table 5.4 Signal overlap values for the nucleus and Nf-kB in control cells and cells treated with degradation products, micelles, and polymersomes, respectively.

	Control	Degradation Products	Micelles	Polymersomes
24 hours	$22.3 \pm 7.9\%$	$91.7 \pm 7.9\%$	$98.3 \pm 1.1\%$	$98.9 \pm 0.3\%$
48 hours	$25.1 \pm 1.3\%$	$93.4 \pm 4.4\%$	$99.6 \pm 0.5\%$	$82.5 \pm 0.5\%$

5.3 Conclusions

The combination of ROP and ROCOP methods allowed the preparation of amphiphilic block polymers using fully by aliphatic polyester blocks and featuring metabolic intermediates as monomers or degradation products. The relative proportions of hydrophilic/hydrophobic blocks were controlled and the materials afforded different self-assembly morphologies, including micelles and vesicles (polymersomes) as determined by DLS and TEM imaging. In the presence of lipases, the self-assembled structures were rapidly disrupted and the polyester itself also displayed fast degradation, as monitored by DLS and SEC. It was established that both the polyester self-assemblies and the corresponding degradation products demonstrate no appreciable cytotoxicity against a range of cell lines, including cancer cells and normal cells. However, an inflammation response was observed in some cases and was confirmed using combined cell counting and confocal microscopy. Both the loading and release characteristics using DOX and biodegradation results of the polyesters demonstrate the potential for the materials to be applied as non-cytotoxic vehicles for controlled drug release. Most importantly, this work expands the scope of the building blocks for the field of

self-assembly because succinic acid is one of several metabolic intermediates that could be applied, including maleic acid, citric acid, glycerol, *etc.*

5.4 References

- (1) Ulery, B. D.; Nair, L. S.; Laurencin, C. T. *J. Polym. Sci. Pol. Phys.* **2011**, *49*, 832-864.
- (2) Zhu, Y.; Yang, B.; Chen, S.; Du, J. *Prog. Polym. Sci.* **2016**, In press.
- (3) Kim, W.; Thevenot, J.; Ibarboure, E.; Lecommandoux, S.; Chaikof, E. L. *Angew. Chem., Int. Ed.* **2010**, *49*, 4257-4260.
- (4) Rhodes, A. J.; Deming, T. J. *J. Am. Chem. Soc.* **2012**, *134*, 19463-19467.
- (5) Rodriguez-Hernandez, J.; Lecommandoux, S. *J. Am. Chem. Soc.* **2005**, *127*, 2026-2027.
- (6) Schatz, C.; Lecommandoux, S. *Macromol. Rapid Commun.* **2010**, *31*, 1664-1684.
- (7) Guo, B.; Finne-Wistrand, A.; Albertsson, A.-C. *Biomacromolecules* **2011**, *12*, 2601-2609.
- (8) Gandini, A.; Lacerda, T. M.; Carvalho, A. J. F.; Trovatti, E. *Chem. Rev.* **2015**, 1637-1669.
- (9) Arrieta, M. P.; López, J.; Hernández, A.; Rayón, E. *Eur. Polym. J.* **2014**, *50*, 255-270.
- (10) Guillaume, C.; Ajellal, N.; Carpentier, J. F.; Guillaume, S. M. *J. Polym. Sci., Part A: Polym. Chem.* **2011**, *49*, 907-917.
- (11) Poetz, K. L.; Mohammed, H. S.; Snyder, B. L.; Liddil, G.; Samways, D. S. K.; Shipp, D. A. *Biomacromolecules* **2014**, *15*, 2573-2582.
- (12) Tamada, J.; Langer, R. *J. Biomater. Sci.-Polym. Ed.* **1992**, *3*, 315-353.
- (13) Engler, A. C.; Ke, X. Y.; Gao, S. J.; Chan, J. M. W.; Coady, D. J.; Ono, R. J.; Lubbers, R.; Nelson, A.; Yang, Y. Y.; Hedrick, J. L. *Macromolecules* **2015**, *48*, 1673-1678.
- (14) Suriano, F.; Coulembier, O.; Hedrick, J. L.; Dubois, P. *Polym. Chem.* **2011**, *2*, 528-533.
- (15) Brignou, P.; Carpentier, J. F.; Guillaume, S. M. *Macromolecules* **2011**, *44*, 5127-5135.
- (16) Darensbourg, D. J.; Choi, W.; Karroonnirun, O.; Bhuvanesh, N. *Macromolecules* **2008**, *41*, 3493-3502.
- (17) Kricheldorf, H. R.; Rost, S. *Macromolecules* **2005**, *38*, 8220-8226.
- (18) Zhang, S.; Zou, J.; Zhang, F.; Elsabahy, M.; Felder, S. E.; Zhu, J.; Pochan, D. J.; Wooley, K. L. *J. Am. Chem. Soc.* **2012**, *134*, 18467-18474.
- (19) Liu, X.; Ni, P.; He, J.; Zhang, M. *Macromolecules* **2010**, *43*, 4771-4781.
- (20) Clément, B.; Grignard, B.; Koole, L.; Jérôme, C.; Lecomte, P. *Macromolecules* **2012**, *45*, 4476-4486.
- (21) Xiao, H.; Qi, R.; Liu, S.; Hu, X.; Duan, T.; Zheng, Y.; Huang, Y.; Jing, X. *Biomaterials* **2011**, *32*, 7732-7739.
- (22) Yan, Q.; Hu, J.; Zhou, R.; Ju, Y.; Yin, Y. W.; Yuan, J. Y. *Chem. Commun.* **2012**, *48*, 1913-1915.
- (23) Gaitzsch, J.; Huang, X.; Voit, B. *Chem. Rev.* **2016**, *116*, 1053-1093.
- (24) Le Hellaye, M.; Fortin, N.; Guilloteau, J.; Soum, A.; Lecommandoux, S.; Guillaume, S. M. *Biomacromolecules* **2008**, *9*, 1924-1933.
- (25) Neradovic, D.; van Nostrum, C. F.; Hennink, W. E. *Macromolecules* **2001**, *34*, 7589-7591.
- (26) Discher, D. E.; Eisenberg, A. *Science* **2002**, *297*, 967-973.

- (27) Fukushima, K.; Tan, J. P. K.; Korevaar, P. A.; Yang, Y. Y.; Pitera, J.; Nelson, A.; Maune, H.; Coady, D. J.; Frommer, J. E.; Engler, A. C.; Huang, Y.; Xu, K. J.; Ji, Z. K.; Qiao, Y.; Fan, W. M.; Li, L. J.; Wiradharma, N.; Meijer, E. W.; Hedrick, J. L. *Acs Nano* **2012**, *6*, 9191-9199.
- (28) Lou, X. D.; Detrembleur, C.; Jerome, R. *Macromol. Rapid Commun.* **2003**, *24*, 161-172.
- (29) Seyednejad, H.; Ghassemi, A. H.; van Nostrum, C. F.; Vermonden, T.; Hennink, W. E. *J. Controlled Release* **2011**, *152*, 168-176.
- (30) Zhu, Y.; Romain, C.; Williams, C. K. *Nature* **2016**, Accepted.
- (31) Feng, L.; Liu, Y.; Hao, J. Y.; Li, X. H.; Xiong, C. D.; Deng, X. M. *Macromol. Chem. Phys.* **2011**, *212*, 2626-2632.
- (32) Feng, L.; Liu, Y.; Hao, J.; Xiong, C.; Deng, X. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 1812-1818.
- (33) Darensbourg, D. J.; Tsai, F.-T. *Macromolecules* **2014**, *47*, 3806-3813.
- (34) Tsai, F.-T.; Wang, Y.; Darensbourg, D. J. *J. Am. Chem. Soc.* **2016**, *138*, 4626-4633.
- (35) Wu, G.-P.; Darensbourg, D. J. *Macromolecules* **2016**.
- (36) Zhu, Y.; Yang, B.; Chen, S.; Du, J. *Prog. Polym. Sci.* **2016**.
- (37) Zhang, H.; Lin, X.; Chin, S.; Grinstaff, M. W. *J. Am. Chem. Soc.* **2015**, *137*, 12660-12666.
- (38) Webster, R.; Elliott, V.; Park, B. K.; Walker, D.; Hankin, M.; Taupin, P. In *PEGylated Protein Drugs: Basic Science and Clinical Applications*; Veronese, F. M., Ed.; Birkhäuser Basel: Basel, 2009, p 127-146.
- (39) Wang, W.; Ding, J.; Xiao, C.; Tang, Z.; Li, D.; Chen, J.; Zhuang, X.; Chen, X. *Biomacromolecules* **2011**, *12*, 2466-2474.
- (40) Du, J.; O'Reilly, R. K. *Soft Matter* **2009**, *5*, 3544-3561.
- (41) Save, M.; Schappacher, M.; Soum, A. *Macromol. Chem. Phys.* **2002**, *203*, 889-899.
- (42) Hatzakis, E.; Archavlis, E.; Dais, P. *J. Am. Oil Chem. Soc.* **2007**, *84*, 615-619.
- (43) Spyros, A.; Argyropoulos, D. S.; Marchessault, R. H. *Macromolecules* **1997**, *30*, 327-329.
- (44) Zhu, Y.; Romain, C.; Poirier, V.; Williams, C. K. *Macromolecules* **2015**, *48*, 2407-2416.
- (45) Upadhyay, K. K.; Le Meins, J. F.; Misra, A.; Voisin, P.; Bouchaud, V.; Ibarboure, E.; Schatz, C.; Lecommandoux, S. *Biomacromolecules* **2009**, *10*, 2802-2808.
- (46) Lutz, J.-F.; Weichenhan, K.; Akdemir, Ö.; Hoth, A. *Macromolecules* **2007**, *40*, 2503-2508.
- (47) Fan, L.; Lu, H.; Zou, K.; Chen, J.; Du, J. *Chem. Commun.* **2013**.
- (48) O'Brien, R. W.; Midmore, B. R.; Lamb, A.; Hunter, R. J. *Faraday Discuss. Chem. Soc.* **1990**, *90*, 301-312.
- (49) Liu, Q.; Chen, J.; Du, J. *Biomacromolecules* **2014**, *15*, 3072-3082.
- (50) Agut, W.; Brulet, A.; Taton, D.; Lecommandoux, S. *Langmuir* **2007**, *23*, 11526-11533.
- (51) Jumeaux, C.; Chapman, R.; Chandrawati, R.; Stevens, M. M. *Polym. Chem.* **2015**, *6*, 4116-4122.
- (52) Chen, W.; Du, J. *Sci. Rep.* **2013**, *3*, doi:10.1038/srep02162.
- (53) Sanson, C.; Diou, O.; Thevenot, J.; Ibarboure, E.; Soum, A.; Brulet, A.; Miraux, S.; Thiaudiere, E.; Tan, S.; Brisson, A.; Dupuis, V.; Sandre, O.; Lecommandoux, S. *Acs Nano*

2011, 5, 1122-1140.

(54) Sanson, C.; Schatz, C.; Le Meins, J. F.; Soum, A.; Thevenot, J.; Garanger, E.; Lecommandoux, S. *J. Controlled Release* **2010**, 147, 428-435.

(55) Kowalczyk, A.; Trzcinska, R.; Trzebicka, B.; Müller, A. H. E.; Dworak, A.; Tsvetanov, C. B. *Prog. Polym. Sci.* **2014**, 39, 43-86.

(56) Zhu, H.; Geng, Q.; Chen, W.; Zhu, Y.; Chen, J.; Du, J. *J. Mater. Chem. B* **2013**, 1, 5496-5504.

(57) Louguet, S.; Rousseau, B.; Epherre, R.; Guidolin, N.; Goglio, G.; Mornet, S.; Duguet, E.; Lecommandoux, S.; Schatz, C. *Polym. Chem.* **2012**, 3, 1408-1417.

(58) Chen, W.; Meng, F. H.; Cheng, R.; Zhong, Z. Y. *J. Controlled Release* **2010**, 142, 40-46.

(59) Nomura, D. K.; Long, J. Z.; Niessen, S.; Hoover, H. S.; Ng, S.-W.; Cravatt, B. F. *Cell* **2010**, 140, 49-61.

(60) Mosmann, T. *J. Immunol. Methods* **1983**, 65, 55-63.

(61) Gilmore, T. D. *Oncogene* **2006**, 25, 6680-6684.

(62) Baker, R. G.; Hayden, M. S.; Ghosh, S. *Cell Meta.* **2011**, 13, 11-22.

Chapter 6

Conclusions

6.1 Overviews

Polyester represent a significant volume and value of materials for textiles, packaging, as engineering materials, and as polyol precursors for making polyurethane, foams and adhesives. There is a drive to investigate methods and raw materials which allow more polyesters to be formed from renewable resources. Though robust and currently widely applied in industry, the traditional polycondensation route to make polyesters is limited by requiring precise stoichiometry, high thermodynamic constraints, a lack of polymerization control, and slow polymerization rate. Alternatively, both the ring-opening polymerization (ROP) of lactones and the ring-opening copolymerization (ROCOP) of epoxides and cyclic anhydrides can deliver polyesters with good polymerization control. For the ROP, high molecular weight polyesters can be produced and the manufacturing is compatible with currently used industrial process. For the ROCOP, it can yield alternating polyesters using commercially available epoxides/cyclic anhydrides. Both polymerization methods are able to include aromatic functionality into the polymer backbone and to even incorporate bio-based monomers. However, whether it is possible to make block copolyesters with various thermal/mechanical properties *via* the combination of ROP and ROCOP remains unexplored.

Therefore, this thesis has focused on investigating ROCOP as a means to deliver polyesters with particular chemical functionality and physico-chemical properties. In particular, the thesis investigates whether it is possible to combine ROP and ROCOP to make well controlled block copolymers. Although there are methods by which independent ROP and ROCOP reactions could be run and the polymer products ‘coupled’ together or used as ‘macroinitiators’, the goal was to develop a ‘one-pot, one-step’ procedure allowing both processes to occur, either sequentially or concurrently, to deliver copolymers. The concept relies on being able to use a single catalyst for both polymerization reactions. There was very little investigation of this concept prior to this thesis, although a related ‘switchable’ catalysis was known for CO₂/epoxide ROCOP and lactone ROP using di-zinc catalysts.

6.2 Conclusions

Chapter 2 describes the ROP of ϵ -caprolactone using a di-zinc catalyst and various diols. The catalyst system delivered controlled polymerization, where the polymer molecular weight could be predicted from $[\text{monomer}]/[\text{chain transfer agent}]$. Nonetheless, an unexpected result was that the nature of the hydroxyl groups on diols, influenced significantly the nature of the end groups of the PCL chains. The studies highlight the importance of the catalyst system in controlling the relative rates of initiation vs. propagation, and thereby the ability to produce chains terminated by or extended from the diol. The di-zinc catalyst showed a kinetic selectivity for primary hydroxyl groups and delivered only chains extended from diol. When secondary $-\text{OH}$ or sterically hindered primary $-\text{OH}$ groups were present, then mixtures of chains extended from and terminated by the diols were produced. The composition of the mixtures could be controlled by manipulating the monomer:catalyst loading or by selecting the chemistry of the diol. Such selectivity may be an interesting means to control and target specific polymer chain end groups. The findings set the foundation for the research into polymerizations using mixture of epoxides/cyclic anhydrides/lactones to deliver well-defined block copolyesters.

Given that the key propagating alkoxide is a secondary cyclohexylene species, in order to achieve well-defined block copolyesters architectures, a lactone monomer (ϵ -DL) with secondary alkoxide propagating species was selected. Furthermore, a new di-zinc complex, $[\text{LZn}_2(\text{Ph})_2]$, with phenyl co-ligands was developed because it allowed better control over the initiating species. The new di-zinc catalyst was established to independently catalyze the ring-opening copolymerization of anhydrides/epoxides and ring-opening polymerization of lactones. When polymerizing mixtures of PA/CHO/ ϵ -DL, pure ABA type triblock copolyesters were prepared, in one-pot and occurring, *via* a sequence selective method. The new copolyesters were characterized including by NMR spectroscopy, SEC and DSC measurements. The experiments showed high catalytic selectivity with epoxide/cyclic anhydride enchainment occurring before any ROP of ϵ -DL. The experiments also confirmed the formation of triblock copolymers. The monomers were selected to yield materials of the

‘soft block-hard block-soft block’ composition and this was confirmed by thermal/mechanical measurements in the forth chapter. It was interesting to observe that the PDL-*b*-PCHPE-*b*-PDL triblocks might showed two separate T_g values at some block compositions. The results suggest there might be microphase separation between the hard PCHPE and soft PDL domains. The catalysis was also applied to prepare multi-block copolyesters comprising up to seven blocks of PCHPE and PDL. The third chapter allowed the determination of the ‘ground rules’ for implementing the selective process. It also demonstrated the ability to apply the catalysis using a range of other monomers.

The new catalytic method simplifies the preparation of block copolyesters and was next investigated for the preparation of materials with tailored properties. A range of PCHPE-*b*-PDL multiblocks were chain extended using urethane linkages and thermal/mechanical characterization was conducted. For materials having low incorporation of hard block (26 wt% PCHPE), the polymers were excellent thermoplastic elastomers. The materials showed impressive elongations at break (ca. 2450%) with comparable stress at break (11.5 MPa) to many existing thermoplastic elastomers, such as SBS or SIS. The multiblock copolyester, having the highest proportion of the hard block (59 wt% PCHPE), exhibited shape memory properties over repeated cycles. The process involved a cold-draw, at ambient temperature, and subsequent heating to 55 °C allowed near complete recovery from the deformation. Instead of the transition temperature corresponding to the T_g of PCHPE blocks, as is common in shape memory polymers, a rather rare transition consistent with the enthalpy of relaxation was the trigger to the recovery. The materials are interesting as a low transition temperature combined with a high T_g should allow access to materials useful for (bio)medicine. The materials showed high strain fixity (> 250%) and excellent recovery ratios (> 96%), which are important criteria for any applications. These new multi-block copolyesters are all expected to be degradable, although the rigid blocks are likely more slowly biodegraded. Furthermore, there are precedents for preparing and sourcing all the monomers from renewable raw materials.¹⁻³ Thus, the new materials merit further

development and investigation as renewable and degradable alternatives to the widely applied SBS elastomers and related materials.

The final chapter examines the block copolyesters' applications in biomedicine, especially in drug delivery. The alternating copolymerization of cyclic anhydrides and epoxides is attractive as a means to make block copolyesters with tailored amphiphilicity, stimuli-responsive behaviour and biocompatibility. As a first step to demonstrate the bio-application potential of such block copolyesters, a proof-of-concept study of their self-assembly, drug delivery and biodegradation behaviour was investigated. The preparation of amphiphilic block polymers was achieved using aliphatic polyester blocks (ROP) and featuring metabolic intermediates as monomers or degradation products (ROCOP). The relative proportions of hydrophilic/hydrophobic blocks were controlled. The copolymers afforded different self-assembly morphologies, including micelles and vesicles (polymersomes), in aqueous solutions. The self-assembled structures underwent rapid disruption in the presence of lipases, due to the degradation of the aliphatic polyester blocks. It was established that both the polyester self-assemblies and the corresponding degradation products demonstrated no appreciable cytotoxicity against a range of cell lines, including cancer cells and normal cells. An inflammation response was observed in some cases. Both the loading and release characteristics using DOX and the biodegradation results of the polyesters demonstrate the potential for the materials to be applied as non-cytotoxic vehicles for controlled drug release. Most importantly, succinic acid is one of several metabolic intermediates that could be applied, including maleic acid, citric acid, glycerol, *etc.*, providing scope for future studies.

Overall, the thesis focussed on applying di-zinc catalysts to selectively polymerize lactones, epoxides and cyclic anhydrides. A new switchable and selective catalysis was developed allowing access to well controlled block copolymers featuring alternating (semi-aromatic) polyester blocks and aliphatic polyester blocks. The switchable catalysis was established to be generally applicable to other lactones/epoxides/cyclic anhydrides. It was rationalized to

arise due to both kinetic and thermodynamic factors. The synthesis was exploited to prepare various new amorphous block copolymers which functioned as thermoplastic elastomers, shape memory materials or as self-assembled micelles or vesicles. The polymers were fully characterized and various application areas are proposed.

6.3 Future Outlook

As discussed in Chapters 2-5, more work needs to be conducted to investigate the influences of both the nature of the hydroxyl groups, on the chain transfer agent, and catalysts on the polyester architecture. In addition, studies also need to be carried out to exploit the catalytic selectivity as a means to target particular chain architectures for application.

