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Aluminium Salen and Salan Catalysts for Polymerisation of Novel Monomers and Macrostructures

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University of Edinburgh

Submitted for the degree of Doctor of Philosophy
2015
Declaration

The work described in this thesis is entirely my own, except where I have either acknowledged help from a named person or given reference to a published source. Text taken from another source will be enclosed in quotation marks and a reference given. This thesis has not been submitted, in whole or in part, for any other degree.

Signature:

Date:
Abstract

Aluminium salen and aluminium salan complexes are excellent catalysts for the ring-opening polymerisation of lactide. This thesis studied their efficacy in the polymerisation of novel monomers and their ability to build new macrostructures.

Aluminium salen and aluminium salan complexes were tested as catalysts for ring-opening polymerisation of common aliphatic monomers where controlled polymer synthesis has not yet been achieved with similar systems. Excellent control over molecular weight and dispersity was achieved for ε-caprolactone polymerisation, with high molecular weights accessible. Immortal polymerisation could also be performed with an extremely high level of chain transfer agent (up to 100 equivalents) and the highest monomer turnover (10000 monomer equivalents) with aluminium salen catalysts to date. Addition of functional groups to the monomer was also studied; the effect of steric bulk in polymerisation of methyl-substituted derivatives was significant. Protected alcohol functionalities can also be introduced into easily synthesised homopolymers and copolymers.

The first example of synthesising a polyester with aromatic functionality within the polymer backbone via polymerisation of cyclic ester monomers was studied with an aluminium salen catalyst. 2,3-Dihydro-5H-1,4-benzodioxepin-5-one polymerisation was facile and proceeded under mild conditions. The resulting polymer could be depolymerised back to starting monomer with the same aluminium salen catalyst under dilute conditions. Random, AB diblock and ABA triblock copolymers were readily synthesised with L-lactide and β-butyrolactone as comonomers. Block copolymers with β-butyrolactone could also be selectively depolymerised, to give poly(3-hydroxybutyrate) homopolymers. Attempted polymerisation of a range of other aromatic monomers was unsuccessful due to addition of steric bulk, changing orientation of the monomer ester bond or decreasing the ring size.

Synthesis of homopolymer and ABA triblock copolymers with L-lactide and alkyl-substituted β-lactones was investigated. Homopolymerisation of all alkyl-substituted β-lactones resulted in well controlled polymer, with rate decreasing as
alkyl-substituent length increased. A sequential addition of monomers method with β-butyrolactone, β-valerolactone and β-heptanolactone was employed for copolymer synthesis. Copolymers synthesised from β-butyrolactone and β-valerolactone resulted in tunable glass transition and melting temperatures. Copolymers synthesised from β-heptanolactone resulted in thermoplastic elastomers exhibiting microphase separation, supported by differential scanning calorimetry and small-angle X-ray scattering.

Finally, optimisation of \textit{in situ} generated carbonylation catalysts was studied. Optimisation of literature complexes allowed for synthesis of β-valerolactone, β-heptanolactone, β-tridecalactone, 4-chloro-β-butyrolactone and β-6-heptenolactone on relatively large scales under much easier experimental protocols. Additionally, tuning of \textit{ortho}-phenylene bridged salen ligand framework gave to structure-activity relationships. Using this optimised catalyst system, 4-chloro-β-butyrolactone and β-6-heptenolactone were prepared and used in ring opening polymerisation. Well controlled and efficient polymerisation of 4-chloro-β-butyrolactone was easily achieved with aluminium salen and salan catalysts. Homopolymers and block copolymers with poly(ethylene glycol) and β-6-heptenolactone were readily synthesised.
Acknowledgements

There are a significant number of people who have helped me complete the work for degree. First and foremost, thanks is given Dr Michael Shaver for not only giving me the opportunity to undertake a PhD, but many opportunities given as an undergraduate. I cannot count the number of times he has gone above and beyond for my benefit and the level of support and encouragement received since 2009 is extraordinary.

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˚C                  degrees Celsius
1,3-BDO             4H-1,3-benzodioxin-4-one
1,4-DPO             1,4-dioxepin-5-one
2,3-DHB             2,3-dihydro-5H-1,4-benzodioxepin-5-one
2,6-Me-ε-CL         2,6-dimethyl-epsilon-caprolactone
3,4-DHB             3,4-dihydro-2H-1,5-benzodioxepin-5-one
3-HP                3-hydroxypyridine
3-Me-2,3-DHB        3-methyl-2,3-dihydro-5H-1,4-benzodioxepin-5-one
3-Ph-2,3-DHB        3-phenyl-2,3-dihydro-5H-1,4-benzodioxepin-5-one
4-BOB-ε-CL          4-(4-benzyoxybutyl)- epsilon-caprolactone
4-Cl-β-BL           4-chloro-beta-butyrolactone
4-Me-ε-CL           4-methyl-epsilon-caprolactone
6-Me-ε-CL           6-methyl-epsilon-caprolactone
7-MC                7-methoxycoumarin
β 6                 beta-6-heptenolactone
β-BL                beta-butyrolactone
β-CD                beta-cyclodextrin
β-HL                beta-heptanolactone
β-TDL               beta-tridecalactone
β-VL                beta-valerolactone
δ                   delta-valerolactone
ε                   epsilon-caprolactone
μ                   micrometer
μL                  microliter
AFM                 atomic force microscopy
ArH                 proton attached to an aromatic ring
Bn                  benzyl; CH₂C₆H₅
BVO                 Baeyer-Villager oxidation
ªBu                 normal butyl; CH₂CH₂CH₂CH₃
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Chapter One

Importance of Cyclic Ester Ring-Opening Polymerisation

1.1 Traditional polymers: A rose with thorns

Since the first industrial-scale production of polymers in the 1950’s, society’s reliance on these materials has grown substantially. Production of polymers has risen dramatically from 1.5 million tonnes to nearly 250 million tonnes in 2008.[1] Our increased dependence on polymer-based materials is due to their low-cost and highly desirable and tunable properties in products such as plastics, textiles, rubbers, food packaging, electronics and coatings.[2] The wide range of applications arises from the diversity of readily accessible starting materials with many different functional groups. The low-cost and large scale production is easily achieved to obtain many commercial polymers (Figure 1.1).[3]

To say that polymer-based materials have been beneficial to humanity is an understatement. Lightweight and thermally/chemically stable materials are excellent alternatives to heavier metal-based materials.[4] However, the incredibly stable nature of these materials poses several drawbacks. Once these materials have reached the end of their lifetime, their disposal is often into landfills. The stability of these waste materials mean that they will stay in the landfills for many years.[5] This persistence in landfills has been shown to cause a decreased rate of degradation of other waste materials present.[6] This degradation, when it does occur, often releases harmful
degradation products into the environment causing acute and persistent harm to ecosystems.\[^7\]

Monomers for generating traditional polymers are typically derived from petrochemical sources.\[^8\] It is estimated that the production of plastics is responsible for approximately 7% of the global oil and gas consumption.\[^9\] The non-renewable nature of these starting materials is detrimental. Additionally, the cost of petrochemical based products is tied to the cost of oil; meaning that commodity polymers are at risk of significant cost increases. These issues, among others have led to increased interest and research into novel materials that reduce our dependence on petroleum-derived polymers. For a true paradigm shift, the properties of such materials need to be comparable to traditional plastics. Completely removing traditional polymers from society is likely not possible but replacing some materials with alternatives could have a significant positive impact on the environment and a reduced dependence on oil.

### 1.2 Biodegradable polymers

Biodegradable polymers are materials that can be easily broken down or degraded by naturally occurring microorganisms.\[^10\] When degradation occurs, the final products are (ideally) CO\(_2\) and H\(_2\)O.\[^11\] In polyesters, there are several methods

![Figure 1.1 World production of commodity polymers](image-url)
of degradation that typically result in hydrolytic cleavage of the ester linkages followed by further degradation to smaller molecules by microorganisms.\textsuperscript{[12]}

Bio-based polymers are prevalent in nature with proteins, polysaccharides and poly(hydroxyalkanoate)s as common examples.\textsuperscript{[11-13]} Despite a wide range of materials being produced naturally, the properties of many petrochemical polymers cannot be matched. Thus, research into synthetic biodegradable polymers has increased to produce materials with easily tunable properties.

1.2.1 Mechanisms of polymerisation

Synthesis of biodegradable polymers typically occurs by one of two methods: condensation polymerisation or ring-opening polymerisation (ROP). Condensation polymerisation offers synthesis of polyester via a combination of diols and dicarboxylic acids with the removal of water. Alternatively, this can also be achieved by self-condensation of hydroxyacids (Scheme 1.1).\textsuperscript{[9a]} Condensation polymerisation allows for synthesis of a wide range of polymers as many diols, dicarboxylic acids and hydroxyacids are commercially available. However, molecular weight and dispersity are often difficult to control and high molecular weight polymers are difficult to generate by condensation polymerisation.\textsuperscript{[14]}

\begin{center}
\begin{tikzpicture}
    \node at (0,0) {\text{n} \ HO\cdot\text{R} \cdot\text{O} \cdot\text{H} \cdot\text{O} \cdot\text{R} \cdot\text{O} \cdot\text{H} \cdot\text{O} \cdot\text{R} \cdot\text{O} \cdot\text{H}}; \node at (3,0) {- (n-1) \ H_2O}; \node at (6,0) {\text{HO} \cdot\text{R} \cdot\text{O} \cdot\text{H} \cdot\text{O} \cdot\text{R} \cdot\text{O} \cdot\text{H} \cdot\text{O} \cdot\text{R} \cdot\text{O} \cdot\text{H}};
\end{tikzpicture}
\end{center}

\textbf{Scheme 1.1} General condensation polymerisation scheme

These types of polymers can also be generated via ring-opening polymerisation of cyclic monomers. Examples of common monomers include lactones (lactide, β-butyrolactone, ε-caprolactone), cyclic carbonates (ethylene carbonate, trimethylene carbonate) or cyclic phosphoesters (ethylethylene phosphate, methylpropylene phosphate) (Figure 1.2).\textsuperscript{[11]} This strategy results in a much more controlled polymerisation giving predictable and high molecular weights as well as narrow dispersities. This can also allow for a complementary synthesis of naturally occurring biodegradable polymers such as poly(hydroxyalkanoate)s (PHAs).\textsuperscript{[15]}
Ring-opening polymerisations are also highly atom economical as there is an absence of side reactions resulting in byproducts or termination reactions.\textsuperscript{[16]}

Anionic ring-opening polymerisations were the first examples of ROP (Scheme 1.2).\textsuperscript{[17]} Initiation involves nucleophilic attack at the monomer by an anionic initiator. Propagation then occurs by subsequent nucleophilic attack of (many) more monomer units. Quenching the reaction, typically by addition of a protic source, promotes termination. Anionic ROP is less common in polyester formation but is used extensively in epoxide polymerisation to generate polyethers.\textsuperscript{[18]} Simple salts (i.e. potassium ethoxide, potassium tert-butoxide) are often employed as initiators, although discrete metal complexes have also been used.\textsuperscript{[19]}

\textbf{Figure 1.2 Examples of ROP monomers}

The most common mechanism for ROP of lactones is a coordination-insertion mechanism, shown in Scheme 1.3.\textsuperscript{[20]} A Lewis acid, typically a metal alkoxide, catalyses the reaction. The lactone monomer coordinates to the Lewis acidic metal center. The metal alkoxide is then inserted into the monomer carbonyl.
Cleavage of the former acyl bond then results in formation of a new metal alkoxide species, which can propagate further to generate polyester. Termination is achieved by addition of a large excess of a protic source, such as an alcohol or acid, resulting in protonolysis of the metal complex to form and hydroxyl-terminated polyester.

![Scheme 1.3](image)

**Scheme 1.3** Mechanism of coordination-insertion ROP

A living polymerisation (such as anionic ROP) is one that has no side reactions or termination reactions. Coordination-insertion ROP is typically a controlled polymerisation as it mimics a living polymerisation. Unfortunately, side reactions and termination reactions are only minimised. The major contributor to this is transesterification (Scheme 1.4).

Transesterification can occur either intramolecular or intermolecular, both of which are detrimental to polymerisation control. Transesterification occurs when a metal center of a propagating polymer chain reacts with a polymer chain instead of monomer. Intramolecular transesterification results in the metal center reacting with the growing polymer chain directly attached to it. This yields cyclic polymer and a shorter growing polymer chain. Intermolecular transesterification results in a metal centre reacting with a different polymer chain affording two polymer chains of different lengths. Whilst it is difficult to completely remove transesterification, catalyst and monomer design can allow for a significant reduction of this detrimental reaction.
1.3 Monomer Scope

1.3.1 Lactide

While the earliest ROP systems focused on β-butyrolactone, a significant shift in research efforts was quickly made towards lactide polymerisation. Lactide, the cyclic diester of lactic acid, is intriguing as a monomer for ROP for several reasons. First, as it is derived from lactic acid, a renewable resource obtained from fermentation of various plants, it is considered a renewable monomer.\[23\] This could relieve a significant amount of stress on petrochemical resource-based monomers and polymers. Secondly, lactic acid contains a chiral center, giving three different configurations of lactide (Figure 1.3). It should be noted that the common monomer rac-lactide is a 1:1 mixture of D- and L-lactide.
As a result of the chirality present in lactide, stereoregular polymers can be synthesised (Figure 1.4).\[24\] Starting from an enantiopure monomer source of either D- or L-lactide can only result in isotactic PLA (repeating (R) or (S) stereocenters) synthesis, assuming no racemisation takes place. Starting from rac-lactide can yield two other tacticities: heterotactic and atactic (Figure 1.4). Heterotactic PLA is the alternating insertion of D- and L-lactide, giving a –SSRRSSRSSRRSS– stereocenter configuration. Atactic PLA is the result of random insertions. The last remaining tacticity for PLA is syndiotactic, alternation of stereocenters (–RSRSRSRSRS–) and can be prepared from meso-lactide with selective catalysts.\[25\]

![Figure 1.4 Possible PLA tacticities](image-url)
Producing PLA with varying tacticities gives rise to different properties.\textsuperscript{[24]} Heterotactic and atactic PLA are typically amorphous while syndiotactic and isotactic PLA are semicrystalline. Syndiotactic PLA generally has lower thermal transitions ($T_g \approx 45^\circ C$, $T_m \approx 155^\circ C$) compared to isotactic ($T_g \approx 60^\circ C$, $T_m \approx 170^\circ C$) forms. It has also been found that a stereocomplex isotactic PLA, a mixture of isotactic ($R$) and isotactic ($S$), has a significantly higher melting temperature ($235^\circ C$) than either purely isotactic ($R$) or isotactic ($S$).

Stereoccontrolled polymerisation of lactide is typically performed from rac-lactide. An isotactic PLA polymerisation using a single catalyst can yield two different types of polymer; the purely isotactic PLA discussed previously or a stereoblock PLA polymer.\textsuperscript{[26]} Stereoblock PLA contains blocks of repeating ($R$) or ($S$) segments, followed by a switch to insertion of the other enantiomer (–SSSSSSSSRRRRRRRRRR–). Stereoblock PLA typically has properties between purely isotactic ($R$) or ($S$) and stereocomplex PLA ($T_m = 185 – 195^\circ C$). It should also be noted that as catalysts are used to control this stereoregularity, errors are usually present. Stereoregularity is typically measured as a degree of selectivity. NMR spectroscopy allows for the measurement of stereocenter tetrads to calculate the ratio of different linkages that correspond to each type of tacticity.\textsuperscript{[27]} Many discrete metal complex catalysts have been employed for polymerisation of lactide based on Ca,\textsuperscript{[28]} Mg,\textsuperscript{[29]} Y,\textsuperscript{[30]} Ti,\textsuperscript{[30f, 31]} Hf,\textsuperscript{[31e, 32]} Zr,\textsuperscript{[31e, 32-33]} Zn,\textsuperscript{[34]} Al,\textsuperscript{[35]} Ga\textsuperscript{[36]} and In.\textsuperscript{[37]} Aluminium based catalysts will be discussed in greater detail in Chapter 1.4.

1.3.2 $\varepsilon$-Caprolactone

Another common monomer in ring-opening polymerisation is $\varepsilon$-caprolactone ($\varepsilon$-CL).\textsuperscript{[38]} One driving force of ROP is thought to be loss of ring strain. This makes $\varepsilon$-CL an intriguing monomer as the seven-membered ring has considerably less ring strain compared to lactide.\textsuperscript{[39]} Despite this, $\varepsilon$-CL is an excellent monomer for ROP. Poly($\varepsilon$-caprolactone), PCL, is a fully biodegradable polymer with properties similar to low-density polyethylene.\textsuperscript{[38]} It is typically prepared via ROP using the catalyst $\text{Al(O}^\circ\text{Pr)}_3$ and results in low dispersity linear polymer. PCL has been commercially available since the 1970’s and has found use in many applications, such as films, containers and drug delivery.\textsuperscript{[40]} Copolymers have also been
investigated to enhance the polymer properties. ε-CL contains no chiral center leading to no polymer tacticity. Instead, PCL properties are governed by the molecular weight and dispersity of the polymer. PCL is a semicrystalline thermoplastic with a very low glass transition temperature ($\approx -60^\circ C$) and relatively low melting temperature ($\approx 60^\circ C$). This is considered a drawback for some applications but beneficial in others.

ε-CL polymerisations typically have a higher tendency to undergo transesterification, as the ester linkages of the growing polymer chains are inherently more accessible to the metal catalysts; catalyst choice is thought to be more important in limiting transesterification.$^{[41]}$ This has resulted in particular focus on developing catalysts that minimise the undesired transesterification side reactions.

1.3.3 β-Lactones

β-Lactones are four-membered rings and thus the smallest stable cyclic esters. Despite their inherent ring strain, β-lactone polymerisation through coordination-insertion ROP is considered difficult.$^{[42]}$ Nevertheless, many catalysts have been developed for β-lactone polymerisation. β-butyrolactone (β-BL) is the only commercially available β-lactone and has thus received the most attention to date. Like lactide, β-BL is chiral, and as a result tacticity control is a major research avenue.$^{[43]}$ However, as stereocontrol is thought to often occur as a result of steric interactions with the catalyst, β-BL ROP stereocontrol is considerably more difficult. This is due to the smaller size of the monomer itself and the methyl group pointing away from the carbonyl in β-BL, as well as the catalyst.

β-BL polymerisation was of interest in early years of cyclic ester ROP as the resulting polymer, poly(3-hydroxybutyrate) (P3HB) is naturally occurring polymer produced by bacteria and algae used for energy storage.$^{[44]}$ Naturally occurring P3HB is produced in its isotactic ($R$) form, is high molecular weight and is highly crystalline with a melting temperature $\approx 180^\circ C$. As it is only produced in isotactic ($R$), synthesis of P3HB was intriguing due to other accessible microstructures. Synthetic P3HB typically differs from natural P3HB in that atactic tends to be amorphous and syndiotactic tends to be semi-crystalline.$^{[45]}$
Other β-lactones have also been polymerised. β-Valerolactone (β-VL), with an ethyl substituent, has been of interest as poly(3-hydroxybutyrate-co-3-hydroxypentanoate) copolymers have been synthesised via bacterial fermentation showing improved processability. Homopolymerisation of rac-β-VL was achieved by Coates using a zinc β-diiminate catalyst. A subsequent report from Coates and Thomas, showed that an yttrium catalyst can be used in β-lactone polymerisation. Homopolymerisation of β-VL as well as alternating copolymerisation of β-BL with β-VL was reported.

Despite the potential for β-lactones as a diverse class of monomers, with the synthesis of many different derivatives reported, only a select few have been reported in ROP. Recent advances in their synthesis via metal catalysed carbonylation of epoxides gives β-lactone polymerisation a promising outlook, with a broad range of functional groups available.

1.4 Aluminium ring-opening polymerisation catalysts

Aluminium complexes have been very well studied in ROP. The earliest reports of cyclic ester polymerisation consisted of a simple triethylaluminium/water catalyst to produce P3HB. While the authors had hoped to synthesise P3HB with similar properties to naturally occurring P3HB, the optical properties were not been matched, likely due to starting from rac-β-BL, resulting in an atactic polymer. A subsequent report demonstrated that optical activity could in fact be matched by using an enantioenriched starting material. Starting from 73% (R)-β-BL, the synthesised P3HB had consistent optical rotation to the starting monomer and comparable to natural P3HB.

Discrete aluminium complexes soon became a focus in ROP. The first examples of discrete, single-site aluminium complexes for ROP were based on a porphyrin ligand framework by Inoue (Figure 1.5) initially developed for epoxide polymerisation. This report found that the propagating species was an aluminium carboxylate by 1H NMR spectroscopy. Furthermore, the number of growing polymer chains was directly proportional to the number of aluminium centers present. Interestingly, conducting the polymerisation with a mixture of two different
aluminium porphyrin complexes with varying reactivity, a monomodal polymer distribution is still obtained. As a bimodal distribution would be expected for chains growing independently on each aluminium center, it was suggested that chain exchange was occurring. Further work by Inoue investigated different initiator groups (alcohols), immortal polymerisation (excess initiator relative to metal centers) and accelerated polymerisation using an additional Lewis acid.\cite{53}

As a result of this seminal work by Inoue, there has been significant interest in development of improved discrete aluminium complexes for ROP. Another reason aluminium complexes have gathered such a level of interest is due to their ability to control the stereoregularity of the resulting polymer.

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{aluminium_porphyrin_complexes.png}
\caption{Aluminium porphyrin complexes for ring-opening polymerisation}
\end{figure}

Spassky used the chiral ligand (R)-3,3-dimethyl-1,2-butanediol with triethylaluminium for the polymerisation of rac-β-BL, a ligand he also used with zinc and yttrium.\cite{54} Unfortunately, only low conversion (18\%) was achieved, even after very long reaction times (18 days). Spassky followed up this work with the first report of an aluminium salen complex for ROP.\cite{55} Again, polymerisation of rac-β-BL was quite slow and only oligomeric P3HB was obtained. The further use and development of aluminium salen (and salan) complexes will be discussed in more detail in section 1.5. Other simple aluminium species, such as aluminium trisopropoxide, Al(OiPr)3, have been used been used to polymerise ε-CL,\cite{56} β-BL,\cite{57} lactide\cite{20b} and cyclic anhydrides.\cite{58} Conversions were high with low dispersities (D) in all cases.
Darrensbourg expanded on the idea of aluminum salen species and synthesised aluminium “half salen” complexes (Figure 1.6). Nine aluminium half salen complexes were investigated for the polymerisation of rac-lactide, \(\beta\)-butyrolactone, \(\gamma\)-butyrolactone, \(\delta\)-valerolactone, \(\epsilon\)-caprolactone and trimethylene carbonate. Polymerisations of rac-lactide were generally very well controlled with dispersities often below 1.1. Polymerisation of the other monomers were less controlled with \(D = 1.2 - 1.9\). Expectedly, the more difficult to polymerise \(\gamma\)-butyrolactone did not yield any polymer.

![Figure 1.6 Aluminium catalysts for ROP developed by Darrensbourg](image)

Jones and coworkers have developed three novel classes of aluminium catalysts for ROP (Figure 1.7). The first class, aluminium salalen complexes - a salen/salan hydrid – that feature neutral donors of both the imine and amine type. In their first report, eight complexes were synthesised and screened for ROP of rac-LA. Polymers were generally well controlled (\(D = 1.04 - 1.65\)). Furthermore, the nature of the amine substituent had an effect on PLA tacticity. A subsequent report investigated changing the ligand bridge from ethyl to cyclohexyl with the effect of structure and electronics of the ligands having a large impact on the polymer properties. The Jones group have also synthesised bis aluminium salen catalysts for ROP. The bis aluminium speciation was achieved by employing a 1,4-diimine bridge, making bimetallic configuration favored. These complexes gave relatively well controlled PLA, with slight isoselectivity (\(P_m = 0.67\)). The third and
most recent class are based on imino bis(phenolate) ligands.\textsuperscript{[64]} The dimeric complexes were active in ROP of \textit{rac}-LA, though no stereoselectivity was observed.

\begin{center}
\textbf{Figure 1.7} Aluminium complexes for ROP developed by Jones (complexes 33 – 37 exist as dimers)
\end{center}

Another class of ROP catalysts is aluminium anilido-aldimine complexes (Figure 1.8). Mu reported the synthesis of two novel compounds and their use in \(\varepsilon\)-CL polymerisation.\textsuperscript{[65]} Polymerisations at 70\(^\circ\)C were rapid, reaching high conversion in less than one hour of up to 400 equivalents. Higher monomer loadings were possible (600 and 800 equivalents) but required slightly longer reaction times (up to two hours). Polymerisations conducted at 20\(^\circ\)C reached high conversion after eight hours and afforded lower dispersities. Previous work in the Shaver group has expanded the study of aluminium anilido-aldimine complexes.\textsuperscript{[66]} Six complexes were synthesised and favored formation of a bimetallic species, consistent with the findings of Mu. Despite this, polymerisations were very well controlled. Modification of the ligands focused on the effect of the imine bridge and the polymerisation of \textit{rac}-lactide. Significantly reducing the steric bulk around the amine nitrogen from the complexes reported by Mu still did not result in a monometallic aluminium species. Despite this, polymerisation of \textit{rac}-lactide was still well controlled. Generally, polymerisations at 120\(^\circ\)C were less controlled with higher
dispersities than polymerisations conducted at 70°C and complexes with a methyl substituent on the amine nitrogen giving the highest level of control ($D = 1.07$ for 40 and 42).

1.5 Aluminium salen and salan complexes for ring-opening polymerisation

1.5.1 Salen and salan ligands

The term salen was originally used to refer to the unsubstituted ligand containing an ethylene diimine bridge, N,N’-bis(salicylidene)-1,2-ethanediamine (Figure 1.9). However, salen is now used more widely for bis(salicylidene)diimine ligands with various substitution and diimine bridges. This ubiquitous ligand has been complexed to many transition metals and used in many catalytic reactions. For example, reactions with heterocycles have been studied including manganese complexes for enantioselective olefin epoxidation,[67] cobalt complexes for enantioselective epoxide ring-opening[68] and aluminium and chromium complexes for carbonylation of various heterocycles.[49, 69]

Salan ligands are similar to salen ligands, with the diimine bridge being replaced by a diamine bridge. The term salan was originally used by Atwood to describe saturated salen complexes.[70]
Despite being structurally similar, much fewer metal salan complexes have been investigated for polymerisations, even though synthesis of many metal complexes has been reported.\textsuperscript{[71]} For both ligand frameworks, even though the phenoxide rings allow for theoretical substitution in four positions (R\textsubscript{1} – R\textsubscript{4}), typically positions R\textsubscript{1} and R\textsubscript{3} are the only positions with non-hydrogen substitution.

1.5.2 Aluminium salen and salan complex synthesis

Salen and salan ligands are both prepared by straightforward reactions from commercially available reagents. Additionally, several salen ligands are available commercially. Salen ligands are prepared \textit{via} imine condensation between two equivalents of a substituted 2-hydroxybenzaldehyde and one equivalent of a diamine (Scheme 1.5).\textsuperscript{[72]}

\begin{equation}
\begin{align*}
\text{[H2][salen]} &= \text{[H2][salen]} \\
2 \text{CHO} + \text{H2N} \rightarrow \text{H2O, reflux, 3-18 h} \rightarrow \text{H2N} &= \text{H2N} \\
\text{R1} + \text{R2} + \text{R3} + \text{R4} + \text{R5} \rightarrow \\
\text{R1} + \text{R2} + \text{R3} + \text{R4} + \text{R5} \rightarrow \\
\text{R1} + \text{R2} + \text{R3} + \text{R4} + \text{R5} \rightarrow \\
\text{R1} + \text{R2} + \text{R3} + \text{R4} + \text{R5} \rightarrow
\end{align*}
\end{equation}

\textbf{Scheme 1.5 General synthesis for salen ligands}

Salan ligands are similarly prepared, \textit{via} condensation of two equivalents of a substituted phenol with one equivalent of diamine in the presence of excess formaldehyde (Scheme 1.6).\textsuperscript{[73]}

\begin{equation}
\begin{align*}
\text{[H2][salan]} &= \text{[H2][salan]} \\
2 \text{OH} + \text{NH} \rightarrow \text{MeOH, reflux, 24 h} \rightarrow \text{NH} &= \text{NH} \\
\text{R1} + \text{R2} + \text{R3} + \text{R4} \rightarrow \\
\text{R1} + \text{R2} + \text{R3} + \text{R4} \rightarrow \\
\text{R1} + \text{R2} + \text{R3} + \text{R4} \rightarrow \\
\text{R1} + \text{R2} + \text{R3} + \text{R4} \rightarrow
\end{align*}
\end{equation}

\textbf{Scheme 1.6 General synthesis for salan ligands}
Aluminium salen and salan pre-catalysts can then be easily synthesised by addition of a slight excess of trialkylaluminium and heating to 110°C (Scheme 1.7). Filtration and washing with cold hexane typically affords the desired aluminium species in good to excellent yields.

**Scheme 1.7 General synthesis of aluminium salen and salen complexes**

1.5.3 Catalyst tuning

Both salen and salan ligands are very tunable. As a result, catalyst tuning by simple changes to the catalyst often leads to a large difference in reactivity (Figure 1.10). The first example of cyclic ester ROP using an aluminium salen complex was reported by Spassky. Complex 45 was used to polymerise both oxetanes and β-BL. ROP of β-BL resulted in only low molecular weight poly(3-hydroxybutyrate) (P3HB). Spassky later used 45 in the ROP of rac-lactide, which gave moderate control over the polymerisation. Furthermore, slightly isotactic PLA ($P_m = 0.68$) was obtained. Tuning of this compound was also investigated by introducing a methyl group onto the imine carbons (46). An increase in the rate of polymerisation was reported, nearly three times faster than the fastest aluminium catalysed polymerisation of lactide at the time (Al($O^i$Pr)$_3$, $k_{app} = 138$ h$^{-1}$ vs. $374$ h$^{-1}$). Soon after, Spassky synthesised the first chiral Al[salen] complex for ROP, $(R)$-47. This led to a stereoselective polymerisation of rac-lactide - the preferential insertion of one lactide enantiomer over the other. The resulting enantioenriched PLA was characterised by differential scanning calorimetry (DSC) and showed an increase in the melting temperature compared to isotactic PLA (either P(L-LA) or P(D-LA)). This was attributed to the formation of stereocomplex PLA. Coates extended work with the chiral catalyst $(R)$-47, producing syndiotactically enriched PLA from
Figure 1.10 Aluminium salen complexes for ROP
meso-lactide, the first report of this tacticity for PLA.\textsuperscript{[25, 27b]} Interestingly, using the racemic derivative, \textit{rac-47}, gave stereoblock PLA with an average of 11 repeat lactide units per stereoblock.\textsuperscript{[26, 77]}

Adding electron withdrawing chloro substituents in the R\textsubscript{3} position was carried out by Gibson to increase catalyst activity.\textsuperscript{[78]} Polymerisation of either \textit{rac}-lactide or L-lactide proceeded at room temperature with 48. Unfortunately, conversion only reached 25\% after 24 hours.

Feijen synthesised an Al[salen] complex based on the Jacobsen salen ligand (\textit{rac-49} and (\textit{R})-49); bulky and electron donating tert-butyl groups in the 3 and 5 positions and a cyclohexyl bridge.\textsuperscript{[67a, 79]} This yielded polymers with significantly higher isospecificity ($P_{m} = 0.92$ for (\textit{R})-49, 0.93 for \textit{rac-49}). However, (\textit{R})-49 differed from previous catalysts in that a preference for L-lactide over D-lactide was observed ($k_{L}/k_{D} \approx 14$).\textsuperscript{[34a]}

Achiral Al[salen] complexes have also been used to introduce an isoselective polymerisation.\textsuperscript{[80]} Ioselectivity could to be increased by two different types of changes to the salen framework: using a more flexible amine bridge, such as an alkyl bridge or having a sterically demanding group in the R\textsubscript{1} position. The Gibson group published a detailed study on tuning aluminum salen catalysts featuring many new complexes as well as a reinvestigation of previous catalysts (Table 1.1).\textsuperscript{[35b]}

Despite structural similarities and ease of synthesis, Al[salan] complexes have received much less attention. The first reported cyclic ester ROP using an Al[salan] complex was not until 2004.\textsuperscript{[81]} In this report, eight Al[salan] complexes were synthesised and screened for activity in \textit{rac}-lactide polymerisation. (78 – 85, Figure 1.11). All eight complexes resulted in well-controlled PLA. The rate of polymerisation followed the trend of H > Cl > Me > tert-butyl for phenoxy substitution and methylamino complexes more active than benzylamino complexes. Interestingly, Al[salan] complexes favored both isotactic and heterotactic PLA formation, depending on the catalyst choice. Complexes 78, 80 and 81 gave isotactic enriched PLA while complexes 79, 82 – 85 produced heterotactic enriched PLA.
Feijen later developed a series of Al[salen] complexes containing a cyclohexyl diamine bridge, allowing for both racemic and $(R,R)$ analogues.\[82]\] Catalysts with either no phenoxy substitution or methyl phenoxy substitution gave moderate isotactic enriched PLA ($P_m$ up to 0.66), while chloro phenoxy substitution gave heterotactic enriched PLA ($P_r$ up to 0.73). The complexes also represent the first Al[salen] species tested for meso-lactide polymerisation, yielding syndiotactically enriched PLA ($P_r = 0.70$).

A piperazine bridged Al[salen] complex has also been investigated (89).\[83]\] The authors found that the nature of the initiating X group had minimal impact on polymer conversion ($\epsilon$-CL: 0 - 47%, lactide: 0%). Furthermore, the bimetallic species [salan]Al$_2$X$_4$ were more active than the corresponding monometallic species. This was explored in more detail by Wang and coworkers.\[84]\] Yao reported a tert-butyl derivative (90), which yielded similar results.\[85]\] Jones and coworkers modified the diamine bridge to a homopiperazine (91 – 95) resulting in higher activity for $\epsilon$-CL, $\delta$-VL and $\text{rac}$-lactide.\[86]\]

### Table 1.1 Rac-lactide polymerisation with various Al[salen] complexes

<table>
<thead>
<tr>
<th>$[\text{Al]}$</th>
<th>$M_n$</th>
<th>$D$</th>
<th>$P_m$</th>
<th>$k_{\text{app}}$ ($10^4$ s$^{-1}$)</th>
<th>$[\text{Al]}$</th>
<th>$M_n$</th>
<th>$D$</th>
<th>$P_m$</th>
<th>$k_{\text{app}}$ ($10^4$ s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>4390</td>
<td>1.76</td>
<td>0.68</td>
<td>59</td>
<td>59</td>
<td>7430</td>
<td>1.20</td>
<td>0.85</td>
<td>159</td>
</tr>
<tr>
<td>48</td>
<td>4290</td>
<td>1.43</td>
<td>0.70</td>
<td>103</td>
<td>67</td>
<td>8140</td>
<td>1.19</td>
<td>0.64</td>
<td>3609</td>
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<tr>
<td>60</td>
<td>7130</td>
<td>1.58</td>
<td>0.56</td>
<td>181</td>
<td>68</td>
<td>7570</td>
<td>1.40</td>
<td>0.68</td>
<td>928</td>
</tr>
<tr>
<td>53</td>
<td>5900</td>
<td>1.27</td>
<td>0.83</td>
<td>1</td>
<td>69</td>
<td>9320</td>
<td>1.13</td>
<td>0.63</td>
<td>4380</td>
</tr>
<tr>
<td>61</td>
<td>8220</td>
<td>1.34</td>
<td>0.68</td>
<td>49</td>
<td>70</td>
<td>7920</td>
<td>1.08</td>
<td>0.86</td>
<td>84</td>
</tr>
<tr>
<td>62</td>
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<td>0.60</td>
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<td>0.72</td>
<td>784</td>
</tr>
<tr>
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<td>0.77</td>
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<td>0.50</td>
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</tr>
<tr>
<td>54</td>
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<td>0.75</td>
<td>661</td>
<td>73</td>
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<td>1.33</td>
<td>0.37</td>
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</tr>
<tr>
<td>64</td>
<td>9700</td>
<td>1.08</td>
<td>0.60</td>
<td>1009</td>
<td>74</td>
<td>6560</td>
<td>1.26</td>
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<tr>
<td>58</td>
<td>9590</td>
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<td>0.88</td>
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<tr>
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</tbody>
</table>
Hormnirun reported asymmetrically substituted Al[salan] complexes (96 - 99). Polymerisation of rac-lactide showed excellent control over molecular weight and dispersity, with heterotactically enriched PLA obtained ($P_r = 0.64 - 0.74$). Chloro derivatives gave higher levels of heterotacticity, whilst methylamino diamine bridged complexes gave lower heterotacticity.
The Shaver group has also contributed to the development of Al[salen] and Al[salan] species. Adamantyl-substitution in the R\textsubscript{1} position for both Al[salen] and Al[salan] complexes was investigated for polymerisation of rac-lactide and β-BL (Figure 1.12).\textsuperscript{[88]} 100 produced highly isotactic PLA from rac-lactide ($P_m = 0.89$). Additionally, no decrease in isoselectivity was seen with increased [M]\textsubscript{0}:[Al]\textsubscript{0}, even up to 1000:1 or when performed under immortal ROP (iROP) conditions (10 eq. chain exchange alcohol per aluminium center). The corresponding Al[salan] species, 101, yielded less than 5% conversion under the tested conditions.

![Diagram](image1)

Figure 1.12 Aluminium salen and salan catalysts developed by Shaver for ROP

### 1.5.4 Monomer scope in Al[salen] and Al[salan] catalysed ROP

Often a catalyst will exhibit excellent control over polymerisation of only a small number of monomers while exhibiting no control or no polymerisation over many other monomers. Ideally, a single catalyst or single family of catalysts could facilitate the polymerisation of a wide range of monomers. This could simplify many systems and access more complex copolymerisations. While efforts in developing Al[salen] and Al[salan] complexes for ROP has been a major focus of global research efforts, much less work has been done in investigating the monomer scope
these catalysts can facilitate. The majority of these complexes have been tested for polymerisation of ε-CL or lactide but rarely both. We recently published a book chapter on aluminium salen and salan complexes in ROP.\[^{89}\]

Early work in cyclic ester ROP was primarily focused on β-BL polymerisation (Chapter 1.3.4).\[^{52, 90}\] Despite this, only a small number of Al[salen] complexes had been tested for β-BL polymerisation, presumably due to poor activity observed with 45.\[^{91}\] The Shaver group has demonstrated 58 and 84 are actually amongst the most efficient catalysts for the ROP of rac-β-BL.\[^{88}\] Furthermore, the system was quite robust, handling a variety of solvents and temperatures without any significant loss in control. 58 could polymerise up to 500 equivalents of β-BL, reaching high conversion with predictable molecular weight and low dispersities (1.06 – 1.14). The bulkier Al[salen] complex, 100, produced P3HB with a lower dispersity (≤1.05) but required longer reaction times. Additionally, P3HB could be produced in bulk or in solution (toluene or THF) between 25 – 120˚C, with little to no effect on the polymer properties. To further show the robust nature of the system, iROP polymerisations were also performed. 58 or 84 operated smoothly under iROP conditions, even with extremely high amounts of chain transfer agent: [β-BL]₀:[Al]₀:[ROH]₀ = 1000:1:50. A subsequent report investigated ortho-adamantyl substituted complexes and polymerisation kinetics using the aforementioned complexes and complexes 102 – 105.\[^{92}\] Complexes 102 – 105 were poor catalysts for ROP of β-BL (D = 1.37 – 2.21). The more rigid phenylene-bridged complexes (103 – 105) were significantly slower (\(k_{\text{app}} = 1.5, 2.1\) and \(1.0 \times 10^{-6}\) s\(^{-1}\) for 103, 104 and 105, respectively) than the alkyl substituted complexes (\(k_{\text{app}} = 33.5\) and \(28.7 \times 10^{-6}\) s\(^{-1}\) for 100 and 102, respectively). Beyond β-BL, no other β-lactones have been polymerised using either an Al[salen] or Al[salan] complex.

Controlling δ-valerolactone polymerisation is considered to be more challenging than β-BL, lactide or ε-CL ROP due to the higher reactivity.\[^{93}\] While there have been reports of catalysts structurally similar to Al[salen] and Al[salan] in δ-VL ROP, only a small number of Al[salen] and Al[salan] complexes have been used.\[^{59}\] Jones has investigated the ROP of δ-VL using several Al[salan] complexes (92 – 95). Consistent with difficulty in δ-VL ROP, polymerisations were relatively
uncontrolled (D = 1.77, 1.12, 1.54, 1.50 and 1.25 for 91, 92, 93, 94 and 95, respectively).\[86] Despite 51 exhibiting a relatively low dispersity (1.12), only low conversions were observed (≤ 30%). Cao used Al[salen] complex 106 to polymerise δ-VL. Results were consistent with Al[salan] polymerisations, with only moderate conversion with relatively high dispersities (1.6 - 2.1).\[94]

ε-CL has also been used as a monomer, increasing the ring size to seven. One of the first ε-CL polymerisations using an Al[salen] complex was reported by Cao. 106, as well as its dimer, showed high activity, although control was typically poor (D = 1.21 – 1.65).\[94] Homopiperazine-bridged Al[salan] complexes also served as catalysts for ε-CL ROP, with only 92 offering slight control (D = 1.15), but only at low conversions. Feijen reported ROP of ε-CL and two methyl-ε-CL derivatives, 4-methyl-ε-CL (4-Me-ε-CL) and 6-methyl-ε-caprolactone (6-Me-ε-CL) using (R,R)-49.\[95] While (R,R)-49 reached high conversion (96%) after 2.5 hours at 90°C with moderate dispersity control (1.21), molecular weights were significantly higher (~ two times) than the theoretical molecular weight. 4-Me-ε-CL polymerisation was also possible, requiring much longer reaction times of 6 and 27 hours at 90 and 70°C, respectively. As for PCL, P(4-Me-ε-CL) molecular weights were approximately double the theoretical molecular weight, while dispersities increased slightly (1.25 – 1.28). Interestingly, 6-Me-ε-CL yielded polymers that displayed a much higher level of control (D = 1.04) at 90°C, possibly due to the more sterically hindering methyl group adjacent to the site of ring-opening. This hypothesis is consistent with the extremely long reaction times (336 hours) required to reach high conversion. Unexpectedly, neat polymerisation of 6-Me-ε-CL required even longer reaction times (91%, 530 hours) and increased dispersities

Macrolactones have also been investigated in ROP using Al[salen] complexes. The resulting polymers are of interest due to their long, uninterrupted polyethylene like segments in each monomer repeat unit. As a result, these polymers may serve as alternatives to polyethylene and polyethylene-like polymers. To date, Duchateau has reported the only polymerisation of macrolactones using an Al[salen] species.\[96] 45 and 54 were investigated as catalysts to polymerise the macrolactones decalactone (DL), undecalactone (UDL), pentadecalactone (PDL) and hexadecalactone (HDL) (Scheme 1.8). The catalysts facilitate macrolactone
polymerisations to high conversion (84 – 98%) with relatively broad dispersities (1.6 – 1.8). Rates of polymerisations were slower for macrolactones \( (k_{\text{app}} = 0.01 – 0.04 \text{ min}^{-1}) \) than for smaller lactones such as \( \varepsilon\text{-CL} \ (k_{\text{app}} = 0.25 \text{ min}^{-1}) \) due to less ring strain. It was also noted that the bulkier complex 54 was slower with lower conversion (87%) than when using 45 (99%) under similar conditions. Duchateau followed his initial report by investigating other Al[salen] complexes and copolymers of PDL with \( \varepsilon\text{-CL}.^{[97]} \) All complexes tested (Scheme 1.8) facilitated PDL polymerisation, with high conversion.