The switchable catalytic method, developed in the thesis, shows potential both to allow new types of chemistry and to deliver interesting new materials. There are a number of directions for future applications. Firstly, the catalysis should be expanded to other metal-ligand combinations, such as metal-salen or metal-porphyrin complexes (**Figure 6.1**). The target future catalysts are known to be effective for epoxide/cyclic anhydride ROCOP,^{4,5} although they require addition of co-catalysts. There are also some reports of ‘switch on’ of ROP using metal-porphyrin catalysts and epoxides,⁶ results which were reported after the di-zinc selective catalysis. Thus, it is important to establish whether the metal-salen or metal-porphyrin catalysts show the same ability to link ROP and ROCOP processes and to deliver block copolyesters. The structures of some lead candidates are shown in Fig. 6.1

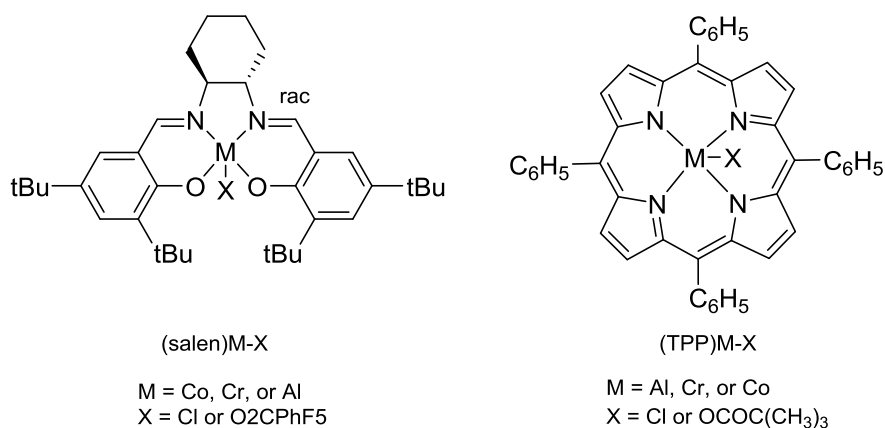
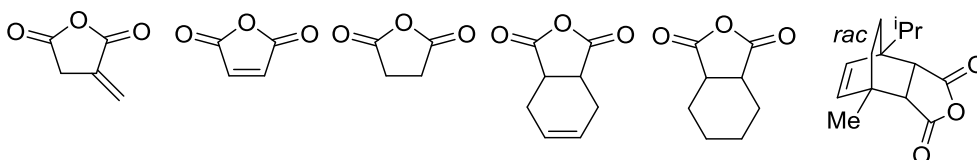


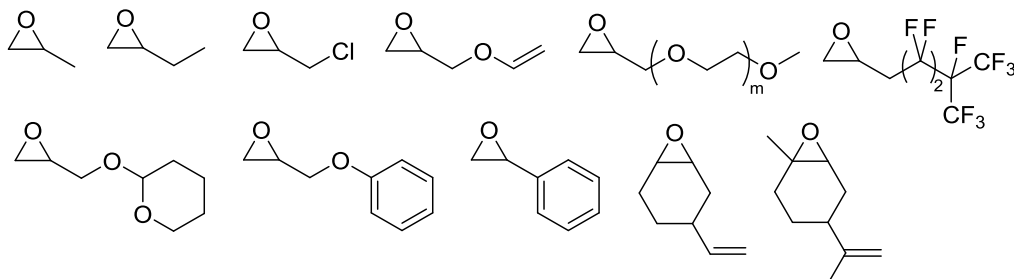
Figure 6.1 The structures of some typical metal-salen and metal-porphyrin complexes.^{7,8}

Moreover, this thesis focussed exclusively on di-zinc catalysts, but the development of more highly active catalysts showing the same selectivity would allow both more switching and a greater diversity of products. A clear future direction should be to prepare magnesium analogues of the di-zinc di(phenyl) catalysts, such as $[\text{LMg}_2(\text{Ph})_2]$ which would be expected to be more active and to maintain control over chain end-groups.⁹ Furthermore, the switchable catalysis needs to be tested using a broader monomer pool (**Figure 6.2**) to afford block copolyesters with various thermal/mechanical properties. For monomers with $\text{C}=\text{C}$, it would be possible to apply post-polymerization modification to further tune the properties. So far, the ‘switch’ is usually activated by the addition or depletion of the key monomer (e.g. cyclic anhydride or epoxide in this thesis). Thus, it is also of great interest in the field to develop ‘smart’ catalysts that respond to external stimuli, such as light and temperature.¹⁰ Such switches might allow more precise control, leading to multi-block polyesters with tuneable block sequence, length and even architecture, which could be used as materials for coding information (**Scheme 6.1**).

Cyclic anhydrides:



Epoxides:



Lactones:

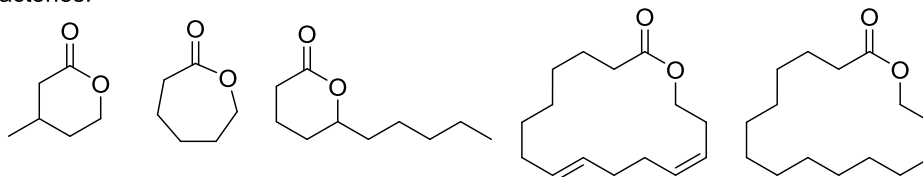
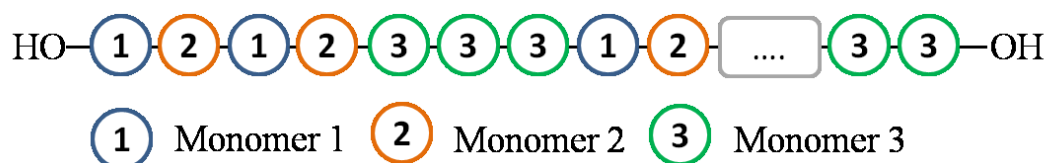


Figure 6.2 Potential monomers which can be used to make block copolyesters *via* chemoselective polymerization method.



Scheme 6.1 Copolyesters with sequence controlled architecture for information coding.

To improve further the mechanical properties of the thermoplastic elastomers, the properties of the ‘hard’ block are critical. In this thesis, multi-block copolyesters comprise PCHPE as the ‘hard’ blocks were described. The blocks already exhibit superior glass transition temperature, comparable tensile strength and Young’s modulus to most of the polyesters and polycarbonates currently used.^{11,12} However, compared to the values obtained using polyolefins as commodity TPEs, PCHPE remains at the lower end of values for its temperature stability, degradation temperature and Young’s modulus. Thus, new monomer combinations need to be developed to make polyesters with crystalline domains (such as stereocontrolled ROCOP) so as to improve the overall polymers’ thermal resistance and stability.

Furthermore, despite the thermoplastic elasticity and shape memory behaviour, the multi-block copolyesters, comprising PA, CHO and ϵ -DL, are expected to generate a toxic compound, phthalic acid, after degradation and thus may not be suitable for biomedical applications *in vivo*. The development of multi-block copolyesters with chemical functionality is attractive as this would allow modification to introduce biomedical properties, including for areas like drug loading/release, antimicrobials and cell affinity. Therefore, screening other aliphatic monomers, especially monomers with functionalities such as vinyl-CHO and vinyl-PO,¹³ could be worth investigating to prepare biodegradable, multifunctional TPEs or shape memory materials for biomedicine.

There also remain challenges prior to biomedical applications of the polyester self-assemblies, especially developing means to overcome the unexpected inflammation response. It will also be important to investigate more fully the biomedical potentials of polymers prepared from other metabolites, such as CO₂, maleic anhydride and glycidyl compounds (**Figure 6.3**). The process benefits from a large monomer pool of both cyclic anhydrides and epoxides, it should therefore be possible to introduce a wide range of functionalities *via* post-polymerization modification methods. For example, reactions like the thiol-ene chemistry or hydroboration could be used to efficiently transform alkenes in vinyl-CHO and vinyl-PO monomers (**Figure 6.4**). Further, it might also be possible to introduce two different functional groups with high degrees of alternation on the polymers prepared by ROCOP (**Figure 6.5**). Such a material might function as a dual stimuli-responsive polymer. Potentially, it might even be possible to achieve new stimuli-responsive behaviour, such as upper critical solution temperature (UCST) in aqueous solution, by introducing functional groups that interact with each other.

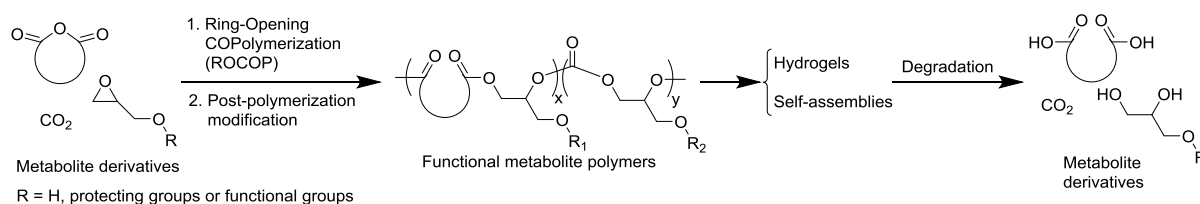


Figure 6.3 Schematic illustration of the synthesis, post-polymerization modification and degradation of metabolite polymers.

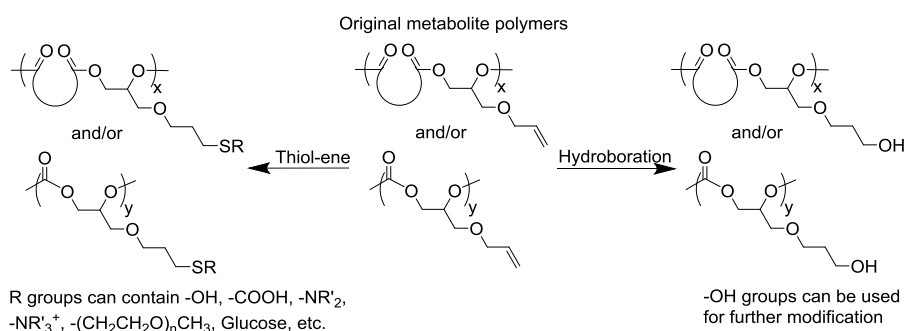


Figure 6.4 Proposed post-polymerization modification routes to afford metabolite polymers with various functionalities.

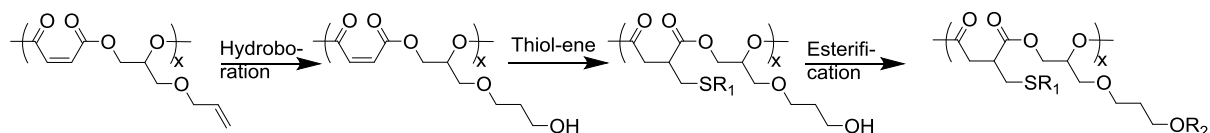


Figure 6.5 Proposed route to afford metabolite polymers with the neighbouring dual functionality.

6.4 References

- (1) Zhu, Y.; Romain, C.; Williams, C. K. *J. Am. Chem. Soc.* **2015**, *137*, 12179-12182.
- (2) Mahmoud, E.; Watson, D. A.; Lobo, R. F. *Green Chem.* **2014**, *16*, 167-175.
- (3) Winkler, M.; Romain, C.; Meier, M. A. R.; Williams, C. K. *Green Chem.* **2015**, *17*, 300-306.
- (4) Aida, T.; Sanuki, K.; Inoue, S. *Macromolecules* **1985**, *18*, 1049-1055.
- (5) Darensbourg, D. J.; Poland, R. R.; Escobedo, C. *Macromolecules* **2012**, *45*, 2242-2248.
- (6) Balasanthiran, V.; Chatterjee, C.; Chisholm, M. H.; Harrold, N. D.; RajanBabu, T. V.; Warren, G. A. *J. Am. Chem. Soc.* **2015**, *137*, 1786-1789.
- (7) DiCiccio, A. M.; Coates, G. W. *J. Am. Chem. Soc.* **2011**, *133*, 10724-10727.
- (8) Bernard, A.; Chatterjee, C.; Chisholm, M. H. *Polymer* **2013**, *54*, 2639-2646.
- (9) Kember, M. R.; Williams, C. K. *J. Am. Chem. Soc.* **2012**.
- (10) Guillaume, S. M.; Kirillov, E.; Sarazin, Y.; Carpentier, J. F. *Chem. Eur. J.* **2015**, *21*, 7988-8003.
- (11) Ulery, B. D.; Nair, L. S.; Laurencin, C. T. *J. Polym. Sci., Part B: Polym. Phys.* **2011**, *49*, 832-864.
- (12) Ikada, Y.; Tsuji, H. *Macromol. Rapid Commun.* **2000**, *21*, 117-132.
- (13) Darensbourg, D. J.; Tsai, F.-T. *Macromolecules* **2014**, *47*, 3806-3813.

Chapter 7

Synthetic Methods

7.1 General Procedures

7.1.1 Materials

All solvents and reagents were obtained from commercial sources (Aldrich and Fisher) and used as received unless stated otherwise. The zinc catalyst $[LZn_2(OAc)_2]$ was synthesized according to the procedure reported previously.¹ Cyclohexene oxide (CHO) was fractionally distilled over calcium hydride once prior to use and stored under an inert atmosphere. 4-Vinyl-1-cyclohexene-1,2-epoxide (vCHO) was dried over calcium hydride prior to the distillation under reduced pressure and stored under N_2 protection at $-35\text{ }^{\circ}\text{C}$. ϵ -Caprolactone (ϵ -CL) was dried over calcium hydride and stored under nitrogen. ϵ -Decalactone (ϵ -DL), δ -valerolactone (δ -VL) was also dried over calcium hydride and stored under nitrogen. *rac*-Lactide (*rac*-LA) was recrystallized three times using dry toluene prior to use and stored under an inert atmosphere. THF and toluene were distilled from sodium and stored under nitrogen. Trans-1,2-cyclohexanediol (CHD) was recrystallized from ethyl acetate and kept under nitrogen atmosphere. Ethylene glycol (EG) was distilled over anhydrous Na_2SO_4 and stored under nitrogen. 2-Methyl-1,3-propanediol (MPD) was distilled over CaO and stored under nitrogen. Poly(ethylene glycol) (PEG 1500) was purified as following: dissolved in methylene dichloride, precipitated using ethyl ether and dried using toluene azeotropic distillation. 1,2-Propane diol and 2-chloro-4,4,5,5-tetramethyl dioxaphospholane were used as received. Phthalic anhydride (PA) was purified via dissolving in benzene and filtering the insoluble impurity (phthalic acid, by ^1H NMR) followed by a recrystallization from $CHCl_3$ and sublimation once. 1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD) was used as received. Methylene diphenyl diisocyanate (MDI) was purified *via* dissolving in hexane and filtering the insoluble impurity, followed by removing all the solvent. Succinic anhydride (SA) was recrystallized from benzene, prior to sublimation, under vacuum, at $100\text{ }^{\circ}\text{C}$. Bis(triphenylphosphine)iminium chloride (PPNCl) was purified by recrystallization from diethyl ether and acetonitrile. Dialysis tubing (14 kDa molecular weight cutoff) was obtained from BioDesign Inc. of New York.

7.1.2 Syntheses of Polymers and Catalysts

*Preparation of 4-tert-butyl-2,6-diformylphenol (compound 4, **Scheme 7.1**)¹*

4-*tert*-Butyl-phenol (20.00 g, 133.2 mmol) and hexamethylenetetramine (29.88 g, 213.2 mmol) were placed in a round bottom flask and TFA (104 mL, 1384.0 mmol) was added slowly to this reaction mixture whilst stirring. The reaction mixture was left to reflux for 17 h at 125 °C. Then the mixture was refluxed for 4 hours at 150 °C using a Dean-Stark condenser to remove water (which formed as a side product). The reaction mixture was cooled to 100 °C and 3M HCl was added (100 mL). The resulting mixture was refluxed for another 40 min, at 100 °C, and then cooled to room temperature and placed in the freezer overnight. The precipitate produced was filtered, washed twice with cold MeOH (-78 °C) and dried, under vacuum to yield yellow crystals (12.57 g, 45 %); δ_{H} (CDCl₃, 400 MHz) 11.50 (s, 1H, -OH), 10.26 (s, 2H, -C(O)H), 8.00 (s, 2H, Ar-H), 1.37 (s, 9H, Ar-C-(CH₃)₃). ¹H NMR spectrum is shown in **Figure 7.1**.

*Preparation of [H₄L](ClO₄)₂ (Compound 3, **Scheme 7.1**)¹*

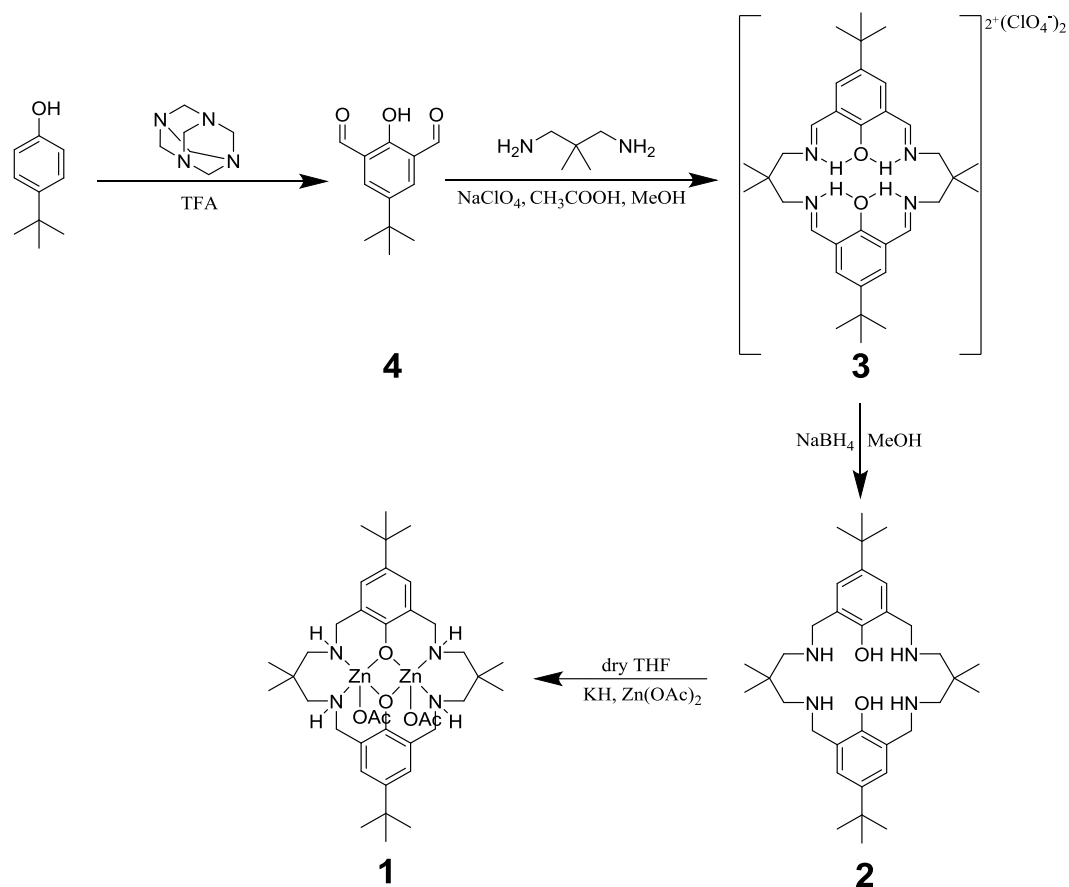
4-*tert*-Butyl-2,6-diformylphenol (2.40 g, 11.6 mmol), NaClO₄ (5.62 g, 46.4 mmol), acetic acid (1.32 mL, 23.2 mmol) and MeOH (180 mL) were placed in a round bottom flask and heated to 70 °C. When the solution began to boil, 2,2-dimethyl-1,3-propanediamine (0.70 mL 5.8 mmol) dissolved in MeOH (60 mL) was added, dropwise. After the addition of the amine, the reaction mixture was cooled to room temperature and stirred overnight. The volume of the resulting red/orange solution was reduced to ca. 120 mL and left to stand for two days. The red crystalline precipitate that formed was filtered and washed with cold MeOH (-78°C) to yield red/orange crystals (2.75 g, 65 %); δ_{H} (DMSO-*d*₆, 400 MHz) 13.60 (br s, 4H, NH/OH), 8.70 (d, 4H, N=CH), 7.66 (s, 4H, Ar-H), 3.88 (s, 8H, CH₂), 1.29 (s, 12H, CH₃), 1.15 (s, 18H, CH₃). ¹H NMR spectrum is shown in **Figure 7.2**.

*Preparation of [H₂L] (Compound 2, **Scheme 7.1**)¹*

$[\text{H}_4\text{L}](\text{ClO}_4)_2$ (2.70 g, 3.62 mmol) was suspended in MeOH (270 mL) and NaBH_4 (3.97 g, 104.94 mmol) was added slowly to the reaction mixture. After the addition of NaBH_4 , the red/orange suspension turned to a colorless solution and was left to stir for another 1 h. Then water was added to the solution, slowly, until a white precipitate persistently appeared and the mixture was left to crystallize overnight. White crystals were obtained (1.2 g, 69%). δ_{H} (CDCl_3 , 400 MHz) 6.96 (s, 4H, Ar-H), 3.76 (s, 8H, CH₂), 2.54 (s, 8H, CH₂), 1.27 (s, 18H, CH₃), 1.03 (s, 12H, CH₃). ^1H NMR spectrum is shown in **Figure 7.3**.

Preparation of $[\text{LZn}_2(\text{OAc})_2]^{\text{I}}$

H_2L (0.40 g, 0.72 mmol) was dissolved in dry THF (10 mL) and transferred into a Schlenk tube containing KH (0.04 g, 1.08 mmol), and cooled to $-78\text{ }^\circ\text{C}$, under nitrogen. The suspension was allowed to warm to room temperature and left to stir for 1 h. The excess KH was filtered and the solution transferred to a Schlenk tube containing $\text{Zn}(\text{OAc})_2$ (0.27 g, 1.48 mmol). The reaction was left to stir for 16 h, after which the THF was removed *in vacuo*, and the product taken up in dry CH_2Cl_2 (10 mL). The suspension was filtered and the CH_2Cl_2 removed, *in vacuo*, to yield the compound as a white powder (0.51 g, 83 %). δ_{H} (Toluene- d_8 , 400 MHz, 383 K) 7.00 (4 H, s, Ar-H), 4.12 (4 H, br s, NH), 3.55 (4 H, br d, CH₂), 3.23 (4 H, br s, CH₂), 2.79 (4 H, br s, CH₂) 2.19 (~ 4 H, br s, CH₂), 1.75 (~ 6 H, s, OAc), 1.24 (18 H, s, Ar-C-CH₃), 0.64 (12 H, br d, CH₂-C-CH₃). ^1H NMR spectrum is shown in **Figure 7.4**.



Scheme 7.1 Synthetic route of bimetallic zinc catalyst $[\text{LZn}_2(\text{OAc})_2]$.

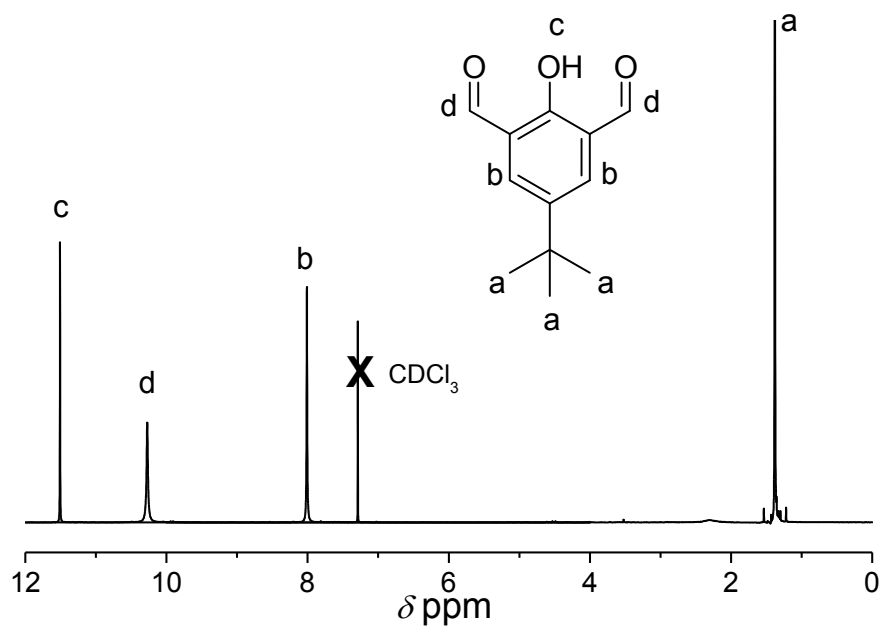


Figure 7.1 ^1H NMR spectrum of 4-tert-butyl-2,6-diformylphenol in CDCl_3 .

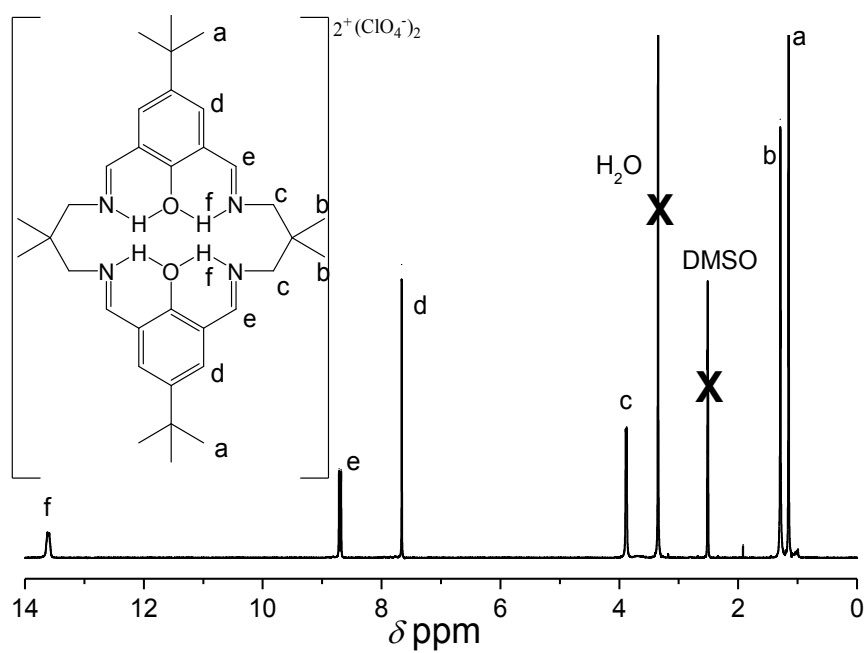


Figure 7.2 ^1H NMR spectrum of $[H_4L](ClO_4)_2$ in $DMSO-d_6$.

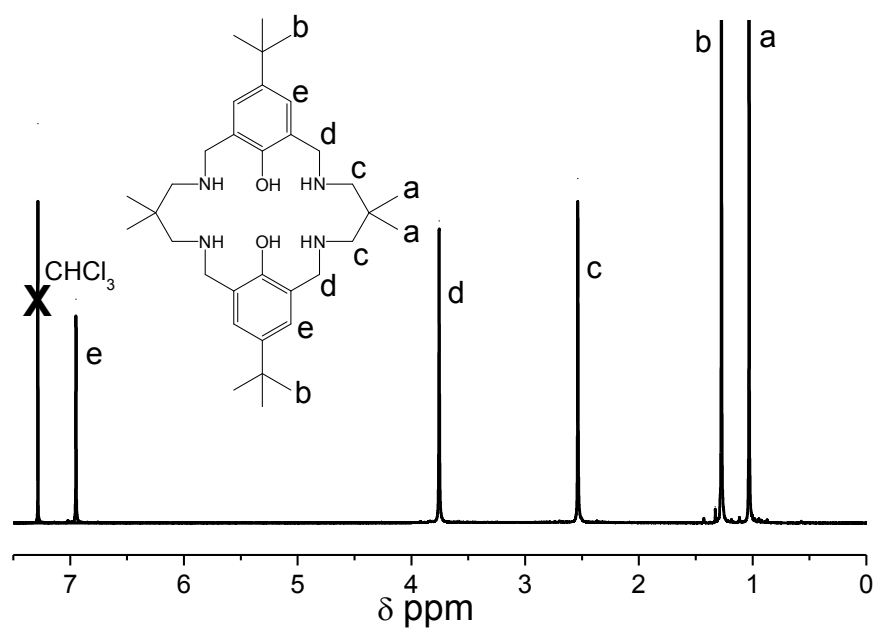


Figure 7.3 ^1H NMR spectrum of $[H_2L]$ in $CDCl_3$.

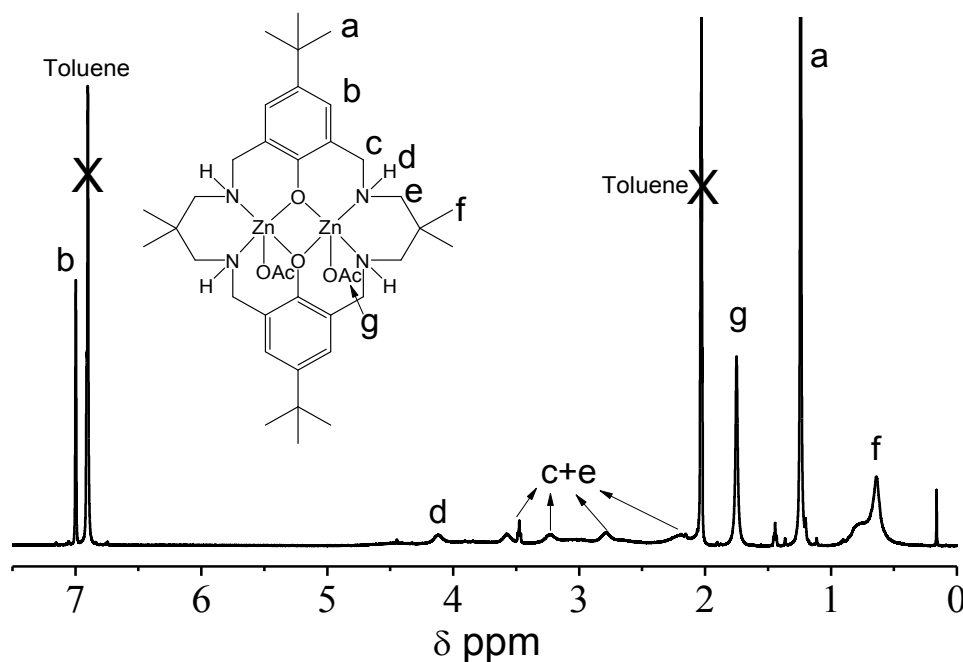


Figure 7.4 ^1H NMR spectrum of $[\text{LZn}_2(\text{OAc})_2]$ in $\text{toluene-}d_8$ at $110\text{ }^\circ\text{C}$.

Monitoring the formation of zinc alkoxide (Figure 7.5) via in-situ ATR-IR spectroscopy

CHO ($1200.0\text{ }\mu\text{L}$, 12.0 mmol) and $[\text{LZn}_2(\text{OAc})_2]$ (48.0 mg , $6.0 \times 10^{-2}\text{ mmol}$) were added into a Schlenk tube, under N_2 , at ambient temperature. A background spectrum was recorded when the detector was just above the liquid level. Then, the reaction temperature was increased to $80\text{ }^\circ\text{C}$ and the mixture was allowed to react for 2 h. Thereafter, the temperature was slowly cooled to ambient temperature and the red solution was left to stir for another 3 h. The molar ratio of $[\text{CHO}]/[\text{LZn}_2(\text{OAc})_2]$ is 200 : 1. The resonances at 1611 cm^{-1} and 1742 cm^{-1} are assigned to the asymmetric stretch of the carboxylate group (κ^2) and to a CHO-bound acetate resonance³, respectively. These two resonances were monitored by ATR-IR spectroscopy.

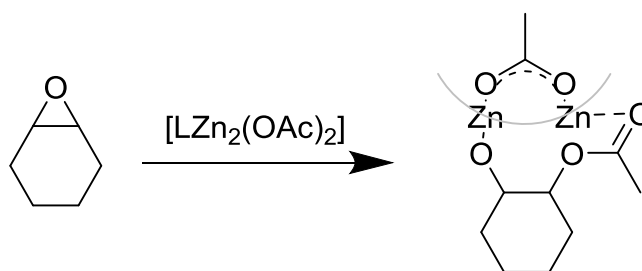


Figure 7.5 The formation of the zinc alkoxide intermediate.

Polymerization of ϵ -caprolactone (ϵ -CL) using the ‘one-pot’ method

In a typical polymerization of ϵ -CL using the ‘one-pot’ method, the $[\text{LZn}_2(\text{OAc})_2]$ (10.0 mg, 1.3×10^{-2} mmol) and ϵ -CL (277.0 μL , 2.5 mmol) were dissolved in CHO (1.1 mL, 11.3 mmol), under N_2 protection in a Schlenk tube, charged with a stir bar. The relative molar ratio of $[\text{LZn}_2(\text{OAc})_2]/[\text{CHO}]/[\epsilon\text{-CL}]$ was 1/900/200. The solution was then heated to 80 $^\circ\text{C}$, and allowed to react for 2.5-3.0 h. Aliquots were taken every 30 min, for ^1H NMR characterization. After 2.5-3.0 h, the polymerization was cooled to room temperature and exposed to air. The final polymer solution was diluted with dichloromethane (DCM, ca. 0.5 mL) and the PCL was purified by precipitation from cold MeOH to yield a white semisolid.

Polymerization of ϵ -caprolactone (ϵ -CL) using the sequential method without the addition of chain transfer agents

In a typical polymerization of ϵ -CL using the sequential method without the addition of chain transfer agents, the $[\text{LZn}_2(\text{OAc})_2]$ (10.0 mg, 1.3×10^{-2} mmol) was dissolved in CHO (1.1 mL, 11.3 mmol), under N_2 protection, in a Schlenk tube, charged with a stir bar. The reaction mixture was then left to react for 1.5 h at 80 $^\circ\text{C}$, to form the zinc alkoxide intermediate. The reaction mixture was then cooled to room temperature, and ϵ -CL (277.0 μL , 2.5 mmol) was carefully transferred to the solution under dynamic N_2 flow. The mixture was allowed to react at 80 $^\circ\text{C}$. The relative molar ratio of $[\text{LZn}_2(\text{OAc})_2]/[\text{CHO}]/[\epsilon\text{-CL}]$ was 1/900/200. Aliquots were taken every 30 min, for ^1H NMR characterization. After 1.0 h, The polymerization was cooled to room temperature and exposed to air. The final polymer

solution was diluted with dichloromethane (DCM, approximately 0.5 mL) and the polymer was precipitated using MeOH (ca. 200 mL) to yield a white solid.

General Procedure for the polymerization of ϵ -caprolactone (ϵ -CL) in the presence of chain transfer agents (CTAs) (Table 2.1 and Figure 7.6)

Typically, the $[\text{LZn}_2(\text{OAc})_2]$ (5.0 mg, 6.25×10^{-3} mmol) and *trans*-1,2-cyclohexanediol (7.3 mg, 6.25×10^{-2} mmol, CHD as CTA) were dissolved in CHO (695.0 μL , 6.25 mmol), in a Schlenk tube charged with a stir bar. The reaction mixture was then heated to 80 $^\circ\text{C}$, and left to stir at this temperature for 1.5 h, to enable complete formation of the zinc alkoxide intermediate. Then, ϵ -CL (340.0 μL , 3.14 mmol) was added into the solution. The mixture was allowed to react at 80 $^\circ\text{C}$. The relative molar ratios, in this case, were $[\text{LZn}_2(\text{OAc})_2]/[\text{CHD}]/[\text{CHO}]/[\epsilon\text{-CL}] = 1/10/1000/500$. Aliquots were taken every 30 min for ^1H NMR characterization. After 2.5-3.0 h, the polymerization was cooled to room temperature and exposed to air. The final polymer solution was diluted with DCM (ca. 1.0 mL). The crude polymer was purified by precipitation from cold MeOH (ca. 200 mL) to afford PCL as a white solid.

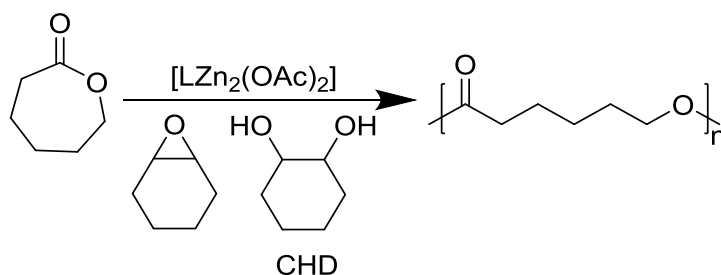


Figure 7.6 Synthetic route of PCL in the presence of chain transfer agent, CHD.

Table 7.1 Relative quantities of reagents used in ϵ -CL ROP listed in Table 2.1

#	Molar ratio	Loadings				CTA type	t (h) ^a
	$[\text{LZn}_2(\text{OAc})_2]/[\text{CTA}]/[\epsilon\text{-CL}]/[\text{CHO}]$	$\text{LZn}_2(\text{OAc})_2$	CTA	$\epsilon\text{-CL}$	CHO		
1	1/10/300/1000	5.0 mg	7.3 mg	210.0 μL	695.0 μL	CHD	2.5
2	1/10/500/1000	5.0 mg	7.3 mg	340.0 μL	695.0 μL	CHD	2.5

3	1/10/700/1000	5.0 mg	7.3 mg	485.0 μ L	695.0 μ L	CHD	2.5
4	1/10/900/1000	5.0 mg	7.3 mg	625.0 μ L	695.0 μ L	CHD	3.0
5	1/10/300/1000	5.0 mg	3.5 μ L	210.0 μ L	695.0 μ L	EG	2.5
6	1/10/300/1000	5.0 mg	4.5 μ L	210.0 μ L	695.0 μ L	PD	2.5
7	1/10/300/1000	5.0 mg	94.0 mg	210.0 μ L	695.0 μ L	PEG	2.5
8	1/10/300/1000	5.0 mg	5.5 μ L	210.0 μ L	695.0 μ L	MPD	2.5

^{a)} Polymerization time after the addition of ϵ -CL Procedure for monitoring the relative quantities of Type I and Type II during the polymerization of ϵ -caprolactone (ϵ -CL) (Section 2.2.5)

The $[\text{LZn}_2(\text{OAc})_2]$ (50.0 mg, 6.3×10^{-2} mmol) and *trans*-1,2-cyclohexanediol (73.0 mg, 6.3×10^{-1} mmol, CHD as CTA) were dissolved in CHO (7.0 mL, 62.5 mmol), in a Schlenk tube charged with a stir bar. The reaction mixture was then heated to 80 °C, and left to stir at this temperature for 1.5 h, to enable complete formation of the zinc alkoxide intermediate. Then, ϵ -CL (3.2 mL, 31.4 mmol) was added into the solution. The mixture was allowed to react at 80 °C. The relative molar ratios were $[\text{LZn}_2(\text{OAc})_2]/[\text{CHD}]/[\text{CHO}]/[\epsilon\text{-CL}] = 1/10/1000/900$. The polymerization was kept at 80 °C for a further 4.5 h after complete ϵ -CL conversion (3.0 h after the addition of ϵ -CL). Aliquots were taken at predetermined time intervals for ^1H NMR and SEC characterization. Then, the polymerization was cooled to room temperature and exposed to air. The final polymer solution was diluted with DCM (ca. 4.0 mL), followed by the addition of cold MeOH (ca. 200 mL) to precipitate the PCL as a white solid.

General Procedure for the polymerization of ϵ -caprolactone (ϵ -CL) in the presence of monofunctional chain transfer agents (CTAs) (Table 2.5)

Typically, the $[\text{LZn}_2(\text{OAc})_2]$ (10.0 mg, 1.3×10^{-2} mmol) and 1-hexanol (7.3 mg, 2.6×10^{-1} mmol, as CTA) were dissolved in CHO (1.3 mL, 13.0 mmol), in a Schlenk tube charged with a stir bar. The reaction mixture was then heated to 80 °C, and left to stir at this temperature for 1.5 h, to enable complete formation of the zinc alkoxide intermediate. Then, ϵ -CL (715.0 μ L, 6.5 mmol) was added into the solution. The mixture was allowed to react at 80 °C and the polymerization was monitored by *in situ* ATR-IR spectroscopy. The relative molar ratios, in

this case, were $[\text{LZn}_2(\text{OAc})_2]/[\text{CHD}]/[\text{CHO}]/[\epsilon\text{-CL}] = 1/20/1000/500$. Aliquots were also taken for ^1H NMR characterization to check the monomer conversion. After 2.5 h, the polymerization was cooled to room temperature and exposed to air. The final polymer solution was diluted with DCM (ca. 1.0 mL). The crude polymer was purified by precipitation from cold MeOH (ca. 200 mL) to afford PCL as a white solid.

Table 7.2 Relative quantities of reagents used in $\epsilon\text{-CL}$ ROP listed in **Table 2.5**.

#	Molar ratio	Loadings				CTA type	t (h) ^a
	$[\text{LZn}_2(\text{OAc})_2]/[\text{CTA}]/[\epsilon\text{-CL}]/[\text{CHO}]$	$\text{LZn}_2(\text{OAc})_2$	CTA	$\epsilon\text{-CL}$	CHO		
1	1/20/500/1000	10.0 mg	31.5 μL	715.0 μL	1.3 mL	1-hexanol	2.5
2	1/20/500/1000	10.0 mg	31.5 μL	715.0 μL	1.3 mL	2-hexanol	2.5
3	1/20/500/1000	10.0 mg	30.5 μL	715.0 μL	1.3 mL	2-methyl-2-pentanol	2.5

^a) Polymerization time after the addition of $\epsilon\text{-CL}$

Typical Procedure for the Ring-opening Copolymerizations (ROCOP) of CHO and PA to prepare poly(cyclohexylene phthalate) (PCHPE) (Figure 7.7, Table 7.X)

Typically, the zinc complex **1** ($[\text{LZn}_2(\text{OAc})_2]$ 10.0 mg, 1.3×10^{-2} mmol) and phthalic anhydride (186.0 mg, 1.3 mmol) were dissolved in CHO (980.0 μL , 10.0 mmol), under N_2 protection, in a screw-cap vial, charged with a stir bar. The solution was then heated to 100 $^\circ\text{C}$, and left to react at 100 $^\circ\text{C}$ for 3.5 h. The relative molar ratios of $[\text{LZn}_2(\text{OAc})_2]/[\text{CHO}]/[\text{PA}]$ were 1/800/100. After the complete consumption of phthalic anhydride, the polymerization was terminated by cooling it to ambient temperature and exposed to air. The crude polymer was isolated by removal of the excess volatiles (CHO) and the sample was analyzed by NMR spectroscopy and SEC. A sample of the crude polymer was also precipitated using pentane to yield a white powder. The purified sample was used for the DSC characterization experiments.

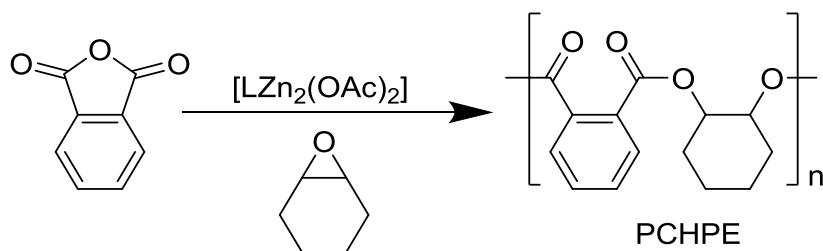


Figure 7.7 Synthetic route to PCHPE.

Table 7.3 Relative quantities of reagents used in ϵ -CL ROP listed in **Table 3.1**.

#	Molar ratio [LZn ₂ (OAc) ₂]/[CHO]/[PA]	Loadings			t (h)
		LZn ₂ (OAc) ₂	CHO	PA	
1	1/800/100	10.0 mg	980.0 μ L	715.0 μ L	3.5
2	1/500/100	10.0 mg	615.0 μ L	715.0 μ L	3.0
3	1/800/100	10.0 mg	980.0 μ L	715.0 μ L	4.0

*Synthesis of PCHPE-*b*-PCL block copolyesters via the sequential method (Figure 7.7)*

The [LZn₂(OAc)₂] (10.0 mg, 1.25×10^{-2} mmol) and phthalic anhydride (37.0 mg, 0.25 mmol) were dissolved in CHO (505.0 μ L, 5.00 mmol), under N₂ protection, in a screw vial, charged with a stir bar. The mixture was then heated to 100 °C and left to react, under inert atmosphere, for 2 h. After the complete consumption of PA, the reaction temperature was reduced to 80 °C, followed by the addition of ϵ -CL into the reaction (210.0 μ L, 1.88 mmol). The mixture was allowed to react for 2 h and monitored by ¹H NMR spectroscopy. The relative molar ratios of [LZn₂(OAc)₂]/[CHO]/[PA]/[ϵ -CL] were 1/400/20/150. The block copolymer was precipitated from the solution using cold MeOH (ca. 200 mL).