![Scheme 1.8 Monomers and catalysts used in macrolactone ROP](image)

1.5.5 Macrostructure control

Another important aspect of ROP is the ability to control the macrostructure of a polymer. By changing the macrostructure, new properties are obtained that are not accessible through conventional homopolymers. Aluminium salen and salan complexes have been used to prepare block copolymer, star polymers and end group controlled polymer macrostructures.\(^{[89]}\)

While many different copolymer structures exist, this thesis has a particular focus on block copolymers. Early work in ROP block copolymers investigated the use of tin catalysts with \( \beta\text{-BL} \) and lactide monomers.\(^{[98]}\) More recently, aluminium salen and salan complexes have been shown to be excellent catalysts for macrostructure control in block copolymer synthesis.\(^{[89]}\)

The Shaver group reported the synthesis of AB diblock copolymers of poly(ethylene glycol) (PEG) and PLA with focus on the impact of PLA tacticity.\(^{[99]}\)
Using a monomethoxy-PEG (mPEG) macroinitiator with aluminium salen complexes (58 or 100), aluminium salan 84 or Sn(oct)2, P(EG-b-LA) was synthesised with isotactic, heterotactic or atactic PLA blocks, respectively. The AB diblock copolymers synthesised formed micelles. As expected for Al[salen] and Al[salan] catalysed lactide polymerisation, dispersities were quite low (1.1 – 1.2). Copolymers with atactic PLA had lower micellar stability compared to heterotactic or isotactic derivatives. Furthermore, atactic and heterotactic samples degraded quicker than isotactic enriched analogues. This was due to higher crystallinity in isotactic samples, a trend observed in degradation times for atactic, heterotactic and isotactic homopolymer PLA samples. Using this, P(EG-b-LA) properties could be easily tuned using Al[salen] and Al[salan] complexes to yield polymers with targeted properties (thermal and self-assembly). Cui, Chen and coworkers have also synthesised block copolymers of PEG/PLA.[100] The authors used the catalysts tendency to chain exchange between metal centers to generate heterotactic/isotactic stereoblock PLA sample using 59 and 84. Both AB diblock and ABA triblock copolymers were generated from mPEG and PEG macroinitiators, respectively. Well controlled polymers with predictable molecular weights were obtained.

Duchateau has synthesised AB block and AB block-like copolymers using two different approaches.[97] The first method was a one-pot reaction and relied on the relative rates of polymerisation of each monomer to generate AB block-like copolymers. Though these were not true AB block copolymers, it was hypothesised that they should have similar properties. PDL and ε-caprolactone copolymers were synthesised but as the polymerisation proceeded, the block-like nature of the polymer decreased due to polymer scrambling from transesterification. In order to overcome this, a second method was developed. Sequential addition of the second monomer was used to generate AB block copolymer P(PDL-b-CL). Polymerisation of the first block, PPDL was achieved by running the reaction until complete monomer consumption was observed. Addition of ε-CL allowed for the synthesis of the desired AB diblock copolymer. Again, polymer scrambling was observed when ε-CL polymerisation was continued past complete monomer conversion; after one hour, the block copolymer had become a random copolymer. Fortunately, this could be controlled by quenching the polymerisation before transesterification dominates.
reactivity. Characterisation of the block copolymer revealed two distinct melting temperatures, one corresponding to each block type. The random copolymer gave a single averaged melting temperature.

Jones and coworkers have also synthesised triblock copolymers using ε-CL, δ-VL and rac-lactide. The authors used a sequential addition of monomers approach with the Al[salan] catalysts 91 – 93.[86] Polymer dispersites were relatively broad (1.63 – 1.77) with monomer conversion high. This may be a result of polymer scrambling from transesterification, as observed by Duchateau, though no further study on this randomisation was reported.

Another efficient method of controlling polymer macrostructures is through the introduction of functional end groups. End group functionality can be achieved by the use of a functional initiator or post-polymerisation reactions. Aluminium salen complexes are tolerant to a variety of initiating groups, as discussed previously.[83] Additionally, as the active catalyst can be easily prepared in situ from an alkyl aluminium complex and an initiating alcohol, there is no need to prepare and isolate a novel catalyst for each new desired end group. Fulton demonstrated this by changing the nature of the initiating group between (methoxide, ethoxide, isopropanoxide, tert-butoxide and triflate) with negligible differences in polymerisation. This can been exploited when more functionally diverse end groups are targeted for post polymerisation reactions. Using both functional initiating and terminal end groups in Al[salen] and Al[salan] catalysed polymerisations allowed for facile post-polymerisation reactions.[101] Four initiating groups (isopropanol, 1,3-propanediol, 1,1,1-tris(hydroxymethyl)ethane and dipentaerythritol) and 11 terminating agents (methanol, acetyl chloride, hexanoyl chloride, benzoyl chloride, isonicotinyl chloride, anthranoyl chloride, isobutyroyl chloride, pivaloyl chloride, hexynoyl chloride, maleimide acid chloride and Me-PEG-COCl) were successfully incorporated. The nature of the terminating agent had almost no effect on the polymer molecular weight and dispersity as all efficiently quenched the reaction. In a subsequent report, Dove extended the work to synthesis cyclic PLA. Using an alcohol functionalised maleimide still allowed for a very controlled polymerisation of lactide with 58, 64 or 84.[102] Post-polymerisation end group functionalisation was also performed to yield α-ω-maleimido functionalised stereoregular PLA. This
produced well-defined cyclic PLA polymers through thiol Michael additions. The Shaver group has also exploited the functional group tolerance in initiating groups with Al[salen] and Al[salan] complexes.\(^{[103]}\) By simply employing a hexyne functionalised initiator (5-hexyn-1-ol), well-defined polymers from rac-lactide, L-lactide and β-BL were synthesised using 17 and could be later used for click chemistry to attach to β-cyclodextrin cores.

Fluorescent initiators have also been successful. Cui, Chen and coworkers have employed a fluorescent initiator for rac-lactide polymerisation with either an Al[salen] (59) or Al[salan] (84) catalyst. ROP under living and immortal conditions with 59 yielded isotactically enriched PLA with a fluorescence activity.\(^{[104]}\) They later demonstrated that using a mixed system, with both aluminium salen and salan catalysts present in the polymerisation, the degree of stereoselectivity could be tuned, resulting in either crystalline or amorphous PLA.\(^{[100]}\)

Thus far, linear polymers have been discussed. However, polymer stars of aliphatic polyesters offer more tuning over rheological, biomedical and mechanical properties,\(^{[105]}\) typically a result of the higher end group:polymer ratio. Early work in this field was carried out by Dove and coworkers.\(^{[101]}\) This work involved the synthesis of well-defined PLA (58, 64 or 84 as catalysts) with modification of end groups to give α,ω-functionality via modification of procedures developed by Jérôme.\(^{[106]}\) While several alcohols were used as initiators to generate linear polymers, dipentaerythritol (DPE) was reported as an initiator and was able to produce a six-arm polymer star. These polymer stars were characterised by \(^1\)H NMR spectroscopy and gel permeation chromatography (GPC); showing the polymerisations were very well controlled. Additionally, various end group functionalities were accessed. Molecular weight was in good agreement with theoretical molecular weights, with expectedly low dispersities of 1.04 – 1.12.

Subsequent reports by the Shaver group investigated the effect of tacticity on both thermal properties and hydrolytic degradation of polymer stars with a DPE core.\(^{[107]}\) It was revealed that there was a correlation between the thermal properties and tacticity bias. Specifically, a significant increase in \(T_g\) and \(T_m\) was observed as the amount of isotacticity bias increases. Interestingly, polymer stars synthesised from rac-lactide with a stereoselective catalyst yielded polymer stars with higher \(T_m\)s
and $T_{\beta}$s than when purely isotactic samples were prepared from $L$-lactide, indicating the potential for stereocomplexation. The level of tacticity also had an impact on hydrolytic degradation. Isotactic polymer stars had increased degradation times. Controlling the number of errors by catalyst choice, and thus the isotacticity bias, gave control over degradation times, correlating with the semi-crystallinity of the samples (measured by powder X-ray diffraction). Additionally, heterotactic enriched stars were more thermally stable but only a slight increase in hydrolytic stability was observed.

The Shaver group has also generated polymer stars from modified $\beta$-cyclodextrin ($\beta$-CD) initiating cores with $rac$-$\beta$-BL, $rac$-lactide, $L$-lactide and $rac$-lactide/glycolide arms.$^{[103]}$ Synthesis of the polymer stars was achieved using the hydroxyl groups of the heptakis(2,6-di-O-methyl)-$\beta$-CD as the initiating groups (core first method). Unfortunately, this led to polymerisations with low yields, inconsistent initiation and unpredictable molecular weights. However, employing an arms first strategy; where alkyne terminated homopolymer was first synthesised, well-defined polymer stars with a $\beta$-CD core could be prepared (arm first method). The alkyne-terminated polymers were attached to an azide functionalised $\beta$-CD core via click chemistry. Homopolymers were synthesised with both tin(II) 2-ethylhexanoate and 58, with only 58 offering good control over the polymer. Polymer stars synthesised from $rac$-lactide (10 – 50 monomer units per arm) were synthesised with excellent control ($D = 1.03 – 1.15$). Similarly, stars synthesised from $\beta$-BL or $L$-lactide were prepared with similarly good control ($\beta$-BL: 10 – 50 monomers per arm, $D = 1.01 – 1.14$; $L$-Lactide: 10 – 50 monomers per arm, $D = 1.01 – 1.05$). Polymer stars with PLA arms were investigated for the controlled release of a fluorescence active molecule, 7-methoxycoumarin (7-MC Uncatalysed hydrolytic degradation was very slow and 7-MC release was diffusion controlled. However, enzymatic degradation occurred much quicker, suggesting potential future application of these stars in controlled release applications, such as drug delivery.

Chen and coworkers have also used their mixed Al[salen] and Al[salan] system with triol initiator tri(2-hydroxyethyl)amine to generate three arm polymer stars.$^{[100]}$ By varying the ratio of 59 and 84, facile tuning of the polymer stereoselectivity bias was achieved. As expected, employing a higher ratio of 84
yielded PLA with a higher amount of heterotactic bias (amorphous stars obtained). Using a higher ratio of 59 produced a more crystalline sample, consistent with a higher isotactic enriched star.

1.6 Project aims

The main aim of this project was to expand the range of monomers used in cyclic ester ROP using well developed aluminium salen and salan complexes (48 and 84 primarily). In Chapter 2, aliphatic cyclic esters were investigated with aluminium salen and salan catalysts. ε-CL has been understudied using aluminium salen and aluminium salan complexes, likely due to poor initial results. However, we expected that these catalysts should serve as excellent catalysts for ROP of ε-CL. Substituted ε-CL monomers were also studied to provide insight on how substitution effects on the ε-CL monomer affects the polymerisation.

Chapter 3 describes aromatic containing monomers in ROP. To date, there have not been any reports of cyclic ester ROP that yields polymers with aromatic functionality into the backbone. It was hypothesised that polymerisation of a novel class of monomers seven-membered ring monomers may allow for the first synthesis of polyesters containing aromatic functionality as part of the polymer backbone generated through cyclic ester ROP.

In Chapter 4, alkyl-substituted β-lactones were investigated as only a few reports of β-lactone ROP have successfully polymerised monomers with substitution larger than a methyl group. It was hypothesised that block copolymers could be synthesised to tune properties based on the nature of the substituent. Ethyl-, n-butyl- and n-decyl-substituted β-lactones were targeted. As there is limited study of β-lactone polymerisation with aluminium salen and aluminium salan complexes, homopolymerisations were also studied to gain further understanding into the system.

Lastly, Chapter 5 explores the optimisation of chromium(III) complexes for carbonylation of epoxides. Building on early work on a chromium(III) salen complex by Coates,[49] derivatives were investigated to gain understanding of the system and how structural changes effect catalytic activity. Simplifying the procedure was also
investigated, as the active catalysts tend to be highly unstable to air and moisture. An
\textit{in situ} generation of the active catalyst using stable Cr(III) intermediates being used.
There was also the aim to generate polymers from the synthesised β-lactone
products. As a result, specific β-lactone targets were chosen. Two functional groups
were initially chosen to explore ROP activity with two aluminium catalysts. 4-
Chloro-β-butyrolactone and β-(6-hepteno)lactone were targeted to study halogen and
alkene tolerance, respectively.
Chapter Two

Controlling Uncontrolled Aluminium Catalysed Ring-Opening Polymerisation Systems

2.1 Ring-opening polymerisation of ε-caprolactone

To date, many catalysts have been effective in ROP of ε-CL, with low dispersities and predictable molecular weights often being achieved (polymerisation shown in Scheme 2.1). Early catalyst systems were based on simple metal alkoxides, similar to those used in β-propiolactone and β-butyrolactone ROP. Kricheldorf reported ε-CL polymerisation using various metal-based catalysts, including Al(O\text{Pr})_3, Ti(OBu)_4, Zr(OPr)_4, (n^{Bu})_2SnOMe, Zn(O^{Bu})_2 and (n^{Bu})_2Sn(OMe)_2.[41] Polymerisations were conducted at 100 and 150˚C with conversion reaching 100% after 24 hours with Al(O\text{Pr})_3. No intermolecular transesterification was observed using Al(O\text{Pr})_3 after 24 hours, which was previously observed in tin systems.[108] Interestingly, the remaining catalysts typically reached high conversion after 24 hours, but conversion decreased as reaction times were increased. This was indicative of transesterification, as low molecular weight polymer chains are often lost during work up.
Despite no intermolecular transesterification being observed when using Al(O\textsubscript{i}Pr\textsubscript{3}), dispersities were still typically quite broad.\textsuperscript{[41]} As a result of this, tin catalysts are more commonly employed commercially with transesterification limited by not allowing polymerisations to continue high conversions (>95%). Of course, tin catalysts have their own drawbacks: tin is toxic and does not mediate ROP well under immortal conditions. Aluminium catalysts remain of significant interest.

As described in Chapter 1, only a limited number of discrete aluminium complexes have been used for ε-CL polymerisation. Anilido-aldimine systems were somewhat successful,\textsuperscript{[109]} aluminium salen and aluminium salan catalysts have been reported for ε-CL and substituted ε-CL polymerisations with relatively poor results,\textsuperscript{[83-85, 94-95]} and more complex macrostructures of AB diblock-like and ABC triblock copolymers were reported by Duchateau and Jones, respectively.\textsuperscript{[62, 109]}

It is surprising that such tunable catalyst systems such as aluminium salen and aluminium salan have not been systematically studied for ε-CL ROP. We investigated two catalysts; aluminium salen complex \textbf{58} and aluminium salan complex \textbf{84} (Figure 2.1). These catalysts were chosen as they were both excellent catalysts for polymerisation of lactide.\textsuperscript{[35b, 81, 88]}

\textbf{Figure 2.1} Aluminium catalysts (\textbf{58} and \textbf{84}) and \text{snoct\textsubscript{2}} used for ROP of ε-CL
2.2 Living polymerisation of ε-caprolactone

We hypothesised that aluminium salen and aluminium salan catalysts may be able to lead to high conversion of ε-CL to poly(ε-caprolactone) (PCL) with excellent control over molecular weight and dispersity. However, polymerisations reported with similar catalysts raised some questions that needed answers. First, the polymerisation temperature was largely unexplored, with polymerisations often being conducted at high temperatures for extended periods of time. Secondly, low dispersities were achieved at low conversion, indicating the polymerisations may only be controlled during the early stage of polymerisation.

Polymerisations were first conducted at high temperatures to compare to early work in the field. Additionally, Sn(oct)$_2$ was also tested under similar conditions as it is the most commonly used catalyst for ε-CL polymerisation. Polymerisation using aluminium catalysts was likely to give broad dispersities and uncontrolled molecular weights. Sn(oct)$_2$ was expected to be better, with improved control at 120˚C. Polymerisation data from these polymerisations are shown in Table 2.1.

Several trends can be observed from the data in Table 2.1. Polymerisations conducted neat at 150˚C were all relatively uncontrolled, independent of catalyst. Molecular weights obtained using Sn(oct)$_2$ or 58 as a catalyst were much less than the theoretical values, while 84 gave much higher molecular weights. While it could be expected that all three, or at least 58 and 84, should follow a trend, the lack of control makes any difficult to observe. However, it is hypothesised that two factors could contribute to the unpredictable molecular weights. At high temperature it is possible that transesterification is favored which could result in either a higher or lower molecular weight than expected. The second possibility is inefficient initiation, even beyond when monomer concentration has effectively reached zero. This could happen if the rate of polymerisation is extremely rapid and is much faster than the rate of initiation, to give polymers that have a higher molecular weight than the theoretical value. Detection should be possible by $^1$H NMR spectroscopy, as if transesterification is the main contributor, the number of benzylic end groups relative to polymer should remain unchanged (or exhibit very little change). If the rate of polymerisation is much higher than the rate of initiation, there should be fewer
benzylic end groups relative to polymer as there are fewer growing chains, effectively increasing the monomer to active catalyst ratio. Regardless of the cause of these unpredictable molecular weights, the dispersities were still very high for ROP (1.55 – 2.58).

Table 2.1 Polymerisation of ε-CL at 120 – 150°C

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Temperature (°C)</th>
<th>Solvent</th>
<th>Time (min)</th>
<th>Conversion (%)</th>
<th>Mₙ,th</th>
<th>Mₙ</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sn(oct)₂</td>
<td>150</td>
<td>neat</td>
<td>40</td>
<td>97</td>
<td>11180</td>
<td>4090</td>
<td>1.85</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>neat</td>
<td>40</td>
<td>86</td>
<td>9920</td>
<td>18430</td>
<td>1.42</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>toluene</td>
<td>180</td>
<td>&gt;98</td>
<td>11520</td>
<td>10450</td>
<td>1.22</td>
</tr>
<tr>
<td>58</td>
<td>150</td>
<td>neat</td>
<td>40</td>
<td>&gt;98</td>
<td>11520</td>
<td>5720</td>
<td>1.55</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>neat</td>
<td>40</td>
<td>&gt;98</td>
<td>11520</td>
<td>2230</td>
<td>1.52</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>toluene</td>
<td>180</td>
<td>&gt;98</td>
<td>11520</td>
<td>8590</td>
<td>1.33</td>
</tr>
<tr>
<td>84</td>
<td>150</td>
<td>neat</td>
<td>40</td>
<td>&gt;98</td>
<td>11520</td>
<td>25370</td>
<td>2.58</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>neat</td>
<td>40</td>
<td>&gt;98</td>
<td>11520</td>
<td>16100</td>
<td>1.58</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>toluene</td>
<td>180</td>
<td>&gt;98</td>
<td>11520</td>
<td>7600</td>
<td>1.40</td>
</tr>
</tbody>
</table>


Decreasing the polymerisation temperature to 120°C results in a decrease in dispersity for each of the catalysts for neat ε-CL polymerisation. For Sn(oct)₂, the dispersity decreased from 1.85 to 1.42, which is still quite uncontrolled. Somewhat interestingly, the observed molecular weight is now significantly higher than the theoretical value. This is the opposite to what is observed at 150°C with Sn(oct)₂, though this may be just an artifact of the extremely low level of control for this system. With 58, only a slight decrease in dispersity is observed and molecular weights are lower than when the reaction is performed at 150°C. Using 84, a
significant decrease in dispersity is observed but molecular weight is still much higher than predicted. Polymerisations conducted at these temperatures are still considered very uncontrolled.

We discovered improvements could be made to all three systems by performing the reactions in toluene, with the Sn(oct)2 system seeing the most significant improvement. In this case, the dispersity has decreased to 1.22, suggesting a moderately controlled polymerisation. Molecular weights were in excellent agreement with the theoretical value. Catalysts 58 and 84 also saw improvements with dispersities decreasing to 1.33 and 1.40, respectively. However, the key improvement observed with 58 and 84 is in the molecular weight of the resulting polymers. The molecular weight of PCL generated with 58 was 8590 Da, which is in good agreement with the predicted molecular weight (11520 Da). 84 yielded slightly lower molecular weight polymer (7600 Da) but is still in good agreement.

While all three systems polymerised ε-CL to high conversion, the control was poor. Both 58 and 84 were relatively ineffective catalysts under these standard conditions. However, we hypothesised that further condition screening could yield improved results. As a result of the data obtained at 120°C and 150°C, further polymerisations were performed in toluene, as neat polymerisations were less controlled for Sn(oct)2, 58 and 84. Polymerisations were conducted at both 85°C and 70°C for all three catalysts (Table 2.2).

**Table 2.2** Polymerisation of ε-CL at 70 – 85°C a

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Temperature (°C)</th>
<th>Conversion (%) b</th>
<th>$M_n,\text{th}$ c</th>
<th>$M_n$ d</th>
<th>$D$ d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sn(oct)2</td>
<td>85</td>
<td>89</td>
<td>10270</td>
<td>8210</td>
<td>1.07</td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>56</td>
<td>6500</td>
<td>4760</td>
<td>1.04</td>
</tr>
<tr>
<td>58</td>
<td>85</td>
<td>&gt;98</td>
<td>11520</td>
<td>8980</td>
<td>1.32</td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>&gt;98</td>
<td>11520</td>
<td>8990</td>
<td>1.34</td>
</tr>
</tbody>
</table>
As ε-CL polymerisation using either 58 or 84 at both 85˚C and 70˚C had reached quantitative conversion, it was hypothesised that transesterification may be occurring after complete monomer consumption was achieved. Therefore, reactions with either 58 or 84 at both 85˚C and 70˚C were repeated for one hour. In all cases, the polymerisation had reached quantitative conversion, indicating that six hours was in fact longer than necessary. However, no change in molecular weight or dispersity had been recorded. This could still be a result of the polymerisation being carried out for too long past the point of quantitative conversion. To measure this, the kinetic profile at 85˚C was studied by monitoring polymerisation of ε-CL with 58 on an NMR scale. After only 5 minutes at 85˚C, complete conversion had occurred, with no change in molecular weight or dispersity observed. This indicated that the reaction is maybe uncontrolled under these conditions and leaving the reaction for an even shorter period would not yield controlled polymer. However, a second possibility is transesterification is occurring once high conversion is reached. To check if this is the case, the reaction would need to be stopped before complete consumption of the monomer. Polymerisation was again repeated but for only one minute at 85˚C. Complete conversion of ε-CL was observed and the dispersity still indicated poor control. It could not be concluded if the polymerisation was uncontrolled throughout, or the broad dispersity was simply a product of transesterification. Using 84 instead of 58 yielded more promising results. After 10 minutes at 85˚C, complete conversion of ε-CL was obtained with molecular weight in moderately good agreement with theoretical molecular weight (M_n = 8940 , M_{n,th} = 11520) and a significantly lower dispersity (1.14 vs. 1.34). As a slight decrease in dispersity (1.31 vs. 1.34) was observed when decreasing the temperature from 85˚C to 70˚C with 84, lower temperatures were investigated. Polymerisations at ambient
temperature showed the rate of polymerisation was exceptionally fast for both 58 and 84, with the pseudo-first order kinetic plots shown in Figure 2.2.

![Figure 2.2 Plot of \(\ln([M]_0/[M]_t)\) vs. time for \(\varepsilon\)-CL polymerisation with 58 (left) and 84 (right)](image)

As can be seen from the kinetic plots, the rate for 58 (0.36 min\(^{-1}\)) is approximately 4.5 times faster than for 84 (0.08 min\(^{-1}\)). However, both are considered to be extremely fast for \(\varepsilon\)-CL polymerisation. Polymerisations were also conducted for significantly longer than once high conversion has been reached showing that transesterification and the resulting broadening of dispersities is occurring after high conversion is reached (Table 2.3).

### Table 2.3 Polymerisation of \(\varepsilon\)-CL at ambient temperature \(^a\)

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Time (min)</th>
<th>Conversion(^b) (%)</th>
<th>(M_{n,th})</th>
<th>(M_n)</th>
<th>(D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>58</td>
<td>15</td>
<td>&gt;98</td>
<td>11520</td>
<td>9780</td>
<td>1.15</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>&gt;98</td>
<td>11520</td>
<td>9710</td>
<td>1.31</td>
</tr>
<tr>
<td></td>
<td>900</td>
<td>&gt;98</td>
<td>11520</td>
<td>10249</td>
<td>1.39</td>
</tr>
<tr>
<td>84</td>
<td>60</td>
<td>&gt;98</td>
<td>11520</td>
<td>8870</td>
<td>1.05</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>&gt;98</td>
<td>11520</td>
<td>8900</td>
<td>1.14</td>
</tr>
<tr>
<td></td>
<td>900</td>
<td>&gt;98</td>
<td>11520</td>
<td>12040</td>
<td>1.18</td>
</tr>
</tbody>
</table>

\(^a\) \(\varepsilon\)-CL polymerisation in \(C_6D_6\) at 22°C with [\(\varepsilon\)-CL]_0: [Al]_0:[BnOH]_0 = 100:1:1. \(^b\) Determined by \(^1\)H NMR spectroscopy. \(^c\) \(M_{n,th} = ([\text{CL}]_0/[\text{BnOH}]_0) \times MW_{\varepsilon,CL} \times (\%\ conv.) + MW_{\text{BnOH}}\). \(^d\) Determined by GPC using \(dn/dc = 0.072\).
84 yields a more controlled polymer than 58, with dispersity as low as 1.05. However, with 58 having a much faster rate, it was possible that an increase in dispersity is occurring in the moments between the reaction reaching quantitative conversion and when it is quenched. For 84, leaving the polymerisation for approximately one hour past quantitative conversion resulted in a slight broadening of dispersity, which correlates well with the broad dispersities observed for all polymerisations at higher temperatures. While 58 yielded slightly less controlled PCL, it is still exceptionally well controlled for an aluminium salen catalysed ε-CL polymerisation. Despite the broadening of dispersity, especially past the point of complete conversion, this represents the lowest dispersities for ε-CL polymerisation for both aluminium salen and aluminium salan catalyst families to date. It should also be noted that these complexes are also the only aluminium salen or aluminium salan ε-CL polymerisations performed at ambient temperature. To determine whether transesterification was causing dispersity broadening after quantitative conversion for 58, polymerisations were conducted for shorter times (Table 2.4). It was hypothesised that the polymerisation was likely very well controlled, as is for 84, whilst monomers are still being inserted.

**Table 2.4** Polymerisation of ε-CL at ambient temperature with 58

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>Conversion (%)</th>
<th>( M_n,\text{th} )</th>
<th>( M_n,\text{NMR} )</th>
<th>( M_n,\text{GPC} )</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>83</td>
<td>9580</td>
<td>9190</td>
<td>8200</td>
<td>1.02</td>
</tr>
<tr>
<td>10</td>
<td>95</td>
<td>10950</td>
<td>10450</td>
<td>9400</td>
<td>1.01</td>
</tr>
<tr>
<td>15</td>
<td>&gt;99</td>
<td>11520</td>
<td>11180</td>
<td>9750</td>
<td>1.13</td>
</tr>
</tbody>
</table>

*ε-CL polymerisation in toluene at 22°C with \([ε-CL]_0:[58]_0:[\text{BnOH}]_0 = 100:1:1.*  
*\( M_{n,\text{th}} = ([ε-CL]_0/[\text{BnOH}]_0) \times MW(ε-CL) \times (�%)\,\text{conv.} + MW(\text{end group})\).  
*\( M_{n,\text{GPC}} \) Determined by GPC using \(dn/dc = 0.072\).  

As can be seen from data in Table 2.4, it was in fact the case that ε-CL polymerisation with 58 is extremely well controlled until quantitative conversion is achieved. Furthermore, dispersity is very low (1.01) at very high conversion (95%), indicating polymerisation is favored over transesterification until no more monomer
is present. This was an excellent result for aluminium salen and aluminium salan catalysed ROP, showing that both catalyst systems can facilitate extremely well controlled synthesis of PCL under very mild reaction conditions of a catalyst family previously reported to be uncontrolled.\(^{[95]}\)

In an attempt to increase the utility of aluminium salen and aluminium salan systems for \(\varepsilon\text{-CL}\) ROP, higher molecular weight PCL was targeted. Molecular weights of approximately 20000, 50000, 100000 and 250000 Da were targeted using 200, 500, 1000 and 2500 equivalents of \(\varepsilon\text{-CL}\), respectively. Data from these polymerisation reactions are shown in Table 2.5.

### Table 2.5 Synthesis of higher molecular weight PCL \(^a\)

<table>
<thead>
<tr>
<th>([\mathrm{CL}]_0:[\mathrm{Al}]_0) (M)</th>
<th>([\varepsilon\text{-CL}]_0) (M)</th>
<th>Time (minutes)</th>
<th>Conversion (^b) (%)</th>
<th>(M_{n,\text{th}}) (^c)</th>
<th>(M_n) (^d)</th>
<th>(D) (^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>200</td>
<td>1.6</td>
<td>40</td>
<td>&gt;99</td>
<td>22930</td>
<td>21590</td>
<td>1.13</td>
</tr>
<tr>
<td></td>
<td>3.2</td>
<td>55</td>
<td>97</td>
<td>22270</td>
<td>21250</td>
<td>1.19</td>
</tr>
<tr>
<td>500</td>
<td>1.6</td>
<td>120</td>
<td>90</td>
<td>51470</td>
<td>43340</td>
<td>1.07</td>
</tr>
<tr>
<td></td>
<td>0.8</td>
<td>60</td>
<td>86</td>
<td>49190</td>
<td>41340</td>
<td>1.03</td>
</tr>
<tr>
<td>1000</td>
<td>1.6</td>
<td>150</td>
<td>97</td>
<td>110820</td>
<td>126620</td>
<td>1.13</td>
</tr>
<tr>
<td></td>
<td>0.8</td>
<td>240</td>
<td>98</td>
<td>111970</td>
<td>133560</td>
<td>1.13</td>
</tr>
<tr>
<td>2500</td>
<td>1.6</td>
<td>900</td>
<td>&gt;99</td>
<td>279750</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td></td>
<td>0.4</td>
<td>480</td>
<td>&gt;99</td>
<td>279750</td>
<td>174780</td>
<td>1.04</td>
</tr>
<tr>
<td></td>
<td>0.4</td>
<td>1440</td>
<td>&gt;99</td>
<td>279750</td>
<td>172320</td>
<td>1.28</td>
</tr>
</tbody>
</table>

Polymerisation of \(\varepsilon\text{-CL}\) in toluene at 22°C with \([58]\)\(_0\):[BnOH] \(_0\) = 1:1. \(^{b}\) Determined by \(^1\)H NMR spectroscopy. \(^c\) \(M_{n,\text{th}} = ([\varepsilon\text{-CL}]_0/[\text{BnOH}]_0) \times \text{MW}_{(\varepsilon\text{-CL})} \times (\% \text{ conv.}) + \text{MW}_{(\text{BnOH})}\). \(^d\) Determined by GPC using \(dn/dc = 0.072\).

In general, polymerisations were relatively well controlled. ROP of 200 equivalents resulted in high conversion and polymers with molecular weights in excellent agreement with theoretical values. As expected, polymerisations conducted
at lower \([\varepsilon-\text{CL}]_0\) showed a slight improvement in control \((D = 1.13)\) than those at higher concentration \((D = 1.19)\). Extending to 500 equivalents, polymerisations were conducted with lower \([\varepsilon-\text{CL}]_0\) to reduce viscosity. These polymerisations reached high conversion with very low dispersities. However, the conversion did not increase past 96%, even at extended reaction times, which appeared to minimise transesterification. Polymerisation of 1000 equivalents at 1.6 and 0.8 M showed essentially no difference in dispersity or molecular weight. Dispersities were relatively low for such a high molecular weight polymer. Polymerisation of 2500 equivalents resulted in very high conversion (> 98% by \(^1\text{H} \text{NMR spectroscopy}) at 1.6 M after 24 hours. Unfortunately, this high molecular polymer was only sparingly soluble in common solvents. As a result of poor solubility in THF, no GPC analysis could be performed. Decreasing the concentration of the reaction (0.4 M) allowed for monitoring of the reaction and quenching once high conversion was achieved. Quantitative conversion was achieved after only eight hours and could be analysed by \(^1\text{H} \text{NMR spectroscopy} and GPC. Analysis showed that the polymerisation could be performed with excellent levels of control Dispersity was as low as 1.04, with broadening occurring when the reaction was left for longer reaction times (24 hours, \(D = 1.28)\). The molecular weight was considerably lower than the theoretical molecular weight, which is common during the synthesis of high molecular weight polymers.

With these results in mind, another mechanism of control was investigated in an attempt to synthesise well controlled PCL by immortal ring-opening polymerisation. Both low and high molecular weight PCL was targeted using this method.

### 2.3 Immortal polymerisation of \(\varepsilon\)-caprolactone

Immortal ring-opening polymerisation (iROP) is a technique in ROP that takes advantage of a catalyst’s ability to mediate the growth of more than one polymer chain (Scheme 2.2).\(^{[110]}\) This is done by using a catalyst that can undergo chain exchange between a growing polymer chain and a free (dormant) polymer
chain. To obtain narrow dispersities through iROP, the rate of chain exchange should be sufficiently larger than the rate of propagation and initiation. \[111\]

Immortal ROP was first reported by Inoue for epoxide polymerisation. \[110\] In this report, the authors described using an aluminium porphyrin complex with addition of excess methanol as a chain transfer agent, with up to 49 equivalents of MeOH per aluminium center added to a propylene oxide (PO) polymerisation. As the equivalents of MeOH increased, the molecular weight of the polymer decreased, with excellent correlation between the number of initiating groups and polymer chains. Additionally, the dispersity was also lowered as the amount of MeOH increased, suggesting iROP can increase the level of control over a polymerisation. Inoue followed up this work by expanding this to lactone polymerisation. \[112\] Using a carboxylic acid as excess initiator (up to 39 equivalents), iROP of β-BL was successfully performed. As for PO polymerisation, well controlled polymers were synthesised. Conversely, as the amount of initiator increased, the dispersity increased. End group analysis was also performed to demonstrate that most polymer chains had end groups consistent with chain transfer agent.

Immortal polymerisation has also been performed using aluminium salen (58, 100) and salan complexes (84). \[88\] iROP of rac-lactide was performed with up to 10 equivalents of BnOH per metal center with excellent control. Molecular weights were predictable and only a slight loss in tacticity control was observed. Increasing the amount of initiating alcohol further gave poor control. iROP with β-BL was tolerant of a higher amount of chain transfer agent (50 equivalents). Polymerisations were still very well controlled, with dispersities less than 1.1. However, when a large amount of chain transfer agent was added, only low molecular weights were targeted (~ 2000 Da), likely a consequence of catalyst limitations of total number of monomer

Scheme 2.2 Schematic of immortal ring-opening polymerisation (iROP)
turnovers. 58 gave lower conversion (up to 75%) under iROP conditions compared to 84 (up to 99%). iROP of β-BL using the bulky adamantyl-substituted aluminium salen complex 100 was unsuccessful, with conversion <5% after 24 hours. However, iROP of rac-lactide with 100 was successful.

Aside from being fundamentally interesting, immortal polymerisations are of importance as they can yield polymers with similar characteristics, while effectively decreasing the catalyst loading. Additionally, immortal polymerisation often induces a greater level of control.\textsuperscript{113} Despite having poorer iROP results than 84 for rac-lactide and β-BL, iROP of ε-CL was investigated with 58 as a catalyst (Table 2.6). 58 was chosen over 84 due to higher activity observed in living polymerisation. These reactions were performed with modest expectations, as the rate of ε-CL polymerisation is incredibly rapid. Whilst this could be beneficial, propagation may be favored over chain exchange, resulting in inefficient initiation for all chains. This would be particularly noticeable when [BnOH\textsubscript{0}]/[58\textsubscript{0}] is lower. Despite these concerns, reactions were carried out with [BnOH\textsubscript{0}]/[58\textsubscript{0}] = 5:1, 10:1, 25:1, 50:1 and 100:1. Initially, [ε-CL\textsubscript{0}]:[BnOH\textsubscript{0}] was kept constant (100:1) to compare to living polymerisations.

\textbf{Table 2.6} Immortal polymerisation of ε-CL with 58 at ambient temperature \textsuperscript{a}

<table>
<thead>
<tr>
<th>[ε-CL\textsubscript{0}]:[BnOH\textsubscript{0}]:[58\textsubscript{0}]</th>
<th>Time (minutes)</th>
<th>Conversion\textsuperscript{b} (%)</th>
<th>M\textsubscript{n,th}\textsuperscript{c}</th>
<th>M\textsubscript{n}\textsuperscript{b}</th>
<th>D\textsuperscript{d}</th>
</tr>
</thead>
<tbody>
<tr>
<td>500:5:1</td>
<td>10</td>
<td>23</td>
<td>2680</td>
<td>2730</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>90</td>
<td>86</td>
<td>9040</td>
<td>9920</td>
<td>-</td>
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<td>135</td>
<td>95</td>
<td>10950</td>
<td>10140</td>
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<td></td>
<td>180</td>
<td>93</td>
<td>10720</td>
<td>11290</td>
<td>1.02</td>
</tr>
</tbody>
</table>

\textsuperscript{a} All reactions performed at ambient temperature.
\textsuperscript{b} Conversion determined by 
\textsuperscript{c} M\textsubscript{n,th} calculated using the Flory equation.
\textsuperscript{d} Polydispersity index (D) calculated from GPC.
Immortal ROP of ε-CL with 58 was very successful. Polymerisations were allowed to continue until high conversion was achieved (> 90%) with molecular weights all in excellent agreement with predicted molecular weights, demonstrating that all excess initiator molecules are efficiently initiating. Additionally, dispersities were very low, with essentially no difference compared to the living polymerisations. However, we also observe iROP has one advantage over living ROP as it minimises the impact of transesterification reactions proceeding after complete monomer consumption. Once complete monomer consumption has been achieved, chain transfer acts as a competing reaction with transesterification. This was an exciting result as it demonstrated that aluminium salen complexes are excellent mediators of controlled living polymerisation and controlled immortal polymerisation.

The kinetics for immortal polymerisations was monitored for all tested ratios. Typical plots for iROP ([ε-CL]₀/[BnOH]₀/[58]₀ = 5000:50:1) kinetics and molecular weight vs conversion are shown in Figure 2.3. Molecular weight agreed with theoretical values throughout the polymerisation, showing control is exceptional from start to finish. In all cases, pseudo-first order kinetics with respect to monomer

<table>
<thead>
<tr>
<th>Ratio</th>
<th>N</th>
<th>T</th>
<th>MW</th>
<th>Mw</th>
<th>Mn</th>
</tr>
</thead>
<tbody>
<tr>
<td>2500:25:1</td>
<td>60</td>
<td>7</td>
<td>910</td>
<td>850</td>
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<tr>
<td></td>
<td>310</td>
<td>47</td>
<td>5470</td>
<td>5390</td>
<td>-</td>
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<tr>
<td></td>
<td>720</td>
<td>78</td>
<td>9010</td>
<td>8990</td>
<td>-</td>
</tr>
<tr>
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<td>11090</td>
<td>1.03</td>
</tr>
<tr>
<td>5000:50:1</td>
<td>360</td>
<td>22</td>
<td>2620</td>
<td>2520</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>1440</td>
<td>68</td>
<td>7870</td>
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<td></td>
<td>2520</td>
<td>87</td>
<td>10040</td>
<td>9980</td>
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<td>3600</td>
<td>95</td>
<td>10950</td>
<td>10470</td>
<td>1.02</td>
</tr>
<tr>
<td>10000:100:1</td>
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<td>1020</td>
<td>1010</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2670</td>
<td>43</td>
<td>5020</td>
<td>5080</td>
<td>-</td>
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<td>4200</td>
<td>68</td>
<td>7870</td>
<td>7750</td>
<td>-</td>
</tr>
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<td></td>
<td>11520</td>
<td>96</td>
<td>10950</td>
<td>11490</td>
<td>1.04</td>
</tr>
</tbody>
</table>

\(^{a}\) Immortal polymerisation of ε-CL in toluene or C₆D₆ at 22°C with [ε-CL]₀ = 1.6 M. \(^{b}\) Determined by \(^{1}\)H NMR spectroscopy. \(^{c}\) M_{n,th} = ([ε-CL]₀/[BnOH]₀) × MW(ε-CL) × (% conv.) + MW (BnOH).

\(^{d}\) Determined by GPC using dn/dc = 0.072.
concentration were observed. As expected, with a decreasing [58]₀, the apparent rate also decreases (Table 2.7).

**Table 2.7 Rate of iROP of ε-CL compared to [58]₀**

<table>
<thead>
<tr>
<th>[ε-CL]₀:[BnOH]₀:[58]₀</th>
<th>[58]₀ (mM)</th>
<th>(k_{app}) (h⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>500:5:1</td>
<td>3.20</td>
<td>1.34</td>
</tr>
<tr>
<td>1000:10:1</td>
<td>1.60</td>
<td>0.942</td>
</tr>
<tr>
<td>2500:25:1</td>
<td>0.64</td>
<td>0.15</td>
</tr>
<tr>
<td>5000:50:1</td>
<td>0.32</td>
<td>0.051</td>
</tr>
<tr>
<td>10000:100:1</td>
<td>0.16</td>
<td>0.017</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ε-CL</th>
<th>BnOH</th>
<th>58</th>
<th>500:5:1</th>
<th>1.34</th>
</tr>
</thead>
<tbody>
<tr>
<td>ε-CL</td>
<td>BnOH</td>
<td>58</td>
<td>1000:10:1</td>
<td>0.942</td>
</tr>
<tr>
<td>ε-CL</td>
<td>BnOH</td>
<td>58</td>
<td>2500:25:1</td>
<td>0.15</td>
</tr>
<tr>
<td>ε-CL</td>
<td>BnOH</td>
<td>58</td>
<td>5000:50:1</td>
<td>0.051</td>
</tr>
<tr>
<td>ε-CL</td>
<td>BnOH</td>
<td>58</td>
<td>10000:100:1</td>
<td>0.017</td>
</tr>
</tbody>
</table>

*Immortal ROP of ε-CL in C₆D₆ at 22°C with [ε-CL]₀ = 1.6 M. Conversion monitored by ¹H NMR spectroscopy*

Synthesis of higher molecular weight PCL was also attempted through iROP (Table 2.8). Polymerisations were carried out with [ε-CL]₀[BnOH]₀:[58]₀ = 2500:5:1 and 5000:5:1 to target PCL with a degree of polymerisation of 500 and 1000, respectively. iROP of ε-CL for synthesis of higher molecular weight PCL was very effective. Reactions were conducted at 30°C for 24 hours. ROP with [ε-CL]₀[BnOH]₀:[58]₀ = 2500:5:1 gave quantitative conversion but only moderate control after 24 hours, likely due to the long reaction times. Molecular weight was slightly higher than the theoretical value, which is the opposite trend observed for living ROP of 500 equivalents. ROP with [ε-CL]₀[BnOH]₀:[58]₀ = 5000:5:1 gave...
quantitative conversion with very well controlled PCL. Despite not optimising reaction conditions, dispersity was lower than for living ROP of 1000 equivalents of \(\varepsilon\)-CL. This demonstrates that iROP may be used to yield polymers with similar, and possibly better, levels of control than living polymerisation while significantly reducing the catalyst concentration.

Table 2.8 Synthesis of higher molecular weigh PCL via iROP

<table>
<thead>
<tr>
<th>([\varepsilon\text{-CL}]_0)[BnOH]_0:([58]_0)</th>
<th>Conversion(^b) (%)</th>
<th>(M_{n,th})^c</th>
<th>(M_n)^d</th>
<th>(D)^d</th>
</tr>
</thead>
<tbody>
<tr>
<td>2500:5:1</td>
<td>&gt;99</td>
<td>57180</td>
<td>68760</td>
<td>1.19</td>
</tr>
<tr>
<td>5000:5:1</td>
<td>&gt;99</td>
<td>114250</td>
<td>124430</td>
<td>1.09</td>
</tr>
</tbody>
</table>

\(^a\) Immortal polymerisation of \(\varepsilon\)-CL with 58 in toluene at 30°C for 24 hours with [\(\varepsilon\text{-CL}\)]_0 = 0.8 M. \(^b\) Determined by \(^1\)H NMR spectroscopy. \(^c\) \(M_{n,th} = (([\varepsilon\text{-CL}]_0/[\text{BnOH}]_0) \times MW(\varepsilon\text{-CL}) \times (\% \text{ conv.}) + MW(BnOH)) . \(^d\) Determined by GPC with \(dn/dc = 0.072\).