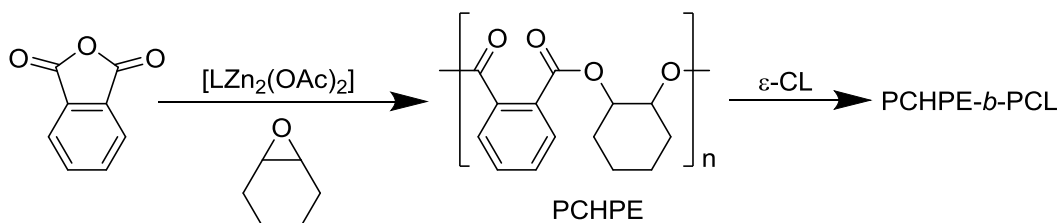


Figure 7.7 Synthesis of PCHPE-*b*-PCL via the sequential method.

Table 7.4 Relative quantities of reagents used in **Table 3.2**.

#	Molar ratio	Loadings				t_1 (h) ^a	t_2 (h) ^a
	[LZn ₂ (OAc) ₂]/[CHO]/[PA]/[ε-CL]	LZn ₂ (OAc) ₂	CHO	PA	ε-CL		
1	1/400/20/100	10.0 mg	505.0 μL	37.0 mg	140.0 μL	2.0 h	2.0 h
2	1/400/20/150	10.0 mg	505.0 μL	37.0 mg	210.0 μL	2.0 h	2.0 h
3	1/400/20/200	10.0 mg	505.0 μL	37.0 mg	280.0 μL	2.0 h	2.0 h
4	1/400/20/0	10.0 mg	505.0 μL	37.0 mg	0.0 μL	2.0 h	2.0 h
5 ^b	1/400/20/150	10.0 mg	505.0 μL	37.0 mg	210.0 μL	2.0 h	2.0 h

^a) the polymerization of PCHPE block is conducted at 100 °C for 2.0 h (t_1) before the addition of ε-CL at 80 °C. The ROP of ε-CL is conducted at 80 °C for another 2.0 h (t_2); ^b) both the polymerization of PCHPE block and PCL block are conducted at 100 °C.

*Synthesis of PCHPE-*b*-PCL block copolyesters from a mixed monomer feedstock of PA, CHO and ε-CL.*

Typically, the [LZn₂(OAc)₂] (10.0 mg, 1.25×10^{-2} mmol), phthalic anhydride (37.0 mg, 0.25 mmol) and ε-CL (210.0 μL, 1.88 mmol) were dissolved in CHO (505.0 μL, 5.00 mmol), under N₂ protection, in a screw vial, charged with a stir bar. The mixture was then heated to 100 °C and left to react, under inert atmosphere, for 2.0 h. The relative molar ratios of [LZn₂(OAc)₂]/[CHO]/[PA]/[ε-CL] were 1/400/20/150. The crude polymer was purified by precipitation using cold MeOH (ca. 200 mL).

Table 7.5 Relative quantities of reagents used in **Table 3.3**.

#	Molar ratio	Loadings				t (h)
	[LZn ₂ (OAc) ₂]/[CHO]/[PA]/[ε-CL]	LZn ₂ (OAc) ₂	CHO	PA	ε-CL	
1	1/400/20/100	10.0 mg	505.0 μL	37.0 mg	140.0 μL	2.0 h
2	1/400/20/150	10.0 mg	505.0 μL	37.0 mg	210.0 μL	2.0 h
3	1/400/20/200	10.0 mg	505.0 μL	37.0 mg	280.0 μL	2.5 h
4	1/400/10/150	10.0 mg	505.0 μL	19.0 mg	210.0 μL	1.5 h
5 ^b	1/400/40/150	10.0 mg	505.0 μL	74.0 mg	210.0 μL	3.5 h

Typical Procedure for the Combined ROP and ROCOP to yield the block copolyesters (PDL-*b*-PCHPE-*b*-PDL) using [LZn₂(OAc)₂] (Figure 7.8)

Typically, the zinc complex **1** ([LZn₂(OAc)₂] 10.0 mg, 1.25×10^{-2} mmol), phthalic anhydride (37.0 mg, 0.25 mmol) and ϵ -DL (205.0 μ L, 1.26 mmol) were dissolved in CHO (1010.0 μ L, 10.00 mmol), under N₂ protection, in a screw-cap vial charged with a stir bar. The mixture was then heated to 100 °C and left to react, under an inert atmosphere, for 4.0 h. The relative molar ratios of [LZn₂(OAc)₂]/[CHO]/[PA]/[ϵ -DL] were 1/800/20/100. The polymerization was terminated by cooling it to ambient temperature. The crude polymer was isolated by removal of the excess volatiles (CHO) and a sample of this material was used for NMR spectroscopy and SEC analysis. A purified sample was also prepared by precipitation from a sample of the reaction solution using cold MeOH (ca. 200 mL), this sample was used for the DSC characterization experiments.

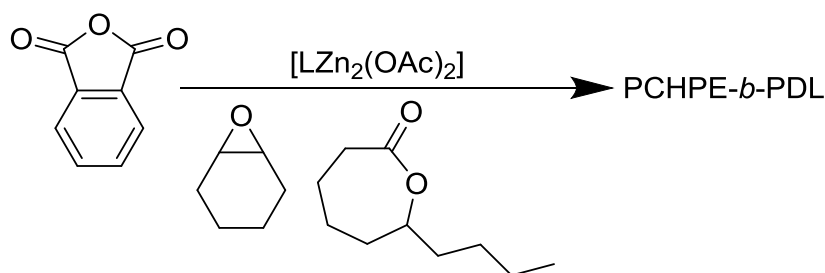


Figure 7.8 Synthesis of PCHPE-*b*-PDL using a mixed monomer feedstock.

Table 7.6 Relative quantities of reagents used in **Table 3.4**.

#	Molar ratio	Loadings				t (h)
	[LZn ₂ (OAc) ₂]/[CHO] /[PA]/[ϵ -DL]	LZn ₂ (OAc) ₂	CHO	PA	ϵ -DL	
1	1/2/800/20/0	10.0 mg	1010.0 μ L	37.0 mg	0.0 μ L	1.0
2	1/2/800/20/100	10.0 mg	1010.0 μ L	37.0 mg	205.0 μ L	2.0
3	1/2/800/20/150	10.0 mg	1010.0 μ L	37.0 mg	308.0 μ L	2.0
4	1/2/800/20/200	10.0 mg	1010.0 μ L	37.0 mg	410.0 μ L	2.5

Preparation of [LZn₂(Ph)₂] (Complex 1)⁴

To a precooled THF solution (-40 °C, 5 mL) of H₂L (318.0 mg, 0.57 mmol) was added a pre-cooled THF solution (-40 °C, 2 mL) of diphenyl zinc (253 mg, 1.15 mmol). After a few minutes, the solution became cloudy. The mixture was allowed to react for 20 h at 25 °C and then, the product was filtered. It was washed with cold THF (10 mL) and was isolated as a white powder (381 mg, 0.46 mmol, 81% yield).

¹H NMR (TCE-*d*₂, 403 K) δ: 7.40 (br, aryl-H, 6H), 7.00 (br, aryl-H, 4H), 5.22-3.90 (br, 4H), 3.60-2.30 (br, 16 H), 1.36 (br, ^tBu, 18H), 1.31 (br, CH₃, 6H), 1.06 (br, CH₃, 6H). ¹³C NMR (TCE-*d*₂, 403 K) δ: 128.1, 126.8, 63.5, 56.8, 31.4, 27.9 and 21.5. (To avoid signals being broadened due to the different complex conformations at low temperature, NMR was conducted at 403 K) Elemental Analysis: Calcd. (%): C, 66.10; N, 7.72; H, 6.70; Found (%): C, 66.03, H, 7.72, N, 6.66.

Typical Procedure for the Ring-opening Copolymerizations (ROCOP) of CHO and PA to prepare poly(cyclohexylene phthalate) (PCHPE) using complex 1, [LZn₂(Ph)₂] (Figure 7.9)

The zinc complex **1** ([LZn₂(Ph)₂]) 10.0 mg, 1.25 × 10⁻² mmol, phthalic anhydride (186.0 mg, 1.26 mmol) and a stock solution of CHD (116.0 μL; 24.0 mg/mL in CHO) were dissolved in CHO (884.0 μL, 8.91 mmol), under N₂ protection, in a screw-cap vial, charged with a stir bar. The solution was then heated to 100 °C, and left to react at 100 °C for 3.5 h. The relative molar ratios of [**1**]/[CHD]/[CHO]/[PA] were 1/2/800/100. After the complete consumption of phthalic anhydride, the polymerization was terminated by cooling it to ambient temperature. The crude polymer was isolated by removal of the excess volatiles (CHO) and the sample was analyzed by NMR spectroscopy and SEC. A sample of the crude polymer was also precipitated using pentane (ca. 200 mL) to yield a white powder. The purified sample was used for the DSC characterization experiments.

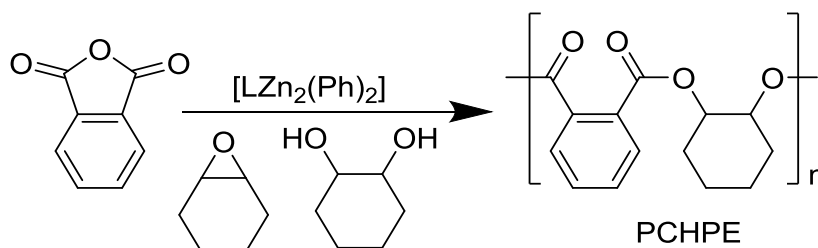


Figure 7.9 Synthetic route to PCHPE.

Table 7.7 Relative quantities of reagents used in **Table 3.5**

#	Molar ratio [LZn ₂ (Ph) ₂]/[CTA]/[CHO]/[PA]	Loadings				t (h)
		LZn ₂ (Ph) ₂	CHD	CHO	PA	
1	1/2/800/100	10.0 mg	2.8 mg	884.0 μ L	186.0 mg	3.0
2	1/4/800/100	10.0 mg	5.6 mg	884.0 μ L	186.0 mg L	3.0
3	1/6/800/100	10.0 mg	8.4 mg	884.0 μ L	186.0 mg	3.5
4	1/8/800/100	10.0 mg	11.2 mg	884.0 μ L	186.0 mg	4.0
5	1/10/800/100	10.0 mg	14.0 mg	884.0 μ L	186.0 mg	4.0

Typical Procedure for the Ring-opening polymerizations (ROP) of ϵ -DL to prepare poly(ϵ -decalactone) (PDL) using complex 1, [LZn₂(Ph)₂] (Figure 7.10)

The zinc complex **1** ([LZn₂(Ph)₂] 10.0 mg, 1.25×10^{-2} mmol), ϵ -DL (410.0 μ L, 2.50 mmol) and a stock solution of CHD (116.0 μ L; 24.0 mg/mL in CHO) were dissolved in CHO (885.0 μ L, 8.91 mmol), under N₂ protection, in a screw-cap vial, charged with a stir bar. The solution was then heated to 100 °C, and left to react at 100 °C for 1.25 h. The relative molar ratios of [**1**]/[CHD]/[CHO]/[ϵ -DL] were 1/2/800/200. The polymerization was terminated by cooling it to ambient temperature. The crude polymer was isolated by removal of the excess volatiles (CHO) and the sample was analyzed by NMR spectroscopy and SEC. A sample of the crude polymer was also precipitated using cold methanol (ca. 200 mL) to yield viscous liquid. The purified sample was used for the DSC characterization experiments.

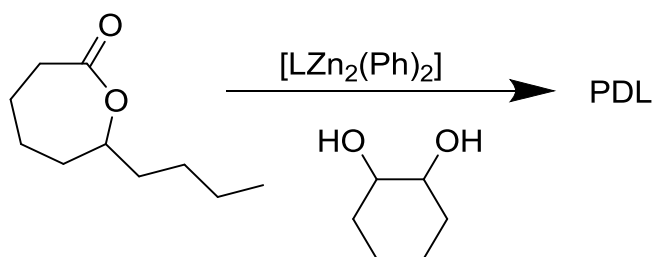


Figure 7.10 Ring-opening polymerization of ϵ -DL, using $[LZn_2(Ph)_2]$.

Table 7.8 Relative quantities of reagents used in **Table 3.6**.

#	Molar ratio	Loadings				t (h)
	$[LZn_2(Ph)_2]/[CTA]/[CHO]/[\epsilon\text{-DL}]$	$LZn_2(Ph)_2$	CHD	CHO	ϵ -DL	
1	1/2/800/200	10.0 mg	2.8 mg	884.0 μL	410.0 μL	1.25
2	1/4/800/200	10.0 mg	5.6 mg	884.0 μL	410.0 μL	1.25
3	1/6/800/200	10.0 mg	8.4 mg	884.0 μL	410.0 μL	1.25
4	1/8/800/200	10.0 mg	11.2 mg	884.0 μL	410.0 μL	1.25
5	1/10/800/200	10.0 mg	14.0 mg	884.0 μL	410.0 μL	1.25

Typical Procedure for the Combined ROP and ROCOP to yield the block copolymers (PDL-*b*-PCHPE-*b*-PDL) using complex 1, $[LZn_2(Ph)_2]$ (Figure 7.11)

Typically, the zinc complex **1** ($[LZn_2(Ph)_2]$ 10.0 mg, 1.25×10^{-2} mmol), phthalic anhydride (186.0 mg, 1.26 mmol), ϵ -DL (205.0 μL , 1.26 mmol) and a stock solution of CHD (116.0 μL ; 24.0 $\text{mg} \cdot \text{mL}^{-1}$ in CHO) were dissolved in CHO (885.0 μL , 8.91 mmol), under N_2 protection, in a screw-cap vial charged with a stir bar. The mixture was then heated to 100 $^\circ\text{C}$ and left to react, under an inert atmosphere, for 4.0 h. The relative molar ratios of $[1]/[CHD]/[CHO]/[PA]/[\epsilon\text{-DL}]$ were 1/2/800/100/100. The polymerization was terminated by cooling it to ambient temperature. The crude polymer was isolated by removal of the excess volatiles (CHO) and a sample of this material was used for NMR spectroscopy and SEC analysis. A purified sample was also prepared by precipitation from a sample of the reaction solution using cold MeOH (ca. 200 mL), this sample was used for the DSC characterization experiments.

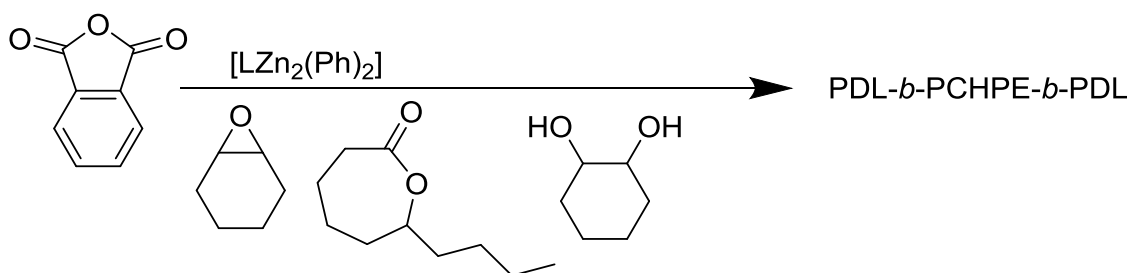


Figure 7.11 Synthesis of PCHPE-b-PDL using a mixed monomer feedstock.

Table 7.9 Relative quantities of reagents used in **Table 3.7**

#	Molar ratio [LZn ₂ (Ph) ₂]/[CTA]/ [CHO]/[PA]/[ε-DL]	Loadings					t (h)
		LZn ₂ (Ph) ₂	CHD	CHO	PA	ε-DL	
1	1/2/800/0/100	10.0 mg	2.8 mg	884.0 μL	0.0 mg	205.0 μL	1.0
2	1/2/800/50/100	10.0 mg	2.8 mg	884.0 μL	93.0 mg	205.0 μL	3.0
3	1/2/800/100/200	10.0 mg	2.8 mg	884.0 μL	186.0 mg	410.0 μL	5.5
4	1/2/800/100/100	10.0 mg	2.8 mg	884.0 μL	186.0 mg	205.0 μL	5.0
5	1/2/800/150/50	10.0 mg	2.8 mg	884.0 μL	280.0 mg	105.0 μL	6.5
6	1/2/800/100/0	10.0 mg	2.8 mg	884.0 μL	186.0 mg	0.0 μL	4.5

Typical procedure for the preparation of PCHPE-b-PDL heptablock copolyesters, using complex 1, [LZn₂(Ph)₂]

The zinc catalyst **1** (10.0 mg, 1.25×10^{-2} mmol), phthalic anhydride (186.0 mg, 1.26 mmol), ε-DL (410.0 μL, 2.50 mmol) and a stock solution of CHD (116.0 μL; $24.0 \text{ mg} \cdot \text{mL}^{-1}$ in CHO) were dissolved in CHO (884.0 μL, 8.91 mmol), under N₂ protection, in an ampoule charged with a stir bar. The mixture was then heated to 100 °C and left to react, under an inert atmosphere, for 4.0 h to reach full conversion of phthalic anhydride and ε-DL. Then, additional phthalic anhydride (93.0 mg, 6.3×10^{-1} mmol) and ε-DL (410.0 μL, 2.50 mmol) were added into the ampoule, under a N₂ flow. The mixture was allowed to react for another 3.0 h, under N₂ protection, at 100 °C. The relative molar ratios of [1]/[CHD]/[CHO]/[PA]/[ε-DL]/[PA (2nd addition)]/[ε-DL (2nd addition)] were 1/2/800/100/200/50/200. The polymerization was terminated by cooling to ambient temperature. The crude polymer was isolated by removal of the excess volatiles (CHO) and a

sample of this material was used for NMR and SEC analysis. Purified polyesters can also be obtained by precipitation from the reaction solution using cold MeOH (ca. 200 mL).

Table 7.10 Relative quantities of reagents used in **Table 3.9**.

#	Molar ratio	Loadings					t (h)
		LZn ₂ (Ph) ₂	CHD	CHO	PA	ε-DL	
	[LZn ₂ (Ph) ₂]/[CTA]/[CHO]/[PA]/[ε-DL]/ [PA (2 nd addition)]/[ε-DL (2 nd addition)]						
1	1/2/800/100/200/50/ 200	10.0 mg	2.8 mg	884.0 μL	186.0 mg	410.0 μL	4.0
		2 nd addition					
2					93.0 mg	410.0 μL	3.0

Typical Procedure for the Combined ROP and ROCOP to yield the block copolyesters using complex 1, [LZn₂(Ph)₂] (Table 3.10)

Typically, the zinc complex **1** ([LZn₂(Ph)₂] 10.0 mg, 1.25×10^{-2} mmol), phthalic anhydride (186.0 mg, 1.26 mmol), ε-DL (205.0 μL, 1.26 mmol) and a stock solution of CHD (116.0 μL; 24.0 mg·mL⁻¹ in vCHO) were dissolved in vCHO (885.0 μL, 8.91 mmol), under N₂ protection, in a screw-cap vial charged with a stir bar. The mixture was then heated to 100 °C and left to react, under an inert atmosphere, for 5.0 h. The relative molar ratios of [**1**]/[CHD]/[vCHO]/[PA]/[ε-DL] were 1/2/800/100/200. The polymerization was terminated by cooling it to ambient temperature. The crude polymer was isolated by removal of the excess volatiles (vCHO) and a sample of this material was used for NMR spectroscopy and SEC analysis. A purified sample was also prepared by precipitation from a sample of the reaction solution using cold MeOH (ca. 200 mL), this sample was used for the DSC characterization experiments.

Table 7.11 Relative quantities of reagents used in **Table 3.10**.

#	Molar ratio	Loadings	t (h)
---	-------------	----------	-------

	[LZn ₂ (Ph) ₂]/[CTA]/[expoxide]/[PA]/[lactone]	LZn ₂ (Ph) ₂	CHD	Epoxide	PA	Lactone	
1	1/2/800/100/200	10.0 mg	2.8 mg	1165.0 μL (vCHO)	186.0 mg	410.0 μL (ε-DL)	5.0
2	1/2/800/100/200	10.0 mg	2.8 mg	884.0 μL (CHO)	186.0 mg	360.0 mg (<i>rac</i> -LA)	5.5
3	1/2/800/100/200	10.0 mg	2.8 mg	884.0 μL (CHO)	186.0 mg	235.0 μL (δ-VL)	6.0
4	1/2/800/100/200	10.0 mg	2.8 mg	1165.0 μL (vCHO)	186.0 mg	235.0 μL (δ-VL)	6.0

Measurement of the Shape-memory Effect

The shape-memory properties (fixed strain ϵ_f , residual strain ϵ_r , strain recovery capability, *etc.*) are defined and quantified using the following equations:

ϵ_f : the fixed strain after being stretched to $\epsilon_{\max} = 300\%$ and left to relax freely at ambient temperature (18 °C).

$$\text{Strain fixity ratio} = \frac{\epsilon_f}{\epsilon_{\max}} \times 100\% \quad (1)$$

ϵ_r : the remaining strain after being heated to 55 °C for 30 s and left to cool to ambient temperature (18 °C).

$$\text{Strain recovery ratio} = \frac{\epsilon_{\max} - \epsilon_r}{\epsilon_{\max}} \times 100\% \quad (2)$$

Shape memory effect as monitored by SAXS: preparation procedure

Sample bars were stretched to 300% and left to relax at ambient temperature (20 °C) to ca. 280% (fixed strain). Thereafter, the stretched sample bars were placed on hot plate (55 °C) for a predetermined time duration to reach different extents of recovery, followed by immediate quenching in liquid nitrogen. Sample bars with a range of strain values (ca. 0%, 75%, 185% and 280%) were then submitted for SAXS characterization.

The Colloidal Self-assembly Protocol

Self-assemblies of the block copolyesters were generally prepared according to the following protocol. The non-solvent, deionized water (4.0 mL) was added dropwise to the block copolyester solution (at a predetermined polymer concentration) in THF (2.0 mL) over a period of 10 min under vigorous stirring (1400 rad/min). Then, de-ionized water (2.0 mL) was poured into the solution to ‘quench’ the self-assembled nanostructures. The residual THF solvent was removed by dialysis with de-ionized water (6×500 mL) over 2 days.