Excellent living and immortal \(\varepsilon\)-CL polymerisation results with 58 and 84 were encouraging, as no aluminium salen or salan complex had exhibited near the same level of control previously. Additionally, it can be argued in terms of homopolymerisation with an aluminium salen or salan complex, \(\varepsilon\)-CL polymerisations are the most robust. High molecular weights, approaching 200000 Da were prepared with excellent levels of control. Immortal polymerisation allowed for up to 100 growing chains and 10000 monomer turnovers per catalyst without significant broadening of dispersity and predictable molecular weights.

2.4 Polymerisation of substituted \(\varepsilon\)-caprolactones and other aliphatic monomers

With the excellent results for living and immortal ring-opening polymerisation of \(\varepsilon\)-CL with 58 and 84, similar aliphatic cyclic esters and substituted caprolactones were targeted as other potential monomers.
2.4.1 Seven membered rings

As discussed in Chapter 1, substituted methyl substituted ε-caprolactones have been employed for ROP with an aluminium salan catalysts.\textsuperscript{95} Polymerisation of 4-methyl and 6-methyl substituted ε-CL was polymerised with significantly reduced rates compared to ε-CL.

For this thesis, four seven membered rings were investigated for ROP: 6-methyl-ε-caprolactone (6-Me-ε-CL), 2,6-dimethyl-ε-caprolactone (2,6-Me-ε-CL), (-)-menthide (Menth) and 1,4-dioxepin-5-one (1,4-DPO) (Figure 2.4). As \textbf{58} was more active for ε-CL polymerisation only this catalyst was investigated for these monomers. These monomers were chosen to gain insight into trends observed in ROP of monomers discussed in Chapter 3.

![Figure 2.4 Structure of seven membered cyclic esters](image)

First, polymerisation of 6-Me-ε-CL and 2,6-Me-ε-CL were investigated. These were chosen as to observe the effect of substitution adjacent to the active ROP site. Polymerisation of 6-Me-ε-CL was successful, though significantly slower than ε-CL. This is consistent with results from Feijen.\textsuperscript{95} Polymerisation of 6-Me-ε-CL conducted at room temperature did not yield any polymer after six hours. Polymerisation could be achieved at 85°C, reaching 76% after 16 hours with moderate control (\(D = 1.16\)). Leaving the reaction for longer reaction times did not increase conversion. Additionally, conducting the polymerisation at 120°C only reached 11% conversion. The kinetics of the reaction at 85°C was also studied (Figure 2.5).
Increasing the amount of bulk by switching to 2,6-Me-ε-C showed a decrease in activity. Polymerisation was attempted at room temperature, 85°C and 120°C, resulting in no polymerisation. This showed that having the increased bulk is unfavorable. It is likely that the monomer is too bulky to allow coordination of the monomer and subsequent ROP.

This trend is also observed in attempted polymerisation of (-)-menthylide. Polymerisations at room temperature, 85°C and 120°C resulted in no polymer with only monomer present in the reaction. It is hypothesised that this is due mostly to the increase in bulk in the 6-position going from methyl to isopropyl as the methyl group in the 4-position is far away from the active site.

The last monomer, 1,4-DPO was chosen to observe the effect of having an additional coordinating atom in the monomer. 1,4-DPO ROP has been extensively studied by Albertsson, with homopolymers, random copolymers, block copolymers and cross-linked polymers being reported.\cite{114} Additionally, materials have been synthesised from 1,4-DPO for porous scaffolds for bone and nerve regeneration.\cite{115} It was expected that polymerisation of 1,4-DPO should occur using 58 as no steric bulk is present (vs. ε-CL) and polymerisation of rac-lactide could be performed in coordinating solvents such as THF.\cite{88} No polymerisation had occurred at room temperature after 24 hours, which was surprising as the difference between 1,4-DPO and ε-CL are minimal. Polymerisation could be achieved at 85°C, albeit at an extremely slow rate. Polymerisation reached maximum conversion after 384 hours with moderate control ($M_{n,th} = 9040$, $M_n = 8010$, $D = 1.20$). Changing the conditions of the polymerisation was unsuccessful in increasing conversion or control. This
showed that having an additional coordinating oxygen in the monomer was detrimental to ROP.

### 2.4.2 4-(4-Benzyloxbutyl)-\(\varepsilon\)-caprolactone

The last aliphatic ROP monomer discussed in this chapter is 4-(4-benzyloxbutyl)-\(\varepsilon\)-caprolactone (4-BOB-\(\varepsilon\)-CL). This work was done in collaboration with Dr Stephen Fletcher at the University of Oxford, who provided samples of rac- and enantioenriched (ca 92% ee) \((R)\)- and \((S)\)-4-BOB-\(\varepsilon\)-CL for ROP. The synthesis of these monomers was reported by this group using a (chiral) copper (I) catalyst with a zirconium salt (Scheme 2.3).\[1^16\]

![Scheme 2.3 Synthesis of 4-BOB-\(\varepsilon\)-CL](image)

Polymerisations of rac- and \((R)\)-4-BOB-\(\varepsilon\)-CL were performed using 58 and 84 and initially attempted at room temperature. After 24 hours at room temperature, no significant polymerisation had occurred. This was consistent with previous substituted caprolactone polymerisations. However, increasing the polymerisation temperature to 70 or 85°C gave high conversion (> 85%) to polymer. Additionally, ROP showed moderate levels of control (\(\mathcal{D} < 1.2\)) (Table 2.09).

Some trends can be observed from data presented in Table 2.09. First, polymerisation of rac-4-BOB-\(\varepsilon\)-CL was considerably slower than \((R)\)-4-BOB-\(\varepsilon\)-CL. This is more pronounced by the polymerisation with 58, with similar conversions being achieved for rac and \((R)\) monomers after 150 and 20 minutes, respectively. The second trend is that polymerisation with 58 is more controlled than polymerisation with 84. This is shown by both molecular weights and dispersities. Dispersities were slightly higher for 84, while molecular weights were in better agreement with theoretical molecular weights with 58. As a result, further ROP of 4-BOB-\(\varepsilon\)-CL were conducted using 58.
Table 2.09 Polymerisation of rac- and (R)-4-BOB-ε-CL with 58 and 84 \(^a\)

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Monomer</th>
<th>Time (minutes)</th>
<th>Conversion (^b) (%)</th>
<th>(M_{n,th}) (^c)</th>
<th>(M_n) (^b)</th>
<th>(D) (^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>58</td>
<td>rac</td>
<td>150</td>
<td>86</td>
<td>11850</td>
<td>13420</td>
<td>1.14</td>
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<tr>
<td></td>
<td>(R)</td>
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<td>88</td>
<td>12270</td>
<td>14720</td>
<td>1.09</td>
</tr>
<tr>
<td>84</td>
<td>rac</td>
<td>60</td>
<td>80</td>
<td>11160</td>
<td>15010</td>
<td>1.18</td>
</tr>
<tr>
<td></td>
<td>(R)</td>
<td>60</td>
<td>88</td>
<td>12270</td>
<td>17060</td>
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</tbody>
</table>

\(^a\) Polymerisation of 4-BOB-ε-CL at 85°C in C\(_6\)D\(_6\) with [4-BOB-ε-CL]_0:[Al]_0:[BnOH]_0 = 50:1:1 with [4-BOB-ε-CL]_0 = 1.6 M. \(^b\) Determined by \(^1\)H NMR spectroscopy. \(^c\) \(M_{n,th} = ([4-BOB-ε-CL]_0[BnOH]_0) \times MW(4-BOB-ε-CL) \times \% \text{conv.} + MW(\text{BnOH})\). \(^d\) Determined by GPC.

Polymers were analysed by both NMR spectroscopy and GPC. \(^1\)H and \(^13\)C NMR spectra are shown in Figure 2.6. Integration of CH\(_2\) resonances adjacent to the ester oxygen in monomer and polymer was used to determine conversion. Furthermore, integration of the benzylic end group compared to polymer signals was used to estimate molecular weight.
As 4-BOB-ε-CL was provided in rac-, (R)- and (S) forms, polymerisation of all three was investigated. We hoped to observe a difference in activity based on the chirality of the monomer. This has been shown in some catalyst systems with preference of one enantiomer of rac-lactide.\textsuperscript{[34a]} The rates for all three monomers were measured and are shown in Table 2.10 and Figure 2.7.

\textbf{Figure 2.6} $^1$H (bottom) and $^{13}$C (top) NMR spectra of P(4-BOB-ε-CL) in CDCl$_3$
Table 2.10 Polymerisation rates of rac-, (R)- and (S)-4-BOB-ε-CL \(^a\)

<table>
<thead>
<tr>
<th>Monomer</th>
<th>Rate (\times 10^2\text{min}^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>rac</td>
<td>1.21</td>
</tr>
<tr>
<td>(R)(^b)</td>
<td>3.88</td>
</tr>
<tr>
<td>(S)(^b)</td>
<td>2.84</td>
</tr>
</tbody>
</table>

\(^a\) Polymerisation of 4-BOB-ε-CL in C\(_6\)D\(_6\) with [4-BOB-ε-CL]_0[58]_0[BnOH]_0 = 50:1:1 and [4-BOB-ε-CL]_0 = 1.6M. \(^b\) 92% ee.

![Figure 2.7 Pseudo first-order kinetic plot for 4-BOB-ε-CL polymerisation with 58; ■ = (R), ▲ = (S), ● = rac](image)

As can seen from data presented in Table 2.12 and Figure 2.7, there was less of a preference for one enantiomer, as the rate of polymerisation of (R) and (S) enantiomers were both faster than the racemic analogue. As the rate of polymerisation for rac-4-BOB-ε-CL was slower than for both (R) and (S) enantiomers, this suggests that the preference is not in which monomer is first inserted, but the enantiomer most recently inserted monomer dictating subsequent preference. That is, if a (R) monomer has most recently been inserted, another (R) monomer is favored. The same trend is observed for (S). This results in a decrease in rate for rac-4-BOB-ε-CL as the effective concentration of ‘favored’ monomer is decreased. The Fletcher group noted difficulty in monomer purification. It is possible that the errors in observed rates are due in part to trace impurities.

It was hypothesised that a block copolymer was also synthetically accessible. The method of choice was sequential addition of monomers (Scheme 2.4). As ε-CL polymerisation was more susceptible to transesterification than 4-BOB-ε-CL, ε-CL polymerisation was performed second. Ten equivalents of rac-4-BOB-ε-CL was first
polymerised by 58 at 70°C for two hours, with a crude sample taken for analysis. As
the molecular weight was low, GPC analysis was not conclusive. However, 1H NMR
spectroscopic analysis indicated > 95% conversion was achieved. The reaction was
cooled to room temperature, 90 equivalents of ε-CL were introduced to the reaction
and polymerisation was continued until no more ε-CL remained (10 – 15 minutes).
1H NMR analysis indicated complete conversion of ε-CL and a 90:10 ratio of
polymers. GPC analysis revealed that copolymer had formed, as indicated by
presence of only a single polymer signal. Copolymers with ε-CL are of interest as it
allows for tunable amount of functionality (4-benzyloxybutyl), which can be used for
post polymerisation reactions.

![Scheme 2.4 Synthesis of block copolymer from ε-CL and rac-4-BOB-ε-CL](image)

Post polymerisation deprotection of the benzyl groups was attempted. Two
methods of deprotection were tried, which have been used to deprotect similar
functional groups in small organic molecules.[117] The first method was using Pd/C
under hydrogen, with a range of solvents under a pressure of hydrogen (75 psi) for
seven days. 1H NMR spectroscopy indicated that no deprotection of the benzyl ethers
was achieved. However, deprotection of the benzyl end group was achieved.
Addition of BBr3 at -78°C, was also unsuccessful with no deprotection observed.

2.4.3 δ-Valerolactone polymerisation

δ-Valerolactone (δ-VL) was chosen as it is very similar to ε-CL structurally
but is significantly more active in ROP.[93] As a result, examples of controlled δ-VL
polymerisation with aluminium salen or salan complexes are even less common.
Jones and coworkers reported δ-VL polymerisation with homopiperazine-bridged
aluminium salen complexes (91 – 95).[86] The authors also showed triblock
copolymers of ε-CL, δ-VL and rac-lactide could be synthesised. As for ε-CL
polymerisation with these complexes, dispersities were relatively broad except where
conversion was low. Cao also reported ROP of δ-VL with an aluminium salan complex (106) with similar results.[94] Poor results in aluminium catalysed δ-VL polymerisation are not unique to salen and salan complexes. An aluminium diamide complex efficiently converted up to 1250 equivalents of δ-VL to polyvalerolactone (PVL) in 30 minutes at 25°C.[118] However, as typical for these very rapid polymerisations, there was little to no control over polymer dispersities (1.9 - 4.9).

Despite quite poor δ-VL polymerisation with similar complexes, the success with ε-CL suggested that polymerisations may be controlled with 58 or 84. As more work had been done with 58 for ε-CL polymerisation, it was first tested for δ-VL polymerisation (Table 2.11).

As shown by data in Table 2.11, a relatively well controlled polymerisation of δ-VL was achieved with 58. Furthermore, high conversion was reached after 40 minutes at room temperature. Leaving the polymerisation for longer did not yield any significant increase in conversion. This was interesting as ε-CL proceeds to quantitative conversion, followed by transesterification. Molecular weights by GPC were calculated using a $dn/dc$ value of 0.063 mL/g, which was calculated from GPC analysis of three different PVL samples of varying molecular weight, with each sample performed at three different concentrations.

**Table 2.11** Polymerisation of δ-VL with 58

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>Conversion (%)</th>
<th>$M_{n,th}$</th>
<th>$M_n$</th>
<th>$M_n$</th>
<th>$D$</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>44</td>
<td>4510</td>
<td>3910</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>25</td>
<td>91</td>
<td>9220</td>
<td>9140</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>40</td>
<td>94</td>
<td>9520</td>
<td>9380</td>
<td>10410</td>
<td>1.16</td>
</tr>
</tbody>
</table>

$^a$ Polymerisation of δ-VL in C$_6$D$_6$ at 22°C with [δ-VL]$_0$/$[58]_0$/$[BnOH]_0 = 100:1:1$. $^b$ Determined by $^1$H NMR spectroscopy. $^c$ $M_{n,th} = ([δ-VL]_0/[BnOH]) × MW(δ-VL) × (% conv.) + MW(BnOH)$. $^d$ Determined by GPC using $dn/dc = 0.063$.

δ-VL polymerisations were also performed using 84. Data from these polymerisations are shown in Table 2.12.
Table 2.12 Polymerisation of δ-VL with 84

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Time (minutes)</th>
<th>Conversion b (%)</th>
<th>M&lt;sub&gt;n,th&lt;/sub&gt;&lt;sup&gt;c&lt;/sup&gt;</th>
<th>M&lt;sub&gt;n&lt;/sub&gt;&lt;sup&gt;b&lt;/sup&gt;</th>
<th>M&lt;sub&gt;n&lt;/sub&gt;&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Đ&lt;sup&gt;d&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>22</td>
<td>15</td>
<td>76</td>
<td>7720</td>
<td>7440</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>20</td>
<td>91</td>
<td>9220</td>
<td>9170</td>
<td>n.d.</td>
<td>n.d.</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>93</td>
<td>9420</td>
<td>9300</td>
<td>10520</td>
<td>1.05</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>22</td>
<td>94</td>
<td>9510</td>
<td>9420</td>
<td>10760</td>
<td>1.09</td>
</tr>
</tbody>
</table>

<sup>a</sup> Polymerisation of δ-VL in C<sub>6</sub>D<sub>6</sub> with [δ-VL]<sub>0</sub>[84]<sub>0</sub>:[BnOH]<sub>0</sub> = 100:1:1. <sup>b</sup> Determined by <sup>1</sup>H NMR spectroscopy. <sup>c</sup> M<sub>n,th</sub> = ([δ-VL]<sub>0</sub>/[BnOH]<sub>0</sub>) × MW(δ-VL) × (% conv.) + MW(BnOH). <sup>d</sup> Determined by GPC using dn/dc = 0.063.

Polymerisations carried out with 84 followed similar trends. Polymerisation was again very rapid with predictable molecular weight but did not reach quantitative conversion. The dispersity with 84 showed significant improvement, now as low as 1.05. This indicated that 84 was a better catalyst for δ-VL polymerisation than 58. While broadened dispersities were initially observed for ε-CL polymerisation with 58, it was later attributed to transesterification after complete monomer consumption. However, this was not the case for δ-VL polymerisation with dispersities remaining high throughout the polymerisation.

As polymerisations were not reaching quantitative conversion, an equilibrium between monomer and polymer was likely being reached. This equilibrium did not appear to be significantly influenced by concentration. This was shown by addition of solvent after maximum conversion was reached; no conversion change was observed after several additional hours.

Higher molecular weight PVL was also targeted. Results for 100 equivalents suggest that one of two outcomes would be observed. The first being that polymerisation proceeds similarly, with conversions ~90%. In this case the conversion is determined by the equilibrium. The second possibility is that conversion is controlled by the polymer properties such as molecular weight. If this
was the case, higher molecular weight PVL should not be easily accessible. Results from attempted synthesis of higher molecular weight PVL are shown in Table 2.13.

Table 2.13 Attempted synthesis of higher molecular weight PVL

<table>
<thead>
<tr>
<th>[δ-VL]₀:[84]₀</th>
<th>Time (minutes)</th>
<th>Conversion (%)</th>
<th>Mₙ,th</th>
<th>Mₙ</th>
<th>Mₙ</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>200:1</td>
<td>30</td>
<td>84</td>
<td>16930</td>
<td>15340</td>
<td>16450</td>
<td>1.02</td>
</tr>
<tr>
<td>75</td>
<td>85</td>
<td>17130</td>
<td>17060</td>
<td>16450</td>
<td>1.02</td>
<td></td>
</tr>
<tr>
<td>500:1</td>
<td>30</td>
<td>14</td>
<td>7120</td>
<td>7120</td>
<td>6470</td>
<td>1.03</td>
</tr>
<tr>
<td>270</td>
<td>16</td>
<td>8120</td>
<td>10290</td>
<td>7140</td>
<td>1.01</td>
<td></td>
</tr>
<tr>
<td>70 e</td>
<td>87</td>
<td>43660</td>
<td>31400</td>
<td>30660</td>
<td>1.07</td>
<td></td>
</tr>
</tbody>
</table>

a Polymerisation of δ-VL in toluene at 22°C with [δ-VL]₀:[84]₀:[BnOH]₀ = 100:1:1 and [δ-VL]₀ = 1.6 M. b Determined by ¹H NMR spectroscopy. c Mₙ,th = ([δ-VL]₀[BnOH]₀) × MW(δ-VL) × (% conv.) + MW(BnOH). d Determined by GPC using dn/dc = 0.063. e [δ-VL]₀ = 8.7 M.

Polymerisation with higher [δ-VL]₀:[BnOH]₀ were inconclusive as to whether conversion was being controlled by molecular weight or equilibrium. It should be noted that δ-VL polymerisations for 100, 200 and 500 equivalents were all performed so that [δ-VL]₀ = 1.6 M. Polymerisation of 200 equivalents still reached relatively high conversion quickly. Molecular weights were approximately 60% larger than for 100 equivalents, suggesting higher molecular weights are accessible. However, when 500 equivalents were polymerised at similar concentrations, only low conversions were observed. This could be overcome by increasing the initial concentration of δ-VL to 8.7 M, which allowed for higher conversion (87%) with only a slight increase in dispersity.

These results showed that aluminium salen and aluminium salan complexes could facilitate the polymerisation of δ-VL with excellent levels of control. Polymerisations were less susceptible to transesterification as there was little to no change in dispersity when the reaction was left for extended reaction times. As a result of excellent results from δ-VL and ε-CL, other aliphatic monomers were studied. These results demonstrate the robust nature of aluminium salen and salan complexes.
complexes. Furthermore, these polymerisations are considerably more controlled that for other discrete aluminium catalysts.

2.5 Conclusions

In conclusion, ring-opening polymerisation of aliphatic monomers with 58 and 84 was investigated. First, polymerisation of ε-CL was studied. Neat and solution polymerisation at 70 – 150˚C were uncontrolled for the most part. Decreasing the temperature 22˚C in exceptionally controlled ROP, with dispersities as low as 1.02. These represent the ε-CL polymerisations with the highest level of control as well as the fastest rates for aluminium catalysts. Synthesis of higher molecular weight PCL could also be achieved with a high level of control, giving molecular weights up to ~175000 Da and Đ = 1.04.

Immortal polymerisation of ε-CL was also successful. Polymerisation of up to 10000 equivalents of ε-CL and 100 equivalents of BnOH per metal center could be performed without any loss in control. Molecular weights up to 125000 Da were synthesised via iROP with excellent control and low catalyst loading.

Addition of a methyl group in the 6-position in 6-Me-ε-CL resulted in a significant decrease in activity. No polymerisation occurred at room temperature and needed 85˚C to achieve ROP. Addition of more bulk in 2,6-Me-ε-CL or Menth shut polymerisation completely with 58 at temperatures up to 120˚C. Substitution of one CH₂ with an oxygen in 1,4-DPO also resulted in a significant decrease in rate.

Polymerisation of rac-, (R)- and (S)-4-BOB-ε-CL was me with success. Polymerisation of enantioenriched monomers was faster than the racemic form, suggesting isotactic polymerisation is favored. A block copolymer with ε-CL was synthesised giving predictable copolymer composition.

Polymerisation of δ-VL could be achieved at room temperature, with no apparent transesterification. Higher molecular weight PVL could be synthesised, with up to equivalents of δ-VL reach highing conversion.

This work has been prepared for publication and has been submitted for peer review to European Polymer Journal and has been accepted subject to revision.
Chapter Three

The First Aromatic/Aliphatic Polyester Synthesised via Ring-Opening Polymerisation

3.1 Introduction to aromatic containing polyesters from ring-opening polymerisation

Early work in biodegradable polymers demonstrated the effect of incorporating pendant phenyl substituents into a poly(L-lactic acid) polymer.\textsuperscript{[119]} This was achieved through addition of phenyllactic acid to L-lactic acid in a condensation polymerisation (Scheme 3.1). The copolymers were fully characterised, including \textsuperscript{1}H NMR spectroscopy, GPC, thermal properties, crystallinity and \textit{in vivo} degradation studies.

\begin{equation}
\text{n} \text{HOOC(OH)} + \text{m} \text{HOOC(OH)} \rightarrow \Delta (n+m-1) \text{H}_2\text{O} \rightarrow \text{HOOC})_{\text{n}}(\text{COO})_{\text{m}}\text{H}
\end{equation}

\textbf{Scheme 3.1} Synthesis of poly(L-lactic acid-co-phenyllactic acid)

There have been few other examples of ring-opening polymerisation of aromatic containing monomers. Copolymerisation of epoxides/anhydrides is
advantageous when incorporating aromatic groups into a polymer, as more commercial reagents are available. Duchateau showed this was possible by producing a copolymer from styrene oxide and phthalic anhydride using salen- and porphyrin-based catalysts of Mn, Co, Cr and Al (Scheme 3.2).\textsuperscript{120} Polymerisations were well controlled; copolymers had nearly 100% alternation.

![Scheme 3.2 Copolymerisation of styrene oxide and phthalic anhydride](image)

Baker and coworkers have also made progress in aromatic containing monomers for ROP. In an initial report, the synthesis and polymerisation of phenylactide was discussed (Scheme 3.3).\textsuperscript{121} Solution polymerisations with Al(O\textit{i}Pr)\textsubscript{3} or Sn(oct)\textsubscript{2} both gave low conversions and catalyst decomposition. However, bulk polymerisations allowed for higher conversion of monomer. As expected for Sn(oct)\textsubscript{2} and Al(O\textit{i}Pr)\textsubscript{3}, transesterification was observed at extended reaction times. Interestingly, racemisation had occurred during the polymerisation, resulting in amorphous atactic poly(phenyllactic acid) (PPLA) with a $T_g$ (50$^\circ$C) that was very similar to that of atactic PLA. The degradation of PPLA was studied and revealed that degradation is approximately five times slower than PLA, a result of increasing the hydrophobicity of the polymer. A subsequent report from Baker involved the synthesis and polymerisation of mandelide, another lactide derivative with pendant aromatic groups.\textsuperscript{122} The loss of a CH\textsubscript{2} linker between the cyclic ester and the phenyl ring (\textit{vs.} phenyllactide) had a significant effect on polymer properties. Poly(mandelic acid) (PMA) had rheological and thermal properties similar to polystyrene. Again, racemisation was observed, resulting in amorphous atactic polymers.

Poly(mandelic acid) has also been derived from other monomer sources. Tighe and coworkers reported the polymerisation of 5-phenyl-1,3-dioxolan-2,4-dione in the presence of pyridine with water as an initiator gave low molecular weight
Brod NMR spectroscopy resonances likely indicate the polymer was atactic. Carbery and Davidson have reported the synthesis of high molecular weight and stereoregular PMA through a similar process. Using a pyridine/mandelic acid organocatalyst, polymers were prepared with excellent molecular weight correlation and narrow dispersities. Additionally, racemisation was minimal and highly isotactic PMA was produced, resulting in a significant increase of the $T_g$ (15°C).

### 3.2 Potential aromatic/aliphatic monomers for ring-opening polymerisation

No ROP of a cyclic ester monomer has incorporated an aromatic functionality as part of the polymer backbone to date. This was viewed as an opportunity to test active and robust aluminium salen and aluminium salan complexes with monomers that have not been used in ROP previously. However, the absence in aromatic/aliphatic polyesters synthesised via ROP is due in part to difficulty in synthesising the starting monomers. As ROP monomers are typically small rings (4–7 atoms), including both an aromatic ring and an ester can be difficult. For example, the simplest possible example contains a four-membered ring: benzpropiolactone, the β-lactone derivative of salicylic acid, is expectedly difficult to synthesise and is highly unstable. Increasing the ring size to a five-membered ring gives a much more stable species, phthalide. Despite being produced commercially, this monomer has never been successfully used in ROP. Increasing

---

**Scheme 3.3** Synthetic routes to polyesters with pendant aromatics

PMA via loss of CO$_2$.$^{[123]}$ Broad $^1$H NMR spectroscopy resonances likely indicate the polymer was atactic. Carbery and Davidson have reported the synthesis of high molecular weight and stereoregular PMA through a similar process.$^{[124]}$ Using a pyridine/mandelic acid organocatalyst, polymers were prepared with excellent molecular weight correlation and narrow dispersities. Additionally, racemisation was minimal and highly isotactic PMA was produced, resulting in a significant increase of the $T_g$ (15°C).

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the ring sizes to six- and seven-membered rings was hypothesised to access species that would be suitable as monomers for ROP.

### 3.2.1 Benzodioxepinones

**2,3-Dihydro-5H-1,4-benzodioxepin-5-one**

Benzodioxepins are bicyclic compounds consisting of one phenyl ring and a seven-membered ring with two oxygen atoms and one double bond. These would not be useful as target monomers as no ester is present. Thus, lactone derivatives were used as target monomers. The first of such monomers explored was 2,3-dihydro-5H-1,4-benzodioxepin-5-one (2,3-DHB) (Figure 3.1). 2,3-DHB is commercially available and produced on relatively large scales. Facile synthesis has been reported through multiple synthetic pathways.[126]

![Figure 3.1 Structure of targeted benzodioxepinone monomers](image)

**3,4-Dihydro-2H-1,5-benzodioxepin-2-one**

A similar benzodioxepinone can be easily synthesised from readily available starting materials. 3,4-Dihydro-2H-1,5-benzodioxepin-2-one (3,4-DHB) is a result of changing the orientation of the ester bond in 2,3-DHB. 3,4-DHB synthesis has been reported *via* Baeyer-Villager oxidation (BVO) of 4-chromanone using *m*-CPBA as an oxidant.[127] We wanted to avoid the use of the harmful *m*-CPBA and instead attempted the synthesis of 3,4-DHB *via* BVO as a more benign oxidant (Scheme 3.4).[128] In this method, the active species are generated *in situ* and sodium percarbonate acts as a buffer, eliminating the need for addition of an additional buffer source. Whilst this route has not been reported for synthesis of 3,4-DHB, similar ketones have been prepared.[128]
Synthesis using this method was successful. Initial reaction times were four hours, resulting in >60% conversion. Leaving the reaction for 16 hours resulted in a moderate increase in conversion (80%). The crude reaction mixture was soluble in most organic solvents. Recrystallisation was successful for accessing relatively low yields of an off-white solid that was sparingly soluble in common NMR solvents. However, repeated recrystallisation did allow for an overall high combined yield. Purification using column chromatography was more straightforward, allowing for isolation of an off-white solid in high yields. The product isolated by either method was only partially soluble in d$_6$-DMSO or hot CDCl$_3$. Additionally, starting material could be recovered and used in subsequent BVO reactions to reduce waste. $^1$H and $^{13}$C NMR spectroscopy was used to characterise 3,4-DHB and was consistent with literature reports.

3-Alkyl/aryl-dihydro-5H-1,4-benzodioxepin-5-ones

Substituted monomers were also investigated. Dong and coworkers have reported the synthesis of substituted 2,3-DHBs.$^{[129]}$ In these reports, hydroacylation of ketoaldehydes using a Rh(I)/phosphine catalyst system was employed. Additionally, highly enantioselective ($\geq$98% ee) synthesis was also achieved by judicious phosphine choice. A diverse range of functional groups was introduced including alkyl, phenyl, substituted phenyl, halo, furyl and thiophene. Using this strategy, methyl- and phenyl-substituted 2,3-DHBs were synthesised for ROP.

Some problems in the synthesis of the ketoaldehyde precursor were encountered (Scheme 3.5). Salicylaldehyde was protected by addition of excess 1,3-propanediol in the presence of tetra-$n$-butylammonium tribromide and triethylorthoformate.$^{[130]}$ After washing with water and drying over Na$_2$SO$_4$, distillation at 110°C under reduced pressure removed impurities to afford the desired product in high yield (>80%). The second step involved condensation of ketal from
the first step and halo-ketone. This worked best at room temperature for 16 hours. While Dong and coworkers used the crude product without purification, this caused some problems. When the yellow oil was used without purification, the ketoaldehyde product from step three would be isolated as a brown oil. Purification of the brown oil by column chromatography or recrystallisation yielded a white solid that would revert back to a brown oil within 12 hours under either inert and non-inert conditions. Using these brown oils in the ring-closing hydroacylation was problematic as only low conversions (~10 – 15%) were obtained. To overcome this, isolation of the keto-acetal in step two was performed. Column chromatography of the yellow oil yielded a white solid that were characterised by $^1$H NMR spectroscopy. Using the purified keto-acetal in the acid catalysed deprotection step resulted in a much cleaner ketoaldehyde. In the final step, the active catalyst was first prepared in situ by stirring $[\text{Rh(nbd)}_2]\text{BF}_4$ with phosphine in CH$_2$Cl$_2$ under H$_2$ for 30 minutes. This results in liberation of norbornane and allows for coordination of the phosphine to the rhodium center. The solution was concentrated and ketoaldehyde in CH$_2$Cl$_2$ was added to the catalyst (5 mol%). Stirring at room temperature for 6 – 24h typically gave high yields (> 95%) and column chromatography afforded the desired monomers. Racemic monomers were obtained using 1,3-bis(diphenylphosphino)propane while enantiopure monomers were obtained using either (R)- or (S)-DTBM SEGPHOS. We note that our optimised procedures do not match those reported in the literature.

![Scheme 3.5](image)

Scheme 3.5 Synthesis of substituted 2,3-DHBs; i) 1,3-propanediol (4 eq.), TBATB, HC(OEt)$_3$ ii) acetone, halo-ketone, K$_2$CO$_3$, KI iii) p-TsOH, THF/H$_2$O iv) $[\text{Rh}]$, phosphine, CH$_2$Cl$_2$, H$_2$
3.2.2 4H-1,3-Benzodioxin-4-one

4H-1,3-Benzodioxin-4-one (1,3-BDO) is a similar monomer to 2,3-DHB, with a six-membered ring in place of a seven-membered ring. Additionally, the removal of a CH$_2$ linkage in the seven-membered ring results in an acetal. This can be beneficial in degradation as acetals are typically easily cleaved by acid-catalysed hydrolysis.\[131\] There are several different routes of synthesis of 1,3-BDO. The synthesis of choice was base-catalysed ring formation from phenylsalicylate and paraformaldehyde.\[132\] The authors reported the synthesis on a one mmol scale with 81% yield after one day. As one mmol scale is relatively small, scale up to 100 mmol was attempted. The reaction proceeded as reported in the literature with isolated yields of >75%. Purification by Kugelrohr distillation at 110°C was straightforward to yield white needle-like crystals.

3.3 Polymerisation of 2,3-DHB

Polymerisation of 2,3-DHB would result in the first aromatic/aliphatic backbone polyester synthesised through cyclic ester ROP. Poly(ethylene terephthalate) (PET) is an example of an aromatic/aliphatic polyester produced commercially on industrial scales. PET is prepared through condensation of terephthalic acid and ethylenediol and has not been prepared through ROP.\[133\] Additionally, PET is among the most produced polymers commercially but has a negative environmental impact. Namely, PET is very persistent in landfills with a very long degradation time.\[134\] The long degradation time is largely due to the high crystalline nature arising from the aromatic regions of the polymer. It should be noted that PET and similar aromatic containing polyesters have been prepared via ROP of cyclic oligomers prepared through condensation.\[135\] This work has been carried out by several groups since the mid 1990’s.\[136\] This route has several
drawbacks. These include energy intensive synthesis of oligomers required for polymerisation, uncontrolled distribution of different oligomer sizes, uncontrolled polymerisation of oligomers and the polymers produced have the drawbacks outlined previously for PET.

There are obvious structural differences between the potential polymer from 2,3-DHB polymerisation, poly-2-(2-hydroxyethoxy)benzoate (P2HEB) and PET; PET is para-linked through the aromatic group while P2HEB is ortho-linked. PET has two ester functionalities versus one in P2HEB. These structural differences should result in differences in thermal and physical characteristic properties. However, the synthesis of P2HEB has advantages in the method of synthesis. Namely, ROP can allow for the synthesis of highly controlled and targeted, tunable properties such as molecular weight and dispersity. We believe this to be a proof of concept study, and not intended to mimic PET properties.

### 3.3.1. Polymerisation of 2,3-DHB using Sn(oct)$_2$

Despite the disadvantages of using Sn(oct)$_2$ as a catalyst for ROP, it was still tested to allow for a comparison of Sn catalysed ROP vs Al catalysed ROP. Results of polymerisations carried out using Sn(oct)$_2$ are shown in Table 3.1. Polymer analysis for 2,3-DHB molecular weights were all calculated using end group analysis in $^1$H NMR spectroscopy and dispersity was calculated using GPC. Molecular weights were not calculated by GPC as difficulties were found in ensuring all the GPC sample pass through the filter in sample preparation, which did not permit samples of the high concentrations needed to calculate a consistent $dn/dc$ value.

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Time (h)</th>
<th>Conversion (%)</th>
<th>$M_{n,th}$</th>
<th>$M_n$</th>
<th>$D$</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>3</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>120</td>
<td>3</td>
<td>58</td>
<td>9600</td>
<td>8300</td>
<td>1.23</td>
</tr>
<tr>
<td>120</td>
<td>6</td>
<td>61</td>
<td>10100</td>
<td>11400</td>
<td>1.44</td>
</tr>
</tbody>
</table>

Table 3.1 Polymerisation of 2,3-DHB using Sn(oct)$_2$ $^a$

$^a$2,3-DHB polymerisation with [2,3-DHB]$_0$/[Sn]$_0$/[BnOH]$_0$ = 100/0.5/1. $^b$ Determined by $^1$H NMR spectroscopy. $^c$ $M_{n,th}$ = ([2,3-DHB]$_0$/[BnOH]$_0$) × MW$_{2,3,OH}$ × (% conv.) + MW$_{BnOH}$. $^d$ Determined by GPC.
Polymerisations were initially carried out at typical concentrations for Sn(oct)_2 catalysed ROP. Under these conditions, no polymer was observed under any of the temperatures tested. Increasing [2,3-DHB]_0 to between 4 and 5 M allowed for polymerisation under specific conditions. As can be seen from Table 3.1, no polymerisation of 2,3-DHB was observed at 70°C after 3 hours in toluene. Leaving the polymerisation for a longer period of time yielded the same result. Increasing the temperature to 120°C did result in conversion of 2,3-DHB to P(2HEB). After 3 hours, 58% of the monomer had been converted to polymer. The molecular weight was in fairly good agreement with the theoretical value. The dispersity indicated the polymerisation was moderately well controlled with D = 1.23. However, leaving the polymerisation for an additional three hours resulted in significant broadening of the polymer dispersity to 1.44 with no significant increase in conversion. These two factors suggest that transesterification is likely occurring. The polymer molecular weight is still in good agreement with theoretical molecular weight, as both intra and intermolecular transesterification would not result in a significant change in the number of benzyl end groups present. While this demonstrated that polymerisation of 2,3-DHB was possible using Sn(oct)_2 and could be moderately controlled, careful attention to polymerisation time is required. Only moderate conversion was possible, resulting in considerable monomer waste. These results show some similarities and differences to ε-CL polymerisation using Sn(oct)_2. Both ε-CL and 2,3-DHB undergo significant transesterification at 120°C. However, ε-CL polymerisation proceeds to high conversion (> 98%) and is well controlled with high conversion at 70°C.

### 3.3.2 Polymerisation of 2,3-DHB using an aluminium salen catalyst

With this in mind, polymerisation of 2,3-DHB was attempted using our preferred aluminium salen complex 58 to try and overcome the drawbacks of Sn(oct)_2 catalysed ROP (Table 3.2). Polymerisations were initially carried out at typical concentrations for Al[salen] catalysed ROP reactions. As for Sn(oct)_2, no polymerisation was achieved at these concentrations and higher concentration polymerisations were required. For the remainder of this thesis, polymerisations are carried out between 4 and 5 M, unless otherwise noted.
Table 3.2 Polymerisation of 2,3-DHB with 58 at 120°C \(^a\)

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Time (h)</th>
<th>Conversion (^b) (%)</th>
<th>(M_{n,\text{th}}) (^c)</th>
<th>(M_n) (^b)</th>
<th>(D) (^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>neat</td>
<td>3</td>
<td>66</td>
<td>10960</td>
<td>11000</td>
<td>1.60</td>
</tr>
<tr>
<td>toluene</td>
<td>3</td>
<td>56</td>
<td>9230</td>
<td>9310</td>
<td>1.76</td>
</tr>
</tbody>
</table>

\(^a\) 2,3DHB polymerisations at 120°C with \([2,3\text{-DHB}]_0/[58]_0/[\text{BnOH}]_0 = 100/1/1. \(^b\) Determined by \(^1\)H NMR spectroscopy. \(^c\) \(M_{n,\text{th}} = ([2,3\text{-DHB}]_0/\text{[BnOH]}_0) \times \text{MW}_(2,3\text{-DHB}) \times \text{conv.}) + \text{MW}_\text{BnOH}.\)

As can be seen from Table 3.2, 58 was in fact capable of polymerising 2,3-DHB at 120°C. Polymerisation could be conducted neat or in toluene. Neat polymerisation reached 66% conversion after three hours with a dispersity of 1.60 and a molecular weight in good agreement with the theoretical molecular weight. Polymerisation in toluene for the same amount of time yielded a lower conversion (55%) and a higher dispersity (1.76). Allowing the reactions to continue past three hours resulted in similar conversions and dispersities. Unfortunately, polymerisation of 2,3-DHB was even less controlled using 58 than Sn(oct)_2. Changing the catalyst to the aluminium salan complex 84 resulted in similar conversion and control. For both, polymerisations halted after reaching only moderate conversion. These results, paired with Sn(oct)_2 catalysed ROP were promising as they represent the first synthesis of a cyclic ester polymerisation to yield aromatic functionality into the backbone but we hoped to achieve a controlled ROP.

In an attempt to minimise the level of transesterification and potentially increase conversion, 2,3-DHB polymerisations were conducted at 70°C (Table 3.3). This was not expected to yield significant polymer as no polymerisation was observed using Sn(oct)_2.

Unexpectedly, as shown in Table 3.3, polymerisations could be conducted neat or in toluene at 70°C. Polymerisations conducted neat had reached 64, 75 and 77% conversion after one, three and five hours, respectively. Increasing the polymerisation beyond five hours had no effect on results. Molecular weights were again in excellent agreement with theoretical values, all within ±15%. The largest
Table 3.3 Polymerisation of 2,3-DHB with 58 at 70°C 

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Time (h)</th>
<th>Conversionb (%)</th>
<th>Mₙ,th</th>
<th>Mⁿ</th>
<th>Dd</th>
</tr>
</thead>
<tbody>
<tr>
<td>neat</td>
<td>1</td>
<td>64</td>
<td>10580</td>
<td>10760</td>
<td>1.13</td>
</tr>
<tr>
<td>neat</td>
<td>3</td>
<td>75</td>
<td>12330</td>
<td>12900</td>
<td>1.13</td>
</tr>
<tr>
<td>neat</td>
<td>5</td>
<td>77</td>
<td>12750</td>
<td>11020</td>
<td>1.14</td>
</tr>
<tr>
<td>toluene</td>
<td>1</td>
<td>75</td>
<td>12370</td>
<td>12510</td>
<td>1.14</td>
</tr>
<tr>
<td>toluene</td>
<td>3</td>
<td>75</td>
<td>12360</td>
<td>12670</td>
<td>1.16</td>
</tr>
<tr>
<td>toluene</td>
<td>5</td>
<td>80</td>
<td>13240</td>
<td>14240</td>
<td>1.17</td>
</tr>
<tr>
<td>toluene</td>
<td>1</td>
<td>28</td>
<td>22710</td>
<td>18830</td>
<td>1.14</td>
</tr>
</tbody>
</table>

a 2,3-DHB polymerisations at 70°C with [2,3-DHB]₀/[58]₀/[BnOH]₀ = 100/1/1. b Determined by ¹H NMR spectroscopy. c Mₙ,th = ([2,3-DHB]₀/[BnOH]₀) × MW(2,3-DHB) × (% conv.) + MW(BnOH). d Determined by GPC. e [2,3-DHB]₀/[Al]₀/[BnOH]₀ = 500/1/1

The difference in these polymerisations compared to those conducted at 120°C was the dispersities obtained. The polymerisations offered a very high level of control with D = 1.13 – 1.14. Additionally, the dispersity had not increased after prolonged polymerisation time. The monomer conversion had not increased significantly between three and five hours (75 vs. 77%), with essentially no change in dispersity (1.13 vs. 1.14). There was also no change in dispersity when the polymerisation was left past five hours. Transesterification is minimised when lowering the reaction temperature to 70°C but conversion had not increased significantly than when conducted at 120°C. This was thought to be potentially due to the viscosity of the reaction mixture as the reactions had become visibly more viscous as the reaction progressed. To determine if this was in fact the case, polymerisations were performed in toluene.

Polymerisations in toluene followed similar trends to neat polymerisations. Conversion after one hour was higher than neat (75 vs. 64%) and maximum conversion was also slightly higher (80 vs. 77%). Again, polymerisations were well controlled with D = 1.14 – 1.17. Since this showed that viscosity of the reaction was not the largest factor contributing to reaching higher conversion, a second hypothesis
was proposed: as the molecular weight of the polymers had all been around the same (12000 – 14000 Da), polymerisations were potentially reaching a maximum molecular weight. To test this hypothesis, a reaction with 500 equivalents of monomer was conducted. After one hour in toluene at 70˚C, 28% of monomer was converted to polymer. This corresponds to a theoretical degree of polymerisation of 140 (≤ 80 for previous experiments). The molecular weight determined by end group analysis determined that the polymer had a molecular weight of 18830 Da, considerably higher than the 12000 -14000 Da observed previously. This suggested that the polymerisations were not reaching a maximum conversion due to a maximum accessible molecular weight. P2HEB could be purified by precipitation into cold methanol. This allowed for isolation of purified polymer that was characterised by ¹H and ¹³C NMR spectroscopy (Figure 3.2). As expected for a polymer, resonances were significantly broader than monomer resonance. It can also been seen that despite the aromatic protons of the benzyl end group overlapping with polymer aromatic signals, a distinct singlet corresponding to the methylene unit is easily observable. This is used to calculate number average molecular weights throughout this chapter.