*Synthesis of the hydrophilic epoxide monomer (ME₃MO) (Figure 7.12)*⁵

The synthesis was conducted according to the procedure reported by Wang *et al.*⁵ A mixture of tetrabutylammonium hydrogen sulfate (TBAHS, 2.53 g, 7.50×10^{-3} mmol), epichlorohydrin (41.41 g, 4.47×10^{-1} mmol) and NaOH aqueous solution (36.0 mL, 50 wt%) was vigorously stirred, at 0 °C. Triethylene glycol monomethyl ether (24.00 g, 1.49×10^{-1} mmol) was added to the mixture, dropwise. After the addition of the triethylene glycol monomethyl ether, the mixture was left to react, at 25 °C, for a further 5 h. DCM (100 mL $\times$ 3) was used to extract the product. The collected organic phases were then washed with brine (200 mL $\times$ 3) and dried (anhydrous Na₂SO₄, overnight). After filtration, the solvent was removed *in vacuo* to yield a bright yellow liquid as the crude product. The pure product was isolated after distillation, from CaH₂, and stored under nitrogen (24.57 g, yield: 65.0 %, see Figure 5.1 for ¹H NMR spectrum)

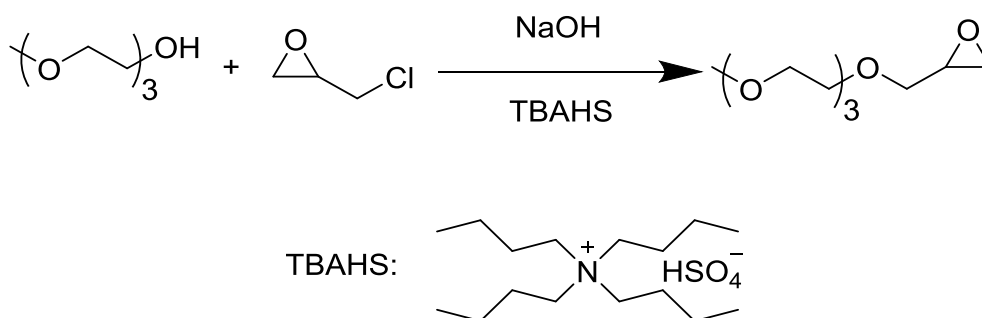


Figure 7.12 Synthesis of the hydrophilic epoxide monomer, ME₃MO.

Synthesis of PCL-OH Macroinitiator (**Figure 7.13**)

Typically, PCL₃₈-OH macroinitiator was synthesized according to the following procedure. The organo catalyst TBD (10.0 mg, 7.20×10^{-2} mmol), ϵ -CL (5.0 mL, 4.31×10 mmol) and 1-hexanol (147.0 μ L, 1.44 mmol) were dissolved in dry toluene (8.6 mL), under N₂ protection, in a Schlenk tube charged with a stir bar. The reaction mixture was allowed to react at 25 °C for 6.5 h. Then benzoic acid (200.0 mg, 1.64 mmol) was added into the mixture, under a N₂ flow to terminate the polymerization. The relative molar ratios of [TBD]/[1-hexanol]/[ϵ -CL] were 1/20/600. The crude PCL was purified by precipitation from the reaction solution by addition of MeOH (50 mL $\times$ 3) to yield white powder.

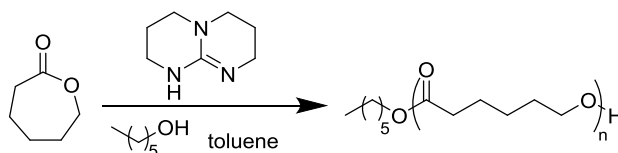


Figure 7.13 Ring-opening polymerization of ϵ -CL, in toluene, using TBD as the catalyst and 1-hexanol as the chain transfer agent.

Table 7.12 Relative quantities of reagents used in **Table 5.1**, entry 1-2.

#	Molar ratio	Loadings			t (h)
	[TBD]/[n-hexanol]/[ϵ -CL]	TBD	n-hexanol	ϵ -CL	
1	1/20/600	10.0 mg	145.0 μ L	5.0 mL	6.5
2	1/20/1000	10.0 mg	145.0 μ L	8.3 mL	10.0

All polymerizations were run in toluene with the initial concentration of ϵ -CL at 5.0 M using n-hexanol as the CTA at 25 °C.

Synthesis of PCL-b-P(SA-alt-ME₃MO) (**Figure 7.14**)

Typically, PCL-*b*-P(SA-*alt*-ME₃MO) was synthesized according to the following procedure. [SalenCrCl] (10.0 mg, 1.58×10^{-2} mmol), PPnCl (9.1 mg, 1.58×10^{-2} mmol), PCL₃₈-OH macroinitiator (640.0 mg, 1.58×10^{-1} mmol), succinic anhydride (237.0 mg, 2.37 mmol) and ME₃MO (600.0 μ L, 2.69 mmol) were dissolved in toluene (1.5 mL), in a Schlenk tube, charged with a stir bar inside the glovebox. The reaction mixture was allowed to react at 80

°C for 6 h. Aliquots were taken regularly to monitor the conversion of succinic anhydride (~80 %). Polymerization was stopped before the full conversion of succinic anhydride. The relative molar ratio of [salenCrCl]/[PPNCl]/[PCL-OH]/[succinic anhydride]/[ME₃MO] were 1/1/10/150/170. The crude polymer was purified by precipitation repeatedly from MeOH (50 mL × 5), to remove any (co)catalysts, residual monomers and free P(SA-*alt*-ME₃MO) chains, until the integral ratio of the PCL and P(SA-*alt*-ME₃MO) remained constant in ¹H NMR.

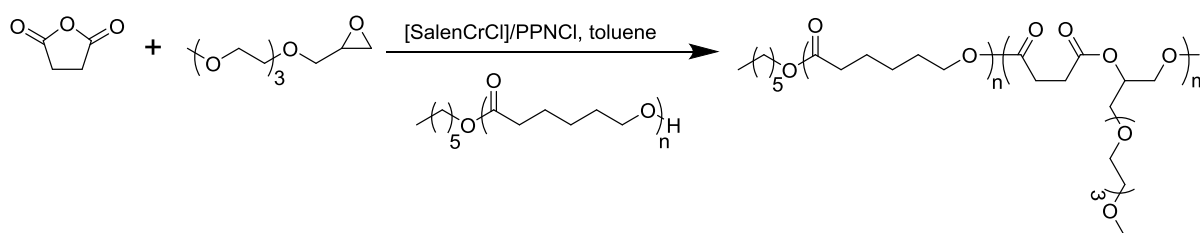


Figure 7.14 Ring-opening copolymerization of SA and ME₃MO, in toluene, using a [SalenCrCl]/PPNCl catalyst system and monofunctional PCL as macroinitiator.

Table 7.13 Relative quantities of reagents used in **Table 5.1**, entry 3-5.

#	Molar ratio	Loadings					t (h)
	[SalenCrCl]/[PPNCl] /[PCL-OH]/[SA]/[ME ₃ MO]	SalenCrCl	PPNCl	PCL-OH	SA	ME ₃ MO	
1	1/1/10/200/220 (PCL ₃₈ -OH)	10.0 mg	9.1 mg	640.0 mg	237.0 mg	600.0 µL	9.0
2	1/1/10/200/220 (PCL ₅₄ -OH)	10.0 mg	9.1 mg	910.0 mg	237.0 mg	600.0 µL	9.0
3	1/1/10/150/170 (PCL ₅₄ -OH)	10.0 mg	9.1 mg	910.0 mg	178.0 mg	465.0 µL	6.0

All polymerizations were run in toluene as the reaction solvent, at 80 °C for 6.0-9.0 h, with an initial concentration of SA at 1.0 M.

7.1.3 Procedures for the evaluation of the drug loading and release

Procedure of making the calibration curve of DOX·HCl in PBS solution

The procedure was previously reported by another group using tris buffer.² In this work, a stock PBS solution (10.0 mM, pH 7.4) of DOX·HCl (500 µg·mL⁻¹) was carefully diluted to a range of concentrations (0.5, 1.0, 2.0, 3.0 and 4.0 µg·mL⁻¹) also using PBS solution (10.0

mM, pH 7.4). The fluorescence intensities of these samples were measured using the Fluorescence Spectrometer described above. The PMT (*photomultiplier* tube) voltage was set to be 570 V. 5 nm was selected as the excitation slit and 5 nm was set as the emission slit. Emission scan (500~800 nm) mode was used during the experiment and the λ_{ex} was fixed to be 461 nm. The peak intensities at 591 nm were taken to prepare the calibration curve. The linear fitting of the calibration curve was conducted in Origin 8.1 and reported in Figure 5.11B. The same instrument settings were used for the investigation of drug releasing profiles.

Colloidal self-assembly drug-loading procedure and *in vitro* release.

The loading of DOX was performed according to the following protocol. The polymer stock solution (2.00 mL, 1.25 mg/mL in THF) was mixed with a DOX stock solution (0.50 mL, 0.05 mg/mL). Then, DI water (5.00 mL) was added, dropwise, to form the polyester vesicles. The organic solvent was removed by flushing the solution with N₂ for 2 h. The residual THF and free DOX (not encapsulated) were removed *via* dialysis using a dialysis tube (MWCO = 14000) against PBS solutions (1.0 L) at 25 °C. The PBS solution was renewed 6 times every 30 min and the concentration of the PBS solutions was increased gradually from 1.0 mM, 2.0 mM, 4.0 mM, 6.0 mM, to 8.0 mM and finally 10.0 mM, to prevent any sudden change in osmotic pressure across the vesicle membrane. Thereafter, the obtained solution was weighed and the fluorescence characterization was conducted to determine the drug loading efficiency (DLE). The *in vitro* drug releasing profile was conducted according to the following procedure. The DOX loaded vesicle solution (5.00 mL) was transferred immediately, to a clean dialysis tube (MWCO = 14000) and dialyzed against PBS solution (100.00 mL of a 10.00 mM solution at pH 7.4) at 37 °C. Aliquots were taken for fluorescence characterization (λ_{ex} = 461 nm; λ_{em} = 591 nm) at pre-determined time intervals. In the control experiment of free DOX delivery, a PBS solution containing DOX was prepared first. The DOX concentration was adjusted to a similar value with the DOX loaded vesicle solution based on the drug loading efficiency measured by the fluorescence spectroscopy. Then, this DOX

solution (5.00 mL) was transferred to a clean dialysis tube (MWCO = 14000 Da) and dialyzed against PBS solution (100.00 mL of a 10.00 mM solution at pH 7.4) at 37 °C. Aliquots were taken for fluorescence characterization ($\lambda_{\text{ex}} = 461 \text{ nm}$; $\lambda_{\text{em}} = 591 \text{ nm}$) at pre-determined time intervals. The calibration for DOX emission was already determined and was applied to determine the value of M_e . The drug loading efficiency (DLE) was calculated according to the following equation.

$$\text{DLE (\%)} = \frac{M_e}{M_f} \times 100\% \quad (3)$$

Where M_e represents the weight of drug encapsulated in vesicles, M_f stands for the starting weight of drug added to the solution.

Enzymatic Biodegradation of the polyester vesicles

Biodegradation of the polyester vesicles was conducted according to the following procedure. The polyester vesicle solution (1.0 mL of a solution of concentration 0.42 mg/mL) was mixed with of *Pseudomonas cepacia* lipase solution (1.0 mL, 200 unit/mL). Control samples were also prepared by mixing the polyester vesicle solution (1.0 mL, 0.42 mg/mL) with DI water (1.0 mL). The mixtures were then placed on a shaker (Eppendorf ThermoMixer, 600 rpm at 37 °C) and aliquots were taken for DLS and SEC measurements at predetermined time intervals.

7.2 References

- (1) Kember, M. R.; Knight, P. D.; Reung, P. T. R.; Williams, C. K. *Angew. Chem., Int. Ed.* **2009**, *48*, 931-933.
- (2) Chen, W. Q.; Du, J. Z. *Sci. Rep.* **2013**, *3*, 2162.
- (3) Buchard, A.; Jutz, F.; Kember, M. R.; White, A. J. P.; Rzepa, H. S.; Williams, C. K. *Macromolecules* **2012**, *45*, 6781-6795.
- (4) Zhu, Y.; Romain, C.; Williams, C. K. *J Am Chem Soc* **2015**, *137*, 12179-12182.
- (5) Wang, W.; Ding, J.; Xiao, C.; Tang, Z.; Li, D.; Chen, J.; Zhuang, X.; Chen, X. *Biomacromolecules* **2011**, *12*, 2466-2474.

Chapter 8

Characterization Techniques

8.1 Techniques and methods

In the formation of block copolymers, it is important to accurately determine the structure. Particularly, it is important to distinguish the block structures of ABA type and AB type block copolymer by analysing the end groups. The methods which are used to characterize the block structures are described in this section below.

SEC: Size Exclusion Chromatography (SEC) is used to determine the molecular weight and dispersity ($\mathcal{D}$) of a polymer sample. Different species can be separated according to their hydrodynamic size, which is achieved by passing the sample through column packed by porous materials. The species with smaller size enters the pores and therefore it takes more time for this species to pass through the column. However, the species with larger size cannot enter the pores and therefore it takes less time for this species to pass through the column.

Therefore, the elution time of certain species is related to its hydrodynamic size and can be converted into the relative molecular weight by using standards to calibrate the column, assuming that all the polymer chains in solution have spherical shape. In this work, narrow polystyrene standards purchased from PSS were used for calibration. It is noteworthy that SEC converts the hydrodynamic size of a species into molecular weight using polystyrene as the reference, so it is strongly influenced by the structure of the polymer. For well-known polymers, correction factors (X) can be applied to the MWs determined using the PS standards.

$$M_{n(\text{corrected})} = X \cdot M_{n(\text{SEC})}$$

When the polymer chains in one polymer sample have closely related lengths, the SEC trace is usually a Gaussian distribution with a narrow distribution. However, when the SEC trace appears to be broad or lopsided, this indicates that not all of the chains have the same propagation rates, which is often due to the presence of different chain structures. SEC is the most commonly applied method to confirm the formation of block copolymers. For an ABA

type block copolymer, SEC trace of ABA shifts to a higher MW than that of the macroinitiator (the B block).

The molecular weights and dispersities were characterized using an Agilent PL GPC-50 instrument, with HPLC grade THF as the eluent at a flow rate of $1.0 \text{ mL} \cdot \text{min}^{-1}$ at 40°C . Two PLgel Mixed D columns (particle size: $5 \text{ }\mu\text{m}$; linear MW operating range: $200\text{--}400000 \text{ g} \cdot \text{mol}^{-1}$) were used in series. Near monodispersed polystyrene standards (Polymer Standards Service) were used to calibrate the instrument. The polyesters were dissolved in HPLC grade THF and filtered prior to analysis. In some cases, a different SEC instrument was used: A Shimadzu LC-20AD, was used to characterize the molecular weights and dispersities, using a Multi-Angle Laser Light Scattering Detector (MALLS) detector, with two Mixed Bed PSS SDV linear S columns and THF as the eluent, at a flow rate of $1.0 \text{ mL} \cdot \text{min}^{-1}$ at 30°C . This is due to the fact that MALLS detector is connected to the Shimadzu system. This instrument was used when the MALLS detector was required to determine the absolute molecular weights. The MALLS detector was calibrated by polystyrene standards and the dn/dc values were measured using an external RID detector (Knauer) with at least 3 different concentrations of the polymer to be analysed (Figure A2 and A4). Basically, the refractive index values of the polymer solutions were plotted against the corresponding concentrations. Linear fitting was applied to the plots (software: Astra 6.1 from Wyatt Technology) and the dn/dc value was taken from the slope of the linear fitting. The limitation of this method is that the dn/dc value of a polymer changes over MW.¹ Therefore, it is important to check the dn/dc value of individual polymers. Crude polymers were used for SEC characterization unless stated otherwise.

NMR: NMR spectroscopy of polymers is usually complicated due to the fact that a polymer sample is a mixture of polymer chains with different MWs, leading to the peak broadening. It is possible to characterize the final repeat unit at the chain end as the chemical shift of that final repeat unit is often distinct. Therefore, it might be possible to calculate the molecular weight of the polymer using the normalized integral of the ^1H NMR signals of both the end

groups and the backbone signals. It is noteworthy that due to the weak signals of the end groups, the MWs calculated *via* ^1H NMR may not be accurate. For polymers with high molecular weight, it could be very hard to detect the end group signals.

^1H , $^{13}\text{C}\{^1\text{H}\}$, $^{31}\text{P}\{^1\text{H}\}$ and 2D NMR (COSY & HSQC) spectra were recorded using a Bruker AV 400 spectrometer at room temperature (unless otherwise stated). Spectra were processed and analyzed using Mestrenova software (version 8.0). All the ^1H NMR data used for end group calculation were recorded with extended relaxation delay (d_1) of 25s. All the $^{31}\text{P}\{^1\text{H}\}$ NMR data used for end group determination were recorded with extended relaxation delay (d_1) of 15 s (longest t_1 was determined to be 3s). It is not always possible to detect the hydroxyl signals in ^1H NMR spectroscopy due to the fast proton exchange of hydroxyl groups with residual water or other protic sources. Therefore, the reaction between hydroxyl groups and 2-chloro-4,4,5,5-tetra-methyldioxaphospholane is used to characterized the nature of the end groups.² This method can be used to characterize polymeric species featuring hydroxyl end groups, by reacting the hydroxyl terminated polymers with a dioxaphospholane, using Bis-phenol A (138.57 ppm) as the internal reference. Typically, hydroxyl groups have ^{31}P signals ranging from 146 ppm to 148 ppm (usually, 146.4-147.8 ppm for primary hydroxyls and 146.1-146.2 ppm for secondary hydroxyls).² Carboxylic acid end groups appear at ca. 135.5-135.7 ppm.²

Sample preparation procedure for end group (–OH) determination using ^{31}P NMR

The preparation procedure was according the procedure reported previously by Spyros et al.² Typically, a stock solution was prepared by dissolving 400 mg of Bisphenol A (BPA) and 5.5 mg of $\text{Cr}(\text{acac})_3$ in 10 mL of pyridine. A polymer solution in CDCl_3 with the concentration of 30 mg/mL was then prepared. A 400 μL of the polymer solution and 40 μL of the stock solution were mixed in a 5 mm NMR tube. Thereafter, excess 2-chloro-4,4,5,5-tetramethyl dioxaphospholane (40 μL) was transferred into the NMR tube. The mixture was allowed to react for 6.0 h prior to characterization.

¹H DOSY NMR Spectroscopy: Diffusion ordered spectroscopy (DOSY) distinguishes the NMR signals based on the different diffusion coefficients of the species, which provides a means to determine whether all NMR signals belong to one species. Spin-echo spectra, with different pulsed field gradient strengths are collected and the signal decays are measured. The spin-echo intensity of a spin active nucleus, (*I*), relates to the diffusion coefficient (*D*) of the molecule by the following equation:

$$\ln\left(\frac{I}{I_0}\right) = -\gamma^2 \delta^2 G^2 \left(\Delta - \frac{\delta}{3}\right) D$$

where γ is the gyromagnetic ratio, δ is the length of the gradient pulse, G is the gradient strength, and Δ is the delay between gradient midpoints, D is diffusion coefficient, I is spin echo intensity.

From the diffusion coefficient of a species, its hydrodynamic radius (R_h) can be calculated using Stokes-Einstein equation:

$$R_h = \frac{k_B T}{6\pi\eta D}$$

where k_B is the Boltzmann constant, T is the temperature, and η is the solvent viscosity at the measured temperature, D is the diffusion coefficient, R_h is the hydrodynamic radius.

DOSY measures the diffusion coefficient which can be converted to the hydrodynamic radius using Stokes-Einstein equation, based on assumptions. In polymer chemistry ¹H DOSY NMR spectrum can be used to characterise block copolymers. For a block copolymer, all the ¹H NMR signals should have the same diffusion coefficient. However, if the block copolymer sample also contains homopolymer species, ¹H NMR signals would show different diffusion coefficients.

In this thesis, ¹H DOSY experiments were performed on a Bruker AV 500 spectrometer at a steady temperature of 298 K with at least 32 gradient increments using the ledbpgp2s sequence. Complete diffusion was ensured using the T1/T2 module of Topspin and DOSY

transformations using either mono, bis- or tri-exponential fitting were performed using the same software after zero filling. Further processing was achieved using the topspin software (version 3.1); DOSY data collection and analysis were carried out by Mr. Peter Haycock at Imperial College London.

MALDI-ToF: Matrix-assisted laser desorption/ionization time of flight analysis (MALDI-ToF) is a soft ionization technique for mass spectrometry. Typically, each polymer chain with a specific molecular weight contributes a separate signal. The difference in m/z between two neighboring signals should equal to the molar mass of the repeat unit of that polymer. When all polymer chains have the same structure but different chain length, only one distribution can be observed. However, if the polymer chains have different end groups, several distributions can be observed. These distributions usually separated by the same repeat unit but differ in the end group mass. In this thesis, potassium ions are used as the ionizing agent in order to generate the spectrum. Therefore, K^+ ion must be taken into account when calculating the theoretical mass. In the case when polymers are end-capped by an anionic end group, e.g. $-COO^-$, then it is possible that one potassium ion forms a salt with the end group and another potassium ion acts as the ionizing agent, leading to the detection of a polymer structure of $P-2K^+$. Although MALDI-ToF is a powerful technique to determine the polymer structure, it is noteworthy that different species are ionized or accelerated in different ways. The intensity of a signal should not be used to quantify the relative concentration of the polymeric species

MALDI-ToF spectra of polyesters were carried out on Waters/Micromass MALDI micro MX spectrometer. For homopolyesters, samples were dissolved in THF along with a dithranol matrix, at a loading of 1:5, using potassium trifluoroacetate (KTFA) as the cationizing agent. For alternating polyesters, samples were dissolved in THF, at a concentration of $1 \text{ mg} \cdot \text{mL}^{-1}$. Trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) was used as the matrix, at a concentration of $10 \text{ mg} \cdot \text{mL}^{-1}$ in THF. Potassium trifluoroacetate (KTFA) was used as the cationizing agent, at a concentration of $1 \text{ mg} \cdot \text{mL}^{-1}$. In both cases, the

solutions of polymer, matrix and salt were mixed in a ratio of 1/1/1 (v/v/v), respectively. The mixed solution was spotted on a stainless steel MALDI plate repeatedly (5 times) and left to dry in the fume hood, overnight. The spectrum was recorded using reflectron mode.