Figure 3.2 ¹H (bottom) and ¹³C NMR spectra for P2HEB
Conducting polymerisations of 2,3-DHB at 70°C instead of 120°C showed that 58 was capable of mediating the ROP to generate very well controlled polymers in bulk or in solution but conversions were still low. Several experiments were performed in an attempt to increase conversion further (Table 3.4).

Table 3.4 Alternative conditions for 2,3-DHB polymerisation

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conversion(^b) (%)</th>
<th>(M_{n,th})(^c)</th>
<th>(M_n)(^b)</th>
<th>(D)(^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(^e)</td>
<td>70</td>
<td>11090</td>
<td>11200</td>
<td>1.14</td>
</tr>
<tr>
<td>2(^f)</td>
<td>77</td>
<td>13600</td>
<td>10800</td>
<td>1.12</td>
</tr>
</tbody>
</table>

\(^a\) 2,3-DHB polymerisations in toluene with \([2,3\text{-DHB}]_0/[58]_0/[\text{BnOH}]_0 = 100/1. \(^b\) Determined by \(^1\)H NMR spectroscopy. \(^c\) \(M_{n,th} = ([2,3\text{-DHB}]/[\text{BnOH}]) \times \text{MW}_{2,3\text{-DHB}} \times (\% \text{ conv.}) + \text{MW}_{\text{(BnOH)}}\). \(^d\) Determined by GPC. \(^e\) Catalyst generated \textit{in situ} prior to monomer addition. \(^f\) \([2,3\text{-DHB}]_0/[\text{Al}]_0/[\text{BnOH}]_0 = 500:1:5.\n
The aluminium salan complex 84, was used in place of 58. Under similar conditions, polymerisations resulted in similar conversion, molecular weight and dispersity. The active catalyst was alternatively generated \textit{in situ} by heating 58 and BnOH in toluene at 70°C for one hour prior to addition of monomer (entry 1, Table 3.4). Again, no significant change was observed. The polymerisation was conducted under immortal conditions (entry 2, Table 3.4; 500:1:5 \([2,3\text{-DHB}]_0/[\text{Al}]_0/[\text{BnOH}]_0\) with a slight decrease in dispersity (1.12 vs. 1.14) being the only difference in the polymerisation.

During a polymerisation being performed on an NMR scale it was noticed that if the solution was left for a period of time after the reaction had reached maximum conversion at 70°C, the solution would become solid. Dissolution of the sample and analysis by \(^1\)H NMR indicated that the conversion had increased past the conversion achieved at 70°C. As a result of this, temperatures lower than 70°C were investigated. Polymerisations were attempted at 60°C and 50°C to determine if polymerisations could be performed at lower temperatures. These data are shown in Table 3.5.

As shown in Table 3.5, 58 was capable of polymerising 2,3-DHB at both 60°C and 50°C. Unexpectedly, the polymerisations at both 60°C and 50°C reached
higher conversion than polymerisations at 70°C or 120°C. As expected with higher conversion, higher molecular weight polymers are generated (13000 – 15000 Da). These polymerisations were also exceptionally well controlled. The dispersities were lowered further than observed for any higher temperature polymerisations with D ≤ 1.10 in each case. Transesterification reactions are still minimal, as going from four hours to six hours at 60°C gave no change in conversion (92%) or dispersity (1.08).

Table 3.5 Polymerisation of 2,3-DHB with 58 at 50 and 60°C

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Time (h)</th>
<th>Conversion (%)</th>
<th>M_{n,th}</th>
<th>M_n</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>4</td>
<td>92</td>
<td>15270</td>
<td>13000</td>
<td>1.08</td>
</tr>
<tr>
<td>60</td>
<td>6</td>
<td>92</td>
<td>15100</td>
<td>13500</td>
<td>1.08</td>
</tr>
<tr>
<td>50</td>
<td>1</td>
<td>59</td>
<td>9710</td>
<td>7720</td>
<td>1.09</td>
</tr>
<tr>
<td>50</td>
<td>6</td>
<td>91</td>
<td>15060</td>
<td>15220</td>
<td>1.07</td>
</tr>
</tbody>
</table>

*a 2,3-DHB polymerisations in toluene with [2,3-DHB]_0/[58]_0/[BnOH]_0 = 100/1/1. b Determined by ^1H NMR spectroscopy. c M_{n,th} = ([2,3-DHB]_0/[BnOH]_0) × MW(2,3-DHB) × (% conv.) + MW(BnOH). d Determined by GPC.

To gain further insight into the polymerisation, kinetic studies were performed at both 60°C and 50°C. It was suggested by data in Table 3.5 that polymerisation at 60°C would be faster than 50°C. Pseudo-first order kinetic plots and molecular weight vs. conversion plots are shown in Figures 3.3 – 3.5. Kinetic studies were performed with [M]_0:[Al]_0:[BnOH]_0 = 50:1:1. The results obtained from polymerisations with 50 equivalents of monomer are transferrable to polymerisations with different monomer to catalyst ratios.
As can be seen by Figures 3.2 and 3.3, kinetic plots revealed that the polymerisations were pseudo-first order with respect to monomer concentration. This is indicative of a well controlled polymerisation by a coordination-insertion mechanism. This is well established for aluminium salen catalysed ROP of cyclic esters. The rates of polymerisations for 60, 50 and 22°C are shown in Table 3.6. As expected, the rate for polymerisation at 60°C was faster ($k_{\text{app}} = 0.0104 \text{ min}^{-1}$) than polymerisation at 50°C ($k_{\text{app}} = 0.0074 \text{ min}^{-1}$). Polymerisation kinetics at 60°C was measured by reaction in an NMR tube in C$_6$D$_6$. While this allowed for facile monitoring of conversion, dispersity could not be measured at each time interval. It should be noted that the pseudo-first order plot does not pass through close to the
theoretical y-intercept value (\(\ln([M]_0/[M]_t) = 0\)). This is due to the technique, as time zero was defined as the moment the instrument reached the desired temperature. However, polymerisation commences at room temperature and will have continued while the instrument was heating. Despite this, the kinetics were only measured once the reaction reached temperature so for sake of comparing rates, the experiment can be considered valid. Polymerisation kinetics at 50°C was performed by removing aliquots of the reaction mixture at desired time intervals for analysis. This allowed for monitoring of the level of control throughout the reaction. GPC analysis of the crude reaction aliquots indicated that dispersity remains relatively unchanged throughout the reaction. The molecular weight calculated by \(^1\)H NMR spectroscopy correlates very well with the theoretical molecular weights and increases linearly with conversion at all three temperatures studied. Additionally, good correlation at low molecular weight shows that there is efficient initiation and all polymer chains begin growing at approximately the same time. Good correlation at high molecular weight shows that after polymer chains stop growing, transesterification is negligible. Higher molecular weight P2HEB was also synthesised (Table 3.6).

Table 3.6 Polymerisation of higher molecular weight P2HEB with 58 \(^a\)

<table>
<thead>
<tr>
<th>[2,3-DHB] (_0):[58] (_0)</th>
<th>Conversion (^b) (%)</th>
<th>(M_{n,th}^c)</th>
<th>(M_n^b)</th>
<th>(D^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>200:1</td>
<td>88</td>
<td>28770</td>
<td>25210</td>
<td>1.10</td>
</tr>
<tr>
<td>500:1</td>
<td>78</td>
<td>63740</td>
<td>52050</td>
<td>1.11</td>
</tr>
</tbody>
</table>

\(^a\) 2,3-DHB polymerisations in toluene at 50°C for 24h. \(^b\) Conversion and molecular weight determined by \(^1\)H NMR spectroscopy. \(^c\) \(M_{n,th} = ([2,3-DHB]_0/[BnOH]_0) \times MW_{(2,3-DHB)} \times (\%\ conv.) + MW_{(BnOH)}\). \(^d\) Determined by GPC.

As a result of the excellent results obtained for polymerisations at 60°C and 50°C even lower temperatures were investigated. First, the kinetics at 22°C was measured (Figure 3.5). As expected, a pseudo-first order relationship with respect to monomer concentration is observed; rate has again decreased. Dispersity vs. conversion is also plotted in Figure 3.4 and shows the level of control is maintained throughout the polymerisation. Good correlation of molecular weight and low dispersity at low conversion is indicative of efficient initiation. This is often difficult
at room temperature; inefficient initiation can lead to a broad molecular weight distribution.

![Figure 3.5](image_url)  
**Figure 3.5** Plot of $\ln([M]_0/[M])$ vs. time (left) and molecular weight vs. conversion (right) for polymerisation of 2,3-DHB at 22°C

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>$k_{app} \times 10^{-2} \text{ min}^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>60$^b$</td>
<td>1.04</td>
</tr>
<tr>
<td>50$^c$</td>
<td>0.74</td>
</tr>
<tr>
<td>22$^c$</td>
<td>0.57</td>
</tr>
</tbody>
</table>

$^a$ 2,3-DHB polymerisations in toluene or toluene-$d_8$ with [2,3-DHB]$_0$:[58]$_0$:BnOH$_0$ = 50/1/1. $^b$ Performed in an NMR tube. $^c$ Aliquots removed under inert atmosphere.

Polymerisations of 2,3-DHB with aluminium salen complex 58 were very successful. They represent the first synthesis of polyester containing aromatic functionality in the backbone from cyclic ester ROP.

### 3.3.3 Polymerisation of 2,3-DHB using organocatalysts

Aluminium salen catalysed polymerisation of 2,3-DHB was incredibly successful with excellent molecular weight control, low dispersities and higher molecular weights accessible. However, one potential drawback was observed with this system; polymerisations were required to be conducted at high concentrations (4 – 5 M) or very little to no conversion was recorded. In an attempt to overcome this,
alternative catalysts were tested. Aluminium salan complex 84 showed very little
difference to complex 58 and could not be conducted at lower concentrations.
Organocatalysts have recently found success in ring-opening polymerisation of
conventional ROP monomers such as lactide and ε-caprolactone.\cite{137} The
organocatalyst 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) has been reported as
incredibly active in lactide polymerisation, reaching complete conversion of 100
equivalents in under one minute.\cite{138} This is significantly more active than even the
most active aluminium salen complexes.

Initial ROP of 2,3-DHB was attempted with two organocatalysts; the basic
1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and the more acidic diphenylphosphate
(DPP) (Figure 3.5). Various conditions were tested for ROP of 2,3-DHB (Table 3.8).
Unfortunately, using these catalysts did not yield any P2HEB under any of the
conditions tested.

![Figure 3.6 Organocatalysts tested for 2,3-DHB polymerisation](image)

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Temperature</th>
<th>Time</th>
<th>Conversion (^b) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DBU</td>
<td>22</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>DPP</td>
<td>22</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>24</td>
<td>0</td>
</tr>
</tbody>
</table>

\(^a\)2,3-DHB polymerisation with \([2,3-DHB]_0[\text{cat}]_0[BnOH]_0 = 100/1/1\) in toluene.

\(^b\) Determined by \(^1\)H NMR spectroscopy.
With no polymerisation observed using either DBU or DPP, the bifunctional organocatalyst TBD was employed in 2,3-DHB ROP (Table 3.9). TBD catalysed polymerisations were successful, with polymer formation under a diverse range of conditions.

**Table 3.9** Polymerisation of 2,3-DHB using TBD

<table>
<thead>
<tr>
<th>Solvent</th>
<th>[M]₀</th>
<th>[M]₀/[Al]₀</th>
<th>Temp. (°C)</th>
<th>Time (min)</th>
<th>Conv. a (%)</th>
<th>Mₙ,th b</th>
<th>Mₙ a</th>
<th>Đ c</th>
</tr>
</thead>
<tbody>
<tr>
<td>toluene</td>
<td>2.38</td>
<td>100</td>
<td>22</td>
<td>30</td>
<td>89</td>
<td>14720</td>
<td>14660</td>
<td>1.19</td>
</tr>
<tr>
<td>toluene</td>
<td>1.30</td>
<td>100</td>
<td>22</td>
<td>60</td>
<td>80</td>
<td>13240</td>
<td>13130</td>
<td>1.14</td>
</tr>
<tr>
<td>toluene</td>
<td>0.52</td>
<td>100</td>
<td>22</td>
<td>190</td>
<td>51</td>
<td>7990</td>
<td>6370</td>
<td>1.14</td>
</tr>
<tr>
<td>toluene</td>
<td>1.30</td>
<td>200</td>
<td>22</td>
<td>240</td>
<td>78</td>
<td>24080</td>
<td>22450</td>
<td>1.15</td>
</tr>
<tr>
<td>toluene</td>
<td>1.30</td>
<td>500</td>
<td>22</td>
<td>360</td>
<td>29</td>
<td>23620</td>
<td>14390</td>
<td>1.42</td>
</tr>
<tr>
<td>toluene</td>
<td>1.30</td>
<td>100</td>
<td>50</td>
<td>60</td>
<td>46</td>
<td>7660</td>
<td>8710</td>
<td>1.11</td>
</tr>
<tr>
<td>CH₂Cl₂</td>
<td>1.30</td>
<td>100</td>
<td>22</td>
<td>120</td>
<td>60</td>
<td>9960</td>
<td>9760</td>
<td>1.14</td>
</tr>
</tbody>
</table>

 a Determined by ¹H NMR spectroscopy. b Mₙ,th = ([2,3-DHB]₀/[BnOH]₀) × % conversion × (2,3-DHB). c Determined by GPC.

Polymerisation of 100 equivalents of 2,3-DHB in toluene was rapid at room temperature and reached high conversion. Initial studies were performed at 2.38 M in 2,3-DHB, significantly lower than the 4 M 2,3-DHB concentration required for ROP with 58 or 84. Conversion reached 89% after only 30 minutes. Leaving the reaction for longer periods of time does not lead to any increase in conversion or molecular weight. Instead, dispersity increases indicating TBD catalysed ROP of 2,3-DHB is susceptible to transesterification. It should also be noted that at 2.38 M [2,3-DHB]₀, the dispersity is higher than polymerisations with 58 at temperatures ≤ 70°C. Decreasing the monomer concentration to 1.38 M still allows for high conversion (80%), albeit with doubled reaction times. Dispersity has decreased to 1.14, now closer to the control observed in the aluminium salen system. The lowest concentration tested was 0.52 M, nearly ten times more dilute than with 58. Polymerisation was possible, although only 51% monomer conversion was achieved. Increasing the initial monomer feed to 200 equivalents showed similar conversion
(78% vs. 81%) but required four times longer reaction times. Molecular weight was still in excellent agreement with the predicted values and dispersity was low. However, when increasing to 500 equivalents of monomer, conversion reached a maximum conversion of only 29% after six hours. A significant loss of control was observed as molecular weight was considerably lower than the theoretical molecular weight and dispersity had risen to 1.42. Despite poor results at 500 equivalents, TBD acts as an excellent catalyst for up to 200 equivalents of 2,3-DHB at much lower concentrations. Polymerisation also proceeded in CH$_2$Cl$_2$ in addition to toluene. Conversion reached only 60% after two hours, indicating polymer formation is less favored in CH$_2$Cl$_2$. However, the polymerisation had similar levels of control as when conducted in toluene.

Similarities between the aluminium salen and organocatalyst systems can be observed. Most notably, increasing the temperature results in a decrease in monomer conversion. This is more dramatic with TBD as conversion decreases from 80% at room temperature to 46% at 50°C. Interestingly, control of the polymerisation is not lost at 50°C ($D = 1.11$ at 50°C, 1.14 at 22°C).

For further comparison to aluminium salen catalysed 2,3-DHB polymerisation, the kinetics of organocatalysed ROP were studied (Figure 3.7, Table 3.10). The resulting kinetic profiles were not conclusive about the reaction order and the reported pseudo first order kinetics were calculated from the linear segments from each plot for comparison to aluminium catalysed ROP. The kinetic plots in Figure 3.7 show the conversion vs. time to best show the more rapid nature of TBD catalysed ROP. Polymerisations were carried out at the three concentrations studied previously for organocatalysed polymerisations (2.38, 1.38 and 0.52 M). C$_6$D$_6$ was substituted for toluene and the reactions were monitored at 22°C by $^1$H NMR spectroscopy. This was difficult for polymerisation at 2.38 M as conversion is rapid, reaching 73% after nine minutes (time between sample preparation and first NMR scan). This rate was calculated to be $4.25 \times 10^{-2} \text{min}^{-1}$, over two times faster than 2,3-DHB polymerisation using 58 at 60°C while at nearly half the concentration, demonstrating one clear advantage to using TBD in place of aluminium salen catalysts. The rates for the lowered concentrations of 1.38 and 0.52 M were calculated to be $3.43 \times 10^{-2} \text{min}^{-1}$ and $0.30 \times 10^{-2} \text{min}^{-1}$, respectively.
Table 3.10 Rate of 2,3-DHB polymerisation with TBD at various concentrations

<table>
<thead>
<tr>
<th>Concentration (M)</th>
<th>$k_{obs}$ ($\times 10^{-2}$ min$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.38</td>
<td>4.25</td>
</tr>
<tr>
<td>1.38</td>
<td>2.43</td>
</tr>
<tr>
<td>0.52</td>
<td>0.30</td>
</tr>
</tbody>
</table>

$^a$ 2,3-DHB polymerisations in CD$_6$ with [2,3-DHB]$_0$:[TBD]$_0$:[BnOH]$_0$ = 100/1/1. Conversion determined by $^1$H NMR spectroscopy

With the success of both aluminium salen and organocatalysed ROP of 2,3-DHB, a brief study into the properties of P2HEB was performed.

Figure 3.7 Plot of conversion vs. time for TBD catalysed ROP of 2,3-DHB at 22°C in Cd$_6$; 2.38 M (top left), 1.38 M (top right) and 0.52 M (bottom left) and MeAl[salen] at 4.7 M (bottom right)
3.3.4 Thermal properties of P2HEB

The thermal properties of a polymer are important characteristics. Poor thermal properties often limit the applications a polymer can be used for. Differential scanning calorimetry was first employed to investigate thermal properties of P2HEB.

Initially, a heat/cool cycle of heat to 250°C, cool to -50°C, heat to 250°C and cool to -50°C was tested. This yielded an interesting DSC thermogram. In the initial heating cycle, a melting temperature at ~78°C is the only transition observed. In the second heating scan, a glass transition at ~30°C is the only transition observed. This was confusing as not only did the melting temperature transition disappear but the glass transition was not present in the first heating cycle. However, this was not the case when the heating cycle temperature was changed from 250°C as a maximum temperature to 150°C. This indicated that an irreversible reaction was perhaps taking place between 150 and 250°C, most likely thermal decomposition of the polymer. To test this, thermogravimetric analysis (TGA) was performed on P2HEB. The sample was heated from room temperature to 500°C at a rate of 10°Cmin\(^{-1}\). The onset of decomposition \((T_{d,onset})\) was recorded as 219°C with 95% sample decomposition at 262°C. This temperature was lower than expected as aliphatic polyesters (such as PLA and P3HB) are significantly higher.\[^{139}\] However, this explained the confusing DSC thermograms with a temperature range of -50 – 250°C. DSC experiments were performed again with the maximum temperature being lower (150°C) than \(T_{d,onset}\) to give accurate thermal transitions (Table 3.11).

<table>
<thead>
<tr>
<th>(T_g) (°C)</th>
<th>(T_c) (°C)</th>
<th>(T_m) (°C)</th>
<th>(T_{d,onset}) (°C)</th>
<th>(T_{d,95}%) (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>-</td>
<td>78</td>
<td>219</td>
<td>262</td>
</tr>
</tbody>
</table>

\(^{a}\) \(T_m\) measured on second heating scan of DSC. \(T_{d,onset}\) and \(T_{d,95}\%\) measured by TGA.
3.4 Monomer-polymer equilibrium and P2HEB depolymerisation

One aspect of ring-opening polymerisation that is often ignored is that each step in the (ideal) catalytic cycle is reversible. This is particularly easy to ignore with aluminium salen and salan catalyst systems as complete conversion is easily obtained for many monomers such as lactide, β-BL and ε-CL. Additionally, when complete conversion is not reached, often dispersities are broader with transesterification or catalyst degradation being attributed as the cause. However, 2,3-DHB polymerisations were quite well controlled, suggesting catalyst degradation and transesterification reactions were minimised. 2,3-DHB polymerisations would reach a maximum conversion and could be left for an additional 24 hours without sacrifice of control or molecular weight. Furthermore, after leaving for the additional 24 hours, more 2,3-DHB monomer could be introduced and be converted to polymer. This suggested that the polymerisation was in equilibrium between monomer and polymer.

3.4.1 Monomer-polymer equilibrium

This equilibrium between monomer and polymer can be controlled through one of two ways; polymerisation temperature or polymerisation concentration. To explore this, a polymerisation was conducted at room temperature for six hours with 58. 1H NMR spectroscopic analysis revealed the reaction proceeded to 88% conversion to P2HEB. The sample was then heated to 90°C for 10 hours. Analysis after 10 hours indicated conversion had decreased to 70% P2HEB. This demonstrated that the equilibrium was reversible and is tuned by polymerisation temperature. This also explains earlier results that showed conversion being lower (ca. 75%) at 70°C than at 60°C (ca. 85%).

To measure the equilibrium effects of concentration, an approach described by Waymouth for organocatalysed ROP of morpholinones was used. Polymerisation of 50 equivalents of 2,3-DHB was performed at three different concentrations and the conversion changed with concentration (Table 3.12). Conversion was then used to calculate [2,3-DHB] in the reaction which should be equal to the equilibrium monomer concentration, [2,3-DHB]eq.
From these polymerisations at varying concentrations, [2,3-DHB]$_{eq}$ can be estimated to be 0.36 M. This indicates that any monomer added to a polymerisation reaction in excess of 0.36 M should be converted. However, polymerisations conducted at 1.0 M showed no conversion to polymer. This is attributed to changing the catalyst concentration. The catalyst concentration can have a large effect on the rate and activity. The rate of polymerisation when [2,3-DHB]$_0$ = 1.0 M was likely too low, resulting in no significant polymerisation being observed. This procedure was repeated using TBD as a catalyst at 22°C. This resulted in a monomer equilibrium concentration of 0.26 M. This demonstrated further that using TBD as a catalyst should allow for higher conversion to P2HEB at lower concentrations.

More interestingly, the monomer equilibrium concentration can also be calculated from depolymerisation experiments for some systems. This is intriguing as if successful, the depolymerisation should selectively yield monomer as the product of depolymerisation. This depolymerisation phenomenon is not typical but has been shown to be possible for some ROP systems.$^{[141]}$ This was tried using purified P2HEB and 58 in toluene at 60°C (Table 3.13). Depolymerisations were performed with more accurate measurements of solvent to ensure an accurate [2,3-DHB]$_{eq}$ was calculated. This method does not work with every polymer that is in equilibrium. For example, δ-VL polymerisations in in Chapter 2 appeared to be in equilibrium as quantitative conversion could not be reached. However, when isolated PVL was subjected to depolymerisation conditions, no reaction occurred.

Depolymerisation experiments resulted in a monomer equilibrium concentration consistent with polymerisation experiments with [2,3-DHB]$_{eq}$ =

---

**Table 3.12** Determination of [2,3-DHB]$_{eq}$ by ROP with 58 at 60°C in toluene $^a$

<table>
<thead>
<tr>
<th>[2,3-DHB]$_0$ (M)</th>
<th>Composition $^b$ (%)</th>
<th>[2,3-DHB]$_0$ $^c$ (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.6</td>
<td>10 90</td>
<td>0.36</td>
</tr>
<tr>
<td>3.9</td>
<td>9   91</td>
<td>0.35</td>
</tr>
<tr>
<td>4.5</td>
<td>8   92</td>
<td>0.36</td>
</tr>
</tbody>
</table>

$^a$ Polymerisation of 2,3-DHB in toluene at 60°C for six hours with [2,3-DHB]$_0$[58]$_0$[BnOH]$_0$ = 50:1:1. $^b$ Determined by $^1$H NMR spectroscopy. $^c$ [2,3-DHB]$_{eq}$ = (100 - % conv.)/100 × [2,3-DHB]$_0$. 
0.36 M. When depolymerisation experiments were repeated using TBD, little to no depolymerisation was achieved, even at concentrations far more dilute than 0.26 M. This suggests that while the TBD catalysed polymerisation will reach a point where polymer formation is no longer favored, only 2,3-DHB with ROP 58 is reversible.

<table>
<thead>
<tr>
<th>[2,3-DHB]₀ (M)</th>
<th>Composition (%)</th>
<th>[2,3-DHB]₀ (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.88</td>
<td>19 81</td>
<td>0.358</td>
</tr>
<tr>
<td>1.37</td>
<td>26 74</td>
<td>0.355</td>
</tr>
<tr>
<td>0.99</td>
<td>34 66</td>
<td>0.355</td>
</tr>
</tbody>
</table>


### 3.4.2 Depolymerisation of P2HEB

As the equilibrium was shown to be highly dependent on concentration as well as it being possible to depolymerise P2HEB, higher levels of depolymerisation were of interest. A sample of P2HEB was diluted to 0.18 M in toluene, half of the monomer equilibrium concentration. The reaction was monitored by ¹H NMR spectroscopic analysis of crude reaction samples (Figure 3.8). Indeed, the reaction proceeds to high conversion back to 2,3-DHB monomer (≥ 90%) after 12 hours.

While the resonances in ¹H NMR spectrum suggested that the depolymerisation product was 2,3-DHB, evidence to support this further was warranted. As the ratio of polymer to monomer was controlled by concentration, a polymerisation followed by depolymerisation followed by a second polymerisation was attempted (Table 3.14).
The reversibility of the polymerisation/depolymerisation showed that monomer was forming and not a separate degradation product. This was further demonstrated by GPC (Figure 3.9) and the consistency in molecular weight and dispersity between the two polymerisations. Conversion (84% vs. 82%), molecular

---

**Table 3.14** Reversible polymerisation of 2,3-DHB

| Entry | Concentration<sup>b</sup> (M) | 2,3-DHB<sup>c</sup> (%) | P2HEB<sup>c</sup> (%) | $M_{n,th}$<sup>d</sup> | $M_n$<sup>e</sup> | $D$
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.1</td>
<td>18</td>
<td>82</td>
<td>13600</td>
<td>12200</td>
<td>1.08</td>
</tr>
<tr>
<td>2</td>
<td>0.2</td>
<td>94</td>
<td>6</td>
<td>1100</td>
<td>1090</td>
<td>1.09</td>
</tr>
<tr>
<td>3</td>
<td>4.1</td>
<td>16</td>
<td>84</td>
<td>13850</td>
<td>13720</td>
<td>1.07</td>
</tr>
</tbody>
</table>

<sup>a</sup>One-pot polymerisation-depolymerisation of 2,3-DHB/P2HEB by varying concentration with [2,3-DHB]<sub>0</sub>:[Al]<sub>0</sub>:[BnOH]<sub>0</sub> = 100:1:1. <sup>b</sup>Concentration = [2,3-DHB]<sub>0</sub>/volume toluene. <sup>c</sup>Determined by GPC. <sup>d</sup>$M_{n,th}$ = ([2,3-DHB]<sub>0</sub>/BnOH)<sub>0</sub> × % conversion × MW<sub>2,3-DHB</sub>. <sup>e</sup>Determined by <sup>1</sup>H NMR spectroscopy.
weight (13720 Da vs. 12200 Da) and dispersity (1.07 vs. 1.08) are all relatively unchanged between the two. Excellent control in repolymerisation is also indicative of a uniform degree of depolymerisation for all chains and minimal catalyst degradation.

As can be seen from Figure 3.9, the GPC traces are nearly identical. It was attempted to continue this cycling further. However, after addition of toluene to the repolymerisation reaction and heating to 60°C overnight, only a small amount of polymer had converted to 2,3-DHB (<20 %). This was thought to be due to degradation of the catalyst. Fresh catalyst was added to the reaction and stirred at 60°C for 12 hours (0.2 M). 1H NMR spectroscopy indicated high conversion to 2,3-DHB (ca. 85%). Repolymerisation of this was possible, although broadening of the dispersity was observed (Đ = 1.27).

This phenomenon is rarely observed and depolymerisation experiments have only been used in the past to calculate monomer equilibrium concentration. However, this can be used as a degradation tool to selectively generate monomer. In most common aliphatic polyesters (i.e. poly(lactic acid)), the polymer is broken down into the corresponding hydroxyacid via acid catalysed hydrolysis. The hydroxyl acid is then oligimerised through condensation. A catalyst is then added to promote transesterification and produce the desired monomer. This is not ideal as
several steps are required with a significant energy cost. With the 2,3-DHB/P2HEB system, the monomer is recovered in one step under mild conditions (Scheme 3.7). Additionally, the same catalyst is capable of synthesising the polymer as well as recovering the monomer.

**Scheme 3.7** Idealised life cycles of PLA (left) and P2HEB (right)

With these successful depolymerisation results, copolymers with P2HEB were considered.

### 3.5 Copolymerisation with 2,3-DHB

As discussed in Chapters 1 and 2, copolymers are incredibly important to modifying polymer properties. Random and gradient copolymers tend to behave similarly to blending of the two homopolymers while block copolymers can lead to more interesting properties. Synthesis of both random/gradient copolymers and block copolymers were attempted.

#### 3.5.1 Random or gradient copolymers

Random/gradient copolymer synthesis was initially targeted. For the remainder of this chapter, random/gradient copolymers will be referred to as gradient copolymers as the difference in monomer reactivity in the cases studied is most likely to lead to gradient copolymer formation as opposed to a true random
copolymers was first attempted using \( \ell \)-lactide as a comonomer with 2,3-DHB (Scheme 3.8). Synthesis was attempted using aluminium salen complex, 58, and organocatalyst, TBD.

### Scheme 3.8 Synthetic approach to P(LA-co-2HEB)

Incompatibility of homopolymerisation conditions of the two comonomers made copolymerisation difficult. That is, polymerisation of 2,3-DHB requires a high concentration in toluene and low temperatures. Under these conditions, \( \ell \)-lactide is largely insoluble. Despite this, polymerisations were performed at 60˚C, hypothesising that a small amount of soluble \( \ell \)-lactide could participate in copolymerisation (allowing for more \( \ell \)-lactide to dissolve), eventually leading to high conversions. Unfortunately, this did not appear to be the case. No 2,3-DHB polymerisation occurs, indicating that the presence of \( \ell \)-lactide hinders the polymerisation of 2,3-DHB. Performing the polymerisation in other solvents (THF, \( \text{CH}_2\text{Cl}_2 \)) yielded similar results. Increasing the temperature while keeping the concentration high resulted in more lactide dissolution but still no polymerisation occurred. Initial monomer concentration was decreased and polymerisations were performed at 60˚C and 85˚C. Again, no 2,3-DHB conversion was achieved. Only low conversions of \( \ell \)-lactide were observed (< 10%). Switching the catalyst to the aluminium salan catalyst 84, gave similar results, with little to no polymerisation observed.

With no significant conversions achieved using 58 or 84, TBD was investigated. This was expected to be more successful as TBD is capable of polymerising both 2,3-DHB and \( \ell \)-lactide at room temperature and under similar concentrations. Polymerisations were performed in \( \text{CH}_2\text{Cl}_2 \) to ensure both monomers were dissolved. Polymerisation of 50 equivalents of \( \ell \)-lactide and 50 equivalents of 2,3-DHB was performed. Polymerisation was initially run for two minutes as \( \ell \)-
lactide polymerisation with TBD typically results in transesterification quickly once complete conversion is achieved. $^1$H NMR spectroscopy revealed that essentially quantitative conversion of L-lactide was achieved. Unfortunately, no conversion of 2,3-DHB had occurred. Allowing the polymerisation to proceed for longer reaction times resulted in transesterification of the P(L-LA) with no conversion of 2,3-DHB. Thus, gradient copolymerisations with L-lactide were not investigated further. Additionally, as TBD fully polymerised L-lactide with no conversion of 2,3-DHB, block copolymers would likely not be possible using TBD if the P(L-LA) block is grown first.

Copolymerisation of 2,3-DHB and L-lactide were unsuccessful, attributed largely to compatibility issues for each homopolymerisation. Copolymerisation with β-BL may not have these same issues: β-BL is a liquid at room temperature and therefore solubility in toluene should be straightforward. Additionally, neat β-BL polymerisations have been successful using aluminium salen complexes at 70°C and using aluminium salan complexes at ambient temperature.\cite{88} Gradient copolymerisation of 50 equivalents of β-BL and 50 equivalents of 2,3-DHB was tested using 58 at 22, 60 and 70°C for 16 hours (Scheme 3.9).

![Scheme 3.9 Synthesis approach to P(3HB-co-2HEB)](image)

As can be seen from data in Table 3.12, copolymerisation of β-BL and 2,3-DHB was successful. The presence of β-BL does hinder 2,3-DHB polymerisation at room temperature, consistent with what was observed with L-lactide, but does not completely stop it. Copolymerisation at 60°C resulted in 77% conversion of both β-BL and 2,3-DHB. Conversion to P2HEB is slightly lower than conversion under a similar concentration for homopolymerisations, likely due to effectively lowering the overall 2,3-DHB concentration with the addition of β-BL into the reaction. Increasing the temperature yielded conversions quite similar, with only a 2%
increase in 2,3-DHB conversion. This does not suggest that lower 2,3-DHB conversion at 60°C was due to β-BL addition as it would be expected that 2,3-DHB conversion should be lower at 70°C. Molecular weights were higher than predicted, indicating there is less control than for homopolymers. The dispersities also showed a loss of control and were relatively broad; copolymerisations often exhibit less control than homopolymerisations.

Table 3.12 Copolymerisation of β-BL and 2,3-DHB with 58

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Conversion β-BL</th>
<th>Conversion 2,3-DHB</th>
<th>M_n,th</th>
<th>M_n</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
<td>&lt; 5</td>
<td>14</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>60</td>
<td>77</td>
<td>77</td>
<td>9360</td>
<td>12070</td>
<td>1.39</td>
</tr>
<tr>
<td>70</td>
<td>77</td>
<td>79</td>
<td>9520</td>
<td>12760</td>
<td>1.59</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>a Copolymerisation of β-BL and 2,3-DHB in toluene with [β-BL]:[2,3-DHB]:[58]:[BnOH] = 50:50:1:1. b Determined by 1H NMR spectroscopy. c M_n,th = (% conv.β-BL × 0.5 × 76.09) + (% conv.2,3-DHB × 0.5 × 164.16) + 108.14. d Determined by GPC.</td>
</tr>
</tbody>
</table>

P(3HB-co-2HEB) copolymers were analysed by 1H NMR spectroscopy to determine conversion and relative ratio of P3HB and P2HEB (Figure 3.10). A new downfield signal (ca 5.45 ppm) from the typical P3HB methine signal is proposed to correspond to a P3HB unit adjacent to a P2HEB unit. Other signals in the spectrum were as expected, consistent with signals from homopolymers. Additionally, this downfield signal may be used to estimate the percentage of P3HB units that are adjacent to a P2HEB unit.

Despite the moderately broad dispersities, this was an exciting result as using a monomer where ROP can be facilitated under similar conditions allows for synthesis of copolymers. This could allow for introduction of small amounts of a specialty polymer (P2HEB) into more common polyesters, such as P3HB to alter the properties. As a result of these copolymerisation experiments, other copolymer macrostructures were studied.
Block copolymers are also important macrostructures and often exhibit significantly different properties than their corresponding gradient copolymers. Furthermore, we expected to be able to synthesise copolymers of 2,3-DHB and L-lactide. Sequential addition of monomers was the initial strategy as it simplifies the process by minimising workup and eliminating the need for fresh catalyst addition for each block growth. AB diblock copolymers were first studied (Scheme 3.10).

**Figure 3.10** $^1$H NMR spectra of P(3HB-co-2HEB) in CDCl$_3$

**3.5.2 Block copolymers**

Block copolymers are also important macrostructures and often exhibit significantly different properties than their corresponding gradient copolymers. Furthermore, we expected to be able to synthesise copolymers of 2,3-DHB and L-lactide. Sequential addition of monomers was the initial strategy as it simplifies the process by minimising workup and eliminating the need for fresh catalyst addition for each block growth. AB diblock copolymers were first studied (Scheme 3.10).

**Scheme 3.10** Sequential addition ROP to form P(L-LA-b-2HEB)
Initially, the P(L-LA) block was synthesised first, followed by addition of 2,3-DHB. This did not yield any polymer for reasons similar to gradient copolymers: the concentration of 2,3-DHB was likely too low to allow for significant conversion. To overcome this, P2HEB was synthesised first under optimised conditions. L-Lactide was then added with toluene so that lactide polymerisation was now favored. This was successful in generating the desired polymers (Table 3.16).

Table 3.16 Polymerisation data for P(L-LA<sub>n</sub>-b-2HEB<sub>m</sub>)<sup>a</sup>

<table>
<thead>
<tr>
<th>Target</th>
<th>Experimental b</th>
<th>M&lt;sub&gt;n,th&lt;/sub&gt;&lt;sup&gt;c&lt;/sup&gt;</th>
<th>M&lt;sub&gt;n&lt;/sub&gt;&lt;sup&gt;b&lt;/sup&gt;</th>
<th>D&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>m</td>
<td>n</td>
<td>m</td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>20</td>
<td>100</td>
<td>18</td>
<td>10030</td>
</tr>
<tr>
<td>100</td>
<td>100</td>
<td>100</td>
<td>93</td>
<td>20830</td>
</tr>
<tr>
<td>20</td>
<td>100</td>
<td>20</td>
<td>100</td>
<td>15390</td>
</tr>
</tbody>
</table>

<sup>a</sup> Block copolymerisation of L-lactide and 2,3-DHB by sequential addition.<br>
<sup>b</sup> Determined by 1H NMR spectroscopy.<br>
<sup>c</sup> M<sub>n,th</sub> = (n × % conv.<sub>L</sub>L × 144.13) + (m × % conv.<sub>2,3</sub>DHB × 164.16) + 108.14.<br>
<sup>d</sup> Determined by GPC.

Synthesis of L-lactide/2,3-DHB copolymers by sequential addition was far more successful than gradient copolymers. Copolymerisation by this method allowed for the synthesis of very well controlled polymers, with dispersities ≤ 1.15. Molecular weights were not completely predictable, with both P(L-LA<sub>100</sub>-b-2HEB<sub>93</sub>) and P(L-LA<sub>20</sub>-b-2HEB<sub>100</sub>) being considerably lower than predicted. This is likely due to how M<sub>n,th</sub> values were calculated in this case. M<sub>n,th</sub> were calculated from <i>n</i> and <i>m</i> experimental values of worked up polymer. As all polymerisations were conducted until complete L-lactide conversion was observed by 1H NMR spectroscopy, <i>n</i> was assumed to be equal to the target <i>n</i> value. Calculation of <i>m</i> was then done by relative integration of resonances. However, this would not account for a decrease in signal due to low molecular weight polymers lost during workup. As a result, theoretical molecular weights may be higher than they should be. A typical 1H NMR spectrum of a P(L-LA)/P2HEB block copolymer is shown in Figure 3.11.
The same approach was taken in growing ABA triblock copolymers. This was not likely to be a successful route as polymerisation of a second P2HEB block was unlikely to form under the dilute conditions. No ABA triblock copolymer was isolated by this method as concentration after the second block formation caused polymer to precipitate. The difficulty when switching from L-lactide polymerisation to 2,3-DHB can be avoided by polymerisation of the middle P2HEB block from a bifunctional initiator (Scheme 3.11). 1,3-Propanediol was chosen as an initiator and resulted in a P2HEB polymer chain growing in both directions. When switching to a favorable L-lactide polymerisation, A blocks of P(L-LA) are grown on both ends, yielding an ABA triblock copolymer. While not a true ABA copolymer due to the propanediol group in the middle, properties should be nearly identical to true ABA triblock copolymer.

Figure 3.11 $^1$H NMR spectrum of P(L-LA$_{100}$-b-2HEB$_{40}$-b-L-LA$_{100}$) in CDCl$_3$, * = residual acetone
This procedure was quite successful, allowing for a range of copolymers with varying monomer ratios to be synthesised (Table 3.14). Similar ratios were chosen to those for P(L-LA<sub>n</sub>-b-2HEB<sub>m</sub>).

<table>
<thead>
<tr>
<th>Target</th>
<th>Experimental</th>
<th>M&lt;sub&gt;n,th&lt;/sub&gt;</th>
<th>M&lt;sub&gt;n&lt;/sub&gt;</th>
<th>Đ</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>m</td>
<td>n</td>
<td>m</td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>20</td>
<td>89</td>
<td>17</td>
<td>15690</td>
</tr>
<tr>
<td>100</td>
<td>100</td>
<td>100</td>
<td>85</td>
<td>28440</td>
</tr>
<tr>
<td>20</td>
<td>100</td>
<td>20</td>
<td>86</td>
<td>16750</td>
</tr>
</tbody>
</table>

*a* Block copolymerisation of L-lactide and 2,3-DHB by sequential addition. *b* Determined by <sup>1</sup>H NMR spectroscopy. *c* M<sub>n,th</sub> = (n × % conv.<sub>L</sub>-LA × 144.13) + (m × % conv.<sub>2,3-DHB</sub> × 164.16) + 108.14. *d* Determined by GPC.

Synthesis of triblock copolymers showed similar levels of control to AB diblock copolymers, with Đ = 1.08 – 1.16. Molecular weights were slightly closer to the theoretical values, albeit still significantly lower than expected.

Analysis by <sup>1</sup>H NMR showed some unexpected results. Enantiopure L-lactide was used and a distinct quartet should be observed for the P(L-LA) methine proton for the *mmm* tetrad. However, overlapping quartets at slightly different chemical shifts is observed (Figure 3.12). The methine resembled that of atactic PLA. As aluminium salen complexes are known to not undergo racemisation in lactide polymerisation, this was attributed to scrambling of P2HEB and P(L-LA). This indicated that copolymers may be more similar to a random or gradient copolymer.
and not a block copolymer. This is less prevalent in the cases with high levels of P(L-LA) and low levels of P2HEB. This scrambling was detected in both AB and ABA block copolymers.

![Graph showing chemical shifts](image)

**Figure 3.12** P(L-LA) methine region for P(L-LAₙ₋₁₋₃HEBₚ₋₁₋L-LAₙ) where n = 100, m = 20 (top left); n = 100, m = 200 (top right); and n = 20, m = 200 (bottom)

It was hypothesised that one possible source for the apparent scrambling of P2HEB/P(L-LA) could be due to polymerisation of unreacted 2,3-DHB in the reaction. Unreacted 2,3-DHB was left in the reaction, as conversions would not surpass 85%. While it is possible that more 2,3-DHB was being polymerised once L-lactide was added, $^1$H NMR of the crude sample after 2,3-DHB polymerisation and after ABA triblock synthesis suggested that conversion of 2,3-DHB were identical in all cases. In an attempt to overcome this, middle P2HEB blocks were synthesised and isolated to be used as a macroinitiator for ABA triblock copolymer synthesis. Unfortunately, little to no difference was observed for all copolymer synthesis. Furthermore, despite removing unreacted 2,3-DHB before block copolymerisation, $^1$H NMR spectroscopic analysis of crude ABA samples indicated the presence of 2,3-DHB. This suggested that a small amount of P2HEB was being converted back to 2,3-DHB.
Block copolymers from β-BL and 2,3-DHB could also be synthesised. Interestingly, P3HB could be synthesised under conditions favorable for 2,3-polymerisation. As a result, P3HB was synthesised first, followed by addition of 2,3-DHB. This appears to have minimised scrambling as $^1$H NMR spectroscopic analysis of the PHB methine region shows no significant second resonance at ~5.45 ppm corresponding to a P3HB unit adjacent to a P2HEB unit (Figure 3.13).

![Figure 3.13 P(3HB) methine region for P(3HB-b-2HEB) (left) and P(3HB-co-2HEB) (right), * = residual CH$_2$Cl$_2$](image)

**3.5.3 Thermal properties of aromatic/aliphatic copolymers**

The thermal properties of copolymers were studied to give insight to how addition of a comonomer changes properties of P2HEB. As discussed in Chapter 3.3.4, P2HEB had a relatively low decomposition temperature. Thermal decomposition of P2HEB had reached 95% at 263°C. It was hypothesised that copolymers with P(L-LA) and P3HB would improve thermal stability. Thermal decomposition data of P2HEB and selected copolymers are shown in Table 3.18.
As shown by the data in Table 3.15, copolymerisation did improve thermal stability of P2HEB. The onset of decomposition has risen by > 30°C in all cases, while the 95% decomposition temperature has increased by nearly 50°C. Copolymers with a higher ratio of P(LA);P2HEB were stable at even higher temperatures. There was no significant difference between AB and ABA copolymers with similar ratios of polymers. P(3HB\textsubscript{50}-b-2HEB\textsubscript{50}) had the lowest onset of decomposition of all copolymers tested but the highest endpoint of decomposition. Thermograms shown in Figure 3.14 show uniform degradation, indicating that the two different polymer types are degrading in the same temperature range and not at two independent temperature ranges.

**Table 3.18 Thermal decomposition of P2HEB and copolymers**

<table>
<thead>
<tr>
<th>Polymer</th>
<th>$T_d$,onset (°C)</th>
<th>$T_d$,endpoint (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P2HEB\textsubscript{82}</td>
<td>219.3</td>
<td>262.8</td>
</tr>
<tr>
<td>P(L-LA\textsubscript{100}-b-2HEB\textsubscript{170}-b-L-LA\textsubscript{100})</td>
<td>251.2</td>
<td>310.7</td>
</tr>
<tr>
<td>P(L-LA\textsubscript{100}-b-2HEB\textsubscript{34}-b-L-LA\textsubscript{100})</td>
<td>278.7</td>
<td>319.3</td>
</tr>
<tr>
<td>P(L-LA\textsubscript{100}-b-2HEB\textsubscript{17})</td>
<td>273.3</td>
<td>321.2</td>
</tr>
<tr>
<td>P(L-LA\textsubscript{16}-b-2HEB\textsubscript{84})</td>
<td>263.1</td>
<td>307.8</td>
</tr>
<tr>
<td>P(3HB\textsubscript{50}-b-2HEB\textsubscript{50})</td>
<td>244.1</td>
<td>338.0</td>
</tr>
</tbody>
</table>

Figure 3.14 TGA traces for P2HEB and copolymers with L-lactide
Copolymerisations and their thermal properties were encouraging as it demonstrated that it was possible to not only form sought after copolymers, but tune their properties.

### 3.5.4 Depolymerisation of P2HEB copolymers

Depolymerisation of copolymers is of interest as it could allow for a tunable and selective degradation of P2HEB, whilst leaving the other polymer unreacted. Of the copolymers that were prepared, those with P(L-LA) were not expected to show a high degree of depolymerisation. This is due to the scrambling that was observed coupled with the unlikelihood that the catalyst would depolymerise a lactic acid unit. As a result, once the catalyst reaches a lactic acid unit in a chain, that chain is unlikely to undergo any further depolymerisation. Four P(L-LA)/P2HEB copolymers were tested and results are shown in Table 3.15.

As expected, depolymerisation of P(L-LA)/P2HEB copolymers was largely unsuccessful. The only copolymer with a reasonably degree of depolymerisation is one that has only a small amount of P(L-LA), P(2HEB\textsubscript{100}-b-L-LA\textsubscript{20}).

**Table 3.19 Depolymerisation of P(L-LA)/P2HEB copolymers with 58 in toluene at 60°C**

<table>
<thead>
<tr>
<th>Copolymer</th>
<th>2,3-DHB (%)</th>
<th>P2HEB (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P(2HEB\textsubscript{20}-b-L-LA\textsubscript{100})</td>
<td>6</td>
<td>94</td>
</tr>
<tr>
<td>P(2HEB\textsubscript{100}-b-L-LA\textsubscript{20})</td>
<td>67</td>
<td>33</td>
</tr>
<tr>
<td>P(L-LA\textsubscript{100}-b-2HEB\textsubscript{40}-b-L-LA\textsubscript{100})</td>
<td>&lt;1</td>
<td>&gt;99</td>
</tr>
<tr>
<td>P(L-LA\textsubscript{100}-b-2HEB\textsubscript{200}-b-L-LA\textsubscript{100})</td>
<td>4</td>
<td>96</td>
</tr>
</tbody>
</table>

\*Depolymerisation of P(L-LA)/P2HEB in toluene with 58 (3 wt. %) at 60°C for 72h. \*\* Determined by \*\*\*H NMR spectroscopy.

Depolymerisation of P(3HB-b-2HEB) was expected to show a significant amount of ring-closing transesterification due to the minimal scrambling that occurred. P(3HB-b-2HEB) was synthesised and once maximum conversion of 2,3-DHB was reached, the solution was diluted so that [2,3-DHB]\textsubscript{app} = 0.17 M. After
heating the dilute solution for 12 hours, $^1$H NMR spectroscopic analysis showed that a high degree of polymerisation was achieved (> 98%) (Figure 3.15). The level of control in the initial P3HB block synthesis is retained upon depolymerisation. GPC analysis showed that the remaining P3HB after depolymerisation was of similar molecular weight and dispersity (Figure 3.16). This, coupled with the high level of depolymerisation, is consistent with the theory that scrambling is not occurring with P(3HB-$b$-2HEB). If scrambling had occurred, it would be expected that once the catalyst encountered a P3HB unit, the chain would no longer undergo depolymerisation. This would yield two differences to what is seen; more P2HEB would be present and the GPC traces would be different to the starting P3HB block.

![Figure 3.15](image)

**Figure 3.15** $^1$H NMR spectra of crude samples for synthesis of P3HB (bottom), P(3HB-$b$-2HEB) (middle) and depolymerisation of copolymer (top) in CDCl$_3$, * = residual solvent
With excellent results for homopolymerisation, copolymerisation and depolymerisation with 2,3-DHB, other aromatic containing cyclic esters were targeted for ring-opening polymerisation.

3.6 Attempted polymerisation of other aromatic monomers

With the great success in 2,3-DHB polymerisation, the first example of polyester from cyclic ester ROP with a phenyl ring as part of the backbone, other aromatic monomers were investigated.

3.6.1 Polymerisation of 3,4-dihydro-2H-1,5-benzodioxepin-2-one

The aromatic monomer most similar to 2,3-DHB is its structural isomer 3,4-DHB. The key difference between 2,3-DHB and 3,4-DHB is the orientation of the ester linkage. 3,4-DHB has a phenyl ester whereas 2,3-DHB has an alkyl ester. It was hypothesised that this could lead to significantly different reactivity. Additionally, the resulting polymer would likely be less rigid than P2HEB (Scheme 3.12). Polymerisations were screened using catalysts that polymerised 2,3-DHB (Sn(oct)$_2$, 58, 84 and TBD) under a range of solvents and temperatures (Table 3.20).

Unfortunately, under all of the conditions tested no polymerisation was observed. Furthermore, solubility was a large problem in these reactions. In toluene, 3,4-DHB was insoluble at temperatures up to 150°C. It was hoped that a small
amount of monomer would dissolve and undergo polymerisation. This did not appear to be the case. Increasing the temperature to 150°C allowed for solubility of 3,4-DHB but no polymerisation occurred in toluene or in bulk. Changing the catalyst to 84, Sn(oct)₂ or TBD all resulted in no conversion to polymer.

Table 3.20 Conditions tested for ROP of 3,4-DHB

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Solvent</th>
<th>Temperature (°C)</th>
<th>Time (h)</th>
<th>Conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>58</td>
<td>toluene</td>
<td>60</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>120</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>150</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>neat</td>
<td>120</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>neat</td>
<td>150</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>84</td>
<td>toluene</td>
<td>60</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>150</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Sn(oct)₂</td>
<td>toluene</td>
<td>120</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>150</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>TBD</td>
<td>toluene</td>
<td>60</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>CH₂Cl₂</td>
<td>60</td>
<td>24</td>
<td>0</td>
</tr>
</tbody>
</table>

a Polymerisation of 3,4-DHB with [2,3-DHB]₀:cat:Sn:BNOH = 100:1:1 or [2,3-DHB]₀:Sn:BNOH = 100:0.5:1. b Determined by ¹H NMR spectroscopy.
No conversion could be a result of many different reasons. One possibility is the nature of the growing polymer chain. In polymerisation of 2,3-DHB (and aliphatic monomers), the growing polymer chain is a metal alkoxide. However, with 3,4-DHB the growing polymer chain is a metal phenoxide. These two different types of metal species can have significantly different reactivity.

The most likely cause for no conversion is the combination of high temperature and dilution needed for 3,4-DHB to be soluble. Temperatures are significantly higher and concentration is significantly lower than 2,3-DHB polymerisation. Attempting 2,3-DHB polymerisation under these conditions also results in no conversion.

As 3,4-DHB was unsuccessful, other monomers were investigated where the orientation of the ester is similar to 2,3-DHB.

**3.6.2 Polymerisation of substituted 2,3-DHBs**

Of the aromatic containing monomers with the ester linkage similar to 2,3-DHB, substituted 2,3-DHB monomers are most closely related. The reported highly enantioselective synthesis means stereoregular polymers are also possible.

Attempted polymerisation of 3-Me-2,3-DHB and 3-Ph-2,3-DHB was performed under optimised conditions for 2,3-DHB conditions. Unfortunately, no polymerisation was achieved. Comparing the reactivity of 2,3-DHB to the reactivity of ε-CL, it can be said that ε-CL is significantly more reactive. Adding a methyl group in the 6-position of ε-CL (6-Me-ε-CL) gave a dramatic decrease in conversion. Polymerisation of ε-CL reached quantitative conversion at room temperature after only 15 minutes. However, addition of the methyl group resulted in no polymerisation at room temperature. Polymerisation at 85°C was possible but required extended reaction times. As 2,3-DHB is already much less active than ε-CL, addition of a methyl or phenyl group in a similar position would likely have a similar effect in activity. This is likely why no polymerisation is achieved at 60°C after 24 hours, even at high concentrations. Increasing the temperature to 85°C for 24 hours still showed no conversion.
3.6.3 Polymerisation of 4H-1,3-benzodioxin-4-one

As adding a substituent to 2,3-DHB had a negative effect on polymerisation, a new monomer without hindering substituents was investigated. 4H-1,3-Benzodioxin-4-one (1,3-BDO) is a similar monomer with a six-membered ring instead of a seven-membered ring. In aliphatic monomers, six-membered rings (δ-VL) tend to be far less active than seven-membered monomers (ε-CL). Despite this, 1,3-BDO was tested under a variety of conditions (Table 3.21). Unfortunately, no polymerisation was achieved under any of the conditions tested. This suggests that aromatic monomers likely follow a similar trend. Interestingly, the reactive acetal did not undergo any side reactions and monomer was the only product present in crude reaction samples.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Temperature (˚C)</th>
<th>Time (h)</th>
<th>Conversion b</th>
</tr>
</thead>
<tbody>
<tr>
<td>58</td>
<td>22</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>85</td>
<td>6</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>120</td>
<td>6</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>TBD</td>
<td>22</td>
<td>24</td>
<td>0</td>
</tr>
</tbody>
</table>

aPolymerisation of 1,3-BDO in toluene with [1,3-BDO]₀:cat:[BnOH]₀ = 100:1:1. b Determined by 1H NMR spectroscopy

In an effort to see some activity, copolymerisation with l-lactide was also attempted at 85˚C for two hours. While this gave 45% conversion of l-lactide no conversion of 1,3-BD was achieved. Changing the catalyst to aluminium salan complex 84 showed yielded similar results for homopolymerisations and copolymerisations.
3.7 Conclusions

Ring-opening polymerisations of several aromatic containing monomers were investigated. Polymerisations were investigated using 58, 84, Sn(oct)$_2$ and organocatalysts.

Sn(oct)$_2$ catalysed ROP was uncontrolled with transesterification occurring. Aluminium based catalysts 58 and 84 yield uncontrolled P2HEB (120°C). or gave only moderate conversion (70°C). Higher conversion was easily achieved by lowering the reaction temperature to 22 – 60°C. Higher molecular weight P2HEB could be synthesised with up to [2,3-DHB]$_0$:[cat]$_0$ = 500:1 tolerated without loss in control. Thermal properties revealed that P2HEB had a relatively low melting temperature (~78°C) and decomposition temperature (onset ~220°C).

Organocatalyst TBD could be used with rapid rates at lower concentrations. Two drawbacks when using TBD were observed; transesterification occurred at long reaction times and low conversion when [2,3-DHB]$_0$:[cat]$_0$ <200:1.

The polymerisation was highly and selectively reversible, which was exploited to depolymerise exclusively back to monomer. This could be cycled; a one-pot polymerisation-depolymerisation-repolymerisation being performed with exceptional control.

Copolymerisation could be achieved with both L-lactide and β-BL using 58. Gradient copolymerisations with L-lactide were unsuccessful but could be synthesised from β-BL, though relatively uncontrolled (1.39 – 1.59), indicating that having both monomers present promotes transesterification. Block copolymers allowed for synthesis of copolymers with L-lactide or β-BL. Copolymers were more thermally stable than P2HEB. Copolymers could also be depolymerised with copolymers of P3HB/P2HEB giving a higher degree of depolymerisation than P(L-LA)/P2HEB.

Other aromatic monomers were investigated. 3,4-DHB, methyl- and phenyl-substituted 2,3-DHBs and 1,3-BDO were all unsuccessful under all conditions and catalysts tested.

This work has been prepared for publication and has been submitted for peer review to Polymer Chemistry and has been accepted subject to revision.
Chapter Four

Tunable Thermal Properties and Microphase Separation in Thermoplastic Elastomer ABA Triblock Copolymers

4.1 Block copolymers in ring-opening polymerisation

Block copolymers were synthesised and discussed in the context of the aromatic containing monomers and L-lactide or β-BL in Chapter 3. Block copolymers represent an incredibly important class of polymer macrostructure. As a result, we explored incorporating β-lactones into block copolymers with lactide. For the purpose of this chapter, ABA triblock block copolymers will be of main focus, while AB diblock and ABC triblock will not be discussed. ABA copolymers were chosen to ensure compatibility between the outer A blocks and can offer advantages over AB analogues.[142]

One of the earliest ABA triblock copolymers using ROP was reported by Kimura in 2000.[98] The ABA copolymers were composed of A blocks of P(L-LA) and the B block of P3HB (Figure 4.1). Synthesis of P(L-LAn-b-3HB2m-b-L-LAn) was achieved by first growing the middle P3HB middle B block from a bifunctional initiator, 1,4-butandiol with a distannoxane catalyst. L-Lactide was then added with Sn(oct)₂ to give A blocks of P(L-LA). Copolymers were thermoplastic elastomers
(TPEs) with properties being controlled by the relative ratios of P3HB and P(L-LA). DSC analysis revealed two distinct glass transition temperatures, corresponding to the P3HB and P(L-LA) segments of the polymer, indicative of microphase separation. This is not typically observed for these types of copolymers when the P3HB block has no stereoregularity. Analysis of the copolymers, and homopolymers synthesised under similar conditions, showed that in this catalyst system produced syndiotactic P3HB. It should be noted that the middle of the copolymer (B block) contains a 1,4-butanediol linkage, resulting in copolymer that is not technically a ABA triblock copolymer. Additionally, the middle B block was first isolated, purified and then used as a macroinitiator, complicating the synthesis. This was necessary as the catalyst used for β-BL polymerisation was different than for L-lactide polymerisation.

While we were working in this area, higher molecular weight P(LA<sub>n</sub>-b-3HB<sub>2m</sub>-b-L-LA<sub>n</sub>) copolymers were synthesised by Mehrkhodavandi and coworkers. In this study, much higher molecular weight block copolymers (> 100000 Da) were prepared using a binuclear indium catalyst. Copolymers were synthesised from both D- and L-lactide via sequential addition of monomers. This minimised waste and workup as only one workup at the end of the reaction and no additional catalyst for each block is required. It also allows for true ABA block formation as an alcohol acts as the initiating group for the first A block, assuming absence of transesterification.

Block copolymers with other monomers have also been investigated. Bhomwick synthesised copolymers from lactide and δ-VL (Figure 4.2). The authors followed a similar route to Kimura, with poly(δ-valerolactone) (PVL) first synthesised as a macroinitiator from 1,6-hexanediol initiator. The copolymers synthesised were low molecular weight (< 12000 Da) and were catalysed by
Sn(oct)$_2$. Interestingly, the copolymers showed microphase separation between the blocks, with independent $T_g$s for PVL and PLA segments.

![Figure 4.2 Structure of P(LA$_n$-b-VL$_{2m}$-b-LA$_n$)](image)

The Hillmyer group has also made significant progress in polyester ABA triblock copolymers. The first report from Hillmyer was of an ABA triblock copolymer of PLA and polyisoprene (PIP) (Figure 4.3).$^{[145]}$ PIP contains no polyester linkages, therefore the resulting copolymers are not fully biodegradable. However, PLA blocks will allow for some hydrolytic degradation. Synthesis was achieved by first synthesising the middle B PIP block through anionic polymerisation. The PIP was then functionalised to give $\alpha,\omega$-hydroxyl groups. PLA was then added by ROP of lactide with triethyl aluminium (AlEt$_3$) to give the desired copolymer. Characterisation by DSC and small-angle X-ray scattering (SAXS) of the copolymers revealed microphase between the PIP and PLA blocks, resulting in TPE properties.$^{[145b]}

![Figure 4.3 Structure of P(LA$_n$-b-IP$_m$-b-LA$_n$)](image)

Subsequent work focused on a novel monomer, menthide (Menth).$^{[146]}$ Menthide is intriguing as it is derived from naturally occurring menthol and can be easily synthesised in two steps. Synthesis of P(LA$_n$-b-Menth$_m$-b-LA$_n$) was achieved starting from the bifunctional initiator diethyl glycol (DEG) (Figure 4.4).$^{[147]}$ Again, SAXS and DSC characterisation revealed microphase separation. The copolymers were pressure sensitive and showed promise in use for pressure-sensitive adhesives. A subsequent report used diethyl zinc to polymerise menthide and AlEt$_3$ to polymerise lactide.$^{[148]}$ This report was followed by a study of the effect of lactide
stereochemistry using rac-lactide to produce atactic PLA blocks or D- or L-lactide to produce semicrystalline PLA blocks. Study of the mechanical properties revealed that PLA stereochemistry had a significant effect on both Young’s Modulus and tensile strength.

![Figure 4.4 Structure of P(LAₙ₋b-Menth₂ₘ₋b-LAₙ)](image)

Hillmyer has since synthesised an ABA triblock copolymer with a polyester free of PLA (Figure 4.5). Polymerisation of Menth was achieved using Sn(oct)$_2$. With DEG as the initiator, $\alpha$-$\omega$-dihydroxyl polymethindie (PMenth) was isolated. Functionalisation of the hydroxyl groups to give $\alpha$-$\omega$-dibromo PMenth was then used as a macroinitiator for the atom transfer radical polymerisation of $\alpha$-methylene-γ-butyrolactone (MBL), which is also sourced from natural resources. Despite the polymer backbone not being fully biodegradable, the copolymer is fully sourced from renewable monomers. However, synthesis of this copolymer is undesirable for two reasons. First, the bifunctional initiator results in an initiator group in the middle of the copolymer. Secondly, changing from ROP to radical polymerisation requires post polymerisation functionalisation of $\alpha$-$\omega$-dihydroxyl PMenth. This adds an extra step of synthesis and purification to allow for radical polymerisation.

![Figure 4.5 Structure of P(MBLₙ₋b-Menth₂ₘ₋b-MBLₙ)](image)

We hypothesised that thermoplastic elastomers could be synthesised using lactide and β-lactones. We targeted a one-pot reaction via sequential addition of monomers to minimise purification and ease of setup. As we hoped to investigate a wide monomer scope, we first studied homopolymerisation of β-lactones to gain
insight into their polymerisation and how they can be best handled for ABA block copolymer synthesis.

4.2 Homopolymerisation of alkyl-substituted β-lactones

Examples of β-lactone polymerisation beyond β-butyrolactone are quite limited. In controlled ROP there are only a few select reports of homopolymerisation of β-valerolactone (β-VL) and one example of a copolymer from β-VL (with β-BL). No examples of controlled ROP of β-heptanolactone (β-HL) or β-tridecalactone (β-TDL), whose synthesis will be discussed in Chapter 5, have been reported (Figure 4.5). As a result of this, homopolymerisation and copolymerisation with the aforementioned alkyl-substituted β-lactones was investigated.

![Figure 4.6 Structure of β-lactones for ROP](image)

The goal of this work was to synthesise both homopolymers from these β-lactones using aluminium catalyst on route to ABA triblock copolymers. ABA triblock copolymers were targeted as they may be used as thermoplastic elastomers, retaining properties from both poly(3-hydroxyalkanoate) (P3HA) and PLA. It was not expected that copolymers from β-BL would yield desirable materials as TPE behavior observed by Kimura was likely due to the syndiotactic nature of P3HB blocks. Using aluminium salen catalysts did not give significant stereoselectivity, with only low levels achieved with judicious catalyst tuning.

The initial part of this study was to investigate the activity of β-VL, β-HL and β-TDL and compare to that of β-BL, which has been studied with 58 and 84. It was hypothesised that the monomers should undergo ROP using either catalyst 58 or 84, with the rate decreasing as the alkyl chain length increased. We also wanted to
investigate several parameters of the reaction including temperature and accessible molecular weight for optimisation of subsequent copolymer synthesis.

**4.2.1 Effect of temperature**

To understand this system and to obtain an idea of optimal reaction conditions, the polymerisation was conducted over a range of temperatures. Using 58 as a catalyst, polymerisations were first conducted at 70°C. This temperature was chosen as previous work suggested that polymerisations below 70°C were ineffective.[88] The data is presented in Table 4.1.

From this data, it was shown that all four of the monomers can be used for ROP at 70°C using 58 and there are some trends that can be observed. The molecular weight of the polymers is in good agreement for both β-BL and β-VL and in excellent agreement for β-HL when comparing to the theoretical values. This is a good indication that the polymerisation is controlled, with very little to no termination reactions present. This is shown further by the very low dispersity of the polymers. P3HB gave the lowest dispersity (1.04) while only slight broadening is observed for the larger β-lactones (D ≤ 1.10). This was an excellent result as it indicated that for the homopolymerisations of alkyl-substituted β-lactones were well controlled with predictable molecular weights even when adding a large substituent up to C<sub>10</sub>H<sub>21</sub>.

**Table 4.1 Homopolymerisation of alkyl-substituted β-lactones at 70°C<sup>a</sup>**

<table>
<thead>
<tr>
<th>Monomer</th>
<th>Time (h)</th>
<th>Conversion (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>M&lt;sub&gt;n&lt;/sub&gt;&lt;sup&gt;c&lt;/sup&gt;</th>
<th>M&lt;sub&gt;n&lt;/sub&gt;&lt;sup&gt;d&lt;/sup&gt;</th>
<th>D&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-BL</td>
<td>6</td>
<td>92</td>
<td>7900</td>
<td>6400</td>
<td>1.04</td>
</tr>
<tr>
<td>β-VL</td>
<td>6</td>
<td>81</td>
<td>8200</td>
<td>6750</td>
<td>1.10</td>
</tr>
<tr>
<td>β-HL</td>
<td>18</td>
<td>91</td>
<td>11750</td>
<td>11200</td>
<td>1.08</td>
</tr>
</tbody>
</table>

<sup>a</sup> Polymerisation conducted in toluene at 70°C with [M]<sub>0</sub>:[58]<sub>0</sub>:[BnOH]<sub>0</sub> = 100:1:1. <sup>b</sup> Determined by 1H NMR spectroscopy. <sup>c</sup> M<sub>n</sub><sub>th</sub> = % conv. × MW<sub>monomer</sub> + MW<sub>BnOH</sub>. <sup>d</sup> Determined by GPC.
To gain a better understanding of the system, the polymerisations were conducted at higher temperatures. The data from these polymerisations are shown in Table 4.2.

Increasing the polymerisation temperature to 85°C gave similar results as those conducted at 70°C. ROP of each monomer reached quantitative conversion. In order to reach quantitative conversion, the reactions of β-VL, β-HL and β-TDL were left longer than at 70°C. The polymer molecular weights are again in excellent agreement with the expected values. The molecular weight using β-TDL gave the biggest discrepancy from the theoretical value (M_n = 23700, M_n,th = 21340), which is expected as the bulkier decyl substituent of the polymer repeat unit could cause difficulty for new monomer to coordinate to the metal center. However, the magnitude of the error is still exceptionally small and is considered to be in excellent agreement with theoretical values. The dispersities of the polymers are again very low (Đ ≤ 1.10). 58 was capable of polymerising β-lactones with much longer alkyl-substituents without any noticeable sacrifice in control. This represents the first reported β-lactone beyond β-BL with an aluminium salen catalyst as well as the first reported polymerisation of β-TDL with any catalyst.

Table 4.2 Homopolymerisation of alkyl-substituted β-lactones at 85°C

<table>
<thead>
<tr>
<th>Monomer</th>
<th>Time (h)</th>
<th>Conversion (%)</th>
<th>M_n,th</th>
<th>M_n</th>
<th>Đ</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-BL</td>
<td>6</td>
<td>&gt; 99</td>
<td>8720</td>
<td>7570</td>
<td>1.04</td>
</tr>
<tr>
<td>β-VL</td>
<td>6</td>
<td>&gt; 99</td>
<td>10120</td>
<td>10080</td>
<td>1.09</td>
</tr>
<tr>
<td>β-HL</td>
<td>18</td>
<td>&gt; 99</td>
<td>12800</td>
<td>12030</td>
<td>1.08</td>
</tr>
<tr>
<td>β-TDL</td>
<td>40</td>
<td>&gt; 99</td>
<td>21340</td>
<td>23700</td>
<td>1.06</td>
</tr>
</tbody>
</table>

*Polymerisation conducted in toluene at 85°C with [M]₀/[58]₀/[BnOH]₀ = 100:1:1. b Determined by ¹H NMR spectroscopy. c M_n,th = conversion × MW_{(monomer)} + MW_{(BnOH)}. d Determined by GPC.

The kinetics of the polymerisation was studied using 58 with [M]₀/[58]₀/[BnOH]₀ = 50:1:1 (Figure 4.7). Kinetic studies were conducted at 85°C, as the rates should be faster than at 70°C. In the case for each monomer, the kinetic
plots showed the reactions were pseudo-first order with respect to monomer concentration, a further indication that the polymerisation is controlled with an absence of termination reactions. The relative rates of polymerisation were as expected with β-BL polymerisation being the fastest ($k_{app} = 0.0194 \text{ min}^{-1}$). The polymerisation rate decreased significantly for β-VL ($k_{app} = 0.0065 \text{ min}^{-1}$) and further for β-HL ($k_{app} = 0.0040 \text{ min}^{-1}$). While the trend of decreasing rate as alkyl-substituent length increased, the magnitude of difference was slightly unexpected. Changing from β-BL to β-VL gave a quite dramatic drop in rate for increasing the substituent length by one carbon. With this, it would be expected that the polymerisation of β-HL would be significantly slower than both β-BL and β-VL. However, only a minor decrease in rate compared to β-VL polymerisation is observed. Increasing the alkyl chain to a decyl chain still allowed quantitative conversion, although requiring 40 hours to reach quantitative conversion. Interestingly, the rate ($k_{app} = 0.0017 \text{ min}^{-1}$) had decreased only to approximately half of the rate of β-HL polymerisation, despite this large increase in substituent chain length.

![Figure 4.7 Pseudo first-order kinetic plots for homopolymerisation of β-BL (■), β-VL (▲), β-HL (●) and β-TDL (×) with 58](image)

Polymerisation of β-VL, β-HL and β-TDL were also conducted at 120°C, as previous work demonstrated that β-BL was polymerised under these conditions (Table 4.3). The polymerisations were run for six hours for β-VL and β-HL and 12 hours for β-TDL. The reactions all reached quantitative conversion with no evidence for decomposition by $^1$H NMR spectroscopy. This was an exciting result as it showed the robust nature of the catalyst system, allowing for quantitative conversion.
of all alkyl-substituted β-lactones at temperatures between 70 and 120°C. The
dispersities for poly(3-hydroxyheptanoate) (P3HH) and poly(3-hydroxytridecanoate)
(P3HTD) saw slight decreases while P3HP saw only a slight increase. Regardless,
the dispersity is essentially unaffected by the rate of polymerisation within the tested
conditions. This result indicates that there appears to be little to no transesterification
occurring, even after monomer concentration reaches zero. Polymerisations were left
past reaching quantitative conversion with essentially no dispersity broadening. The
molecular weights are also in excellent agreement with the expected values, as
expected with the low dispersity values.

Table 4.3 Homopolymerisation of alkyl-substituted β-lactones at 120°C

<table>
<thead>
<tr>
<th>Monomer</th>
<th>Time (h)</th>
<th>Conversion (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>M&lt;sub&gt;n,th&lt;/sub&gt;&lt;sup&gt;c&lt;/sup&gt;</th>
<th>M&lt;sub&gt;n&lt;/sub&gt;&lt;sup&gt;d&lt;/sup&gt;</th>
<th>D&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-VL</td>
<td>6</td>
<td>&gt; 99</td>
<td>10120</td>
<td>9410</td>
<td>1.11</td>
</tr>
<tr>
<td>β-HL</td>
<td>6</td>
<td>&gt; 99</td>
<td>12920</td>
<td>10760</td>
<td>1.07</td>
</tr>
<tr>
<td>β-TDL</td>
<td>12</td>
<td>&gt; 99</td>
<td>21340</td>
<td>17430</td>
<td>1.05</td>
</tr>
</tbody>
</table>

<sup>a</sup>Polymerisation conducted in toluene at 120°C with [M][c][58][c][BnOH]<sub>0</sub> = 100:1:1. <sup>b</sup>Determined by
<sup>1</sup>H NMR spectroscopy. <sup>c</sup>M<sub>n,th</sub> = % conv. × MW<sub>monomer</sub> + MW(BnOH). <sup>d</sup>Determined by GPC.

4.2.2 Effect of catalyst

While 58 was tested for the homopolymerisation of β-BL, β-VL, β-HL and
β-TDL over a wide range of conditions, we also wanted to investigate the impact of
catalyst choice in the polymerisation. To do this, another aluminium salen complex
(64) and the aluminium salan complex (84) were tested. 64 was originally reported
by Gibson for rac-lactide polymerisation and was approximately six times faster than
58 without loss of control.<sup>33b</sup> 84 was chosen due to its efficiency in the
polymerisation of β-BL as well as producing highly heterotactic PLA and its efficacy
in other ring-opening polymerisations described in this thesis.<sup>81, 88</sup>

As discussed previously, 84 was an effective catalyst for the polymerisation
of β-BL over a range of temperatures.<sup>35a</sup> Since 84 polymerised β-BL at room
temperature, similar conditions were tested for β-VL and β-HL. Interestingly, both polymerisations of β-VL and β-HL were ineffective at room temperature, forming only a small amount of polymer (ca. 5%) after 48 hours. This could be due to a bulkier nature of the monomer/polymer chain compared to β-BL/P3HB causing chains to become dormant.

The polymerisation of β-VL and β-HL were conducted at 85˚C for 18 hours, the time in which 58 converted monomer to polymer quantitatively (Table 4.4). This result confirmed that 84 would facilitate the polymerisation of monomers with longer alkyl-substitution than β-BL. At 85˚C, the dispersities had decreased slightly more than when using 58 (P3HP, D = 1.05 vs. 1.09, P3HH, D = 1.04 vs. 1.08). The polymerisations were then conducted at 120˚C, with polymerisation of both β-VL and β-HL reaching high conversion to polymer after six hours. Dispersities were still well controlled while increasing slightly and molecular weights were still in good agreement with theoretical values, indicating trends were similar.

The kinetic profile was also investigated for 84 to compare to ROP with 58 (Figure 4.8). For this, only β-VL was used as a monomer. The kinetic data demonstrated that the catalyst choice had very little effect on the rate of polymerisation, with 84 ($k_{app} = 0.0071 \text{ min}^{-1}$) being essentially the same as using 58 ($k_{app} = 0.0065 \text{ min}^{-1}$). This information could be beneficial for further experiments in block copolymerisation, as the catalyst choice will play a key role. While no stereorecontrol was observed for either 58 or 84 in β-lactone polymerisation, the catalysts gave isotactic and heterotactic enriched PLA from rac-lactide, respectively.\textsuperscript{35b, 81} Using this information, 58 should be used if isotactic enriched polymerisation of rac-lactide or polymerisation of D- or L-lactide and 84 should be used if heterotactic enriched polymerisation of rac-lactide is desired.
<table>
<thead>
<tr>
<th>Monomer</th>
<th>Temperature (°C)</th>
<th>Time (h)</th>
<th>Conversion (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>M&lt;sub&gt;n,th&lt;/sub&gt;&lt;sup&gt;c&lt;/sup&gt;</th>
<th>M&lt;sub&gt;n&lt;/sub&gt;&lt;sup&gt;d&lt;/sup&gt;</th>
<th>D&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-VL</td>
<td>22</td>
<td>48</td>
<td>&lt;5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>85</td>
<td>18</td>
<td>&gt;99</td>
<td>10120</td>
<td>8300</td>
<td>1.05</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>6</td>
<td>&gt;99</td>
<td>10120</td>
<td>9530</td>
<td>1.08</td>
</tr>
<tr>
<td>β-HL</td>
<td>22</td>
<td>48</td>
<td>&lt;5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>85</td>
<td>18</td>
<td>&gt;99</td>
<td>12920</td>
<td>10250</td>
<td>1.04</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>6</td>
<td>96</td>
<td>12410</td>
<td>9860</td>
<td>1.07</td>
</tr>
</tbody>
</table>

<sup>a</sup>Polymerisation conducted in toluene with [M]<sub>0</sub>[84]<sub>0</sub>[BnOH]<sub>0</sub> = 100:1:1. <sup>b</sup>Determined by <sup>1</sup>H NMR spectroscopy. <sup>c</sup>M<sub>n,th</sub> = % conv. × MW<sub>(monomer)</sub> + MW<sub>(BnOH)</sub>. <sup>d</sup>Determined by GPC.

A second aluminium salen catalyst, 64, was tested for the polymerisation of β-lactones and its kinetic profile measured (Figure 4.9). The rate of β-HL polymerisation was significantly faster with 64 (<i>k<sub>app</sub> = 0.0223 min<sup>-1</sup></i>) compared to 58 (<i>k<sub>app</sub> = 0.0040 min<sup>-1</sup></i>). The difference in rate is the same as observed for rac-lactide polymerisation, with the rate being approximately 5.5 times faster.<sup>[35b]</sup> Polymerisation proceeded to high conversion (> 98% after three hours) with good molecular weight and dispersity control, further demonstrating the robust nature of the aluminium salen family of complexes. Only β-BL has been previously reported in β-lactone polymerisation.
4.2.3 Effect of molecular weight

While all previous homopolymerisations were conducted with a ratio of 
\([M_0/Al_0/BnOH]_0 = 100:1:1\) \([M_0/Al_0/BnOH]_0 = 501:1\) for kinetic studies), 
higher molecular weight polymers were also of interest (Table 4.5). Previous work in 
the Shaver group demonstrated that higher molecular weight 
P3HB was accessible 
using 58 and 85 at 70°C.\(^{[88]}\) Using 58 gave high (> 80%) conversion for β-BL 
polymerisation with \([M_0/Al_0/BnOH]_0 = 250:1:1\) and 500:1:1 with \(D < 1.15\). 
However, using 85 was less effective in ROP of β-BL with \([M_0/Al_0/BnOH]_0 = 
250:1:1\), reaching only 41% conversion after 18 h. Furthermore, ROP with 
\([M_0/Al_0/BnOH]_0 = 500:1:1\) formed < 5% polymer after 18 hours. Due to this, 58 
was used as a catalyst for further β-VL and β-HL polymerisations. Higher molecular 
weight P3HP and P3HH was targeted using \([M_0/Al_0/BnOH]_0 = 200:1:1\) and 
500:1:1. Polymerisations were initially conducted at 85°C to allow for a faster 
polymerisation. Both β-VL and β-HL polymerisations with 200 equivalents gave 
high conversion, with β-VL (95% conversion) being slightly lower than β-HL (>99% 
conversion). Increasing the initial monomer to catalyst ratio to 500:1 allowed for 
quantitative conversion of β-VL to P3HP, although requiring 72 hours. Using this 
initial feed ratio with β-HL, only gave 72% conversion after 48 hours and 78% 
conversion after 72 hours. This indicated that the polymerisation was stopping, 
potentially due to the catalyst center becoming inaccessible due to the large, bulky 
growing polymer chain. To overcome this, the polymerisations with \([M_0/Al]_0 =
500:1 were conducted again at 120°C. β-VL had reached quantitative conversion after 48 hours. While β-HL did not reach quantitative conversion, an increase in conversion (89% after 48 hours) was observed. Samples prepared with [M]₀/[Al]₀ = 200:1 gave low dispersities for both β-VL and β-HL polymerisation (1.10 and 1.08, respectively), molecular weight were significantly lower than the theoretical values. The GPC traces were consistent with this result, with both samples showing a small shoulder, indicating that there are likely two sets of growing polymer chains. As there may be more polymer chains growing than initial initiator added, the monomer concentration is effectively decreased. The dispersity had remained low as the peaks for the two sets of polymer chains.

<table>
<thead>
<tr>
<th>Monomer</th>
<th>[M]₀/[58]₀</th>
<th>Temp. (˚C)</th>
<th>Time (h)</th>
<th>Conv. (%)</th>
<th>Mₙ,th</th>
<th>Mₙ</th>
<th>Đ</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-VL</td>
<td>200</td>
<td>85</td>
<td>40</td>
<td>95</td>
<td>19130</td>
<td>13020</td>
<td>1.10</td>
</tr>
<tr>
<td></td>
<td>500</td>
<td>85</td>
<td>72</td>
<td>&gt; 99</td>
<td>50170</td>
<td>27890</td>
<td>1.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>120</td>
<td>48</td>
<td>&gt; 99</td>
<td>50170</td>
<td>26680</td>
<td>1.21</td>
</tr>
<tr>
<td>β-HL</td>
<td>200</td>
<td>85</td>
<td>40</td>
<td>&gt; 99</td>
<td>25740</td>
<td>19380</td>
<td>1.08</td>
</tr>
<tr>
<td></td>
<td>500</td>
<td>85</td>
<td>72</td>
<td>78</td>
<td>50010</td>
<td>27600</td>
<td>1.08</td>
</tr>
<tr>
<td></td>
<td></td>
<td>120</td>
<td>48</td>
<td>89</td>
<td>56820</td>
<td>23870</td>
<td>1.10</td>
</tr>
</tbody>
</table>

*Polymerisation conducted in toluene. Determined by 1H NMR spectroscopy. Mₙ,th = % conv. × MW(monomer) + MW(BnOH). Determined by GPC.

### 4.2.4 Thermal properties

To gain a further understanding of the polymer properties, the thermal properties of P3HP and P3HH were investigated by DSC. The thermal properties were compared to P3HB and are shown in Table 4.6.
Table 4.6 Thermal properties of poly(3-hydroxyalkanoate) homopolymers

<table>
<thead>
<tr>
<th>Polymer</th>
<th>$T_g$ (°C)</th>
<th>$T_c$ (°C)</th>
<th>$T_m$ (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P3HB</td>
<td>-5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>P3HP</td>
<td>-19.8</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>P3HH</td>
<td>-30.8</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*Transitions obtained from the second heating scan from -90°C to 200°C. $T_g$ values determined from the midpoint of the transition.*

As typical for atactic P3HA, an amorphous polymer, no crystallisation or melting transitions were observed for P3HP or P3HH. As the length of the alkyl-substituent increased, the $T_g$ decreased. Increasing the alkyl chain length should further disrupt order in the polymer chain (vs. P3HB).

These homopolymerisation results demonstrate the robust nature of aluminium salen and aluminium salan complexes in ROP. The monomer scope for these catalysts, and ROP as a whole, was expanded with larger alkyl-substitution being readily polymerised. Thermal properties indicated that polymers with low $T_g$s could be synthesised from β-lactones, important to our target synthesis of more complex macrostructures.

4.3 Copolymers with L-lactide

4.3.1 Synthesis of gradient copolymers

Previous work in the Shaver group has shown that synthesis of copolymers from rac-lactide and β-BL results in more of a gradient copolymer than a random copolymer.[88] This was demonstrated by the $^1$H NMR spectroscopic monitoring of the reaction showing greater initial incorporation (faster rate) of rac-lactide into the polymer. This was interesting as under similar conditions, the homopolymerisation of rac-lactide was slower than the homopolymerisation of β-BL. Copolymerisation of L-lactide with other β-lactones should follow the same trend.
Copolymerisation of \([L\)-lactide \((50\) equivalents) with \([\beta\)-lactone \((100\) equivalents) was attempted for \([\beta\)-BL, \([\beta\)-VL and \([\beta\)-HL. Copolymerisation with \(58\) at \(70^\circ\)C did not yield the desired polymer. \([L\)-Lactide fully converted to P(\([L\)-LA) while \([\beta\)-lactone remained unreacted. Fortunately, increasing the temperature to \(85^\circ\)C did result in copolymer for all \([\beta\)-lactones tested. High conversion was achieved in each reaction after times of \(10\) and \(18\) hours for \([\beta\)-BL and \([\beta\)-HL, respectively. Polymerisation data is shown on Table 4.7.

### Table 4.7 Gradient copolymerisation data of \([L\)-lactide and \([\beta\)-lactone at \(85^\circ\)C

<table>
<thead>
<tr>
<th>([\beta)-Lactone</th>
<th>% PLA</th>
<th>(M_{n,\text{th}})</th>
<th>(M_n)</th>
<th>(D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>([\beta)-BL</td>
<td>50</td>
<td>51</td>
<td>15920</td>
<td>9710</td>
</tr>
<tr>
<td>([\beta)-VL</td>
<td>50</td>
<td>51</td>
<td>17330</td>
<td>12250</td>
</tr>
<tr>
<td>([\beta)-HL</td>
<td>50</td>
<td>52</td>
<td>20130</td>
<td>18280</td>
</tr>
</tbody>
</table>

\(a\) Copolymerisation of \([L\)-lactide and \([\beta\)-lactone at \(85^\circ\)C in toluene with \([L\)-LA]_\text{c}:[\beta\)-AL]_\text{c}:\([\text{BnOH}]_\text{c} = 50:100:1:1.\) \(b\) Determined by \(^1\)H NMR spectroscopy. \(c\) \(M_{n,\text{th}} = (0.5 \times \% \text{ conv.}(\([L\)-LA) \times 144.13) + (\% \text{ conv.}(\([\beta\)-AL)) \times \text{MW}(\([\beta\)-AL)) + 108.14.\) \(d\) Determined by GPC.

The data in Table 4.7 show the polymerisations were very well controlled, with dispersities between 1.05 and 1.13. Despite the excellent dispersity control, the molecular weight in both cases was lower than the expected molecular weight. In the case of P(\([L\)-LA-co-3HB) and P(\([L\)-LA-co-3HP) the molecular weight varied significantly more than for P(\([L\)-LA-co-3HH).