In situ ATR-IR Spectroscopy: *In situ* ATR-IR spectroscopy allows a reaction to be monitored in real time, by monitoring the intensity changes of the vibrational modes of certain compounds. An ATR-IR probe is placed inside the reaction mixture and spectra are recorded at predetermined time intervals. In this thesis, it was used to determine whether or not the two polymerisation approaches (ROCOP and ROP) are occurring simultaneously or sequentially. Characteristic peaks are assigned to the species (monomers or polymers) *via* control experiments (conventional ATR-IR of the pure species).

The conversion at specific time points can be determined using ^1H NMR spectroscopy of aliquots and the following relation used.

$$\text{Conversion} = \frac{I - I_0}{I_{\max}} \times \text{conversion at } I_{\max}$$

where I = Intensity, I_0 = Initial intensity, $I_{\max}$ = Intensity at complete conversion.

The polymerizations were monitored using a Mettler-Toledo ReactIR 4000 spectrometer equipped with a MCT detector and a silver halide DiComp probe. The data was calibrated by independent determination of the conversion of the monomer, using ^1H NMR spectroscopy. Typically, PA (89.0 mg, 0.6 mmol), CHO (2.0 mL, 19.2 mmol), ϵ -DL (210.0 μL , 1.2 mmol) and $[\text{LZn}_2(\text{Ph})_2]$ (10.0 mg, 0.012 mmol) were added into a two neck Schlenk tube under nitrogen, inside the glove box. Then, the React-IR probe was placed in this two neck Schlenk tube. The reaction mixture was allowed to react at 100 $^\circ\text{C}$ under nitrogen. Aliquots were taken at certain intervals under a positive flow of N_2 to check the monomer conversion. The reaction was quenched by exposure to air. The polymer was purified by precipitation from excess cold MeOH (ca. 200 mL).

Thermal Analyses: Differential Scanning Calorimetry (DSC) compares the heat required to increase the temperature of a sample against the reference, which can be used to characterise the thermal transitions of polymer samples. Typically, the sample and reference are maintained at the same temperature, while the temperature is increased linearly. The amount of heat required to keep the sample temperature the same as the reference temperature is measured. When a thermal transition of the polymer sample occurs, endothermic or exothermic heat flow can be detected. Glass transition is related to a change in heat capacity of a sample and causes a baseline shift. Melting is an endothermic process and crystallisation is an exothermic process. A typical DSC curve is a plot of heat flow (Y axis) against temperature (X axis). The enthalpies associated with the thermal phase transitions can be calculated by integration of a certain transition, given that the mass of the sample is known and accurate.

$$\Delta H = KA$$

where ΔH is the enthalpy of the transition, K is the calorimetric constant and A is the area of the transition.

For amorphous polymers studied in this thesis, the main transition determined by DSC is the glass transition temperatures (T_g). The glass transition temperature is related to the chain mobility and is affected by the chain length, the backbone structure, the nature of the side chains and end groups. Polymers with high T_g values are usually rigid plastics, while polymers with low T_g values ($<$ room temperature) are usually soft materials.

The thermal properties of a copolymer can indicate its structure. For instance, distinct T_g values can be observed in DSC when the blocks are not miscible. Also, these T_g values of the blocks should appear in the similar region to the T_g values of their homopolymer analogues. However, when the blocks are completely miscible, only a single T_g can be observed. In this case, the Fox-Flory equation can be used to predict the T_g value.

$$\frac{1}{T_g} = \frac{w_1}{T_{g,1}} + \frac{w_2}{T_{g,2}}$$

where w_1 = weight fraction of 1st block; $T_{g,1}$ = glass transition temperature of 1st homopolymer at infinite chain length; w_2 = weight fraction of 2nd block; $T_{g,2}$ = glass transition temperature of 2nd homopolymer at infinite chain length; T_g = glass transition temperature of the copolymer.

However, the results given by the Fox-Flory equation are only correct when the blocks are fully miscible. Therefore, if the experimental T_g value is in poor agreement with the Fox-Flory result, this indicates that the blocks may not be fully miscible.

The thermal properties were measured using DSC Q2000 (TA Instruments, UK). A sealed empty crucible was used as a reference, and the DSC was calibrated using indium. Samples (usually, 5-10 mg) were heated from room temperature to the predetermined temperature, at a rate of 10 °C·min⁻¹, under helium flow (50 mL·min⁻¹), and were kept at that temperature for 2 min to erase the thermal history. Subsequently, the samples were cooled to another predetermined temperature, at a rate of 10 °C·min⁻¹, and kept at that temperature for further 2 min, followed by a heating procedure from the predetermined lower temperature to the higher temperature, at a rate of 10 °C·min⁻¹. Each sample was run for three heating-cooling cycles. The glass transition temperatures (T_g) reported are taken from the third cycle. Usually, the heat capacity of the polymer increases above the glass transition temperature. Therefore, DSC is a good method to determine the glass transition temperature, T_g . However, the glass transition usually occurs over a range of temperatures rather than at one unique temperature. Thus, glass transition temperature is usually defined as the temperature in the middle of the inclined temperature range. The DSC data collection and analysis in this work were carried out using Universal Analysis 2000 (version 4.3A from TA Instruments). It is important to note that the glass transition temperature determined by DSC also depends on the heating rate. Using high heating rate (> 10 °C·min⁻¹) benefits the T_g detection because the heat flow signal during the glass transition can be enhanced with less increase in noise. However, the glass

transition temperature shifts to higher temperature at higher heating rate due to the fact that the glass transition is a ‘structural relaxation’. If the heating rate is much larger than the relaxation time of the polymer, the ‘structural relaxation’ does not have enough time to occur during the observation time, leading to the increase in the T_g value.³ Considering that most of the DSC measurements in literature were conducted at a rate of $10\text{ }^{\circ}\text{C}\cdot\text{min}^{-1}$, the same heating rate was also applied in this work to allow the comparison between the value reported in this work and in literature.

Thermo-gravimetric analysis (TGA) measures the weight change of a sample against temperature, which usually use to characterize the thermal degradation of a material. Typically, a sample (10-20 mg) is placed in a sample pan and heated linearly (constant heating rate) to a predetermined temperature in air or an inert gas (N_2 in this work), while the weight of the sample is monitored over the experimental period. Usually, the furnace temperature is calibrated using standard materials like alumel, zinc or perkalloy. The microbalance is calibrated using a standard weight (100 mg). A TA instrument (TGA 550) was used to characterize all the multiblock copolymer samples in this work. All measurements were conducted under nitrogen with a heating rate of $20\text{ }^{\circ}\text{C}\cdot\text{min}^{-1}$, from the ambient temperature to $450\text{ }^{\circ}\text{C}$.

Mechanical Measurements: Solvent-cast polyester sheets were prepared by pouring DCM solutions of the polymer into a Teflon mold. The solvent was slowly evaporated, in the fume hood, at room temperature for 2 months. ^1H NMR spectroscopy was used to check for any solvent residues. After 2 months, the DCM peak could no longer be observed, indicating the polyester sheets are sufficiently dry for mechanical tests. Dumbbell-shaped sample bars were then cut from the polyester sheet (35 mm in length, 2.1 mm in gauge width as described in the standard, ISO 527) using a Zwick Punch (Zwick D-7900, Ulm-Einsingen Type 7102, Werk-Nr. 85688) with cutting blades in the lab of Prof. Milo Shaffer. The operation training of the Zwick Punch was conducted by Dr. David Anthony from Prof. Milo Shaffer’s group at Imperial College London. Approximately 6 months after the solvent-casting experiments, the

mechanical properties including strength, elongation and Young's modulus (**Table 4.2** and **Figure 4.4**) were measured in the lab of Prof Marc Hillmyer at the University of Minnesota. The operation training was conducted by Mr. Guilhem De Hoe from Prof Marc Hillmyer's group. The measurements were conducted at ambient temperature and humidity (22.0 °C and 16 %) on a Shimadzu AGS-X 500N Tensile Stress Tester instrument, at 10 mm/min extension rate, using the ISO-527 standard. The results were analyzed using TRAPEZIUMX V1.4.0 software. The thickness of a sample bar was measured using a caliper and the average value was calculated using the thickness measured at three different positions on an individual sample bar. The length of a sample bar between two pneumatic grips was also measured using a caliper. The average thickness, width and the length between grips were input into the software prior to testing. The stress, strain values and Young's modulus were calculated using the same software.

The plastic-to-rubber transition (**Figure 4.5**) were measured at ambient temperature and humidity (21.8 °C and 21 %) on a Linkam TST350 Tensile Stress Tester instrument at 10 mm/min extension rate and 10 mm/min retraction rate, in the lab of Prof. Milo Shaffer. The operation training was conducted by Dr. David Anthony from Prof. Milo Shaffer's group at Imperial College London. The cross section has to be set as $0.001 \times 0.001 \text{ mm}^2$ in the software prior to testing. Therefore, the strain and stress values given by the software need to be corrected manually using the original values of the cross section. The thickness and width of a sample bar were measured using a caliper and the average value was calculated using the values measured at three different positions on an individual sample bar for further calculation. Also, the starting length of a sample bar between two grips was also measured using a caliper for further calculation.

In this thesis, only the engineering stress and the engineering strain were calculated and plotted, instead of the true stress and the true strain. The engineering stress is the applied force divided by the original area of the cross section of a material, while the true stress is the

applied force divided by the actual cross section area of the sample bar at that force. The engineering stress values were calculated using the following equation:

$$\sigma = F/A_0$$

Where σ is the engineering stress value, F is the applied force and A_0 is the original area of the cross section.

The engineering strain values were calculated using the following equation:

$$\varepsilon = \Delta l/l_0$$

Where ε is the engineering strain value, Δl is the change in length and l_0 represents the original value of the gage length.

It is noteworthy that the crosshead displacement value was used to calculate the engineering strain, which overestimates the true displacement value. Therefore, the upper bound of the engineering strain was calculated based on the crosshead displacement, assuming that machine compliance and any slip in the grips are negligible.

Dynamic Mechanical Thermal Analysis (DMTA): DMTA is a very versatile and sensitive technique to measure the polymer viscoelastic mechanical properties. The viscoelastic properties can be studied either over a set temperature or a set frequency. In a typical DMTA experiment, a sinusoidal stress is applied to the sample and the strain is measured. For a completely elastic material, the strain will be perfectly in phase with the stress, (phase angle = 0°). However, for a viscous fluid, a 90° phase lag of the strain will be observed, comparing to the stress. Viscoelastic materials, like polymers, exhibit a phase lag in between these 2 values.

In this thesis, DMTA tests were performed on the solvent cast samples using an RSA (RSA G2, TA instrument). The dynamic moduli were measured as a function of temperature, at a frequency of 1 Hz, a strain value of 1%, and a ramp rate of $3^\circ\text{C}\cdot\text{min}^{-1}$ from -55 to 100°C .

The tests were conducted under the tensile mode. Therefore, to avoid the sample bar turning into viscous liquid inside the instrument, the upper temperature was set to be 100 °C based on the T_g value given by DSC measurements. The characterization conditions (e.g. frequency, heating rate and strain value) were chosen from literatures to allow the comparison between the values in this work and the values reported in the literatures. During the DMTA analysis, the viscoelastic properties of the material are characterized *via* the application of a sinusoidal deformation at certain frequencies and the response of the material is monitored. Polymers are viscoelastic materials. This means the response of a polymer to an applied deformation depends on the speed of the deformation.⁴ By definition, frequency is the inverse of time (1/t), thus high frequency means short time while low frequency means long time. Therefore, the storage modulus and the glass transition temperature of a polymer increase with frequencies.⁴ Although the T_g values measured by DMTA are not discussed in this thesis, it is important to note that the glass transition is a ‘structural relaxation’, involving the segmental motion. Since the rate of the segmental motion depends on temperature, the relaxation occurs at higher temperature with increasing frequency. This results in the increase of T_g values with increasing frequency. The increase of T_g values can also be observed when the heating rate is increased in DSC measurements, as discussed in the DSC section.

SAXS characterization: SAXS is a technique which can be used to evaluate the structure with the length scales of 1~100 nm. The scattering vector, q , is used in scattering characterizations. The scattering vector is defined by the following equation:

$$q = \frac{4\pi \sin \theta}{\lambda}$$

where q is the scattering vector; λ is the wavelength of the X-ray; θ is the Bragg scattering angle.

The scattering vector can be converted into the real space (d) using the following equation:

$$d = \frac{q}{2\pi}$$

Since SAXS provides the morphology information from a much greater volume than TEM, it is more statistically representative. Highly intense X-rays can be acquired from a synchrotron X-ray source. Using the synchrotron X-ray facility, large detector distances can be used to facilitate the detection of signals at very low q , which allows the evaluation of morphologies at the scale of hundreds of nanometres.

SAXS analysis in this thesis was conducted in collaborations with Prof. Marc Hillmyer and was performed by Dr Madalyn R. Radlauer at the Advanced Photon Source (APS) at Argonne National Laboratory at the DuPont-Northwestern Dow Collaborative Access Team (DND-CAT) Synchrotron Research Centre located at Sector 5 of the APS. For these experiments, the energy was 16.4000 keV, and scattering intensities were monitored using a CCD area detector, at a sample to detector distance of 850 cm. All experiments were conducted at ambient temperature using solvent-cast polymer sheets. The solvent was slowly evaporated, in the fume hood, at room temperature for 2 months. The solvent peak (DCM) can no longer be observed after 2 months, indicating the polyester sheets are sufficiently dry. Some dry polymer sheets were further annealed at 130 °C under N₂ over 48.0 h, prior to SAXS characterization. To obtain 1-D spectra, the 2-D scattering patterns were azimuthally integrated to give the scattering intensity with respect to the scattering vector (q).

WAXS characterization: The scattering of X-rays by the crystalline structure generates a characteristic pattern. The intensities and positions of the scattering pattern can be used to evaluate the crystallographic information and in terms of polymeric materials, the crystallinity. The relationship between the scattering angle and the real space distance can be described using the Bragg's Law:

$$n\lambda = 2d\sin\theta$$

where n is a positive integer; λ is the wavelength of X-ray; θ is the scattering angle and d is the real space distance.

WAXS analysis is usually performed at wide angle ($2\theta \geq 5^\circ$), which is corresponding to the length scale of ca. 1 nm. Although WAXS should be considered as a non-destructive technique, it might be destructive to polymers having weak inter-chain bonds or low melting temperature. In this thesis, WAXS was used to check whether the multiblock copolyesters discussed in chapter 4 is amorphous. The WAXS characterization was conducted by Mr Richard Sweeney from the Department of Materials at the Imperial College London. All characterizations were conducted at ambient temperature using the same samples as the ones previously used for SAXS characterization

Transmission Electron Microscope (TEM): Instead of using photons, TEM uses electrons to characterize the microstructure of the samples. At sufficiently high accelerating voltages, the de Broglie wavelength of an electron is significantly less than interatomic distances. By using electron optical lenses, it is possible to illuminate and form images of samples at much higher resolution than is possible in a conventional light microscope. By changing the accelerating voltage of an electron source, the electron energy can be easily controlled. In order to avoid the interaction between electrons and atmosphere atoms, it is critical to apply high vacuum to the TEM column (usually, 10^{-4} mbar to 10^{-13} mbar). The electrons are generated from the sharp tip of the electron filaments (thermionic emitters) when heat is applied to the filaments. Usually, a field emitter has a tungsten filament and an electric field. After the generation of electrons, several electromagnetic lenses are used to focus the electron beam to the samples within the TEM column. The interaction between the sample and the electron beam produces the image. It is important to prepare the sample with very thin thickness (< 100 nm) to allow the electrons to transmit through the sample. The final image can be seen on a fluorescent screen and can also be captured using a CCD camera.

Microtoming and TEM for TPEs and Shape Memory Polymers. Samples were trimmed by hand to reveal a stub with a superficial area of $250 \times 250 \mu\text{m}^2$, then stained with ruthenium tetroxide (RuO_4) vapour for 4 hours, to enhance contrast between microphases.⁵ RuO_4 selectively stains the aromatic PCHPE domains, resulting in the (PCHPE) phase appearing

darker than the PDL domain during imaging. Furthermore, the RuO₄ vapor also hardens the polymer samples, allowing for room-temperature microtoming.⁶ After staining, the samples were microtomed, at room temperature, and cut speeds of 2 to 4 mm/s, using a Leica EM UC6 ultramicrotome and a MicroStar diamond knife. Usually, the microtoming of soft materials like polymer needs to be conducted using liquid N₂ to prevent the morphology being scrambled by the shear force applied during the microtoming. This unconventional procedure (sample hardening *via* heavy metal staining) permitted the blends to be readily and rapidly microtomed to give sections approximately 80 nm thick. These sections were then collected on a tabbed copper grid (PELCO, 300 mesh), and imaged using a FEI Tecnai G2 Spirit BioTWIN transmission electron microscope operating at a 120 kV accelerating voltage.

TEM for Self-assembled Nanostructures. Copolyester solutions were diluted 10 fold at 20 °C, prior to sample preparation. Amorphous carbon-coated copper TEM grids (Agar Scientific) were plasma glow-discharged for 30 s, to generate a hydrophilic surface. Individual samples (10 µL) were placed onto the freshly discharged grids for 1 min, before being blotted with a filter paper to remove any excess liquid. Uranium acetate (0.75 w/v %) was used to stain the aggregates; by soaking the sample-loaded grids for 20 s. Then, the excess staining solution was carefully removed and the grids were dried under vacuum. The sample-loaded grids were further dried inside the fume hood overnight prior to characterization. Characterization was conducted by Dr. Jens Gaitzsch from Prof. Giuseppe Battaglia's group at UCL on a Phillips CM100 instrument at 100 kV, equipped with a Gatan 1 k CCD camera. The TEM images were collected and processed using the Gatan Microscopy Suite software.

Dynamic light scattering (DLS): DLS was used to determine the hydrodynamic radius (R_h) and polydispersity of the self-assemblies formed from PCL-*b*-P(SA-*alt*-ME₃MO) block copolymers in aqueous solution. The DLS measurements were conducted using a Zetasizer Nano series instrument (Malvern Instruments Zen1600). The scattering angle was fixed at 173°. Data processing was carried out using cumulant analysis of the experimental correlation function and analyzed using the Stokes–Einstein equation to calculate the hydrodynamic

radius of the aggregates. All the aqueous aggregate solutions were analyzed using disposable polystyrene cuvettes.

The field correlation function, $g^{(1)}(t)$, is calculated from the measured intensity auto correlation function, $g^{(2)}(t)$ through the Siegert equation below.

$$g^{(2)}(\tau - 1) = \beta |g^{(1)}(\tau)|^2$$

In a polydispersed spheres solution, the $g^{(1)}(t)$ (first-order electric field correlation function) is related to $G(\Gamma)$ (the line width distribution function) by the following equation⁷

$$g^{(1)}(t) = \int_0^\infty G(\Gamma) e^{-\Gamma t} d\Gamma$$

where t refers to the delay time. Both the cumulant analysis and the CONTIN analysis are employed as data processing methods. The cumulant analysis (the following equation) can be applied to describe logarithm of $g^{(1)}(t)$ as a series expansion of time (t).

$$\ln[g^{(1)}(t)] = -\langle \Gamma \rangle t + \left(\frac{\mu_2}{2}\right)t^2 - \left(\frac{\mu_3}{6}\right)t^3 + \dots$$

$\langle \Gamma \rangle$, the first cumulant, is the decay rate of the process which yields the z-averaged diffusion coefficient and the second cumulant (μ_2) is correlated to the second moment of the distribution of relaxation times by the following equation:

$$\mu_2 = \int_0^\infty G(\Gamma)(\Gamma - \langle \Gamma \rangle)^2 d\Gamma$$

where $G(\Gamma)$ is a line width distribution function and Γ is given by the following equation

$$\Gamma = Dq^2$$

where D is the translation diffusion coefficient, and $q [(4\pi n/\lambda_0) \sin (\theta/2)]$ is the scattering vector, θ is the scattering angle, n is the refractive index of the solvent, and λ_0 is the wavelength of the incident light.

$\langle \Gamma \rangle$ and μ_2 can be acquired directly by the cumulant methods and meanwhile the hydrodynamic radius distribution $f(R_h)$ can be obtained by the CONTIN program in the correlator. Then with the assistance of the Laplace inversion, the line width distribution function $G(\Gamma)$ can be calculated based on the measured $g^{(1)}(t)$. For a diffusive relaxation, Γ can be interrelated to D (the translational diffusion coefficient) by Eq. 6. Based on the mathematical relation mentioned above, $G(\Gamma)$ can be converted to $f(R_h)$ according to the following equation, namely the Stokes-Einstein equation.

$$\langle R_h \rangle = \frac{k_B T}{6\pi\eta D}$$

where k_B is the Boltzmann constant, T is the absolute temperature, and η is the viscosity of the solvent.

Zeta Potential: The particle charge controls the physical stability of emulsions and suspensions. Higher particle charge means higher electrostatic repulsion between the particles, leading to better physical stability. Typically, the particle charge is evaluated by the zeta potential. In this thesis, the physical stabilities of the micelles or vesicles as a function of temperature are characterized by the zeta potential. Generally, due to the presence of surface functional groups, particles have surface charge, also known as the Nernst potential. The degree of the dissociation of the surface functional groups is influenced by the pH value of the colloid solution, thus zeta potential is a pH-dependent value.