As the rate of \([\beta\)-BL polymerisation was slower than the rate of lactide polymerisation in copolymerisations with \(58\), the rate of \([\beta\)-VL and \([\beta\)-HL polymerisation is also expected to be slower. This is due to the slower rates for \([\beta\)-VL and \([\beta\)-HL homopolymerisation compared to \([\beta\)-BL and the suppressed rate of \([\beta\)-BL polymerisation in the copolymerisation with lactide. A full kinetic study was not completed to measure the individual rates of \([\beta\)-lactone and \([L\)-lactide polymerisation. However, aliquots were taken from the reaction at various times to estimate how much \([\beta\)-lactone had been incorporated by the time \([L\)-lactide had been fully converted.
to polymer (Table 4.8). L-lactide reached quantitative conversion after two hours in copolymerisation with either β-VL or β-HL. This indicated that the targeted random/gradient copolymers were more similar to an AB diblock copolymer with the A block being a gradient P(L-LA-co-3HA) type and the B block being pure P3HA.

**Table 4.8 Conversion vs. time for β-VL and β-HL copolymerisation with L-lactide in toluene**

<table>
<thead>
<tr>
<th>Monomer</th>
<th>Time (h)</th>
<th>Conversion a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>L-lactide</td>
</tr>
<tr>
<td>β-VL</td>
<td>0.5</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>89</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>&gt;99</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>&gt;99</td>
</tr>
<tr>
<td>β-HL</td>
<td>0.5</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>&gt;99</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>&gt;99</td>
</tr>
</tbody>
</table>


Conversion of β-HL increased with time. The [β-HL]₀ in the copolymerisation was higher than previous homopolymerisations and resulted in higher conversion at similar time intervals. β-HL polymerisation rates appear to increase after L-lactide has been fully consumed by comparing conversion at two hours vs. three hours. Determination of β-VL conversion was more difficult. Crude aliquots were withdrawn from the polymerisation and dried under vacuum prior to analysis. This likely resulted in some β-VL loss due to the monomers lower boiling point, causing apparent conversion of β-VL to be higher than true conversion. Comparing observed β-VL conversion at one, two and three hours could suggest that β-VL conversion is much higher after two hours than at both one and three hours, suggesting significant depolymerisation may have occurred. As this was highly
unlikely, apparent conversion of $\beta$-VL was assumed to be inaccurate by this method. We can say that at least 56% of $\beta$-VL is remaining by the time L-lactide has reached quantitative conversion ($\geq$63% for $\beta$-HL). Despite this, the technique could still be used as a method of estimating when L-lactide had reached quantitative conversion.

To avoid the complication of removing $\beta$-VL during drying, the copolymerisations were performed on an NMR scale with the reaction mixture remaining in a closed system. The results are shown in Table 4.9.

**Table 4.9** Conversion vs. time for $\beta$-VL and $\beta$-HL copolymerisation with L-lactide in C$_6$D$_6^a$

<table>
<thead>
<tr>
<th>Monomer</th>
<th>Time (h)</th>
<th>Conversion $^b$ (%)</th>
<th>l-lactide</th>
<th>$\beta$-lactone</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta$-VL</td>
<td>1</td>
<td>53</td>
<td>10</td>
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</tr>
<tr>
<td></td>
<td>2</td>
<td>77</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>87</td>
<td>24</td>
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</tr>
<tr>
<td></td>
<td>4</td>
<td>95</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>$&gt;99$</td>
<td>40</td>
<td></td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
<td>$\beta$-HL</td>
<td>1</td>
<td>56</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>79</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>93</td>
<td>23</td>
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<tr>
<td></td>
<td>4</td>
<td>97</td>
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<tr>
<td></td>
<td>14</td>
<td>$&gt;99$</td>
<td>89</td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Copolymerisation of l-lactide and $\beta$-lactone at 85°C in refluxing C$_6$D$_6$ with [L-LA]$_0$:[$\beta$-AL]$_0$:[BnOH]$_0$ = 50:100:1:1. $^b$ Determined by $^1$H NMR spectroscopy.

Trends for copolymerisations conducted in C$_6$D$_6$ were similar to those conducted in toluene. The polymerisations in C$_6$D$_6$ were performed at slightly lower concentrations to ensure all sample remained dissolved when cooled to perform $^1$H NMR spectroscopic analysis. This resulted in a slightly decreased rate of
polymerisation for both β-lactone and L-lactide. With the slower rate of polymerisation, L-lactide had reached quantitative conversion after five hours (vs. three hours in toluene). Interestingly, the rate of polymerisation for β-HL did not differ much from the rate for β-VL and the two rates were much closer in the copolymerisations than the corresponding homopolymerisations. After five hours, L-lactide had reached full conversion, while 67 and 70% of unreacted β-VL and β-HL remained, respectively. Using this data, the random copolymers are more block like with P((L-LA100-co-3HP33)-b-3HP67) and P((L-LA100-co-3HP30)-b-3HP70) formed.

4.3.2 Synthesis of ABA triblock copolymers

As discussed in Chapter 1, ABA block copolymers are sought after structures as in some specific cases, microphase separation between the A and B blocks is observed. Microphase separated materials are intriguing as they offer properties from each block and thermoplastic elastomers are often the result of microphase separated block copolymers. Using the data and trends observed for the homopolymer P3HAs, it was hypothesised that using the alkyl-substituted β-lactones as monomers for a middle B block in ABA triblock copolymers with poly(L-lactic acid) may yield thermoplastic elastomeric behavior. It should also allow for a systematic study of the relationship between the length of the alkyl-substituent in the middle B block and the resulting polymer properties.

Effect of polymerisation temperature

Initial efforts to synthesise block copolymers was to use a sequential addition method for simplicity, a higher level of control and greater yield (Scheme 4.1). Since homopolymers from both β-lactone and lactide can be readily synthesised at 70°C, this temperature was investigated first. The homopolymerisation of L-LA was conducted for three hours, after which the reaction vessel was quickly cooled and returned to the glovebox. This should cause growing polymer chains to become dormant as no polymerisation occurred at room temperature. A sample was taken for analysis that showed >98% conversion and molecular weights ±10% of the expected values in each case. β-Lactone was then added to form the middle B block and the
reaction vessel was removed from the glovebox and heated again to 70°C for 18 hours. The process from the first A block was repeated for analysis. The $^1$H NMR spectrum showed that no β-lactone had converted to polymer. This was unsurprising, as random copolymerisation was unsuccessful at 70°C. It may be the energy required to insert a β-lactone molecule into a growing PLA chain is higher than that of an aluminium–benzoxy bond or of a growing P3HA polymer chain. Alternatively, the polymer chains were being terminated after monomer concentration had reached zero. This could be occurring upon cooling of the reaction after complete consumption of L-lactide. To determine if the polymer chains were terminating, the β-lactone was added to the polymerisation via cannula after three hours. Unfortunately, adding the monomer at room temperature (to polymerisation at 70°C) or at 70°C again showed no conversion to AB diblock copolymer. This indicated that it was likely inhibition of insertion of β-lactone into the growing polymer chain was higher energy. To overcome this, once the PLA A block reached complete conversion, the temperature was increased to 120°C for β-lactone block polymerisation. Adding the monomer either in the glovebox at room temperature or at 70°C and heating to 120°C for 18 hours did afford P3HA block formation but $^1$H NMR spectra showed evidence for decomposition and unreacted β-lactone. This indicated that decomposition was occurring before β-lactone was fully converted. As a result, careful monitoring of conversion over time would not allow for formation of well-defined AB diblock copolymers. This result was unexpected as both L-lactide and β-lactone could be easily polymerised at 120°C in homopolymerisation reactions.

![Scheme 4.1 Initial attempted route for AB block copolymer synthesis](image)

To circumvent this decomposition, the polymerisations were performed at 85°C (Scheme 4.2). This temperature was chosen as it could offer enough energy to
allow the insertion of β-lactone into the growing P(l-LA) chain while avoiding the decomposition observed at 120°C. Using the method first described where the β-lactone was added in the glovebox at room temperature, an ABA triblock copolymer was synthesised from l-LA and β-HL (Figure 4.10).

![Scheme 4.2 Successful synthesis route for ABA triblock copolymers](image)

GPC analysis of the first A PLA block confirmed excellent control (D = 1.09). Upon addition of the P3HH B block, the dispersity remained relatively unchanged, with D = 1.10. However, upon addition of the second PLA A block, the dispersity had increased significantly with D = 1.30. While this is still a relatively low dispersity for an ABA triblock copolymer synthesised via ROP, the increase from AB diblock to ABA triblock was surprising. To investigate a possible source of dispersity broadening, the effect of monomer addition temperature was investigated.

![Figure 4.10 First successfully synthesised ABA triblock copolymer](image)
**Effect of monomer addition temperature**

In order to synthesise well defined ABA block copolymers, the temperature at which monomer was added was crucial. Initial ABA block copolymers were synthesised under the following procedure: polymerisation of L-lactide with 58 at 70°C was conducted until complete conversion to polymer (ca. four hours). β-lactone was added at ambient temperature. The reaction mixture that was a solution while at 70°C had become a viscous oil or solid upon cooling. The reaction was then heated to 85°C until complete conversion to P3HA was achieved. The process was repeated for the second PLA A block. While this did yield copolymer with complete consumption of starting monomers, the dispersities were relatively broad. For example, in the case of P(L-LA₂₀₀-b-3HH₂₀₀-b-L-LA₂₀₀), P(L-LA₂₀₀) was synthesised with Đ = 1.09. After addition of 20 units of β-HL, P(L-LA₂₀₀-b-3HH₂₀₀) was isolated with very little change in dispersity (Đ = 1.10). However, after the addition of 100 more units of L-lactide, there was significant broadening of dispersity for P(L-LA₂₀₀-b-3HH₂₀₀-b-L-LA₂₀₀), with Đ = 1.30. While it was initially thought of as a result of broadening due to synthesising a larger polymer, repeating the process with less L-lactide revealed that the dispersity still broadened for smaller copolymers. Another possibility was as the polymer length increased, the solution became viscous resulting in inefficient insertion of monomer. The process was repeated with additional solvent being added with each monomer to offset viscosity. While a slight improvement was observed, copolymers were still relatively uncontrolled.

As the increase was occurring upon polymerisation of the second PLA block and not upon polymerisation of β-HL, it may be due to the relative rates of the polymerisation. As mentioned previously, upon cooling of the reaction to room temperature, the polymer formed had often become insoluble. The monomer was added to the insoluble material and upon reheating, the mixture became homogeneous. Since polymerisation of the B and second A blocks would occur between any dissolved polymer and unreacted monomer once the temperature reached 85°C, it was believed to be due to inefficient initiation between P(L-LA₂₀₀-b-3HH₂₀₀) and L-lactide. Polymerisation would commence from dissolved chains once the reaction had reached 85°C. However, since the solid inside the reaction vessel had not fully dissolved, uniform reinitiation was not occurring. This would cause a
significant increase in dispersity for L-lactide polymerisation as significant propagation occurs before all dissolved metal centers have reinitiated. This is consistent with no significant increase in dispersity for β-HL B block polymerisation. Since the rate of β-HL polymerisation is much lower than L-lactide, very little polymerisation occurs before all chains have fully dissolved. To avoid this, the polymerisation vessel was kept at 85°C and monomer (85°C in toluene) was added via cannula. The results are shown in Table 4.10.

**Table 4.10 Effect of temperature of monomer addition and polymer dispersities**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Monomer addition temperature</th>
<th>25^b</th>
<th>85^c</th>
</tr>
</thead>
<tbody>
<tr>
<td>P(L-LA_{200})</td>
<td>1.09</td>
<td>1.09</td>
<td></td>
</tr>
<tr>
<td>P(L-LA_{200}-b-3HH_{20})</td>
<td>1.10</td>
<td>1.10</td>
<td></td>
</tr>
<tr>
<td>P(L-LA_{200}-b-3HH_{20}-b-L-LA_{200})</td>
<td>1.30</td>
<td>1.14</td>
<td></td>
</tr>
</tbody>
</table>

^a Sequential addition block copolymerisation. ^b Monomer added in glovebox at room temperature. ^c Monomer added in toluene at 85°C.

The polymerisation with monomer being added at 85°C showed essentially no dispersity difference between P(L-LA_{200}) and P(L-LA_{200}-b-3HH_{20}). Addition of the second PLA block maintained control over the polymerisation, with only a small increase in dispersity observed (D = 1.14). This confirmed that the dispersity was in fact broadening due to inefficient reinitiation between AB diblock copolymer and ABA triblock copolymer. As a result, all ABA triblock copolymers for the remainder of this chapter were synthesised by sequential addition of monomer to polymer at 85°C.
4.3.3 Homopolymer and copolymer characterisation

$^1$H NMR spectroscopy

$^1$H NMR spectroscopy was used to determine the conversion of monomer to polymer in homopolymerisation and copolymerisation reactions. Conversion for homopolymerisations was determined by relative integration of monomer methine regions (~4.5 ppm) to polymer methine regions (~5.1 – 5.3 ppm). Determination of conversion for copolymerisations was slightly more complicated. While reactions were run until observation of an absence of monomer signals, relative P(L-LA):P3HA ratios was difficult to determine in some samples as a result of overlapping signals. Polymers composed of P(L-LA) and P3HB allowed for separate integration of the methine region for P(L-LA) from the methine region for P3HB. However, the methine regions of both P3HP and P3HH are overlapping with the P(L-LA) methine region. $^1$H NMR spectra are shown in Figure 4.11 to illustrate the subtle differences in the P(L-LA) methine region for each of the triblock copolymers.

![Figure 4.11 $^1$H NMR methine regions for P(L-LA$_{100}$-b-3HA$_{100}$-b-L-LA$_{100}$); HA = HB (top left), HP (top right) and HH (bottom)]

Integration relative to the terminal CH$_3$ of the P3HA alkyl substituent allowed for measurement of relative polymer ratios for all samples. To ensure
consistency, polymer ratios in P(L-LA<sub>m-b</sub>-3HB<sub>n-b</sub>-L-LA<sub>n</sub>) were also measured relative to the P3HB methyl group. Figure 4.12 shows ¹H NMR spectra of crude samples taken after each step of the polymerisation for P(L-LA<sub>100-b-3HH<sub>100-b</sub>-L-LA<sub>100</sub></sub>). In each spectrum, no residual monomer is observed.

![Figure 4.12 ¹H NMR spectra of 1) P(L-LA<sub>100</sub>), 2) P(L-LA<sub>100-b-3HH<sub>100</sub></sub>) and 3) P(L-LA<sub>100-b-3HH<sub>100-b</sub>-L-LA<sub>100</sub></sub>)](image)

Ratios of P(L-LA):P3HA calculated from the crude samples taken before polymer workup was performed. These data are shown in Table 4.11. ¹H NMR spectroscopy was performed on crude polymer samples after each block growth to ensure that all monomer had been consumed and the relative ratio of P(L-LA) to P3HA was close to the experimental value. Integration of the previously described regions of the ¹H NMR spectra revealed that for all samples taken after each block, P(L-LA) content was within ± 10% of the theoretical amount. Thus, the molecular weight of the resulting polymers should be close to the theoretical molecular weight, assuming a well-controlled polymerisation.
Table 4.11 Theoretical vs. experimental PLA content in ABA triblock copolymers

<table>
<thead>
<tr>
<th>n</th>
<th>m</th>
<th>% PLA&lt;sub&gt;theo&lt;/sub&gt;&lt;sup&gt;a&lt;/sup&gt;</th>
<th>% PLA&lt;sub&gt;NMR&lt;/sub&gt;&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Me</th>
<th>Et</th>
<th>tBu</th>
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<td>16</td>
<td>15.3</td>
<td>15.1</td>
<td>15.3</td>
<td></td>
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<tr>
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<td>100</td>
<td>29</td>
<td>28.1</td>
<td>27.9</td>
<td>28.6</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>100</td>
<td>50</td>
<td>50.5</td>
<td>50.1</td>
<td>46.5</td>
<td></td>
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<tr>
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<td>100</td>
<td>60</td>
<td>59.8</td>
<td>58.4</td>
<td>55.7</td>
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</tr>
<tr>
<td>100</td>
<td>100</td>
<td>67</td>
<td>66.8</td>
<td>67.5</td>
<td>66.0</td>
<td></td>
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<tr>
<td>100</td>
<td>75</td>
<td>72</td>
<td>72.8</td>
<td>72.8</td>
<td>73.4</td>
<td></td>
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<tr>
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<td>50</td>
<td>80</td>
<td>81.0</td>
<td>82.1</td>
<td>81.4</td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>20</td>
<td>90</td>
<td>91.6</td>
<td>90.9</td>
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<td></td>
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<td>100</td>
<td>10</td>
<td>95</td>
<td>94.6</td>
<td>95.2</td>
<td>95.5</td>
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</tr>
</tbody>
</table>

<sup>a</sup> % PLA<sub>theo</sub> = 2n/(2n+m) × 100. <sup>b</sup>% Determined by <sup>1</sup>H NMR spectroscopy

The methine region of the ABA triblock copolymers offers insight to whether transesterification has occurred and disrupted the ABA nature of the triblock copolymer. The PLA methine region is often used to measure levels of isoselectivity in rac-LA polymerisation by exploiting a slight change in chemical shift for possible tetrads (rac-rac-rac, rac-rac-meso, rac-meso-meso, etc…).

Relative tetrad concentration is typically measured by selectively <sup>1</sup>H decoupled <sup>1</sup>H NMR spectroscopy, with coupling of the methyl protons to the methine proton being suppressed, resulting in distinct singlets for the methine proton tetrads. Without any decoupling, it can still be seen that there is only one major quartet for the P(L-LA) methine, arising from long uninterrupted segments of P(L-LA). Intermolecular transesterification would result in scrambling of P3HB into P(L-LA). The possible tetrads are shown in Figure 4.13 (assuming no epimerisation of P(L-LA) occurs). This is best seen in samples of P(L-LAnr-b-3HBmr-b-L-LAn) where the methine region of the P3HB B block does not overlap with PLA methine region. While this does not completely discount transesterification or estimate the level of transesterification, it does indicate there is not a high level of transesterification and true ABA triblock is the dominant species.
For true ABA triblock copolymer, each polymer chain should have two of each LA-LA-LA-HA, LA-LA-HA-HA and LA-HA-HA-HA tetrad for both regions where A block changes to B block. The LA-HA-LA-HA tetrad could arise from one of two sources; intermolecular transesterification or addition of β-lactone or second portion of L-lactide being introduced before complete consumption of previous monomer. The latter should not occur as $^1$H NMR spectroscopy indicated complete conversion in each case. A small peak at 3.76 ppm appears in many of the $^1$H NMR spectra of the A block (pure P(L-LA)) and the ABA triblock copolymers. No peak in this region is observed for the AB diblock copolymers. It is hypothesised that this peak is due to a small amount of transesterification occurring during quenching with methanol resulting in polymers with a methoxy end group. Polymerisation of lactide initiated with an aluminium methoxide salen complex resulted in P(L-LA) with a singlet at 3.76 ppm; NMR experiments confirmed methoxy end group assignment.$^{[35a]}$ This suggests that transesterification during workup is more prominent in P(L-LA) than in P3HA polymerisation.
**Gel permeation chromatography**

Gel permeation chromatography (GPC) was used to characterise ABA block copolymers. Most importantly, this was used to show that polymer growth was occurring upon addition of $\beta$-lactone and second portion of $L$-lactide and not a mixture of homopolymers. Crude samples were removed after every block growth to ensure this was the case. A typical series of GPC traces is shown in Figure 4.14.

![Figure 4.14 GPC traces for P(L-LA) (blue), P(L-LA-b-3HH) (red), and P(L-LA-b-3HH-b-L-LA) (green)](image)

Block growth is clearly observed. The low molecular weight end of the trace of $P(L-LA)$ does not overlap with the low molecular weight end of $P(L-LA-b-3HH)$, indicating that all chains are likely undergoing addition of B block. As dispersity does not change, transesterification is minimal. Copolymers of $P(L-LA_n-b-3HB_m-b-L-LA_n)$ were first characterised with data from these polymers in Table 4.12.

The molecular weight and dispersity data for samples of $P(L-LA_n-b-3HB_m-b-L-LA_n)$ indicated that the ABA triblock copolymers generated were well controlled. Molecular weights were in excellent agreement with the calculated theoretical values. Dispersities were low for an ABA block copolymer with all polymers having $D \leq 1.18$ but were higher than when using $\beta$-VL or $\beta$-HL (*vide supra*); the opposite trend than that that is observed for homopolymerisation of these $\beta$-lactones.
Table 4.12 GPC data for P(L-LA<sub>n</sub>-b-3HB<sub>m</sub>-b-L-LA<sub>n</sub>)

<table>
<thead>
<tr>
<th>n</th>
<th>m</th>
<th>M&lt;sub&gt;n,th&lt;/sub&gt;&lt;sup&gt;a&lt;/sup&gt;</th>
<th>M&lt;sub&gt;n&lt;/sub&gt;&lt;sup&gt;b&lt;/sup&gt;</th>
<th>D&lt;sup&gt;b&lt;/sup&gt;</th>
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<td>10</td>
<td>15270</td>
<td>15110</td>
<td>1.18</td>
</tr>
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</table>

<sup>a</sup> M<sub>n,th</sub> = (n × 144.13) + (m × 76.09) + 108.14. <sup>b</sup>Determined by GPC.

GPC data obtained for P(L-LA<sub>n</sub>-b-3HP<sub>m</sub>-b-L-LA<sub>n</sub>) copolymers is shown in Table 4.13. In the case of P(L-LA<sub>n</sub>-b-3HP<sub>m</sub>-b-L-LA<sub>n</sub>) the trends are the same as P(L-LA<sub>n</sub>-b-3HB<sub>m</sub>-b-L-LA<sub>n</sub>). Molecular weights are again in excellent agreement with the calculated theoretical values. The largest gap between calculated theoretical molecular weight and experimental molecular weight arises for the largest of the ABA block copolymer in the series (n = 100, m = 100). The dispersities have a slightly different trend, namely the copolymers with a higher ratio of P3HP:P(L-LA) demonstrated better control. Dispersities for n = 10, 20 or 50 and m = 100 had very low dispersity of 1.10 and the copolymer with n = 75, m = 100 had D = 1.13. The remaining samples, which had more P(L-LA) content, had D = 1.15 – 1.17, which is still very well controlled for ABA triblock copolymers. It is also shown that in general the samples are better controlled than when the middle block is composed of P3HB.
Table 4.13 GPC data for P(L-LA<sub>n</sub>-b-3HP<sub>m</sub>-b-L-LA<sub>n</sub>)

<table>
<thead>
<tr>
<th>n</th>
<th>m</th>
<th>M&lt;sub&gt;n,th&lt;/sub&gt;&lt;sup&gt;a&lt;/sup&gt;</th>
<th>M&lt;sub&gt;n&lt;/sub&gt;&lt;sup&gt;b&lt;/sup&gt;</th>
<th>D&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
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</tr>
<tr>
<td>100</td>
<td>20</td>
<td>16420</td>
<td>16490</td>
<td>1.17</td>
</tr>
<tr>
<td>100</td>
<td>10</td>
<td>15410</td>
<td>14760</td>
<td>1.15</td>
</tr>
</tbody>
</table>

<sup>a</sup> M<sub>n,th</sub> = (n × 144.13) + (m × 100.12) + 108.14. <sup>b</sup> Determined by GPC.

GPC data for P(L-LA<sub>n</sub>-b-3HH<sub>m</sub>-b-L-LA<sub>n</sub>) copolymers is shown in Table 4.14. In the case of P(L-LA<sub>n</sub>-b-3HH<sub>m</sub>-b-L-LA<sub>n</sub>), the trend of increasing the length of the alkyl substituent in the middle block decreasing the dispersity is continued. Dispersities are even lower than observed for P(L-LA<sub>n</sub>-b-3HP<sub>m</sub>-b-L-LA<sub>n</sub>) and as low as D = 1.08. Dispersities only rise as high as D = 1.16 and follow the same trend as for P(L-LA<sub>n</sub>-b-3HB<sub>m</sub>-b-L-LA<sub>n</sub>); the higher molecular weight copolymers tend to have a higher dispersity.

The molecular weights of P(L-LA<sub>n</sub>-b-3HH<sub>m</sub>-b-L-LA<sub>n</sub>) had a little more variation from the calculated theoretical molecular weight, although most samples were still in excellent agreement. The larger β-HL monomer yields higher molecular weight polymer for samples with similar monomer feed ratios (vs β-BL, β-VL).
Table 4.14 GPC data for P(LAᵣ-b-3HHₘ-b-LAᵣ)

<table>
<thead>
<tr>
<th>n</th>
<th>m</th>
<th>M_{n,th}ᵃ</th>
<th>M_{n}ᵇ</th>
<th>Dᵇ</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>100</td>
<td>14260</td>
<td>19180</td>
<td>1.09</td>
</tr>
<tr>
<td>20</td>
<td>100</td>
<td>15700</td>
<td>15720</td>
<td>1.08</td>
</tr>
<tr>
<td>50</td>
<td>100</td>
<td>20020</td>
<td>22340</td>
<td>1.10</td>
</tr>
<tr>
<td>75</td>
<td>100</td>
<td>23630</td>
<td>24850</td>
<td>1.14</td>
</tr>
<tr>
<td>100</td>
<td>100</td>
<td>27230</td>
<td>33700</td>
<td>1.16</td>
</tr>
<tr>
<td>100</td>
<td>75</td>
<td>24020</td>
<td>25140</td>
<td>1.16</td>
</tr>
<tr>
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<td>50</td>
<td>20820</td>
<td>21650</td>
<td>1.14</td>
</tr>
<tr>
<td>100</td>
<td>20</td>
<td>16970</td>
<td>17850</td>
<td>1.14</td>
</tr>
<tr>
<td>100</td>
<td>10</td>
<td>15690</td>
<td>15230</td>
<td>1.13</td>
</tr>
</tbody>
</table>

ᵃ M_{n,th} = (n \times 144.13) + (m \times 128.16) + 108.14. ᵇ Determined by GPC.

A single ABA triblock copolymer with a P3HTD middle B block was generated. Only one sample was prepared as a result of the long polymerisation time of β-TDL at 85°C. Additionally, the dispersity of this sample was significantly higher than other ABA triblock copolymers formed (~1.4).

For all samples, molecular weights are calculated by two different methods and compared to ensure they are being calculated accurately. The equations for the three detectors used by triple detection GPC are:

RI output (mV) = K_{RI} \times dn/dc \times concentration

Viscometry output (mV) = K_{IV} \times IV \times concentration

Light scattering output (mV) = K_{LS} \times MW \times (dn/dc)^2 \times concentration

Using these equations, molecular weight can be calculated by a known sample concentration or a known dn/dc value. For calculating molecular weight from a known concentration, the dn/dc value is calculated from the RI output, and is then used in the light scattering output to generate the molecular weight. For samples with a known dn/dc value, the same principle is applied, calculating a dn/dc value and in turn, the molecular weight. The values reported are those calculated using a known
concentration, as it is thought to be more precise than taking molar ratios of \( P(\text{L-LA}) \) to P3HA estimated by \(^1\text{H} \text{NMR} \) spectroscopy to estimate a \( dn/dc \).

In the case of copolymers, the \( dn/dc \) value can be estimated using molar ratios of the polymers in the sample. For samples of \( P(\text{L-LA})_{n-b-3\text{HB}}_{m-b-\text{L-LA}}\), the \( dn/dc \) values of both \( P(\text{L-LA}) \) and P3HB are known (0.050 and 0.065 in THF, respectively) and are used to calculate polymer molecular weight. Molecular weights were recalculated using a known concentration and were all comparable to the values previously calculated.

For the copolymers derived from \( \beta\)-VL, \( \beta\)-HL and \( \beta\)-TDL, the \( dn/dc \) values of P3HP, P3HH and P3HTD were not known. To overcome this, the \( dn/dc \) values were first calculated from the homopolymers generated in Chapter 4.1.1. To accurately determine the \( dn/dc \) value, three samples over a range of molecular weights were run at varying concentrations to calculate a \( dn/dc \) value that is reproducible. The \( dn/dc \) values for P3HP, P3HH and P3HTD were calculated to be 0.0595, 0.0591 and 0.0590, respectively. These values followed the trend that was expected based on predictions based on the structure of the monomers (and polymers). The \( dn/dc \) (mL/g) value is a measure of how much the refractive index of a solution changes for a given change in concentration. Adding longer alkyl chains would be expected to decrease (slightly) the change in refractive index (vs. \( \beta\)-BL), fitting with what is observed.

Using the \( dn/dc \) values calculated from several homopolymer P3HA samples, molecular weights of the ABA triblock copolymers were calculated and compared to the values calculated by using known concentrations. Values showed very little difference between the two methods of calculation, demonstrating the accuracy in the \( dn/dc \) values that were previously calculated.

Due to the inherently low \( dn/dc \) values of these copolymers (and homopolymers), samples needed to be prepared in very high concentration. This is a result of the light scattering output relying on the squared \( dn/dc \) value as well as molecular weight. As all of these samples are of low molecular weight and (relatively) low \( dn/dc \), a high concentration is needed to observe a light scattering signal and calculate molecular weight. This is challenging, especially as the system splits flow before reaching the detectors; half going to the RI detector and half going
to the combined light scattering and viscometer detector. As flow rate is maintained by eluent, this effectively reduces the concentration by half for each detector, requiring sample concentrations to be double vs. if only using a single light scattering detector (no RI detector). Solubility was thus a problem for many of the samples. Samples that contained a high amount of P(L-LA) (n = 100) could not be fully dissolved in THF, the GPC eluent. These samples were dissolved in CHCl₃ and injected into the GPC with the eluent still being THF. One concern was that there was the possibility that samples would crash out of solution once they were injected into THF. This would lead to two problems; inaccurate concentration values or blockages in the GPC tubing. However, since samples were somewhat soluble in THF at lower concentrations and only a small amount of sample (100 µL of a ~20 mg/mL solution) was being injected, neither of these problems was observed. A second concern was that since the polymers were being injected in CHCl₃, the $dn/dc$ value may need to be adjusted. To investigate this, homopolymer P(L-LA) was analysed by this method. First, the traces of polymer and a blank CHCl₃ samples were compared. This demonstrated that the polymer and the CHCl₃ that were being passed through the system were showing distinct signals and no overlap observed. This showed that, as expected, the CHCl₃ being injected was interacting with the columns of the GPC, allowing the larger polymer to pass through first. This results in the $dn/dc$, which is solvent dependent, to be considered accurate, as the polymer signal is being observed in THF and free of CHCl₃. However, to ensure accuracy, homopolymer P(L-LA) was run in both THF and CHCl₃ in similar concentration and the results were compared (Table 4.15, Figure 4.15).

Very little difference is observed when dissolving the sample in THF compared to CHCl₃. Calculating molecular weight either by using known concentration or $dn/dc$ also showed very little difference. The sample that was dissolved in THF had only a difference of 510 Da, while the sample prepared in CHCl₃ only varied by 110 Da. Furthermore, the difference between the sample prepared in THF and the sample prepared in CHCl₃ showed the same level of discrepancy.
Table 4.15 GPC data of P(L-LA) in THF and CHCl₃

<table>
<thead>
<tr>
<th>Solvent</th>
<th>(M_{n,\text{th}}^a)</th>
<th>(M_{n,\text{conc}}^b)</th>
<th>(M_{n,\text{dn/dc}}^c)</th>
<th>(D^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>THF</td>
<td>14520</td>
<td>13010</td>
<td>13520</td>
<td>1.03</td>
</tr>
<tr>
<td>CHCl₃</td>
<td>14520</td>
<td>13390</td>
<td>13500</td>
<td>1.02</td>
</tr>
</tbody>
</table>

PLL) samples at 13 mg/mL in either THF or CHCl₃. 

\(M_{n,\text{th}}^a\) = % conv. \(\times MW_{\text{lactide}} + MW_{\text{BnOH}}\).

\(M_{n,\text{conc}}^b\) calculated using known concentration.

\(M_{n,\text{dn/dc}}^c\) calculated using \(dn/dc = 0.050\) (PLL in THF).

\(D^d\) Determined by GPC.

This is shown further by the GPC traces (Figure 4.14). It can be seen that the traces are nearly identical, with peak shapes, peak intensity and retention volume matching, independent of the solvent, with the only difference being the presence of a chloroform peak when dissolving the sample in chloroform. This confirms that the method used to determine the molecular weight of copolymers is valid.

![GPC traces of PLL dissolved in THF (left) and CHCl₃ (right)](image)

**Differential scanning calorimetry**

To investigate the physical properties of the synthesised ABA triblock copolymers, differential scanning calorimetry (DSC) was used. This was done to observe any thermal transitions exhibited by the samples. DSC measurements presented in Tables 4.16 – 4.18 were collected with the assistance of Dr Matthew Parker and Dr Barny Greenland at the University of Reading. It was expected that samples with lower poly(lactic acid) would be less likely to exhibit either a \(T_c\) or \(T_m\), as the amorphous P3HA block would likely disrupt the crystallinity of the polymer. However, all samples were expected to exhibit a \(T_g\). The thermal properties for
samples of P(LAₙ-b-3HBₘ-b-LAₙ) are shown in Table 4.16 with DSC thermograms shown in Figure 4.16.

**Table 4.16** Thermal properties for samples of P(LAₙ-b-3HBₘ-b-LAₙ) a

<table>
<thead>
<tr>
<th>n</th>
<th>m</th>
<th>Tᵥ (˚C)</th>
<th>Tₘ (˚C)</th>
<th>Tᶜ (˚C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>100</td>
<td>0.7</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>20</td>
<td>100</td>
<td>9.9</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>50</td>
<td>100</td>
<td>21.9</td>
<td>138.8</td>
<td>108.6</td>
</tr>
<tr>
<td>75</td>
<td>100</td>
<td>23.3</td>
<td>155.6</td>
<td>99.2</td>
</tr>
<tr>
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<td>100</td>
<td>28.9</td>
<td>152.2</td>
<td>101.6</td>
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<td>75</td>
<td>34.8</td>
<td>153.6</td>
<td>103.0</td>
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<td>50</td>
<td>43.9</td>
<td>157.7</td>
<td>104.4</td>
</tr>
<tr>
<td>100</td>
<td>20</td>
<td>51.4</td>
<td>159.6</td>
<td>111.9</td>
</tr>
<tr>
<td>100</td>
<td>10</td>
<td>52.4</td>
<td>162.4</td>
<td>104.4</td>
</tr>
</tbody>
</table>

a DSC heating cycle: heat to 150°C (10°C/min), cool to -100°C (10°C/min), heat to 250°C (20°C/min). Transitions measured on second heating cycle.

Several trends can be observed from the DSC data. First, the samples with low P(i-LA) content (n = 10, 20 and m = 100) showed only a single Tᵥ and no Tₘ or
$T_c$. For the remaining samples, a $T_c$ is observed in each. There does not appear to be any trend with respect to relative polymer ratios, with $T_c = 99.2 - 111.9$ °C. This is indicative of the crystalline regions of the polymer sample not being much different between samples. However, comparing the $T_m$ for each of the polymer samples, a trend is observed. As the relative ratio of P(l-LA) to P3HB increases, the melting temperature increases as well, with temperatures ranging from 138.8°C (P(l-LA$_{50}$-b-3HB$_{100}$-b-l-LA$_{50}$)) to 162.4°C (P(l-LA$_{100}$-b-3HB$_{10}$-b-l-LA$_{100}$)). This was a desired result, as the amount of P(l-LA) in the sample increases, the samples become more like P(l-LA) homopolymer and less like P3HB homopolymer which leads to the observed trend. A similar trend to this is observed for the resulting $T_g$s. With the $T_g$ of homopolymer P(l-LA) ≈ 60°C and the $T_g$ of homopolymer P3HB ≈ 0°C, it was expected that one of two things would be observed. The first possibility being if the polymer sample exhibits microphase separation; the two block types behaving independently. In this case, two distinct $T_g$s would likely be observed, one for the P(l-LA) block and one for the P3HB block. The other possibility being for a non-microphase separated sample. In this case, a single $T_g$ is observed and likely has a value between the $T_g$s for the two homopolymers. As can be seen from the data, the latter is the case. Only a single glass transition is observed for each of the samples, which increases from 0.7°C (low P(l-LA) ratio) to 52.4°C (high P(l-LA) ratio). Even though the initial goal was to synthesise ABA triblock copolymers that exhibited microphase separation, this was still an excellent result. This demonstrated that using the sequential addition method for ABA triblock copolymer synthesis is an efficient way to produce well controlled polymers with predictable and tunable thermal properties (Figure 4.17) as demonstrated by linear increase in $T_g$ and $T_m$ as the amount of P(l-LA) increases. Namely, both a melting temperature and glass transition temperatures can be tuned by altering the relative ratio of P(l-LA) to P3HB. For example, a glass transition between 0 – 60°C can be chosen and easily synthesised.

This result is a significant improvement over previous work with aluminium salan and aluminium salen complexes generating the random copolymer P(LA-co-3HB).\textsuperscript{[88]} While P(LA-co-3HB) did result in thermal properties that were similarly predictable based on the relative incorporation of each monomer, there was large
difficulty in accurately predicting how much of each monomer would be included in the polymer, particularly when polymerisations were conducted in bulk. PLA was largely favored to be included in the polymer, making it incredibly difficult to predict polymer properties on initial feed ratios. Solution copolymerisations were better controlled with more predictable copolymer compositions.

Similarly, the thermal properties of samples of P(L-LA<sub>n</sub>-b-3HB<sub>m</sub>-b-L-LA<sub>n</sub>) were also investigated (Table 4.17, Figure 4.18, 4.19). It was hypothesised that increasing the length of alkyl-substituent from methyl to ethyl may result in enough of a difference to lead to microphase separation. The change from methyl to ethyl in homopolymerisation gave a dramatic decrease in \( T_g \), consistent with the expected decrease in order. The semi-crystalline P(L-LA) are thus more likely to prefer to have less interaction with the ‘more amorphous’ P3HP segments.

**Figure 4.17** Plot of \( T_g \) (left) and \( T_m \) (right) vs. PLA content of P(L-LA<sub>n</sub>-b-3HB<sub>m</sub>-b-L-LA<sub>n</sub>)

**Figure 4.18** DSC thermograms for P(L-LA<sub>n</sub>-b-3HP<sub>m</sub>-b-L-LA<sub>n</sub>) (increasing PLA% top to bottom). Heating rate = 10 °C min<sup>-1</sup>
In Table 4.17, the trends are largely the same for P(\text{-}-LA\text{-}-b-3HP\text{-}-b-L-LA\text{-}) as for P(\text{-}-LA\text{-}-b-3HB\text{-}-b-L-LA\text{-}). A single $T_g$ is observed, indicating no microphase separation, as well as increasing $T_g$ and $T_m$ as the PLA content increases. However, as a result of the lower $T_g$ of homopolymer P3HP (~19.8°C) compared to P3HB (~0˚C), the range of $T_g$ that can be prepared through block copolymerisation was now expanded by approximately 15˚C. Again, the melting temperature also followed the same trend, with $T_m$ increasing linearly with increasing P(\text{-}-LA) content. Furthermore, the observed (and accessible) $T_m$ range had increased by nearly 10˚C, with the lowest observed $T_m = 130.7$°C (138.8°C for P(\text{-}-LA\text{-}-b-3HB\text{-}-b-L-LA\text{-})). This showed that by simply changing the alkyl substituent allows for a significant increase for the range of $T_g$s and $T_m$s accessible. The thermal properties for samples of P(\text{-}-LA\text{-}-b-3HH\text{-}-b-L-LA\text{-}) were also measured and are shown in Table 4.18 and plots of $T_g$ and $T_m$ vs. PLA content are shown in Figure 4.19.
Table 4.18 Thermal properties for samples of P(L-LAn-b-3HHm-b-L-LAn)

<table>
<thead>
<tr>
<th>n</th>
<th>m</th>
<th>T_g (°C)</th>
<th>T_m (°C)</th>
<th>T_c (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>100</td>
<td>-25.7</td>
<td>-</td>
<td>-</td>
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<tr>
<td>20</td>
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<td>50</td>
<td>100</td>
<td>-23.5</td>
<td>130.2</td>
<td>64.2</td>
</tr>
<tr>
<td>75</td>
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</tr>
<tr>
<td>100</td>
<td>100</td>
<td>-24.4</td>
<td>152.0</td>
<td>82.5</td>
</tr>
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<td></td>
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<td></td>
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<td></td>
</tr>
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</tr>
<tr>
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<td>10</td>
<td>47.4</td>
<td>157.0</td>
<td>95.2</td>
</tr>
</tbody>
</table>

*a DSC heating cycle: heat to 150°C (10°C/min), cool to -100°C (10°C/min), heat to 250°C (20°C/min). Transitions measured on second heating cycle.

Figure 4.19 Plot of T_g (left) and T_m (right) vs. PLA content of P(L-LAn-b-3HPm-b-L-LAn).

From the data presented in Table 4.18, samples of P(L-LAn-b-3HHm-b-L-LAn) follow observed T_m trends for P(L-LAn-b-3HBm-b-L-LAn) and P(L-LAn-b-3HPm-b-L-LAn) but showing striking differences in T_g behavior. As the amount of PLA incorporated increases, the T_m also increases. The minimum T_m observed did not vary
from the lowest observed for P(L-\(\text{LA}_{n}\)-b-3\(\text{HP}_{m}\)-b-L-\(\text{LA}_{n}\)). It was expected that increasing the alkyl substituent from ethyl to \(n\)-butyl would have the same effect that was seen when increasing from methyl to ethyl. The crystallisation temperatures decreased even further to 64.2 – 95.2°C. The longer alkyl substituent could further disrupt and decrease the crystallinity of the semi-crystalline P(L-\(\text{LA}\)).

The glass transitions of these samples revealed a very interesting trend. First, two samples (P(L-\(\text{LA}_{100}\)-b-3\(\text{HB}_{100}\)-b-L-\(\text{LA}_{100}\)) and P(L-\(\text{LA}_{100}\)-b-3\(\text{HB}_{100}\)-b-L-\(\text{LA}_{100}\))) exhibited two distinct \(T_g\)s each. This is indicative of a microphase separated copolymer. Furthermore, the observed \(T_g\)s for these samples were relatively close to the \(T_g\)s for homopolymer P(L-\(\text{LA}\)) and P3HH (Figure 4.21) showing the transitions correspond to regions of the polymer that are in similar environment to homopolymer. The remaining samples are likely microphase separated as well, despite showing only a single \(T_g\). The samples of P(L-\(\text{LA}_{n}\)-b-3\(\text{HP}_{m}\)-b-L-\(\text{LA}_{n}\)) where \(n < 100, m = 100\) have \(T_g\)s between -21.1 and -25.7°C and are relatively unchanged from one another. These samples are only showing the \(T_g\) for P3HH regions, while the P(L-\(\text{LA}\)) \(T_g\) is not observed due to a weak signal. This is not unexpected as the P(L-\(\text{LA}\)) is in relatively low concentration. Samples where \(n = 100, m \leq 50\) have \(T_g\)s

\[\text{Figure 4.20 DSC thermograms for P(L-\(\text{LA}_{n}\)-b-3\(\text{HP}_{m}\)-b-L-\(\text{LA}_{n}\)) (increasing PLA% top to bottom). Heating rate = 10 - 30°C min}^{-1}\]
between 40.0 and 47.4˚C, corresponding to P(l-LA). This is due to the same reason as for samples with low P(l-LA) content showing only a $T_g$ corresponding to P3HH.

The transitions in Figure 4.20 are difficult to see. The expanded $T_g$ region of the two microphase separated samples and a suspected microphase separated sample are shown in Figure 4.22. Even when expanded, the transitions are quite small. Only a single $T_g$ is observed for P(l-LA$_{100}$-b-3HB$_{75}$-b-L-LA$_{100}$) at a lowered heating rate (10˚C min$^{-1}$); the increased heating rate (30˚C min$^{-1}$) allows for the second $T_g$ to be observed. Unfortunately, increased heating rate did not reveal second transitions for the remaining samples. Samples of P(l-LA$_n$-b-3HH$_m$-b-L-LA$_n$) and P(l-LA$_{100}$-b-3HP$_{50}$-b-L-LA$_{100}$) were also run at 30˚C min$^{-1}$ with no observed differences.
SAXS

While differential scanning calorimetry indicated at least two samples of P(L-LA<sub>n</sub>-b-3HH<sub>m</sub>-b-L-LA<sub>n</sub>) exhibited microphase separation, further characterisation was pursued to show this was in fact the case. This was done by small angle X-ray scattering (SAXS). SAXS was used in place of transmission electron microscopy (TEM) or atomic force microscopy (AFM), which are typically used to characterise microphase separation. SAXS offer advantage for characterisation of polymers if variation in temperature is of concern. SAXS was performed on the two samples showing two T<sub>g</sub>s at two temperatures, -50°C and 25°C (Figure 4.23). SAXS and WAXS measurements were carried out by our collaborator Prof. Ian Hamley at the University of Reading and Daniel Hermida-Merino at European Synchotron Radiation Facility.

As can be seen in Figure 4.23, SAXS traces were indicative of microphase separation. Furthermore, it indicates that both samples were microphase separated at both temperatures examined. For P(L-LA<sub>100</sub>-b-3HH<sub>75</sub>-b-L-LA<sub>100</sub>), the peak at q = 0.3 nm<sup>-1</sup> corresponds to an irregularly microphase separated sample with a domain spacing of 21 nm. Interestingly, P(L-LA<sub>100</sub>-b-3HH<sub>75</sub>-b-L-LA<sub>100</sub>) showed different morphology. Peaks at 0.28 nm<sup>-1</sup>, 0.56 nm<sup>-1</sup> and 0.90 nm<sup>-1</sup> suggested a lamellar order with a domain spacing of 22.4 nm.

Wide angle X-ray scattering (WAXS) was also used with a temperature range from -50°C to 150°C. For both samples, peaks were present corresponding to microphase separation across the measured temperature range. This confirmed that the two samples investigated had microphase separated morphology across both glass transition temperatures.
Tensile Properties

With DSC, SAXS and WAXS indicative of microphase separation, the tensile properties were also investigated. Tensile properties were measured for $P(LA_{100} - b - 3HH_{75} - b - LA_{100})$ (HH75) and $P(LA_{100} - b - 3HH_{100} - b - LA_{100})$ (HH100) at -50°C and 25°C; arrows point at peaks corresponding to microphase separation.

![Figure 4.23 SAXS intensity profiles for $P(LA_{100} - b - 3HH_{75} - b - LA_{100})$ (HH75) and $P(LA_{100} - b - 3HH_{100} - b - LA_{100})$ (HH100) at -50°C and 25°C; arrows point at peaks corresponding to microphase separation.]

**Figure 4.23** SAXS intensity profiles for $P(LA_{100} - b - 3HH_{75} - b - LA_{100})$ (HH75) and $P(LA_{100} - b - 3HH_{100} - b - LA_{100})$ (HH100) at -50°C and 25°C; arrows point at peaks corresponding to microphase separation.

**Tensile Properties**

With DSC, SAXS and WAXS indicative of microphase separation, the tensile properties were also investigated. Tensile properties were measured for $P(LA_{100} - b - 3HH_{100} - b - LA_{100})$. It was originally attempted to cast films of samples from $P(LA_n - b - 3HB_m - b - LA_n)$, $P(LA_n - b - 3HP_m - b - LA_n)$, $P(LA_n - b - 3HH_m - b - LA_n)$ and $P(LA_n)$ to compare properties across all polymers synthesised. Attempts to cast coherent films of $P(LA)$ ($M_n \approx 14000$) were unsuccessful. Films generated were brittle with many defects (Figure 4.24). The defects in the film resulted in inability to measure the tensile properties. This was not unexpected as PLA is known to be brittle, resulting in difficulty in casting coherent films. Fortunately, PLA has been well characterised previously. Higher molecular weight $P(LA)$ has been shown to be brittle, with poor elastomeric behaviour (elongation at break $<3.9\%$).[^153]

Film preparation of $P(LA_n - b - 3HB_m - b - LA_n)$ was unsuccessful. Samples where $n = 10, 20, 50, m = 100$ were transparent, but were not fully solid. The samples were viscous oils that could not be used in tensile measurements. Samples where $n = 75, 100, m = 100, 75, 50, 20$ and 10 resulted in opaque and brittle with numerous defects. All attempts resulted in films that were not suitable for tensile measurements.
measurements. While there are literature reports studying the tensile properties of 
P(L-LAₙ-b-3HBₘ-b-L-LAₙ), the middle P3HB block was syndiotactic. In our samples, the middle block is composed of atactic P3HB, which could be why film formation is more challenging defects. Samples of P(L-LAₙ-b-3HPₘ-b-L-LAₙ) followed the same trend and did not result in any films for tensile testing.

Many samples of P(L-LAₙ-b-3HHₘ-b-L-LAₙ) followed the same trend for samples with low P(L-LA) content, resulting in films of viscous oils not suitable for measurements. Fortunately, a film was able to be cast of P(L-LA₁₀₀-b-3HH₁₀₀-b-L-LA₁₀₀) (Figure 4.24). The transparent film was easily cast from slow evaporation of a CHCl₃ solution and dried under vacuum prior to testing. The tensile properties are shown in Table 4.19 and Figure 4.25. Smaller strips with dimensions of 3 mm × 40 mm were taken from the middle of film to avoid any defects around the edges and placed between cardboard to prevent slippage or damage from the instrument grips.

![Figure 4.24 Films of P(L-LA₁₀₀) (left) and P(L-LA₁₀₀-b-3HH₁₀₀-b-L-LA₁₀₀) (right)]

<table>
<thead>
<tr>
<th>Tensile strength (MPa)</th>
<th>Young’s Modulus (MPa)</th>
<th>Elongation at break (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.5</td>
<td>80.2</td>
<td>31.4</td>
</tr>
</tbody>
</table>
The tensile properties demonstrated the elastomeric nature of the polymers. The tensile strength was 5.5 MPa, with a Young’s Modulus of 80.2 MPa and an elongation at break of 31.4%. Since there are not many systems of this nature, it is difficult to directly compare. The Young’s Modulus is significantly lower than that for P(L-LA) which is expected for an elastomeric material. This is further demonstrated by the elongation at break being much higher than the elongation at break for P(L-LA) (< 3.9%). These results indicate that the elongation at break is lower than samples of P(L-LA_{n-b-3HB_{m-b-LA_{n}}} prepared by Kimura. The P(L\(-LA_{n-b-3HB_{m-b-LA_{n}}} in this report are of lower molecular weight, which explains a higher elongation at break. Furthermore, the elongation at break is higher than that reported for higher molecular weight P(L-LA_{n-b-3HB_{m-b-LA_{n}}} reported by Mehrkhodavandi. While the results seem to point towards a correlation between ABA copolymer molecular weight and elongation at break, each of the three samples are made of a different middle block.

**Figure 4.25** Typical stress-strain curve for P(L-LA_{100-b-3HH_{100-b-LA_{100}}})

### 4.3.4 Effect of lactide stereochemistry

Stereocomplex poly(lactic acid) has shown an interesting change in thermal properties compared to other stereoregular PLA samples.\[^{26, 35a}\] Both atactic and heterotactic PLA are amorphous with no observed melting temperature.\[^{154}\] However, changing the tacticity to syndiotactic PLA yields a polymer with a melting
temperature of approximately 155°C while purely isotactic PLA has a slightly higher melting temperature (~ 170°C). Isotactic enriched PLA derived from rac-lactide gives rise to increased melting temperatures (185 – 195°C).\cite{35a} Isotactic enriched PLA has been shown to have alternating isotactic $R$ and isotactic $S$ segments, a result of a chain end control mechanism for stereo errors in the polymerisation. The increase in melting temperature was attributed to co-crystallisation of the poly(L-lactic acid) and poly(D-lactic acid) segments of the polymer chains (Scheme 4.3). While both intermolecular and intramolecular co-crystallisation can occur, it is likely that both occur simultaneously in a given sample. The stereoblock PLA is semicrystalline and that there are regions of the polymer sample that the co-crystallisation occurs alongside amorphous regions.

![Scheme 4.3 Simplified schematic of stereoblock PLA self assembly](image)

This can be further demonstrated by forming stereocomplex PLA (co-crystallisation of pure poly(D-lactic acid) and poly(L-lactic acid), Scheme 4.4), with a greatly increased $T_m$ of approximately 235°C.\cite{155} The increased melting temperatures arising from the co-crystallisation of poly(D-lactic acid) and poly(L-lactic acid) is a result in a more crystalline material. As for stereoblock PLA, stereocomplex PLA is a semicrystalline polymer where both amorphous and (co-)crystalline regions are present in the sample. This phenomenon could be exploited for ABA triblock copolymers to enhance the level of phase separation. To do this, one of the poly(L-lactic acid) A blocks was replaced with a poly(D-lactic acid) block to give an ABA’ type triblock copolymer (Figure 4.26).
$P(L-LA_n-b-3HH_m-b-D-LA_n)$ samples were synthesised similarly to $P(L-LA_n-b-3HH_m-b-L-LA_n)$ samples, with the addition of $d$-lactide instead of $l$-lactide for the second $A$ block. Three analogues were synthesised ($n = 20, m = 100; n = m = 100; \text{and } n = 100, m = 20$) and not the entire series as we were only interested in observing if there were any differences to previous samples and not trends of the entire series. The polymer characterisation data are shown in Table 4.20.

Table 4.20 Polymerisation data for $P(L-LA_n-b-3HH_m-b-D-LA_n)^a$

<table>
<thead>
<tr>
<th>$n$</th>
<th>$m$</th>
<th>Conversion (%)</th>
<th>$M_{n,th}^c$</th>
<th>$M_n^d$</th>
<th>$D^d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>100</td>
<td>$&gt;98$</td>
<td>15810</td>
<td>11190</td>
<td>1.06</td>
</tr>
<tr>
<td>100</td>
<td>100</td>
<td>$&gt;98$</td>
<td>27340</td>
<td>22880</td>
<td>1.09</td>
</tr>
<tr>
<td>100</td>
<td>20</td>
<td>$&gt;98$</td>
<td>17080</td>
<td>19760</td>
<td>1.10</td>
</tr>
</tbody>
</table>

$^a$Polymerisations performed by sequential addition method. $^b$ Determined by $^1$H NMR spectroscopy. $^c$ $M_{n,th} = (n \times 144.13) + (m \times 128.16) + 108.14$. $^d$ Determined by GPC.
As can be observed from the data presented in Table 4.20, polymerisations were well controlled, with low $D$s and relatively predictable molecular weights. Additionally, the dispersities for the ABA’ type copolymers were slightly lower (1.06 – 1.10) than the ABA type copolymers (1.09 – 1.16) but the molecular weights varied slightly more.

The thermal properties of the three ABA’ triblock copolymers were investigated by DSC analysis and showed some interesting data that supplements the thermal data for the ABA type triblock copolymers (Table 4.21). For P(L-LA$_{20}$-b-3HH$_{100}$-b-D-LA$_{20}$), there is nearly no difference in data than that collected for P(L-LA$_{20}$-b-3HH$_{100}$-b-L-LA$_{20}$). In both samples, no crystallisation or melt temperature is observed, which is expected as the sample primarily consists of an amorphous P3HH block. The $T_g$ is nearly identical as well with -22.8°C for ABA’ type and -22.1°C for ABA type. While this initially hinted that there would be little to no effect on the polymer thermal properties when changing one of the poly(l-lactic acid) A blocks to poly(d-lactic acid), the remaining two samples showed interesting variation.

For P(L-LA$_{100}$-b-3HH$_{100}$-b-D-LA$_{100}$), the first and second heating cycles yielded different results. Both heating cycles revealed only a single $T_g$ (corresponding to the P3HH block) at approximately -30°C, which is slightly lower than that observed for P(L-LA$_{100}$-b-3HH$_{100}$-b-L-LA$_{100}$) (-24.4°C), possibly indicating that there is less interaction between the PLA blocks and the P3HH blocks. The $T_c$ of the sample was significantly lower on the first heating cycle (74.5°C vs. 94.2°C). It should also be noted that the $T_c$ exothermic peak was broader than for P(L-LA$_{100}$-b-3HH$_{100}$-b-L-LA$_{100}$). Unexpectedly, the $T_m$ had not changed (153.1°C vs. 153.2°C) as it was hoped for an increased $T_m$, as seen for stereocomplex PLA. The second heating cycle had given some insight to the broad $T_c$ in the first heating cycle. Interestingly, there were now two distinct exothermic peaks (55.3°C and 88.5°C) corresponding to crystallisation temperatures.
Table 4.21 Thermal properties of $P(L\text{-}LA_{n\cdot}\text{-}b\text{-}3HH_{m\cdot}\text{-}b\text{-}L\text{-}LA_{n})$ and $P(L\text{-}LA_{n\cdot}\text{-}b\text{-}3HH_{m\cdot}\text{-}b\text{-}D\text{-}LA_{n})$

<table>
<thead>
<tr>
<th>Sample</th>
<th>$T_g$ (°C)</th>
<th>$T_c$ (°C)</th>
<th>$T_m$ (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P(L\text{-}LA_{20\cdot}\text{-}b\text{-}3HH_{100\cdot}\text{-}b\text{-}L\text{-}LA_{20})$</td>
<td>-21.1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>$P(L\text{-}LA_{20\cdot}\text{-}b\text{-}3HH_{100\cdot}\text{-}b\text{-}D\text{-}LA_{20})$</td>
<td>-22.8</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>$P(L\text{-}LA_{100\cdot}\text{-}b\text{-}3HH_{100\cdot}\text{-}b\text{-}L\text{-}LA_{100})$</td>
<td>-24.4</td>
<td>94.2</td>
<td>153.2</td>
</tr>
<tr>
<td>$P(L\text{-}LA_{100\cdot}\text{-}b\text{-}3HH_{100\cdot}\text{-}b\text{-}D\text{-}LA_{100})^a$</td>
<td>-27.8</td>
<td>74.5</td>
<td>153.1</td>
</tr>
<tr>
<td>$P(L\text{-}LA_{100\cdot}\text{-}b\text{-}3HH_{100\cdot}\text{-}b\text{-}D\text{-}LA_{100})^b$</td>
<td>-30.7</td>
<td>55.3</td>
<td>147.1</td>
</tr>
<tr>
<td>$P(L\text{-}LA_{100\cdot}\text{-}b\text{-}3HH_{20\cdot}\text{-}b\text{-}L\text{-}LA_{100})$</td>
<td>46.9</td>
<td>95.2</td>
<td>157.0</td>
</tr>
<tr>
<td>$P(L\text{-}LA_{100\cdot}\text{-}b\text{-}3HH_{20\cdot}\text{-}b\text{-}D\text{-}LA_{100})$</td>
<td>-22.0</td>
<td>41.7</td>
<td>147.5</td>
</tr>
</tbody>
</table>

$^a$ First heating cycle. $^b$ Second heating cycle.

For $P(L\text{-}LA_{100\cdot}\text{-}b\text{-}3HH_{20\cdot}\text{-}b\text{-}D\text{-}LA_{100})$ only a single $T_g$ is observed. Interestingly, it is now the P3HH transition whereas $P(L\text{-}LA_{100\cdot}\text{-}b\text{-}3HH_{20\cdot}\text{-}b\text{-}L\text{-}LA_{100})$ had only showed a $P(L\text{-}LA)$ transition. This supports the previous notion that it is likely all $P(L\text{-}LA_{n\cdot}\text{-}b\text{-}3HH_{m\cdot}\text{-}b\text{-}D\text{-}LA_{n})$ samples have some degree of microphase separation but the transitions are difficult to observe by conventional DSC. The thermogram also showed a much lower $T_c$ (41.7°C), which overlaps the region of the expected PLA $T_g$.

### 4.4 Conclusions

The ring-opening polymerisation of four alkyl-substituted β-lactones to generate homopolymers and copolymers with lactide was studied using aluminium salen and salan catalysts. Homopolymerisation rate for β-lactones decreased as the length of the alkyl-substituent increased.

Gradient copolymers were synthesised, allowing for copolymers with predictable molecular weights and polymer composition. Copolymerisation at 85°C
gave copolymers with high conversion and low dispersity with ratio of poly(3-hydroxyalkanoate) and poly(l-lactic acid) being extremely predictable.

ABA block copolymers were synthesised via a sequential addition of monomers method. Each block growth was performed until quantitative conversion was reached, followed addition of the next monomer. This allowed for the synthesis of well defined ABA triblock copolymers of the type P(\(L\)-LA\(_n\)-b-3HA\(_m\)-b-L-LA\(_n\)). Dispersities were low for copolymers where HA = HB, HP or HH. When copolymers from \(\beta\)-TDL were synthesised, broad dispersities (> 1.4) were obtained.

DSC characterisation of the copolymers showed that P(\(L\)-LA\(_n\)-b-3HB\(_m\)-b-L-LA\(_n\)) and P(\(L\)-LA\(_n\)-b-3HP\(_m\)-b-L-LA\(_n\)) yielded materials with tunable thermal properties. In particular, the glass transition temperature of the materials ranged between -20°C to 60°C. Additionally, it was possible to target \(T_g\)s with excellent accuracy based on monomer feed ratios. Copolymers of P(\(L\)-LA\(_n\)-b-3HH\(_m\)-b-L-LA\(_n\)) exhibited microphase separation with two distinct \(T_g\)s. Microphase separation, which was further shown by SAXS measurements. The tensile properties of microphase separated materials was also studied, showing thermoplastic elastomeric behavior and significantly improved elastomeric properties compared to homopolymer PLA. Synthesis of P(\(L\)-LA\(_n\)-b-3HH\(_m\)-b-D-LA\(_n\)) was then performed. These polymers were synthesised in the same manner and yielded polymers with similar properties.

This work has been peer reviewed and accepted for publication.\[^{156}\]
5.1 Introduction to epoxide carbonylation

5.1.1 Traditional β-lactone synthesis

Efficient synthesis of β-lactones has been of interest for many years. Beyond polymer science, there are a large number of biologically active compounds containing β-lactone, both natural and synthetic, including the anti-obesity drug Xenical (tetrahydrolipstatin).\textsuperscript{[157]} Additionally, β-lactones often act as key intermediates to products in both organic synthesis and material science.\textsuperscript{[158]}

The synthesis of β-lactones can be achieved \textit{via} several different routes. Traditionally, \([2 + 2]\) cycloaddition of a (substituted) ketene with an aldehyde was the preferred route (Scheme 5.1).\textsuperscript{[159]} This route is advantageous as many starting aldehydes are available resulting in a wide range of functionality. Additionally, the use of chiral catalysts has been shown to produce enantioenriched products.\textsuperscript{[160]}

Despite having a wide range of available starting materials, there are drawbacks to cycloaddition. Most notably, high catalyst loading, low conversion and undesired side products. A more recent approach involves carbonylation of epoxides to produce the desired β-lactones.
5.1.2 Epoxide carbonylation using organic/Co catalysts

In the mid 1990s, there was a returned interest in epoxide carbonylation, sparked by a patent filed by Drent and Kragtwijk. In this patent, the inventors described the synthesis of β-lactones via insertion of carbon monoxide into epoxides with a simple catalyst (Scheme 5.2). The active catalyst was generated from dicobalt octacarbonyl and 3-hydroxypyridine (3-HP) with two epoxides being tested (R = H, Me). Additionally, it was noted that either leaving the reaction for long reaction times or performed at high temperatures resulted in significant poly(3-hydroxyalkanoate) and ketone formation.

Other researchers have since expanded on this work, which has led to a significant growth in development in catalysts for carbonylation. The Alper group studied the effect of different Lewis acids and solvent on carbonylation using PPN (PPN = bis(triphenylphosphine)iminium, [(C₆H₅)₃P=]₂N⁺) as a cocatalyst (Figure 5.1). The authors demonstrated that functional group tolerance can be increased (R = t-Bu, t-Hex, CH₂OPr, CH₂OH (CH₂)ₙCH=CH₂, CH₂Cl). Additionally, aziridines could also be used to produce the corresponding β-lactams. Interestingly, styrene
oxide (\(R = \text{Ph}\)) resulted in no conversion to \(\beta\)-lactone. In all cases the reactions required high pressures of carbon monoxide (900 psi).

![Diagram of 3-HP and PPN](image)

**Figure 5.1** Organocatalysts for epoxide carbonylation

### 5.1.3 Epoxide carbonylation using aluminium catalysts

Aluminium catalysts have also found success in epoxide carbonylation. The simplest aluminium catalyst is \(\text{AlMe}_3/\text{Co}_2(\text{CO})_8\) with dyglyme (suspected active catalyst = \(\text{Me}_2\text{Al}[\text{Co}_2(\text{CO})_4]_2(\text{diglyme})\)).\(^{[163]}\) The authors studied the carbonylation of propylene oxide (PO), showing that the number of turnovers could be increased by increasing temperature. High conversion and selectivity to \(\beta\)-BL was achieved.

The Coates group has dominated epoxide carbonylation research, having reported several excellent catalyst families. The first report with a discrete aluminium catalyst was supported by a salen ligand framework (\(\{\text{Co}(\text{CO})_4\}_2\text{Al}[\text{salen}]^{[98]}\), Figure 5.2).\(^{[69b]}\) Carbonylations were generally quite successful. Starting from \((R)\)-PO oxide yielded \((R)\)-\(\beta\)-BL without loss of chirality. However, high temperatures and pressures were still required. A subsequent report looked at changing the diimine bridge to a cyclohexyl.\(^{[164]}\)

Another aluminium carbonylation catalyst reported by the Coates group was complexed by a porphyrin ligand (\(\{\text{Co}(\text{CO})_4\}_2\text{Al}[\text{TPP}]^{[93]}\)).\(^{[165]}\) In this report, double carbonylation of epoxides to succinic anhydrides was of main focus. However, it was shown that high selectivity of mono carbonylation to \(\beta\)-lactone occurs before second carbonylation, indicating the reaction could be stopped to yield high conversion of \(\beta\)-lactone. The substrate scope had been increased further, with alkyl, alkene, alcohol, ester, ether, amide, silyl ether and aromatic functionalities tolerated.
Most recently, Coates reported the use of several salen and salalen aluminium complexes, with \([\text{Co(CO)}_4\text{Al[salen]}^{\text{CyPy}}\) and \([\text{Co(CO)}_4\text{Al[salen]}^{\text{CyMes}}\) being the most active (Scheme 5.3).\(^{166}\) Perhaps most interesting with these catalysts is their ability to give different regioselectivity. Using the aluminium salen complex, the expected (sterically) product is formed. However, using the aluminium salalen complex, the non-favored product is formed. Additionally, the cis β-lactone is given from trans epoxide. A subsequent report investigate two aluminium salen that followed gave similar results.\(^{167}\) In this report, trans β-lactones are the product from cis epoxides. This could be used in the synthesis of aldol-type products from β-lactones with high enantiomeric excess.\(^{168}\)

While aluminium catalysts have been shown to be excellent catalysts for carbonylation, tolerating a wide range of functional groups, there are a few key drawbacks. High pressures (≥ 900 psi) and high catalyst loading (≥ 1 mol%) were required for all reported carbonylations.
5.1.4 Epoxide carbonylation using chromium (III) catalysts

As for aluminium, the Coates group is at the forefront of chromium (III) carbonylation catalyst design (Figure 5.3). The first catalysts reported were coordinated to porphyrin ligands.\[^{50}\] These two catalysts offered significant improvement over aluminium catalysts. Substrate scope was still broad including epoxides containing alkyl, alkene, ether, ester, amide and silyl ether functionality efficiently converted to $\beta$-lactones. Internal epoxides were also tolerated. This system also allowed for improvement on required catalyst loading, ranging from 1.3 mol % (amide) to as low as 0.01 mol % (alkyl). Unfortunately, high pressures were still required. Ibrahim and coworkers showed the active catalyst could be generated \textit{in situ} from the corresponding chromium (III) chloride salt with Co$_2$(CO)$_8$.\[^{169}\] This was beneficial as it eliminates the need to isolate the extremely air-sensitive chromium cobaltate salts. Additionally, the chromium (III) chloride species are air- and moisture-stable; workups are even performed in H$_2$O. Under these conditions they demonstrated that 900 psi was not required as reactions could be performed at 500 psi without loss in conversion.

Perhaps the greatest discovery to date in metal catalysed carbonylation of epoxides was with the salen catalyst [Co(CO)$_4$]Cr[salen]$^\text{Ph}$. This catalyst system was still very tolerant to many functional groups and the carbonylations could be performed at low pressures. Carbonylations were first performed at 60 psi, eliminating the need for expensive equipment to handle high pressures as these reactions could be performed in glass bottles. Most interestingly, carbonylations could also be performed under one atmosphere of carbon monoxide, eliminating the need for specialised equipment to handle pressures and could be conducted in standard lab glassware with a balloon of carbon monoxide. Reactions were typically scalable up to at least 5 grams, with epichlorohydrin being the only exception reported.
Other ligands to support chromium catalysts have also been used (Figure 5.4). Bildstein tested three complexes with ligands developed by Jacobsen as well as 10 novel indole-aldimine based complexes for carbonylation of PO.\(^{[170]}\) These catalysts generally gave lower turnover and conversion compared to salen and porphyrin systems but did show some degree of enantioselectivity (up to 19% ee).

We needed to exploit carbonylation to generate β-lactones for polymerisation (\textit{vide supra}) and alongside this work sought to optimise current catalysts for improved carbonylation activity. Furthermore, we wanted to extend the \textit{in situ} method developed by Ibrahim to allow for efficient screening.\(^{[169]}\)

Synthesis of functionally diverse β-lactones (non alkyl-substituted) was also targeted with intention of showing proof of concept for their polymerisation. This was studied using aluminium salen and salan complexes discussed in Chapters 1-4.

\textbf{Figure 5.3} Chromium (III) carbonylation catalysts developed by Coates

![Catalysts](image.png)
5.2 Optimisation of *in situ* generation of chromium tetraphenylporphyrin catalysts

The first part of catalyst optimisation was to investigate the tetraphenylporphyrin chromium catalyst. As this catalyst was excellent for carbonylation of many epoxides, it was targeted as a catalyst for alkyl-substituted β-lactones to be used for homopolymerisation and copolymerisation (*vide supra*).[50] Additionally, Ibrahim showed the catalyst could be generated *in situ* but only demonstrated this for carbonylation of one terminal epoxide (1,2-epoxybutane) as their focus was internal epoxides.[169]

Carbonylations were initially carried out in a 45 mL pressure vessel at 70°C with an initial carbon monoxide pressure of 500 psi (Scheme 5.4). Using this vessel, up to 3.0 grams of epoxide (1,2-epoxybutane) could be efficiently converted to β-lactone (β-valerolactone). As the length of the alkyl substituent increased both the maximum scale and \([\text{epoxide}]_0: [\text{Cr}]_0\) decreased. Coates reported that for \([\text{Co(CO)}_4]\text{Cr[OEP]}\), as the length of alkyl substituent increased from ethyl to decyl, the \([\text{epoxide}]_0: [\text{Cr}]_0\) actually increased (3500:1 to 10000:1)[50] due to improved...
catalyst solubility. In our study ClCr[TPP] was less soluble in 1,2-epoxydodecane than in 1,2-epoxybutane. However, having eight ethyl substituents around the porphyrin should greatly increase solubility in a less polar epoxide such as 1,2-epoxydodecane.

The size of the pressure vessel was increased to 100 mL, allowing the scale of the reaction to be increased significantly (nearly double) (Table 5.1). Carbonylations could be carried out on scales up to 5.8 g (1,2-epoxybutane). The same trends were observed as for reactions in the smaller vessel.

![Scheme 5.4 Carbonylation of terminal epoxides with ClCr[TPP]/Co$_2$(CO)$_8$](image)

Table 5.1 Optimisation for carbonylation of alkyl substituted terminal epoxides

<table>
<thead>
<tr>
<th>Epoxide</th>
<th>[epoxide]$_0$: [Cr]$_0$</th>
<th>Mass epoxide (g)</th>
<th>Conversion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,2-epoxybutane</td>
<td>500:1</td>
<td>5.8</td>
<td>&gt;99</td>
</tr>
<tr>
<td></td>
<td>4000:1</td>
<td></td>
<td>&gt;99</td>
</tr>
<tr>
<td></td>
<td>10000:1</td>
<td></td>
<td>81</td>
</tr>
<tr>
<td>1,2-epoxyhexane</td>
<td>500:1</td>
<td>4.0</td>
<td>&gt;99</td>
</tr>
<tr>
<td></td>
<td>2000:1</td>
<td></td>
<td>&gt;9</td>
</tr>
<tr>
<td></td>
<td>4000:1</td>
<td></td>
<td>95</td>
</tr>
<tr>
<td>1,2-epoxydodecane</td>
<td>500:1</td>
<td>3.0</td>
<td>&gt;99</td>
</tr>
<tr>
<td></td>
<td>1000:1</td>
<td></td>
<td>&gt;99</td>
</tr>
<tr>
<td></td>
<td>2000:1</td>
<td></td>
<td>91</td>
</tr>
<tr>
<td>1,2-epoxy-5-hexene</td>
<td>2000:1</td>
<td>4.0</td>
<td>&gt;99</td>
</tr>
<tr>
<td>Epoxide</td>
<td>Ratio</td>
<td>[Cr]</td>
<td>[Co]</td>
</tr>
<tr>
<td>-----------------</td>
<td>-------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td>Epichlorohydrin</td>
<td>100:1</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>Epibromohydrin</td>
<td>50:1</td>
<td>0.2</td>
<td>0</td>
</tr>
</tbody>
</table>

*Carbonylation conditions: [epoxide]₀ = 1.0M, 70°C in THF, 3-18 h, [Cr] = ClCr[TPP], [Cr]₀:[Co₂(CO)₄]₀ = 1:1.5. * Determined by ¹H NMR spectroscopy.

These results were not unexpected but demonstrated this catalyst system could be used to easily synthesise the desired alkyl-substituted β-lactones. Alkene functionalities were still tolerated, with carbonylation of 1,2-epoxy-5-hexene being easily converted to β-6-heptenolactone with only 0.05 mol % catalyst loading. As expected for porphyrin supported chromium catalysed carbonylation, no conversion of epichlorohydrin or epibromohydrin was observed. Epichlorohydrin has been noted as one of the most difficult epoxides for carbonylation, with many catalysts unable to facilitate the carbonylation.[49]

Purification of the β-lactones was easily achieved, with distillation under reduced pressure from the catalyst affording β-VL, β-HL and β-6-HEL. For reactions that did not reach quantitative conversion, starting materials were removed under reduced pressure. β-TDL could not be purified by distillation as decomposition of the lactone occurred. Instead, column chromatography (SiO₂, 10% EtOAc in hexanes) was used to afford the monomer.

With excellent results for in situ generation of the active catalyst [Co(CO)₄]Cr[TPP] and carbonylation of alkyl- and alkene-substituted epoxides, this method was extended to another catalyst system that has a higher functional group tolerance but had not been investigated for in situ catalyst generation.

### 5.3 Optimisation of in situ generation of chromium salen catalysts

As discussed in Chapter 5.1.4, a chromium (III) salen catalyst has been shown to be an excellent catalyst for carbonylation with a significantly broader functional group tolerance.[49] It was hypothesised that in situ generation of the active catalyst could be used to avoid the isolation of the extremely air- and moisture-
sensitive active chromium cobaltate salt. If this was successful, it could also act as a method to quickly identify catalysts of interest for further screening.

As a result of the salen ligand being readily tunable, two different types of ligand modification were proposed. The first was to investigate the phenoxide ring substitution. In the reported Cr[salen] complex, tert-butyl substitution is employed. Electron withdrawing chloro and bulky and donating methyl/adamantyl substitution was targeted. This should indicate the effect on phenoxide electronics as well as steric effect for electron donating complexes. Secondly, the diimine bridge was to be investigated. As Coates showed that less rigid backbones yielded excellent results for aluminium salen and salalen, there is potential for similar results in chromium complexes.\textsuperscript{[167]}

Ligands were synthesised by heating two equivalents of substituted salicylaldehyde with one equivalent of diamine in ethanol for three hours. The flask was cooled and the precipitate was collected by filtration and washed with cold ethanol. The synthesis of salen supported chromium (III) complexes is well established and all complexes were synthesised according to these methods.\textsuperscript{[49, 171]} Complex synthesis was achieved by adding chromium (II) chloride (1.15 equivalents) to a stirring solution of salen ligand in THF. The solution was stirred at room temperature for four hours under inert conditions followed by 18 hours under air. The solution was added to diethyl ether, washed with NaHCO\textsubscript{3}(aq), NaCl\textsubscript{(aq)}, dried over Na\textsubscript{2}SO\textsubscript{4} and dried to leave a deep red or brown solid. Recrystallisation from hot acetonitrile gave the desired chromium salen complexes. ESI mass spectrometry was used to confirm the nature of the chromium complexes.

To benchmark ligand effects, a simple epoxide substrate was chosen. 1,2-Epoxycyclobutane (EB) was chosen, as it was efficiently converted to β-VL in the parent catalyst system. Additionally, as conversion was to be measured by $^1\text{H}$ NMR spectroscopy, this allows easy integration of product resonances with very little peak overlap with starting material or byproducts. The drawback of this method is that 1,2-epoxybutane is volatile. To avoid loss of starting material, crude analysis was performed without removing volatiles. As a result, a large excess of solvent (THF or dimethoxyethane, DME) was present. While this may cause slight inaccuracies in integration of resonances, they should be consistent and allow for comparison
between complexes. Initial carbonylation reactions were performed with 1 mol % of chromium salen, 1.5 mol % of Co$_2$(CO)$_6$ in THF for one hour.

### 5.3.1 Modification of ligand phenoxides

The three complexes to investigate ligand phenoxide modification are shown in Figure 5.5. Synthesis of ClCr[salen]$^{BuPh}$ and ClCr[salen]$^{ClPh}$ was as expected; ESI mass spectrometry was used to characterise the compounds. Synthesis of ClCr[salen]$^{AdPh}$ was more challenging. When conducted under similar conditions, the reaction medium was a suspension and ESI mass spec suggested impurities were present, even after repeated recrystallisation. Performing the synthesis more dilute and for longer periods of time appeared to solve these issues. Results from carbonylation are shown in Table 5.2.

As can be seen from data in Table 5.2, in situ generation of the active catalyst reported by Coates was successful, with carbonylation reaching quantitative conversion after two hours at 50°C. While this temperature was higher, carbonylation could be performed at room temperature, though the reaction rate was lowered. It should also be noted that the product formed was exclusively β-lactone. No side product (poly(3-hydroxypentanoate) or 2-butanone) were observed by $^1$H NMR spectroscopy.

![Figure 5.5](image.png)

*Figure 5.5 Structure of ClCr[salen]$^{BuPh}$, ClCr[salen]$^{ClPh}$ and ClCr[salen]$^{AdPh})*
Table 5.2 Carbonylation of EB with ClCr[salen]$_{BuPh}$, ClCr[salen]$_{ClPh}$ and ClCr[salen]$_{AdPh}$

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Conversion $^b$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ClCr[salen]$_{BuPh}$</td>
<td>&gt;99</td>
</tr>
<tr>
<td>ClCr[salen]$_{ClPh}$</td>
<td>0</td>
</tr>
<tr>
<td>ClCr[salen]$_{AdPh}$</td>
<td>10</td>
</tr>
</tbody>
</table>

$^a$ Carbonylation of 1,2-epoxybutane with [EB]$_0$[Cr$_4$:Co$_2$(CO)$_8$]$_0$ = 100:1:1.5 in THF at 50˚C for 2 h with [EB]$_0$ = 1.0M and initial $P_{CO}$ = 200 psi. $^b$ Determined by $^1$H NMR spectroscopy.

Chloro substitution of the phenoxide ring shut the catalyst down completely, with only starting epoxide present in the crude reaction mixture, indicating electron withdrawing groups are detrimental to catalytic activity. Bulky ortho-adamantyl substitution also had a negative impact on activity. Only 10% conversion to β-lactone was achieved after two hours. This was proposed to be due to insolubility as at the beginning of the reaction not all catalyst had dissolved. Nevertheless, these were still excellent results as they showed two promising features; in situ screening is valid and high selectivity to β-lactone is observed.

With these results in mind, modification of the diimine bridge was investigated next.

5.3.2 Modification of ligand diimine bridge

The next modification of the ligand framework was to change the diimine bridge from ortho-phenylene to 1,2-ethylene and 1,3-propylene (Figure 5.6). Four catalysts were investigated for the effect of diimine bridge. Two catalysts with tert-butyl phenoxide substitution with either a 1,2-ethylene or 1,3-propylene bridge and two are derivatives with chloro phenoxide substitution. This should allow for understanding of the importance of the ridged diimine bridge in the literature catalyst and determine whether chloro phenoxide substitution shuts down other carbonylation catalyst systems. Synthesis of these catalysts proceeded as expected with all catalysts characterised by ESI mass spectrometry. Carbonylation reactions were conducted under identical conditions to those performed in Chapter 5.3.1 to allow for fair comparison. Data from these carbonylations are presented in Table 5.3.
Carbonylations with tert-butyl phenoxide substitution and alkyl bridged diimine were relatively poor catalysts reaching 31 and 27% for 1,2-ethylene and 1,3-propylene bridged complexes, respectively (Table 5.3). An argument may be made for the higher conversion for the ethylene bridged catalyst having a more ridged backbone, more similar to ClCr[salen]\(^{BuPh}\), although the conversion is only 4% higher.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Conversion (^b) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ClCr[salen](^{BuEt})</td>
<td>31</td>
</tr>
<tr>
<td>ClCr[salen](^{BuPr})</td>
<td>27</td>
</tr>
<tr>
<td>ClCr[salen](^{ClEt})</td>
<td>0</td>
</tr>
<tr>
<td>ClCr[salen](^{ClPr})</td>
<td>0</td>
</tr>
</tbody>
</table>

\(^a\) Carbonylation of 1,2-epoxybutane with \([EB]_0[:Cr]_0[:Co_2(CO)_8]_0 = 100:1:1.5\) in THF at 50 °C for 2 h with \([EB]_0 = 1.0\) M and initial \(P_{CO} = 200\) psi. \(^b\) Determined by \(^1\)H NMR spectroscopy.

Chloro phenoxide substituted complexes completely shut the catalyst activity off with no conversion to \(\beta\)-lactone observed after two hours. As for ClCr[salen]\(^{ClPr}\), only starting EB is observed in the crude reaction mixture by \(^1\)H NMR spectroscopy, indicating side reactions are not taking place.
As alkyl bridged chromium (III) salen complexes were inefficient catalysts for carbonylation of EB, further alterations to the diimine bridge were targeted. However, as only an ortho-phenylene bridged complex was the only catalyst to reach high conversion, more subtle changes to that system were studied to gain insight to how the electronics of the backbone affect activity.

### 5.3.3 Substituted phenyl diimine bridged complexes

To study the effect of electronics of the ortho-phenylene bridged catalyst, seven complexes were targeted (Figure 5.7). Synthesis of all of the ligands have been reported in literature and proceeded as expected with one exception: \( \text{H}_2[\text{salen}]^{\text{BuPh-NO}_2} \). This synthesis of this ligand was first attempted under similar conditions to other salen ligands. Only low conversion to the desired product was obtained and high conversion to a different product was observed. This side product was characterised by \(^1\text{H}\) and \(^{13}\text{C}\) NMR spectroscopy and believed to be the product of hydrolysis of the imines (Figure 5.8). The \(^1\text{H}\) NMR spectrum showed no resonances in the expected frequency for imine proton with two singlets at approximately 5.2 ppm corresponding to aminoalcohol protons.

![Figure 5.7 Substituted ortho-phenylene bridged chromium (III) salen complexes for carbonylation](image)

![Figure 5.8 Likely impurity of H\(_2\)[salen]\(^{\text{BuPh-NO}_2}\) synthesis](image)
To overcome this, the reaction was performed under inert conditions. The solvent was changed from ethanol to dry methanol. The workup was performed in air but exposure was minimised. This allowed for isolation of the desired ligand with $^1$H and $^{13}$C NMR spectroscopy used as characterisation.

Synthesis of the precatalysts was straightforward, again with one exception. Workup of ClCr[salen]$^\text{BuPh-NO}_2$ was problematic as a mixture of products was obtained. This is likely due to the workup being performed in air followed by washing with brine, both of which could impact the ligand quality. Recrystallisation did not appear to increase the product purity. As a result, ClCr[salen]$^\text{BuPh-NO}_2$ was not tested in carbonylation.

Initial carbonylations of EB were performed under similar conditions to previous screening with ClCr[salen]$^\text{BuPh}$ with the only difference being a reaction time of one hour instead of two (Table 5.4).

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Conversion $^b$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ClCr[salen]$^\text{BuPhF}$</td>
<td>&gt;99</td>
</tr>
<tr>
<td>ClCr[salen]$^\text{BuPhCl}$</td>
<td>&gt;99</td>
</tr>
<tr>
<td>ClCr[salen]$^\text{BuPh}$</td>
<td>&gt;99</td>
</tr>
<tr>
<td>ClCr[salen]$^\text{BuPhMe}$</td>
<td>&gt;99</td>
</tr>
<tr>
<td>ClCr[salen]$^\text{BuPhOMe}$</td>
<td>&gt;99</td>
</tr>
<tr>
<td>ClCr[salen]$^\text{BuPhMeMe}$</td>
<td>&gt;99</td>
</tr>
</tbody>
</table>

$^a$ Carbonylation of 1,2-epoxybutane with [EB]$^*_0$[Cr]$^*_0$:[Co$_2$(CO)$_8$]$^*_0$ = 100:1:1.5 in THF at 50˚C for 1 h with [EB]$^*_0$ = 1.0M and initial $P_{CO}$ = 200 psi. $^b$ Determined by $^1$H NMR spectroscopy.

All carbonylations reached quantitative conversion after only one hour at 50˚C. While adding chloro substitution on the phenoxide completely shut off the catalyst, chloro and fluoro substitution on the ortho-phenylene bridge still allowed for complete conversion exclusively to β-lactone. To investigate these catalysts further, five were chosen and used in carbonylation of EB at 30˚C for one hour (Table 5.5).
### Table 5.5 Carbonylation of EB with ClCr[salen] BuPh-XY complexes at 30˚C \(^a\)

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Conversion (^b) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ClCr[salen] BuPhCl</td>
<td>32</td>
</tr>
<tr>
<td>ClCr[salen] BuPh</td>
<td>30</td>
</tr>
<tr>
<td>ClCr[salen] BuPhMe</td>
<td>27</td>
</tr>
<tr>
<td>ClCr[salen] BuPhOMe</td>
<td>22</td>
</tr>
<tr>
<td>ClCr[salen] BuPhMeMe</td>
<td>19</td>
</tr>
</tbody>
</table>

\(^a\) Carbonylation of 1,2-epoxybutane with [EB]\(_0\)[Cr]\(_0\):[Co\(_2\)(CO)\(_8\)]\(_0\) = 100:1:1.5 in THF at 30˚C for 1 h with [EB]\(_0\) = 1.0M and initial \(P_{CO}\) = 200 psi. \(^b\) Determined by \(^1\)H NMR spectroscopy.

Carbonylations conducted at 30˚C for one hour gave lower conversions and thus could be used to observe structure-activity relationships. Quantitative conversions could be achieved for all these complexes at this lower temperature by increasing the reaction times. The trend observed was opposite to the expected trend from the phenoxide substitution studies. The more electron withdrawing chloro actually showed higher conversion than the electron donating methyl, methoxy and dimethyl derivatives. This suggests that the electronics of the diamine bridge affect the activity differently than the electronics of the phenoxide rings.