In the media containing electrolytes, ions adsorb onto the particle surface. The first adsorbed monolayer of ions is the inner Helmholtz layer and the second layer is the outer Helmholtz layer. The combination of the inner and outer Helmholtz layers is the Stern layer. Outside the Stern layer, there is a ‘diffuse layer’ consisting of freely diffusing ions. The interface between the ‘diffuse layer’ and the media is where the surface charge of the particle is completely compensated. The zeta potential is measured based on the electrophoretic particle mobility in an electrical field. During the movement of the particle, the ‘diffuse layer’ of the particle is

sheared off and this potential at the plane of shear is defined as the zeta potential.

Zeta potential studies were conducted over the temperature range 20-85 °C (temperature interval: 5 °C), using a ZETASIZER Nano series instrument (Malvern Instruments). Data collection and processing were carried out using Zetasizer software (version 7.11 from Malvern Instruments). All experiments were conducted using clear disposable zeta cells using distilled water as the dispersant. The pH value was measured prior to the monitoring. The temperature equilibrium time was set to be 120 s. The zeta potential data were taken from the average values of three individual runs and reported in Figure A5.

Fluorescence Spectroscopy: A fluorophore can be excited to an excited state when it absorbs a photon of light at a specific wavelength. Then another photon at a higher wavelength will be emitted by the fluorophore when it relaxes to its ground state. This photon is detected by the detector and the signal is converted into the intensity of the fluorescence. The brightness of a fluorophore is influenced by the quantum yield and the molar extinction coefficient. The molar extinction coefficient indicates the ability of a fluorophore absorbing light at a certain wavelength, while the quantum yield suggests the efficiency of a fluorophore. Beer-Lambert law (see below) can be used to determine the concentrations of dilute fluorophores:

$$A = \varepsilon l C$$

where A = absorption, ε = molar extinction coefficient ($\text{L} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}$), l = path length (cm) C = concentration ($\text{mol} \cdot \text{L}^{-1}$).

Fluorophores are characterised by their specific excitation and emission spectra. In this thesis, fluorescence experiments were carried out to evaluate the drug-loading efficiency, DOX was used as the anti-cancer drug (also as the fluorophore). Experiments were conducted using a Cary Eclipse Fluorescence Spectrometer (VARIAN).

8.2 References

- (1) Candau, F.; François, J.; Benoit, H. *Polymer* **1974**, *15*, 626-630.
- (2) Spyros, A.; Argyropoulos, D. S.; Marchessault, R. H. *Macromolecules* **1997**, *30*, 327-329.

- (3) Bower, D. *An Introduction to Polymer Physics*; Cambridge University Press, 2002.
- (4) Menard, K. P. *Dynamic Mechanical Analysis: A Practical Introduction, Second Edition*; CRC Press, 2008.
- (5) Trent, J. S.; Scheinbeim, J. I.; Couchman, P. R. *Macromolecules* **1983**, *16*, 589-598.
- (6) Huong, D. M.; Drechsler, M.; Cantow, H. J.; Moller, M. *Macromolecules* **1993**, *26*, 864-866.
- (7) Li, N.; Ye, G.; He, Y.; Wang, X. *Chem. Comm.* **2011**, *47*, 4757-4759.

Appendices

Appendix A – Data

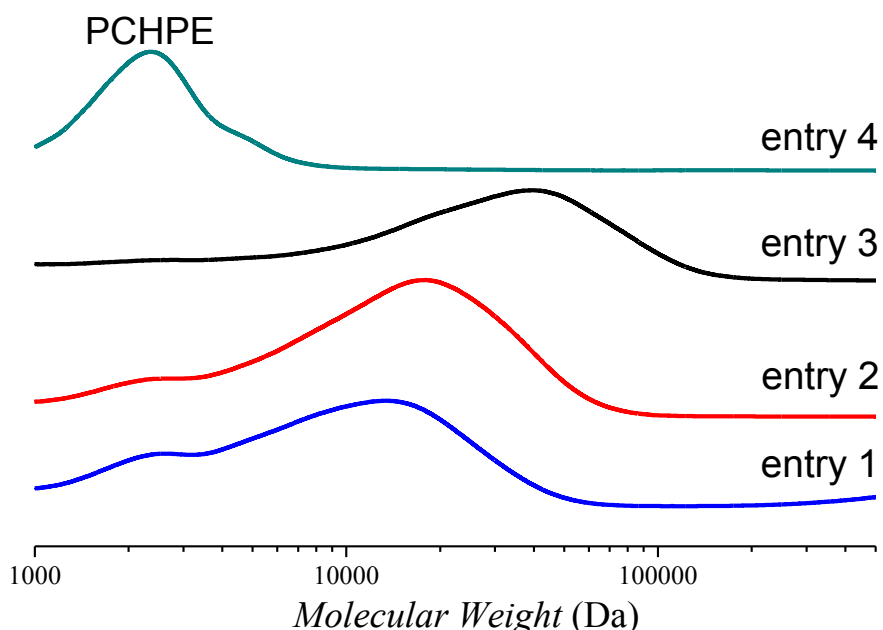


Figure A1. SEC traces of PCHPE-*b*-PCL and PCHPE. The low molecular weight shoulders can be assigned to free PCHPE. Curves correspond to entries 1-4 in Table 3.2, respectively.

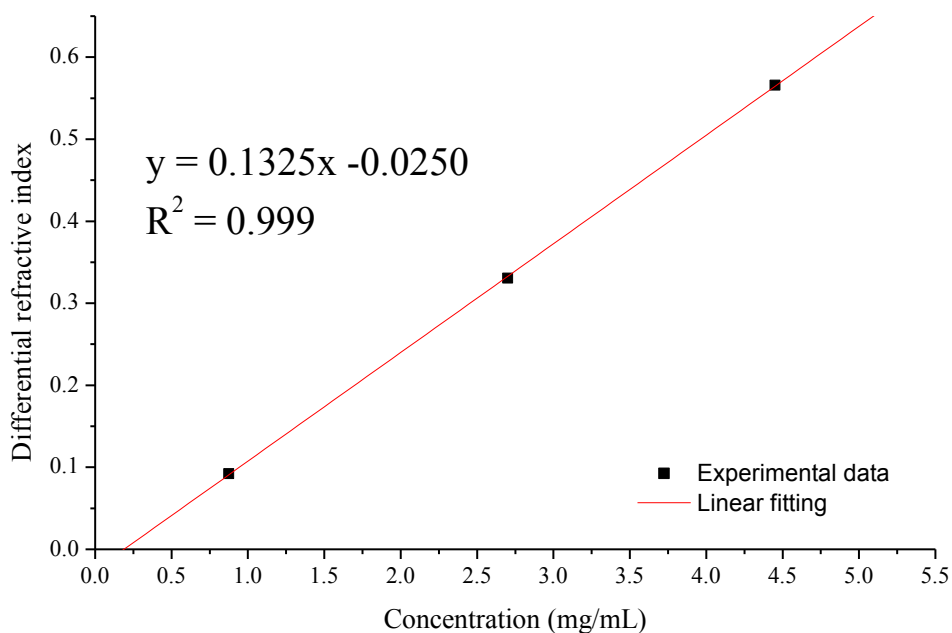


Figure A2. Plots of differential refractive index against the concentration of the alternating polyester (PCHPE) in THF at 25 °C. The dn/dc value is determined *via* linear fitting as $0.133 \pm 0.001 \text{ mL} \cdot \text{g}^{-1}$.

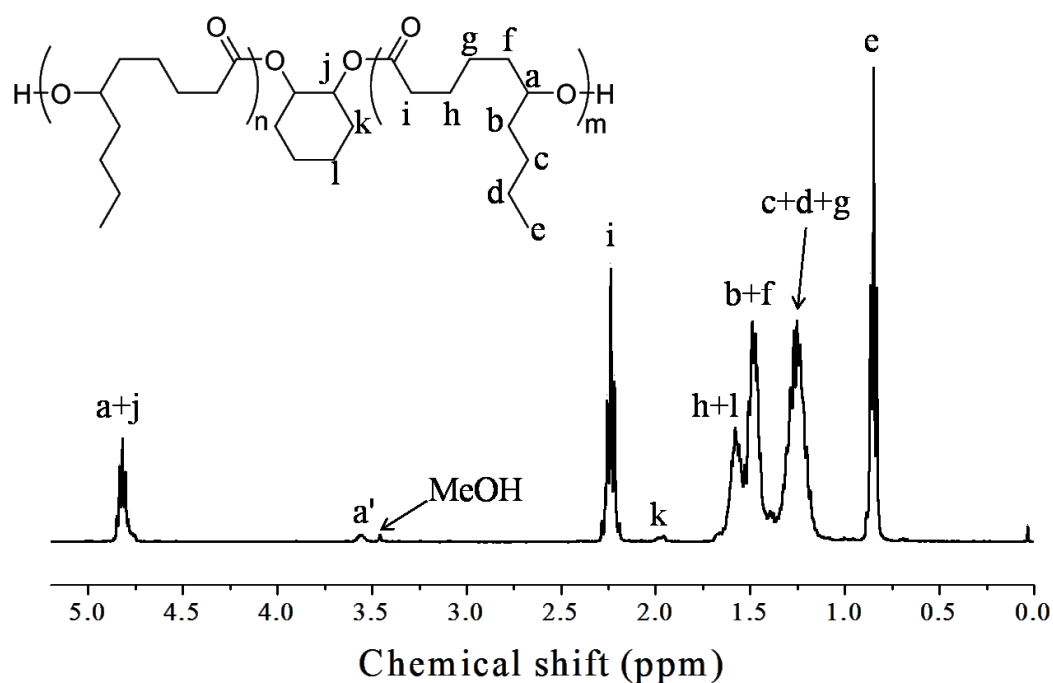


Figure A3. ^1H NMR spectrum of PDL homopolymer (Table 3.6, entry 5) in CDCl_3 .

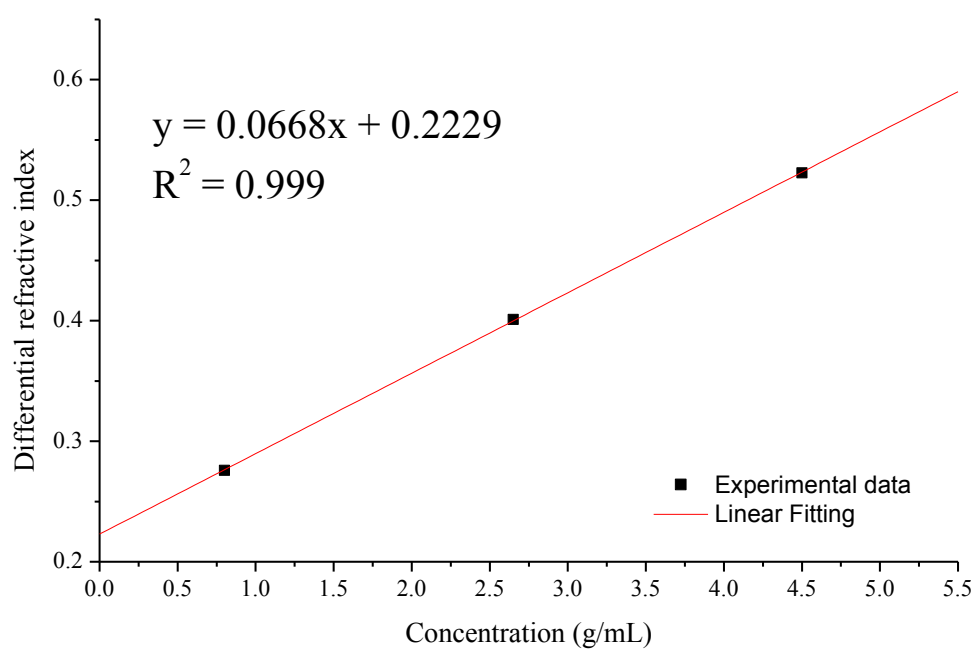


Figure A4. Plots (Table 3.6, entry 2) of the differential refractive index against the concentration of the polyester, poly(decylactone) (PDL) in THF at 25 °C. The dn/dc value is determined *via* linear fitting as $0.067 \pm 0.001 \text{ mL} \cdot \text{g}^{-1}$.

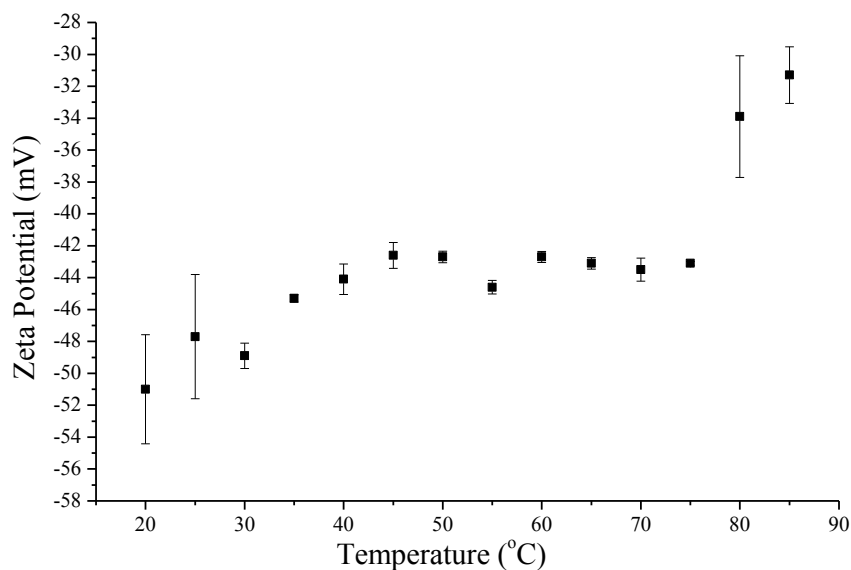


Figure A5. The thermoresponsive behavior monitored by the change in zeta potential at different temperature in distilled water. The pH value at 20 °C was measured to be 6.8. The LCST of the hydrophilic block in the copolyester vesicles is 75 °C, suggesting that the hydrophilic corona of the vesicles is stable at physiological temperature.

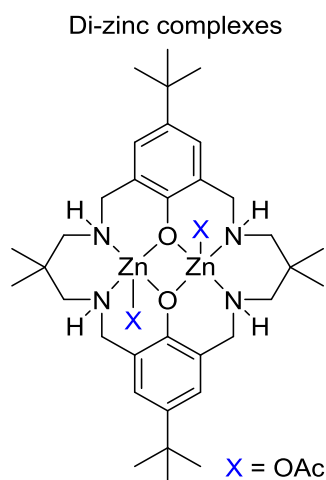


Figure A6. The chemical structure of the di-zinc complex with acetate co-ligand.

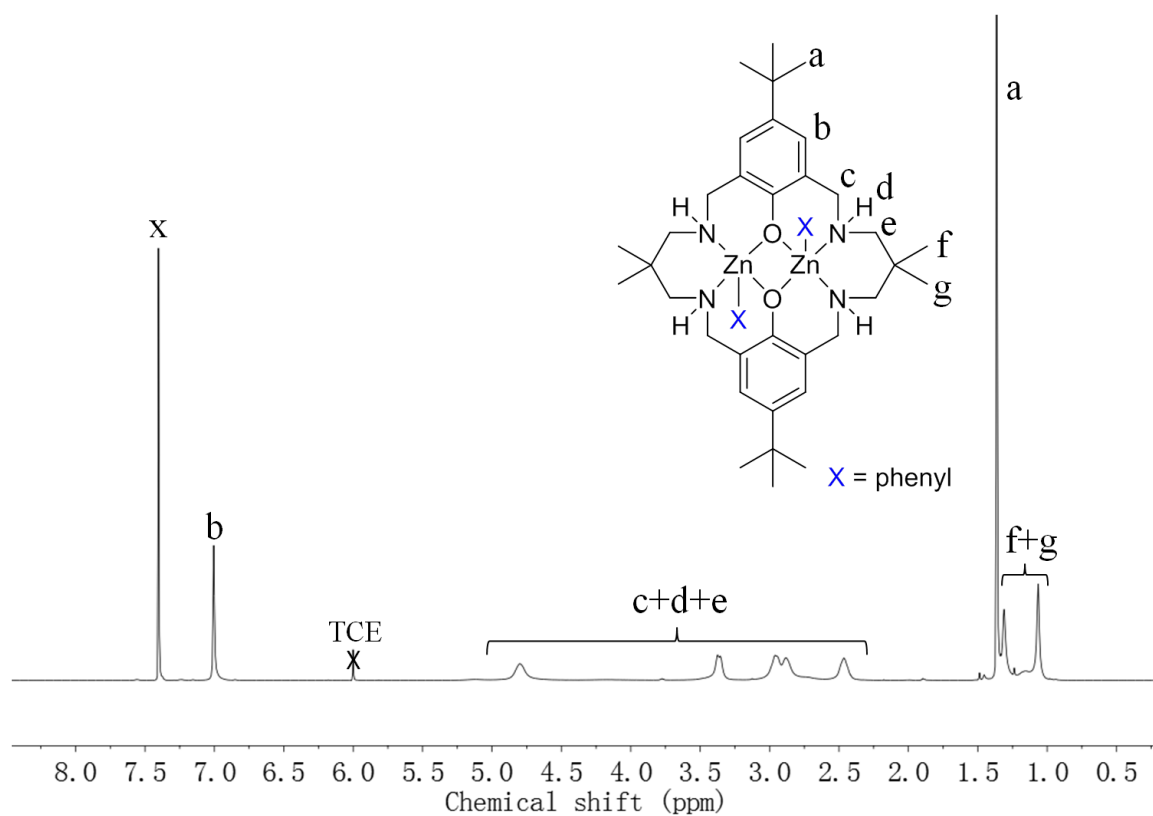


Figure A7. ^1H NMR spectrum of $[\text{LZn}_2(\text{Ph})_2]$ in $\text{TCE-}d_2$ at 403 K.

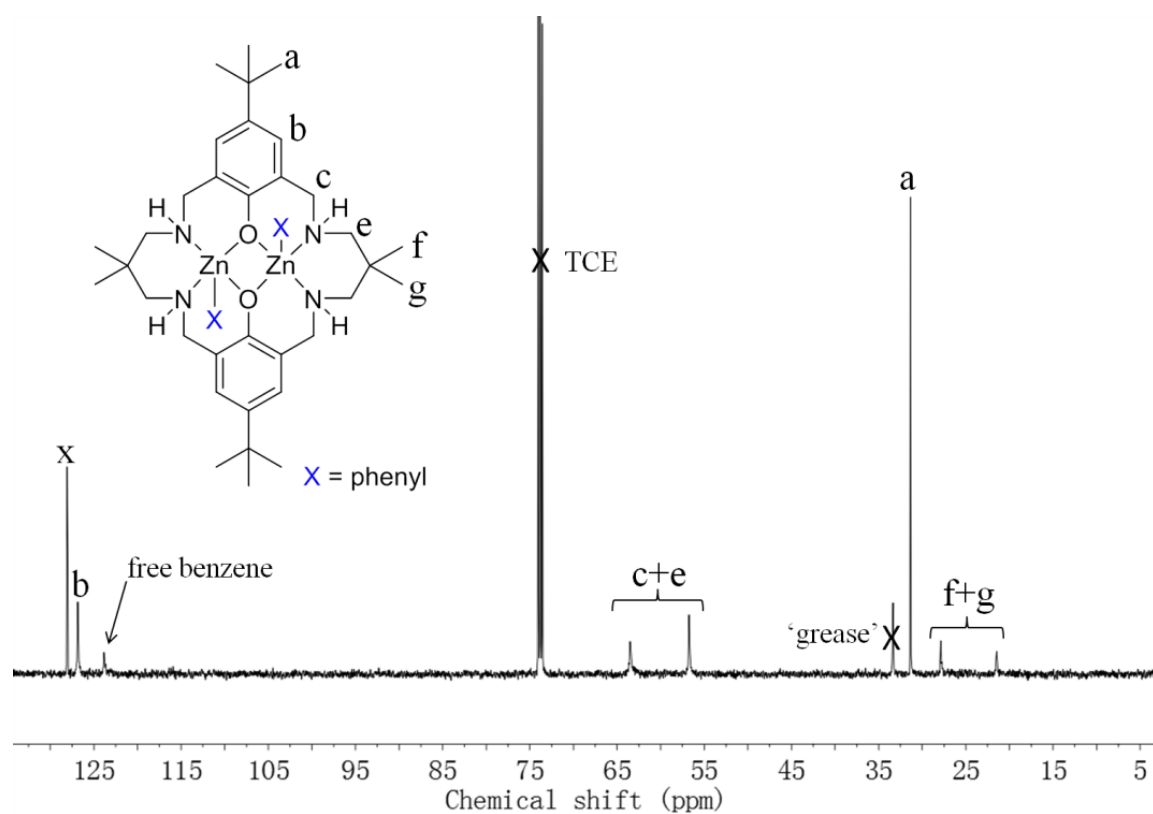


Figure A8. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of $[\text{LZn}_2(\text{Ph})_2]$ in $\text{TCE-}d_2$ at 403 K. Free benzene was formed due to the reaction between $[\text{LZn}_2(\text{Ph})_2]$ and trace of water in the $\text{TCE-}d_2$ solvent at 403 K.

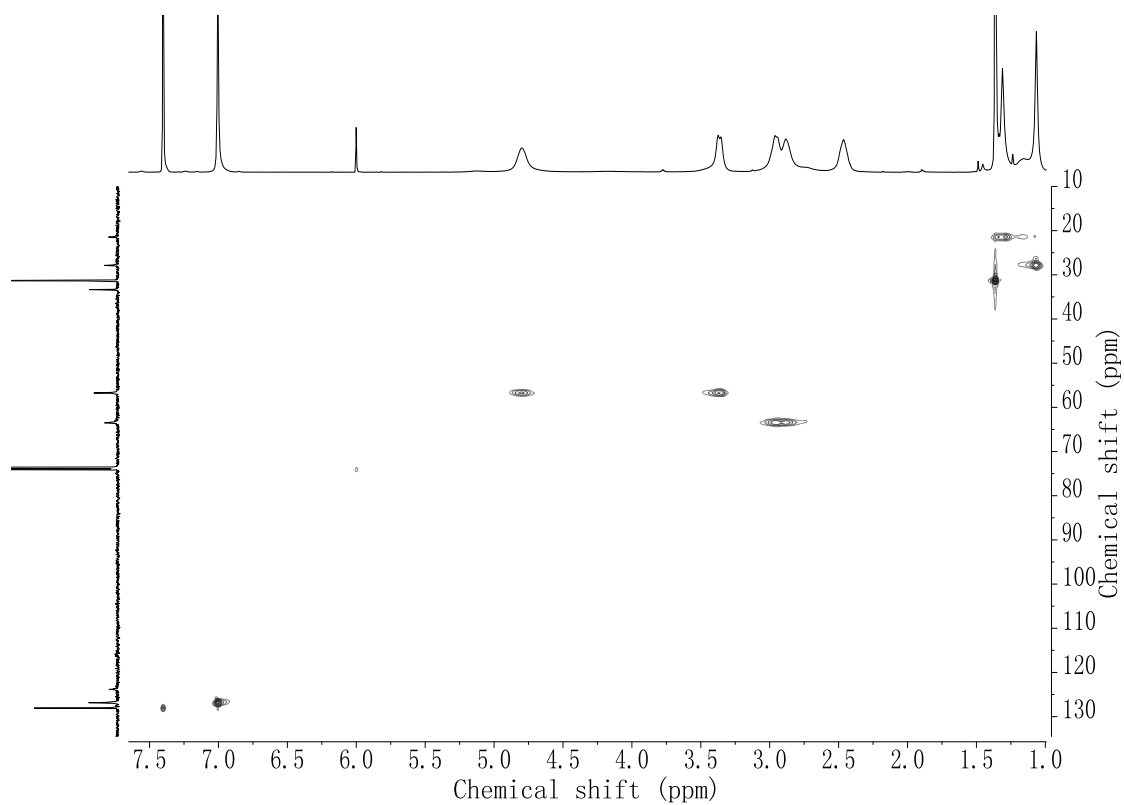


Figure A9. $^1\text{H-}^{13}\text{C}$ HSQC spectrum of $[\text{LZn}_2(\text{Ph})_2]$ in $\text{TCE-}d_2$ at 403 K.

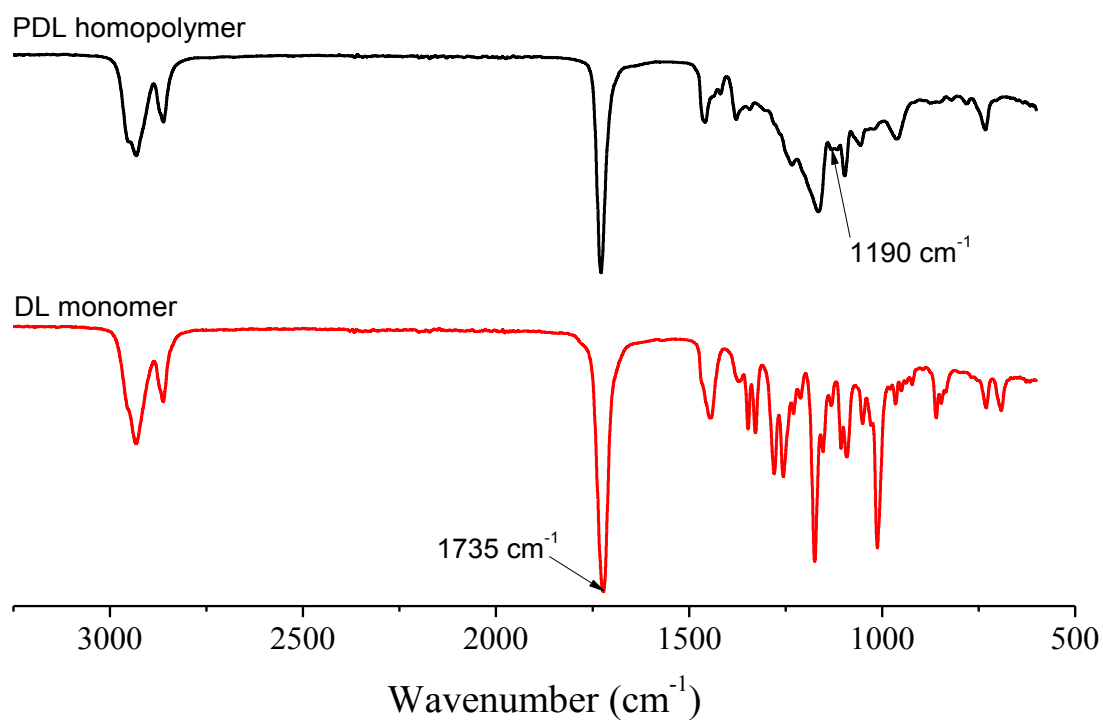


Figure A10. The ATR-IR spectra of pure ϵ -DL monomer and PDL homopolymer. Absorptions at 1735 and 1190 cm⁻¹ are assigned to ϵ -DL and PDL, respectively. Although there are other absorptions of ϵ -DL monomer at lower wavenumbers, they overlap with the solvent (cyclohexene oxide) absorptions.

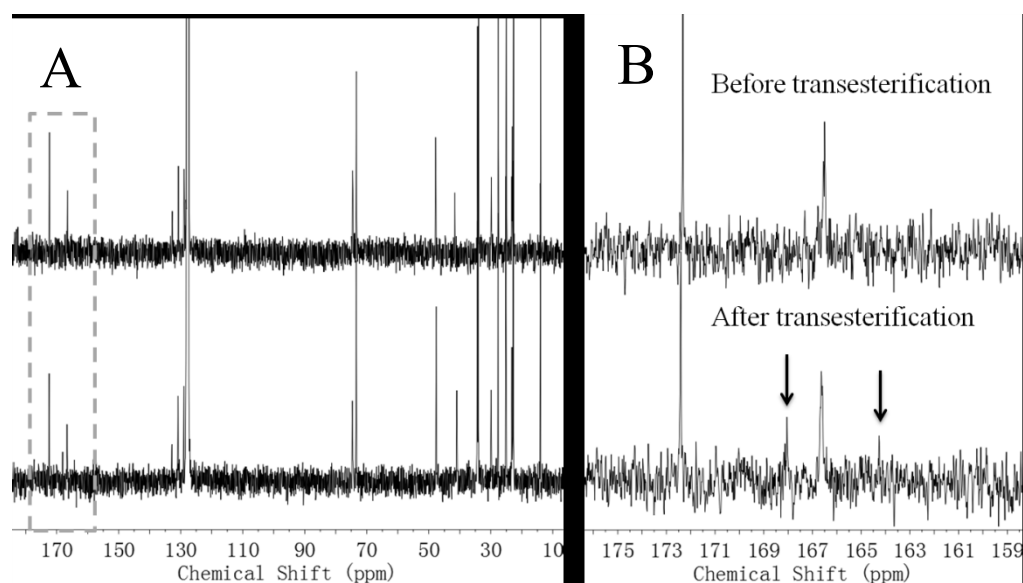


Figure A11. The $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of the (A) PDL-*b*-PCHPE-*b*-PDL copolyester treated with 1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD) at 60 °C for 48 h in an NMR tube, using toluene- d_8 as solvent, under N_2 ; (B) Enlarged carbonyl region corresponding to the selected area in (A), the new carbonyl signals evolving after transesterification are highlighted.

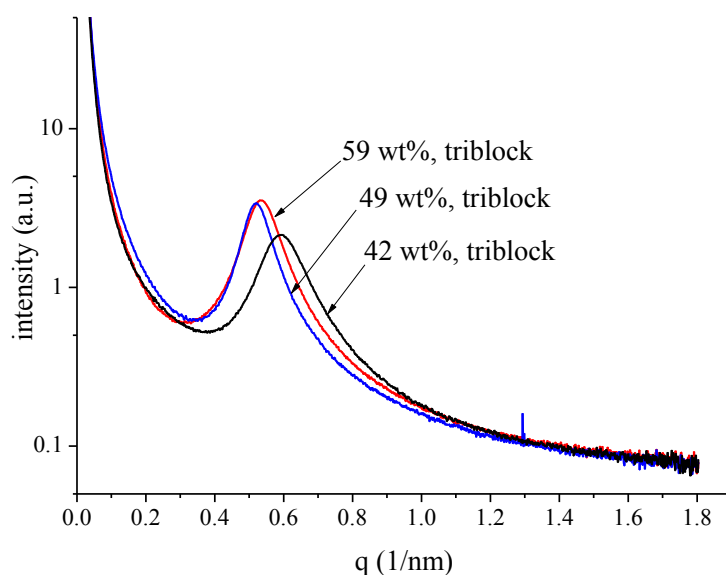


Figure A12. SAXS profiles of PDL-*b*-PCHPE-*b*-PDL triblock copolyesters. Domain spacing (D) values are calculated ($D = 2\pi/q$) to be 10.6 nm, 12.1 nm and 11.8 nm, corresponding to #2, #3 and #4 in Table 4.1, respectively.

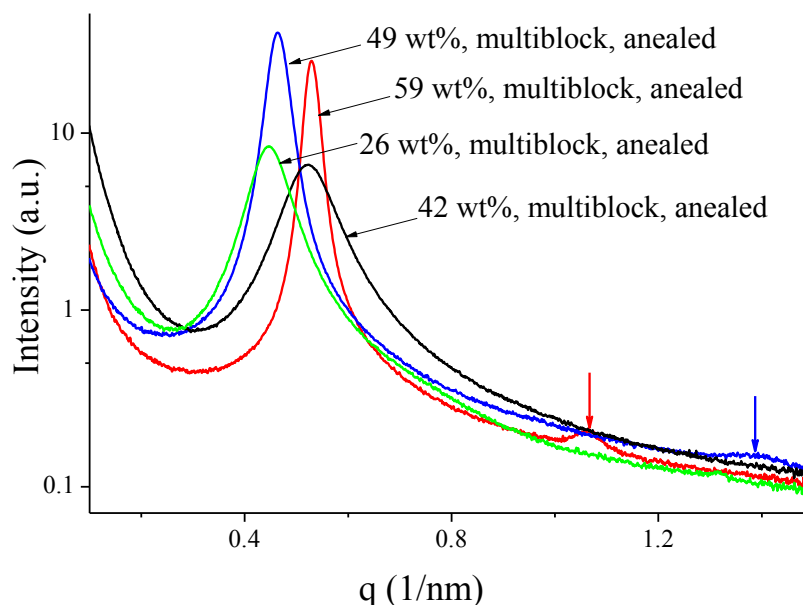


Figure A13. SAXS profiles of PDL-*b*-PCHPE-*b*-PDL multiblock copolyesters after thermally annealed at 130 °C for 48.0 h. Domain spacing (D) values are calculated ($D = 2\pi/q$) to be 14.1 nm, 12.1 nm, 13.5 nm and 11.9 nm, corresponding to #1, #2, #3 and #4 in Table 4.1, respectively. Secondary peaks can be observed in the 49 wt% and 59 wt% samples after annealing, indicating long range order.

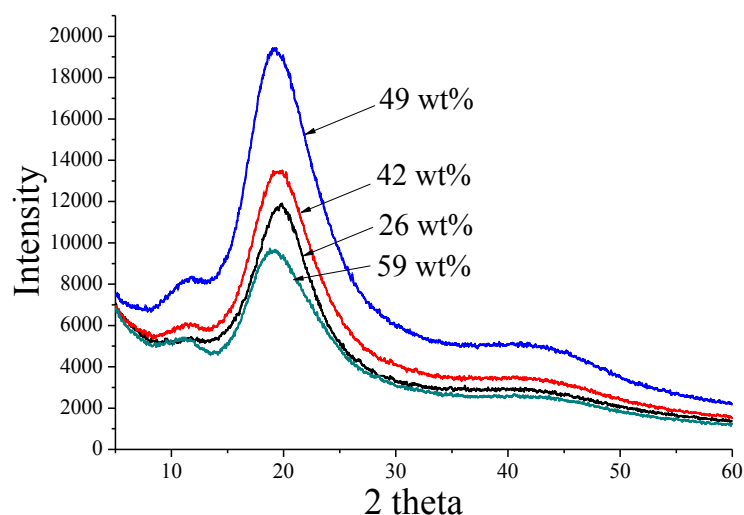


Figure A14. WAXS profiles of PDL-*b*-PCHPE-*b*-PDL multiblock copolyesters after thermally annealed at 130 °C for 48.0 h. corresponding to #1, #2, #3 and #4 in Table 4.1, respectively.

Appendix B – Permissions

Figure 1.8

JOHN WILEY AND SONS LICENSE TERMS AND CONDITIONS

Sep 22, 2016

This Agreement between Yunqing Zhu ("You") and John Wiley and Sons ("John Wiley and Sons") consists of your license details and the terms and conditions provided by John Wiley and Sons and Copyright Clearance Center.

License Number	3954170249872
License date	Sep 22, 2016
Licensed Content Publisher	John Wiley and Sons
Licensed Content Publication	Angewandte Chemie International Edition
Licensed Content Title	Chemoselective Polymerization Control: From Mixed-Monomer Feedstock to Copolymers
Licensed Content Author	Charles Romain, Charlotte K. Williams
Licensed Content Date	Jan 22, 2014
Licensed Content Pages	4
Type of use	Dissertation/Thesis
Requestor type	University/Academic
Format	Electronic
Portion	Figure/table
Number of figures/tables	1
Original Wiley figure/table number(s)	Figure 1
Will you be translating?	No
Title of your thesis / dissertation	Design, synthesis and material property investigation of degradable block copolymer prepared via the combination of ROCOP and ROP
Expected completion date	Nov 2016
Expected size (number of pages)	230
Requestor Location	Yunqing Zhu B1.04 Griffon Studios London, SW11 2ED United Kingdom Attn: Yunqing Zhu
Publisher Tax ID	EU826007151
Billing Type	Invoice
Billing Address	Yunqing Zhu B1.04 Griffon Studios London, United Kingdom SW11 2ED Attn: Yunqing Zhu
Total	0.00 GBP

Figure 1.14

**JOHN WILEY AND SONS LICENSE
TERMS AND CONDITIONS**

Sep 22, 2016

This Agreement between Yunqing Zhu ("You") and John Wiley and Sons ("John Wiley and Sons") consists of your license details and the terms and conditions provided by John Wiley and Sons and Copyright Clearance Center.

License Number	3954161509654
License date	Sep 22, 2016
Licensed Content Publisher	John Wiley and Sons
Licensed Content Publication	Advanced Materials
Licensed Content Title	A High-Performance Recycling Solution for Polystyrene Achieved by the Synthesis of Renewable Poly(thioether) Networks Derived from d-Limonene
Licensed Content Author	Keith Hearon, Landon D. Nash, Jennifer N. Rodriguez, Alexander T. Lonnecker, Jeffery E. Raymond, Thomas S. Wilson, Karen L. Wooley, Duncan J. Maitland
Licensed Content Date	Nov 19, 2013
Licensed Content Pages	7
Type of use	Dissertation/Thesis
Requestor type	University/Academic
Format	Electronic
Portion	Figure/table
Number of figures/tables	1
Original Wiley figure/table number(s)	Figure 2
Will you be translating?	No
Title of your thesis / dissertation	Design, synthesis and material property investigation of degradable block copolymer prepared via the combination of ROCOP and ROP
Expected completion date	Nov 2016
Expected size (number of pages)	230
Requestor Location	Yunqing Zhu B1.04 Griffon Studios London, SW11 2ED United Kingdom Attn: Yunqing Zhu
Publisher Tax ID	EU826007151
Billing Type	Invoice
Billing Address	Yunqing Zhu B1.04 Griffon Studios London, United Kingdom SW11 2ED Attn: Yunqing Zhu

Figure 1.16

E-theses letter template: request to reproduce an extract from a third party's published work

22/09/2016

Dear PNAS,

I am completing my PhD thesis at Imperial College London entitled 'Design, synthesis and material property investigation of degradable block copolymer prepared via the combination of ROCOP and ROP'.

I seek your permission to reprint, in my thesis an extract from: Xiong, M. Y.; Schneiderman, D. K.; Bates, F. S.; Hillmyer, M. A.; Zhang, K. C. Scalable production of mechanically tunable block polymers from sugar. PNAS 2014, 111, 8357-8362. The extract to be reproduced is: Figure 1

I would like to include the extract in my thesis which will be added to Spiral, Imperial's institutional repository <http://spiral.imperial.ac.uk/> and made available to the public under a [Creative Commons Attribution-NonCommercial-NoDerivs](#) licence.

If you are happy to grant me all the permissions requested, please return a signed copy of this letter. If you wish to grant only some of the permissions requested, please list these and then sign.

Yours sincerely,

Yunqing Zhu



Permission granted for the use requested above:

I confirm that I am the copyright holder of the extract above and hereby give permission to include it in your thesis which will be made available, via the internet, for non-commercial purposes under the terms of the user licence. However, the PNAS material should be exempt from the CC license. Any Creative Commons license conflicts with the PNAS license to publish, so we request a note or disclaimer that specifically excludes the PNAS material from the CC license.

[please edit the text above if you wish to grant more specific permission]

Signed: Kay McLaughlin for Diane M. Sullenberger, Executive Editor – 9/23/2016
Name: Kay McLaughlin for Diane M. Sullenberger, Executive Editor – 9/23/2016
Organisation: National Academy of Sciences
Job title: PNAS Permissions Staff

Figure 1.17

**ROYAL SOCIETY OF CHEMISTRY LICENSE
TERMS AND CONDITIONS**

Sep 22, 2016

This Agreement between Yunqing Zhu ("You") and Royal Society of Chemistry ("Royal Society of Chemistry") consists of your license details and the terms and conditions provided by Royal Society of Chemistry and Copyright Clearance Center.

License Number	3954170876536
License date	Sep 22, 2016
Licensed Content Publisher	Royal Society of Chemistry
Licensed Content Publication	Polymer Chemistry
Licensed Content Title	Sustainable thermoplastic elastomers derived from renewable cellulose, rosin and fatty acids
Licensed Content Author	Yupeng Liu,Kejian Yao,Xiaoming Chen,Jifu Wang,Zhongkai Wang,Harry J. Ploehn,Chunpeng Wang,Fuxiang Chu,Chuanbing Tang
Licensed Content Date	Dec 20, 2013
Licensed Content Volume Number	5
Licensed Content Issue Number	9
Type of Use	Thesis/Dissertation
Requestor type	academic/educational
Portion	figures/tables/images
Number of figures/tables /images	1
Format	electronic
Distribution quantity	2
Will you be translating?	no
Order reference number	
Title of the thesis/dissertation	Design, synthesis and material property investigation of degradable block copolymer prepared via the combination of ROCOP and ROP
Expected completion date	Nov 2016
Estimated size	230
Requestor Location	Yunqing Zhu B1.04 Griffon Studios London, SW11 2ED United Kingdom Attn: Yunqing Zhu
Billing Type	Invoice
Billing Address	Yunqing Zhu B1.04 Griffon Studios London, United Kingdom SW11 2ED

Figure 1.18

**JOHN WILEY AND SONS LICENSE
TERMS AND CONDITIONS**

Sep 22, 2016

This Agreement between Yunqing Zhu ("You") and John Wiley and Sons ("John Wiley and Sons") consists of your license details and the terms and conditions provided by John Wiley and Sons and Copyright Clearance Center.

License Number	3954171074197
License date	Sep 22, 2016
Licensed Content Publisher	John Wiley and Sons
Licensed Content Publication	Macromolecular Rapid Communications
Licensed Content Title	Self-Assembled Block Copolymer Aggregates: From Micelles to Vesicles and their Biological Applications
Licensed Content Author	Adam Blanz, Steven P. Armes, Anthony J. Ryan
Licensed Content Date	Jan 22, 2009
Licensed Content Pages	11
Type of use	Dissertation/Thesis
Requestor type	University/Academic
Format	Electronic
Portion	Figure/table
Number of figures/tables	1
Original Wiley figure/table number(s)	Figure 1
Will you be translating?	No
Title of your thesis / dissertation	Design, synthesis and material property investigation of degradable block copolymer prepared via the combination of ROCOP and ROP
Expected completion date	Nov 2016
Expected size (number of pages)	230
Requestor Location	Yunqing Zhu B1.04 Griffon Studios London, SW11 2ED United Kingdom Attn: Yunqing Zhu
Publisher Tax ID	EU826007151
Billing Type	Invoice
Billing Address	Yunqing Zhu B1.04 Griffon Studios London, United Kingdom SW11 2ED Attn: Yunqing Zhu
Total	0.00 GBP
Terms and Conditions	

Reuse of my own publication

ELSEVIER ORDER DETAILS

Sep 22, 2016

Order Number	501182720
Order date	Sep 22, 2016
Licensed Content Publisher	Elsevier
Licensed Content Publication	Progress in Polymer Science
Licensed Content Title	Polymer vesicles: Mechanism, preparation, application, and responsive behavior
Licensed Content Author	Yunqing Zhu,Bo Yang,Shuai Chen,Jianzhong Du
Licensed Content Date	Available online 3 June 2016
Licensed Content Volume Number	n/a
Licensed Content Issue Number	n/a
Licensed Content Pages	1
Start Page	
End Page	
Type of Use	reuse in a thesis/dissertation
Intended publisher of new work	other
Portion	full article
Format	electronic
Are you the author of this Elsevier article?	Yes
Will you be translating?	No
Order reference number	
Title of your thesis/dissertation	Design, synthesis and material property investigation of degradable block copolymer prepared via the combination of ROCOP and ROP
Expected completion date	Nov 2016
Estimated size (number of pages)	230
Elsevier VAT number	GB 494 6272 12
Requestor Location	Yunqing Zhu B1.04 Griffon Studios London, SW11 2ED United Kingdom Attn: Yunqing Zhu
Total	Not Available