The apparent rate of carbonylation could also be measured. The overall rate of the reaction has been thoroughly investigated by the Coates group for aluminium salen complexes and should be consistent for all catalysts of the type [Lewis acid][Co(CO)\(_4\)].\(^{172}\) In this report, the overall rate was:

\[
d[\beta\text{-VL}]/dt = k[\text{EB}]^\theta P_{CO}^\theta [\text{cat}][\text{solvent}]
\]

As the pressure of carbon monoxide and concentrations of catalyst and solvent are being kept constant throughout the reaction (and between reactions), the apparent rate can be measured and compared between catalysts. To do this, the reaction was quickly and carefully vented at different time points during the reaction and a crude sample was removed for \(^1\)H NMR spectroscopic analysis. The reaction
vessel was then quickly repressurised. A typical plot is shown in Figure 5.9 and the apparent rates for four catalysts are shown in Table 5.6.

![Zero-order plot of EB carbonylation with ClCr[salen]BuPh/Co(CO)8](image)

**Figure 5.9** Zero-order plot of EB carbonylation with ClCr[salen]BuPh/Co(CO)8

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>$k_{app}$ ($\times 10^{-3}$ M min$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ClCr[salen]BuPhCl</td>
<td>4.39</td>
</tr>
<tr>
<td>ClCr[salen]BuPh</td>
<td>4.20</td>
</tr>
<tr>
<td>ClCr[salen]BuPhMe</td>
<td>3.56</td>
</tr>
<tr>
<td>ClCr[salen]BuPhMeMe</td>
<td>2.24</td>
</tr>
</tbody>
</table>

*a Carbonylation of 1,2-epoxybutane with [EB]$_0$[Cr][Co$_2$(CO)$_8$]$_0$ = 100:1:1.5 in THF at 30°C with [EB]$_0$ = 1.0M and initial $P_{CO}$ = 200 psi. ^b Determined by $^1$H NMR spectroscopy.

From the calculated apparent rates, it can be seen that they correlate well with the trend observed for conversion after one hour at 30°C. In all cases, linear kinetics was observed under zero-order conditions. The opposing trends observed for phenoxy substitution and diamine bridge modification made it difficult to say conclusively whether making novel catalysts with a more or less electron donating ligand vs. salen ligands is likely to offer improvement. This poses difficulty in future catalyst design, with no conclusive evidence for the impact of the electronic nature of the ligand.
5.4 Synthesis and polymerisation of functional β-lactones

The need for catalysts that can facilitate the polymerisation of many different monomers is described in Chapter 1. However, testing a wide range of functional monomers is difficult as only a very limited number of ROP monomers are available commercially. Even though functional β-lactones are not available commercially, previous work in this chapter highlights the (improved) simplicity in synthesis of β-lactones. Two functional β-lactones were chosen as targets for as proof of concept polymerisations. A chloro-substituted β-lactone was chosen due to the inherent difficulty in synthesis, while β-6-heptenolactone was chosen for post-polymerisation reactions to be performed with collaborators.

5.4.1 Synthesis and polymerisation of 4-chloro-β-butyrolactone

The first monomer targeted was 4-chloro-β-butyrolactone (4-Cl-β-BL, Scheme 5.5). This monomer was chosen as it is challenging to synthesise. Coates and coworkers reported that synthesis could be achieved with the most functional group tolerant catalyst, [Co(CO)₄]Cr[salen]BuPh.⁴⁹ They also stated that this was the only β-lactone whose synthesis could not be scaled beyond 2 mmol of starting epoxide. There are potential challenges in polymerising a monomer containing a chlorine with aluminium catalysts, as decomposition of aluminium salen and aluminium salan complexes is observed immediately when NMR spectra are collected in halogenated solvents. The resulting polymer, poly(4-chloro-3-hydroxybutyrate) (PClHB) is also intriguing as it may be modified through simple post-polymerisation modification. One example of the polyether analogue, polyepichlorohydrin, has shown the chlorine could be easily replaced by an azide by reaction with NaN₃.¹⁷³

The first part of 4-Cl-β-BL of this study was to optimise the synthesis. In situ generation of the catalyst [Co(CO)₄]Cr[salen]BuPh was chosen to study as it is known to efficiently convert epichlorohydrin (ECH) to 4-Cl-β-BL. As shown in Table 5.1, [Co(CO)₄]Cr[TPP] was unable to convert ECH to 4-Cl-β-BL, with only starting material present after the reaction. Data from carbonylations are presented in Table 5.7.
Table 5.7 Optimisation of epichlorohydrin carbonylation

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Temp. (˚C)</th>
<th>ECH₀ (mmol)</th>
<th>Time (h)</th>
<th>ECHᵇ (%)</th>
<th>4-Cl-β-BLᵇ (%)</th>
<th>CAᵇ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DME</td>
<td>25</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>2</td>
<td>2</td>
<td>79</td>
<td>21</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>15</td>
<td>0</td>
<td>90</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>15</td>
<td>40</td>
<td>54</td>
<td>6</td>
</tr>
<tr>
<td>THF</td>
<td>50</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>

ᵃ Carbonylation of ECH with [ECH]₀:[Cr]₀:[Co₂(CO)₈]₀ = 100:1.1.5 and [ECH]₀ = 1.0 M.ᵇ Determined by ¹H NMR spectroscopy.

DME was initially chosen as it was the solvent of choice for carbonylations performed by Coates. At 25˚C, no conversion to 4-Cl-β-BL was observed after two hours, with only ECH present in the ¹H NMR spectrum. This shows a difference between synthesising the active catalyst and generating in situ, as using the isolated active catalyst gave high yields at 25˚C after two hours. Increasing the temperature to 50˚C while maintaining a 2 mmol scale saw 21% conversion to 4-Cl-β-BL, with the remaining 79% being starting material. Complete consumption can be achieved after 15 hours, with 10% being converted into the undesired side product, chloroacetone (CA).

Increasing the scale up to 20 mmol yielded the same ratio of 4-Cl-β-BL:CA, but only a total conversion of 60% was achieved. Using a solvent that is more strongly coordinating, namely THF, allowed for a significantly faster reaction,
consistent with the mechanism of carboxylation.\textsuperscript{[172]} 100% conversion to exclusively 4-Cl-β-BL was achieved after only five hours at 50˚C. Larger scales were attempted with lower conversions observed.

Using these optimised conditions, synthesis was repeated several times and 4-CL-β-BL was isolated by distillation under reduced pressure for ROP. This allowed for isolation of large enough quantities for polymerisation. Only a single report of 4-CL-β-BL has been published, using ethylaluminium oxide as a catalyst.\textsuperscript{[152a]} This resulted in poorly controlled polymers and low conversion.\textsuperscript{[152a]} Polymerisation of 4-Cl-β-BL was attempted using aluminium salen (58) and aluminium salan (84) catalysts (Scheme 5.6). Data from these polymerisations are shown in Table 5.8.

\begin{center}
\textbf{Scheme 5.6 Polymerisation of 4-Cl-β-BL}
\end{center}

Polymerisations carried out at 120˚C with 58 were uncontrolled. This was demonstrated by only reaching 85% conversion after ten hours, high dispersity and molecular weight less than half of the predicted value. The polymerisation was uncontrolled throughout the reaction as dispersity remained high and did not increase from low to high. Decreasing the temperature to 85˚C with 58 resulted in a significant increase in polymerisation control, as noted be a considerable decrease in dispersity (1.03). Experimental and theoretical molecular weights were much closer as well. The polymerisation reached a maximum conversion of 69% after seven hours. While this was not ideal, excellent control was still achieved, a first for 4-Cl-β-BL polymerisation.

In general, polymerisations with 84 were more successful. Conducting the polymerisation at 120˚C resulted in moderately well controlled polymer, with $D = 1.17$ and predictable molecular weight. Besides being a much more controlled polymerisation, another advantage to using 84 was achieving quantitative conversion after ten hours. Decreasing the temperature to 85˚C showed similar trends as for 58.
Dispersity had again dropped to 1.03 and molecular weights were predictable. Again, quantitative conversion was achieved, this time after only seven hours. This shows that the polymerisation at 120°C was likely complete before the ten hour time point. As significant broadening of dispersity was not observed, it can be said that transesterification is not dominant. Interestingly, 4-Cl-β-BL polymerisation with 84 could be conducted at room temperature. As expected, the polymerisation is slowed dramatically, requiring 11 days to reach 96%.

Table 5.8 Polymerisation of 4-Cl-β-BL with 58 and 84

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Temperature (°C)</th>
<th>Time (h)</th>
<th>Conversion (%)</th>
<th>$M_{n,th}$</th>
<th>$M_n$</th>
<th>$D$</th>
</tr>
</thead>
<tbody>
<tr>
<td>58</td>
<td>120</td>
<td>10</td>
<td>85</td>
<td>10350</td>
<td>4340</td>
<td>1.73</td>
</tr>
<tr>
<td></td>
<td>85</td>
<td>7</td>
<td>69</td>
<td>8220</td>
<td>6890</td>
<td>1.03</td>
</tr>
<tr>
<td>84</td>
<td>120</td>
<td>10</td>
<td>&gt;99</td>
<td>12150</td>
<td>10300</td>
<td>1.17</td>
</tr>
<tr>
<td></td>
<td>85</td>
<td>7</td>
<td>&gt;99</td>
<td>12150</td>
<td>11900</td>
<td>1.03</td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>120</td>
<td>78</td>
<td>9510</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>264</td>
<td>96</td>
<td>11680</td>
<td>9540</td>
<td>1.02</td>
</tr>
</tbody>
</table>

$^a$Polymerisation of 4-Cl-β-BL in toluene with $[4$-Cl-$\beta$-BL]$_0$:$[\text{Al}]_0$:$[\text{BnOH}]_0 = 100:1:1$. $^b$Determined by $^1$H NMR spectroscopy. $^c M_{n,th} = ([4$-Cl-$\beta$-BL]$_0$:$[\text{BnOH}]_0) \times \% \text{conv} \times MW_{(4$-Cl-$\beta$-BL)} + MW_{(\text{BnOH})}$. $^d$Determined by GPC using $dn/dc = 0.058$.

The kinetics of 4-Cl-β-BL polymerisation at room temperature with 84 were monitored (Figure 5.10) to determine if the polymerisation followed pseudo-first order kinetics for the duration of the reaction. As aluminium salan catalysed ROP should follow pseudo-first order kinetics, a non-linear plot may indicate decomposition of the catalyst. It was shown in Chapter 2 that 58 did not show signs of catalyst degradation after long reaction times of eight days for ε-CL polymerisation. However, long reaction times in ε-CL ROP was not extended to 84 and 4-Cl-β-BL is more likely to cause degradation due to having a chloro substituent.
As kinetics were monitored at room temperature, it is difficult to make a comparison to β-lactone polymerisations discussed in Chapter 4 (kinetics at 85°C). However, it can be said that polymerisation of 4-Cl-β-BL with 84 is more rapid than polymerisation of β-HL and β-TDL, as quantitative conversion is achieved after seven hours (4-Cl-β-BL) vs. approximately 18 and 40 hours for β-HL and β-TDL, respectively.

Polymerisation of 4-Cl-β-BL demonstrated that both 58 and 84 were capable of polymerising monomers with more functionally diverse substituents. Furthermore, polymerisations could be performed with a high degree of control with attention to reaction conditions. As a result, ROP of a second functional monomer was investigated.

5.4.2 Polymerisation of β-6-heptenolactone

Another intriguing functional group in polymerisation is alkenes. Several β-lactones containing alkene functionality have been synthesised, both internal and terminal. The synthesis of β-6-heptenolactone (β-6-HEL) was briefly discussed in Chapter 5.2 using in situ generation of [Co(CO)$_4$]Cr[TPP]. The synthesis was also easily achieved using in situ generation of [Co(CO)$_4$]Cr[salen]$_{BuPh}$, though higher catalyst loading (1 mol %) was required.

Polymerisation of β-6-HEL has been reported previously by Carpentier and Guillaume. Isotactic and syndiotactic enriched poly(3-hydroxy-6-heptenoate) (P3HHene) was produced from diiminate zinc and amine-bis(phenolate) yttrium.
catalysts, respectively. Their work mainly focused on post polymerisation modification via hydroboration.

We sought to determine if the polymerisation could be facilitated using aluminium salen, 58, and if copolymers could be synthesised. Copolymerisation was the main target to prepare materials in collaboration with the Elizabeth Gillies group at the University of Western Ontario. Homopolymerisation of β-6-HEL proceeded as expected, with 100 equivalents easily converted to polymer. Polymer characteristics such as rate and dispersity were similar to polymerisation of the saturated analogue, β-HL (Chapter 4). This demonstrated that polymerisation with alkene functionalities does not inhibit polymerisation.

Synthesis of block and block-random copolymers starting from a methoxy poly(ethylene glycol) (mPEG) macroinitiator were synthesised (Scheme 5.7). Varying ratios were targeted as changing from low to high composition of poly(3-hydroxyalkanoate) should change the micellar structure and stability. The synthesis of the block copolymers, P(EG<sub>45</sub>-b-3HHene<sub>n</sub>) was attempted. Data from these polymerisation are shown in Table 5.9.

![Scheme 5.7 Synthesis of P(EG<sub>45</sub>-b-3HHene<sub>n</sub>) and P(EG<sub>45</sub>-b-(3HHene<sub>n</sub>-co-3HH<sub>m</sub>))](attachment:image.png)
Table 5.9 Synthesis of P(EG\textsubscript{45}-b-3HHene\textsubscript{n}) \textsuperscript{a}

<table>
<thead>
<tr>
<th>\textit{n\textsubscript{monomer}}</th>
<th>\textit{Conversion} \textsuperscript{b} (%</th>
<th>\textit{n\textsubscript{polymer}} \textsuperscript{b}</th>
<th>\textit{M\textsubscript{n,th}} \textsuperscript{c}</th>
<th>\textit{M\textsubscript{n,NMR}} \textsuperscript{b}</th>
<th>\textit{D} \textsuperscript{d}</th>
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<td>26</td>
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<tr>
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<td>47</td>
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<tr>
<td>90</td>
<td>&gt;99</td>
<td>87</td>
<td>13130</td>
<td>12950</td>
<td>1.09</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Polymerisation of β-6-HEL with [β-6-HEL]\textsubscript{0}:[58]:[mPEG]\textsubscript{0} = n:1:1 in toluene for 20 hours.
\textsuperscript{b} Determined by \textsuperscript{1}H NMR spectroscopy.
\textsuperscript{c} \textit{M\textsubscript{n,th}} = (\textit{n\textsubscript{polymer}} \times 126.15) + 2000.
\textsuperscript{d} Determined by GPC.

As can be seen from the data presented in Table 5.10, copolymers were formed quantitatively. Values for \textit{n\textsubscript{polymer}} were calculated by \textsuperscript{1}H NMR spectroscopy by integration of PEG peaks vs. P3HHene methine peaks. In the polymer samples, \textit{n\textsubscript{polymer}} values were in excellent agreement with \textit{n\textsubscript{monomer}} values, indicating all monomer is being incorporated in the polymer. Molecular weights were calculated similarly and were in excellent agreement with the theoretical values. Dispersities were broad for samples of P(EG\textsubscript{45}-b-3HHene\textsubscript{n}) where \textit{n} = 24 or 47 (\textit{D} = 1.35). Changing polymerisation duration and concentration were attempted in an effort to decrease dispersity without success.

The next goal was to synthesise block copolymers with the PHA block being a random copolymer. These could be hypothetically synthesised by having both β-6-HEL and β-HL in the polymerisation with mPEG macroinitiator. As the two monomers are structurally quite similar and showed essentially identical rates of homopolymerisation, it is hypothesised that they would form a block of P(3HHene\textsubscript{n-}co-3HH\textsubscript{m}) as a random copolymer. These copolymers are of interest as it gives control over the amount of alkene functionality, which can be beneficial for post polymerisation reactions. Data from these polymerisations are shown in Table 5.10.
Table 5.10 Synthesis of P(EG<sub>45</sub>-b-(3HHene<sub>n</sub>-co-3HH<sub>m</sub>))<sup>a</sup>

<table>
<thead>
<tr>
<th>n+m&lt;sub&gt;monomer&lt;/sub&gt;</th>
<th>Conversion&lt;sup&gt;b&lt;/sup&gt; (%)</th>
<th>n&lt;sub&gt;polymer&lt;/sub&gt;&lt;sup&gt;b&lt;/sup&gt;</th>
<th>m&lt;sub&gt;polymer&lt;/sub&gt;&lt;sup&gt;b&lt;/sup&gt;</th>
<th>M&lt;sub&gt;n,th&lt;/sub&gt;&lt;sup&gt;c&lt;/sup&gt;</th>
<th>M&lt;sub&gt;n,NMR&lt;/sub&gt;&lt;sup&gt;b&lt;/sup&gt;</th>
<th>D&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
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<td>23</td>
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<td>8040</td>
<td>1.11</td>
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<td>91</td>
<td>43</td>
<td>41</td>
<td>12180</td>
<td>12680</td>
<td>1.08</td>
</tr>
</tbody>
</table>

<sup>a</sup>Copolymerisation of β-6-HEL and β-HL with [β-6-HEL]<sub>c</sub>:[β-HL]<sub>c</sub>:[mPEG]<sub>c</sub> = n:m:1:1 in toluene for 20 hours with n = m. <sup>b</sup>Determined by <sup>1</sup>H NMR spectroscopy. <sup>c</sup>M<sub>n,th</sub> = (n<sub>polymer</sub> × 126.15) + (m<sub>polymer</sub> × 128.17) 2000. <sup>d</sup>Determined by GPC.

There were some similarities between properties of P(EG<sub>45</sub>-b-3HHene<sub>n</sub>) and P(EG<sub>45</sub>-b-(3HHene<sub>n</sub>-co-3HH<sub>m</sub>)). The similarities include the high predictability of incorporation of β-lactones and molecular weights. Interestingly, the dispersities were significantly lower for the block-random copolymers (1.08 – 1.13).

<sup>1</sup>H NMR spectroscopy was used to determine conversion and incorporation of the monomers (Figure 5.11). As the methine regions of P3HHene and P3HH overlapped, the total of the combined methine regions compared to PEG resonances was used to calculate n<sub>polymer</sub> + m<sub>polymer</sub>. The relative amount of n<sub>polymer</sub> to m<sub>polymer</sub> could be calculated by comparing the integration of alkene resonances to total methine resonances.

In general, the synthesis of block copolymers was successful. Block copolymers of the type P(EG<sub>45</sub>-b-3HHene<sub>n</sub>) were less controlled than those of P(EG<sub>45</sub>-b-(3HHene<sub>n</sub>-co-3HH<sub>m</sub>)). Regardless, their synthesis (and P3HHene synthesis) demonstrates that aluminium salen complexes can tolerate a range of functional groups and allows for incorporation of functional monomers into homopolymers and copolymers.
5.5 Conclusions

In situ generation carbonylation active catalysts, [Lewis acidic][Co(CO)] of chromium (III) supported by salen and porphyrin ligands was an excellent route to β-lactone synthesis with no loss in selectivity or functionality tolerance. This method of catalyst synthesis allowed for facile study of changes to phenoxide and diimine bridge substitution vs. catalytic activity. Changing phenoxide substitution to electron withdrawing chlorines ceased carbonylation activity completely. Having electron donating and bulky ortho-adamantyl hindered activity. Activity was also decreased by changing the diimine bridge from ortho-phenylene to 1,2-ethylene or 1,3-propylene. As a result, substituted ortho-phenylenediamine bridges were employed. Electron withdrawing substituents increased the rate of carbonylation while electron donating substituents decreased the rate.

Finally, polymerisation of two β-lactones containing functional groups was investigated for proof of concept. 4-Chloro-β-butyrolactone was polymerised with very little control at 120°C. Decreasing the reaction temperature to 85°C resulted in

Figure 5.11 ¹H NMR spectrum of P(EG₄₅-b-(3HHene₁₃-co-3HH₁₃)) in CDCl₃
very well controlled polymers. Using 58 as a catalyst resulted in moderate conversion while 84 resulted in quantitative conversion. Additionally, 84 could facilitate the reaction at room temperature, requiring longer reaction times. Alkene functionality was introduced into homopolymers and copolymers with PEG/P3HH by polymerisation of β-6-heptenolactone. Homopolymerisation was well controlled with similar dispersity and rate to β-HL polymerisation. Copolymers were synthesised via macroinitiation of mPEG to give products with predictable molecular weights and alkene incorporation. Random copolymerisation of β-6-HEL and β-HL with mPEG macroinitiator yielded copolymers with tunable amounts of alkene functionality where molecular weight could be kept consistent.
Chapter Six
Conclusions and Future Work

The work in this thesis demonstrates that despite significant development of ring-opening polymerisations with aluminium salen and aluminim salan catalysts, there was still much to explore.

First, the polymerisation of common aliphatic monomers was carried out. To date, aluminium salen and salan complexes have been poor at facilitating controlled polymerisation of ε-caprolactone and δ-valerolactone. By controlling the temperature and concentration of the reaction, ε-caprolactone and δ-valerolactone polymerisation resulted in extremely well controlled polymers with extremely fast polymerisation rates. Poly(ε-caprolactone) with molecular weights approaching 200 kDa was prepared with unprecedented dispersity. More interestingly, immortal polymerisation could be preformed with up to 100 equivalents of chain transfer agent, a number considerably higher than ever reported for aluminium catalysts. The use of chain transfer agent was not limited to low molecular weight polymers, with up to 10000 ε-CL turnovers per metal center possible. High molecular weight samples could be prepared through immortal ring-opening polymerisation without sacrifice to polymer control. Extending this to substituted ε-caprolactones showed that addition of steric bulk around the active site caused hindrance in activity. 6-Methyl-ε-caprolactone polymerisation required higher temperatures while bulkier 2,6-dimethyl-ε-caprolactone and (-)-menthidi did not undergo polymerisation at all. Lastly, a functional monomer, 4-(4-benzyloxybutyl)-ε-caprolactone, was investigated.
Racemic and enantioenriched \((R)\) and \((S)\) monomers were studied, showing a likely preference for isotacticity. A block copolymer with \(\varepsilon\)-caprolactone was also prepared; demonstrating a targeted amount of functional monomer can be incorporated into a polymer.

Polymerisation of 2,3-dihydro-5\(H\)-1,4-benzodioxepin-5-one with aluminium salen and salan complexes resulted in the first example of a polyester containing aromatic functionality in the polymer backbone *via* ring-opening polymerisation of cyclic ester monomers. Polymerisation at 120°C resulted in uncontrolled polymer, while 70°C gave only moderate conversion. Performing polymerisations at \(\leq 60^\circ C\) gave high conversion and low dispersity. These polymerisations were in equilibrium between monomer and polymer that could be easily shifted by changing temperature or concentration. AB and ABA block-like copolymers with \(\mathcal{L}\)-lactide were synthesised through sequential addition of monomers, starting from a bifunctional initiator. Scrambling of monomer units during the polymerisation suggested the copolymers were random or gradient like more than block like. Regardless, these copolymers showed considerable thermal stability compared to homopolymers. Copolymers with \(\beta\)-butyrolactone were also synthesised. Polymerisation of \(\beta\)-butyrolactone first allowed for true block copolymers. Exploitation of equilibrium between monomer and polymer was used for depolymerisation of polymer back to monomer, exclusively. This process could be cycled to give polymerisation-depolymerisation-repolymerisation with no loss of control upon repolymerisation. Depolymerisation could be extended to copolymers. As copolymers with \(\mathcal{L}\)-lactide were gradient like, only low degrees of depolymerisation were observed. The block-like nature of copolymers with \(\beta\)-butyrolactone allowed for high depolymerisation of P2HEB to return essentially P3HB homopolymer. Polymerisation of substituted 2,3-DHBs was also attempted but was unsuccessful. This was hypothesised to be due to increased steric bulk hindering activity. This occurred in (substituted) \(\varepsilon\)-caprolactone polymerisation. Other aromatic containing monomers were studied but unsuccessful. These monomers showed that both ring size and orientation of the ester linkage is crucial for polymerisation activity.

Polymerisation of alkyl-substituted \(\beta\)-lactones was carried out using aluminium salen and aluminium salan catalysts. Homopolymerisation was very
successful with 58, 64, and 84. Polymerisation of could be performed with any of the
catalysts between 70 and 120°C with no significant change to polymer properties.
Increasing the ratio of monomer to initiation/catalyst had the best results with 58 at
higher temperatures. Random copolymerisation of β-lactone and L-lactide with 58
was successful, with gradient-block copolymers being formed. Well defined ABA
triblock copolymers were synthesised from L-lactide (A block) and β-butyrolactone,
β-valerolactone and β-heptanolactone with varying ratios of monomer feeds.
Thermal analysis revealed that copolymers generated from β-butyrolactone and β-
valerolactone gave tunable thermal properties that could be accurately controlled by
changing monomer feed ratios. Copolymers from β-heptanolactone gave copolymers
with microphase separation as confirmed by DSC and SAXS characterisation. These
copolymers were thermoplastic elastomers and could be cast into transparent films.
The tensile properties were also measured and showed a significant increase in
elastomeric behavior compared to poly(lactic acid) homopolymer. Copolymers with
a poly(D-lactic acid) and a poly(L-lactic acid) block were also prepared and showed
similar characteristics.

In situ generation of active catalysts for epoxide carbonylation was studied.
Large scale synthesis of alkyl-substituted β-lactones could be achieved using a
tetraphenylporphyrin chromium (III) catalyst system. Extending to salen supported
cromium (III) complexes allowed for modification to the ligand framework to show
their effect on catalytic activity. Changing phenoxide substitution from tert-butyl to
either electron withdrawing chloro groups or electron donating but excessively bulky
adanantyl groups resulted in significant suppression on activity. Changing the
diimine bridge from a rigid ortho-phenylene to more flexible alkyl bridge also
resulted in decreased activity. Modification of Coates’ literature salen supported
cromium (III) catalyst was investigated by addition of electron donating or electron
withdrawing groups to the ortho-phenylene bridge. While the changes resulted in
only a small change in catalyst rate, a trend was observed. Electron withdrawing
groups increased the rate of carbonylation while electron donating groups slowed
activity slightly.

In situ generation of Coates salen catalyst was optimised to produce 4-chloro-
β-butyrolactone. Polymerisation of 4-chloro-β-butyrolactone was easily achieved,
with low dispersity and fast rates at 85°C. Additionally, polymers were very well controlled, with dispersity < 1.05. 84 was more efficient than 58 as higher conversions were achieved. Increasing the polymerisation temperature to 120°C resulted in broad dispersities while decreasing to 22°C slowed polymerisation considerably. Synthesis of β-6-heptenolactone was achieved with the tetraphenylporphyrin chromium (III) system. This monomer could be used in homopolymerisation with excellent control. Using monomethyl poly(ethylene glycol) as a macrorinitiator, block and block-random (with β-heptanolactone) copolymers were synthesised. This resulted in tunability in ratio of poly(ethylene glycol) to poly(3-hydroxyalkanoate) as well as relative amount of alkene functionality.

There are many avenues of research the work presented in this thesis could lead to. For aliphatic seven-membered rings, further study of ε-CL and substituted ε-CLs is warranted. Expanding to different aluminium salen catalyst may allow for tuning of rate (Figure 6.1). Using a bulkier catalyst (100) could decrease the rate of ROP for ε-CL and reduce transesterification. Conversely, using a less bulky catalyst (45) could increase the rate of polymerisation, allowing for more rapid polymerisation of 6-Me-ε-CL. Additionally, this may allow for ROP with the bulkiest substituted ε-CLs studied, 2,6-Me-ε-CL and Menth. This may also be achieved by using complex 66, which was one of the fastest catalysts for rac-lactide polymerisation.

ROP results of 4-(4-benzylloxbutyl)-ε-caprolactone are very promising, with the rates of polymerisation for racemic and enantioenriched monomers being studied. However, the properties of these materials are still underexplored. Namely, the
thermal properties warrant future study. As the tacticity for poly(lactic acid) has a large effect on thermal properties, this polymer could have a similar effect. Thermal properties of isotactic enriched polymer and atactic polymer are to be studied. A difference in thermal properties could give insight as to whether the difference in rate of polymerisation is in fact due to an isotactic polymerisation. Additionally, deprotection of homopolymer and copolymers will also be investigated further. A wider range of conditions and deprotection routes will be attempted. If successful, these (co)polymers may serve as excellent brush copolymer macroinitiators. Brush copolymer synthesis (Scheme 6.1) with a range of ring-opening polymerisation will be investigated.

\[\text{Scheme 6.1 Proposed synthesis of P(4-BOB-\epsilon-CL-br-LA) and P(4-BOB-\epsilon-CL-br-3HB)}\]

Aromatic containing polymer backbones are incredibly beneficial in commercial polymers. The discovery of polyesters with aromatic backbone functionality could open up significant research efforts. Effort will be put towards synthesis of polymers from substituted 2,3-DHBs. Introduction of substitution could yield significant improvement. Methyl-substitution may offer many of the advantages of poly(lactic acid) tunability. In particular, the ability to control stereoregularity though either stereospecific catalyst or an enantioenriched monomer source will allow for this study. Phenyl-substitution may also offer improvements. Using salen catalysts 45 and 66 may allow for ROP for the reasons discussed for substituted \(\epsilon-\text{CL ROP}\).
Exploiting the depolymerisation observed in converting P2HEB to 2,3-DHB is a potential route to synthesise substituted 2,3-DHB monomers (Scheme 6.2). First, synthesis of the corresponding polyesters would be achieved through condensation polymerisation, followed by selective depolymerisation to afford substituted 2,3-DHB monomer. This would offer an advantage over the route used in this thesis in that an expensive rhodium catalyst would be replaced with a less expensive aluminium catalyst.

![Scheme 6.2 Alternative synthesis of substituted 2,3-DHBs](image)

ABA block copolymers were very tunable, with the tunability achieved through changing the alkyl-substituent of the β-lactone. Results from Kimura showed that the tacticity of the polymer could also have a large impact on polymer properties. Heterotactic and atactic poly(lactic acid) should be investigated to determine how important the semi-crystalline nature of the poly(lactic acid) blocks are towards properties. In particular, this would be interesting to investigate whether changing the poly(lactic acid) blocks in samples that exhibit phase separation to an amorphous poly(lactic acid) block has an effect on said phase separation. This would give insight on whether the incompatibility of the two polymer types is driven by amorphous/semi-crystalline interactions or hydrophobic/hydrophilic interactions. Additionally, stereoregularity of the poly(3-hydroxyalkanoate) block should also be studied. This could be done by using an enantiopure monomer source (isotactic) or a designed catalyst (isotactic or syndiotactic). The use of a designed catalyst may take away from the one pot nature of the system if sequential addition of monomers cannot be used but still warrants study. Higher molecular weight ABA triblock copolymers could also be synthesised. This would allow for better comparison to literature polymers prepared where the molecular weight exceeds 100 kDa.
In situ generation of active carbonylation catalysts allows for facile screening of catalysts. This will be expanded to novel chromium (III) complexes. Attempted synthesis of anilido aldimine and phosphasalen complexes was performed (Scheme 6.3, 6.4). The synthesis of these complexes was attempted but results were not included in this thesis. Initially, synthesis of the chromium (III) anilido aldimine complex was attempted through a similar route as the analogous salen complexes. This yielded an impure purple oil. Isolation of the deprotonated anilido aldimine ligand, followed by salt metathesis with CrCl₃(THF)₃ appeared to be more successful. A deep red solid was afforded and was characterised by ESI mass spec and Evans method (for magnetic susceptibility). Unfortunately, no suitable crystal for X-ray diffraction was obtained. Synthesis of chromium (III) phosphasalen complexes was attempted via a similar route. The potassium salt of the ligand was first isolated, followed by salt metathesis with CrCl₃(THF)₃ yielded deep green coloured solids that were characterised by ESI mass spectrometry and Evans method. Again, no suitable crystals for X-ray diffraction were obtained. Incomplete characterisation made carbonylation screening results inconclusive as to whether they were reliable. Future work will optimise the synthesis of these families of catalysts and obtain full characterisation.

Scheme 6.3 Attempted synthetic routes for a chromium (III) anilido aldimine complex
Functional β-lactone synthesis and subsequent polymerisation will be studied in greater detail. More specifically, the range of functional groups for polymerisation will be expanded. Many functional β-lactones can be synthesised and should be used for polymerisation. Additionally, functional groups that have not been included in β-lactone synthesis will also be screened. For example, phosphonate-substituted epoxides are easily accessible but have not been tested for carbonylation (Scheme 6.5). Phosphonate functionality may be useful in many of the reactions β-lactones are used as intermediates in, including ring opening polymerisation.

Polymerisation of 4-chloro-β-butyrolactone should be followed up. In particular, post polymerisation modification of the chloro group could be extremely useful. Similar polyethers have been reacted to convert the chloro group to an azide group. This could allow for facile addition of many groups through click chemistry. Post polymerisation modification is not limited to chloro substituted polymers. Alkene functionalised polymers from β-6-heptenolactone polymerisation are excellent candidates for post polymerisation reactions. One possible route is to incorporate a wide range of functional groups through alkene cross-metathesis. This would allow for introduction to a large range of functional groups.
Chapter Seven

Experimental Procedures

7.1 General considerations

All experiments involving moisture- and air-sensitive compounds were performed under a nitrogen atmosphere using an MBraun LABmaster sp glovebox system or a Vigor glovebox equipped with a −35 °C freezer and [H₂O] and [O₂] analysers or using standard Schlenk techniques. Gel permeation chromatography (GPC) was carried out in THF at a flow rate of 1 mL min⁻¹ on a Malvern Instruments Viscotek 270 GPC Max triple detection system with 2 × mixed bed styrene/DVB columns (300 × 7.5 mm). GPC analysis was performed using OmniSEC 5.0 software. ¹H and ¹³C NMR spectra were recorded at 298 K with Bruker Avance spectrometers (400 or 500 MHz) in CDCl₃ or C₆D₆. The dn/dc values for PLA, P3HB and PCL were 0.051, 0.065 and 0.072, respectively. The dn/dc values for P3HP, P3HH and P3HTD were calculated using OmniSEC 5.0 software to be 0.060, 0.059 and 0.059, respectively. Calculation of dn/dc values was achieved by duplicate GPC runs of two samples for three different molecular weights with known concentration for each sample. dn/dc values were taken as the average of all calculated dn/dc calculated by OmniSEC 5.0 software. Differential scanning calorimetry (DSC) was carried out using a TA Instruments DSC Q2000 instrument. The samples were heated from -90°C to 200°C at a rate of 20°C/min after an initial heating scan to 200°C (heating rate of 20°C/min) to remove any residual solvent. Values of Tₓ, Tₘ.
and $T_c$ were obtained from the 2nd heating scan (-90°C to 200°C). $T_g$ values were determined from the midpoint of the transition, while $T_m$ and $T_c$ values were calculated as the peak endotherm or exotherm of the respective transitions. Synchrotron small-angle X-ray scattering (SAXS) measurements were performed by Prof. Ian Hamley and Daniel Hermida-Merino on BM26B (DUBBLE) at the European Synchrotron Radiation Source, Grenoble, France. The sample to SAXS detector distance was ca. 2.095 m using a wavelength $\lambda = 1.033$ Å. A Dectris-Pilatus 1M detector with a resolution of 981 × 1043 pixels and a pixel size of 172 × 172 µm was employed used to record the 2D SAXS scattering patterns. Standard corrections for sample absorption and background subtraction have been performed. The data were normalized to the intensity of the incident beam (in order to correct for primary beam intensity fluctuations) and were corrected for absorption, background scattering. The scattering pattern from rat tail collagen were used for the calibration of the wavenumber ($q = 4\pi\sin(q/l)$) scale of the scattering curve. The sample was placed in a DSC pan modified with kapton windows and heated using a Linkam hotstage from -50°C to 150°C and cooled back to -50°C and then heated again to 150°C all at a rate of 5°C/min. SAXS data frames were acquired each 30 seconds during this process. Tensile measurements were obtained using a TA XTplus Texture Analyser using Texture Exponent 32 software under ambient conditions. Films were cast by slow evaporation of CHCl₃ followed by drying. Samples of 3mm×40mm were cut from the middle of the film to avoid edge defects. To avoid sample slippage or damage from the instrument grips, the top and bottom of the sample were placed between cardboard before loading. 2.7.2. mPEG ($M_n = 2000$ Da) was purchased from Sigma Aldrich and dried by heating under vacuum for several hours at 60°C. 1,2-Epoxybutane, 1,2-epoxyhexane, 1,2-epoxy-5-hexene, epichlorohydrin and epibromohydin were dried by stirring over CaH₂ for 18 hours, followed by distillation under inert atmosphere prior to use. 1,2-Epoxydodecane was dried by stirring over CaH₂ for 18 hours and filtration under inert atmosphere prior to use. $H_2\text{[salen]}^{\text{BuPh}}$, $H_2\text{[salen]}^{\text{ClPh}}$, $H_2\text{[salen]}^{\text{Ph}}$, $H_2\text{[salen]}^{\text{BuEt}}$, $H_2\text{[salen]}^{\text{BuPr}}$, $H_2\text{[salen]}^{\text{ClEt}}$, $H_2\text{[salen]}^{\text{ClPr}}$, $H_2\text{[salen]}^{\text{BuPh-Cl}}$, $H_2\text{[salen]}^{\text{BuPh-F}}$, $H_2\text{[salen]}^{\text{BuPh-Me}}$ and $H_2\text{[salen]}^{\text{BuPh-OMe}}$ and $H_2\text{[salen]}^{\text{BuPh-MeMe}}$ were synthesised.
according to modified literature procedures. All $^1$H and spectra were consistent with literature reports.

### 7.2 Materials

58 and 84 were synthesised via modified literature procedures.\[^{81, 183}\] Benzyl alcohol was dried by refluxing over calcium hydride for 24 h, distilled under inert atmosphere and degassed by three freeze–pump–thaw cycles prior to use. Toluene was obtained from an Innovative Technologies solvent purification system, consisting of columns of alumina and copper catalyst and was degassed by three freeze–pump–thaw cycles prior to use. C$_6$D$_6$ was refluxed over potassium for 72h, distilled under inert atmosphere and degassed by three freeze-pump-thaw cycles prior to use. $\varepsilon$-Caprolactone was stirred over calcium hydride for 24 hours, distilled under inert atmosphere and degassed by three freeze-pump-thaw cycles prior to use. L-$\alpha$-Lactide was purified by three vacuum sublimations and dried under reduced pressure for 18 h prior to use. 2,3-dihydro-5$H$-1,4-benzodioxepin-5-one (2,3-DHB) was recrystallised three times from EtOAC:hexanes (50:50) followed by drying under vacuum at 60˚C for 18h prior to use. $\beta$-VL and $\beta$-HL were synthesised (vide supra), distilled to remove catalyst residue, stirred over CaH$_2$ for 24 hours, distilled under inert atmosphere and degassed by three freeze-pump-thaw cycles prior to use. $\beta$-TDL was synthesised (vide supra) and purified by column chromatography before use (SiO$_2$, 10% EtOAc in hexanes).

### 7.3 Synthesis of starting materials and catalysts

**Synthesis of 2-(1,3-dioxan-2-yl)phenol:** Tetra-$n$-butylammonium tribromide (0.12 g, 0.5 mmol) was slowly added to a stirring solution of salicylaldehyde (6.00 g, 49.1 mmol), 1,3-propanediol (14.96 g, 196.5 mmol) and triethylorthofomate (8.01 g, 54.0 mmol) at ambient temperature. The solution was stirred for three hours at room temperature. After three hours, 50 mL of EtOAc was added to the solution. The solution was then washed with 25 mL of brine. The organic layer was dried over Na$_2$SO$_4$ and concentrated to leave pale yellow oil. Impurities were then removed by
distillation (Kugelrohr, 115°C) to leave 6.50 g (73%) of the desired product as a white crystalline solid. \(^1\text{H}\) NMR characterisation was consistent with literature reports.\(^ {184}\) \(^1\text{H}\) NMR (400MHz, CDCl\(_3\)): \(\delta\) 7.89 (s, 1H, \(\text{O}H\)), 7.24, (m, 2H, Ar\(H\)), 6.91 (m, 2H, Ar\(H\)), 5.67 (s, 1H, Ar\(\text{CHO}_2\)), 4.33 (dd, \(J = 13.2, 4.9\text{Hz}\), 2H, O\(\text{CH}_3\)\(\text{H}_2\)\(\text{CH}_2\)), 4.03 (ddd, 2H, \(J = 12.2, 3.9, 2.5\text{Hz}\) O\(\text{CH}_3\)\(\text{H}_2\)\(\text{CH}_2\)), 2.29 (dtt, \(J = 13.5, 12.5, 5.0\text{Hz}\), 1H, O\(\text{CH}_3\)\(\text{H}_2\)\(\text{CH}_2\)), 1.52 (dtt, \(J = 13.2, 2.6, 1.4\text{Hz}\), 1H, O\(\text{CH}_3\)\(\text{H}_2\)\(\text{CH}_2\)).

**Synthesis of 1-(2-(1,3-dioxan-2-yl)phenoxy)propanone:** 2-(1,3-Dioxan-2-yl)phenol (4.46 g, 25 mmol) was dissolved in 50 mL of acetone. K\(_2\)CO\(_3\) (6.9 g, 50 mmol) of was added to the solution and the resulting suspension was stirred for 30 minutes. After 30 minutes, KI (5.0g, 30 mmol) was added followed by dropwise addition of chloroacetone (2.40 mL, 30 mmol). The suspension was then stirred for 18 hours at room temperature or 6 hours under reflux. After the desired time, the suspension was filtered and the filtrate was added to 50mL of EtOAc, washed with brine, dried over Na\(_2\)SO\(_4\) and concentrated to leave a deep yellow residue. The residue was purified by column chromatography (EtOAc:hexanes 1:10) to yield a white solid (4.11g, 70%). \(^1\text{H}\) NMR characterisation was consistent with literature reports.\(^ {129a}\) \(^1\text{H}\) NMR (500MHz, CDCl\(_3\)): \(\delta\) 8.01 (dt, \(J = 8.4, 1.4\text{Hz}\), 1H, Ar\(H\)), 7.66 (dd, \(J = 7.5, 1.7\text{Hz}\), 1H, Ar\(H\)), 7.62 (dt, \(J = 7.5, 1.4\text{Hz}\), 1H, Ar\(H\)), 7.50 (dd, \(J = 7.5, 3.7, 1.7\text{Hz}\), 1H, Ar\(H\)), 7.28 (dd, \(J = 8.4, 7.5, 1.7\text{Hz}\), 1H), 7.04 (td, \(J = 7.5, 0.8\text{Hz}\), 1H, Ar\(H\)), 6.84

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(dd, J = 8.3, 0.8 Hz, 1H, ArH), 5.94 (s, 1H, ArCHO₂), 5.25 (s, 1H, OCH₂COPh), 4.21 (ddd, J = 11.8, 5.0, 1.2 Hz, 2H, OCH₃H₈CH₃H₂D), 3.95 (ddd, J = 12.4, 3.9, 2.5 Hz, 2H, OCH₃H₈CH₃H₂D), 2.22 (m, 1H, OCH₃H₈CH₃H₂D), 1.40 (dtt, J = 13.4, 2.5, 1.3 Hz, 1H, , OCH₃H₈CH₃H₂D).

Synthesis of 2-(2-oxopropoxy)benzaldehyde:

Method A

1-(2-(1,3-Dioxan-2-yl)phenoxy)propanone (1.78 g, 7.5 mmol) was dissolved in 18 mL of THF, cooled to 0°C, and stirred for 15 minutes. After 15 minutes, 2M HCl (7.5 mL, 15 mmol) was added dropwise. The solution was then allowed to heat to room temperature and stir for 16 h. After 16 h, the solution was neutralised with NaHCO₃(aq) and extracted with EtOAc. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. The remaining residue was purified by column chromatography (EtOAc:hexanes 1:4) to yield 1.18g (88%) of the desired product. ¹H NMR characterisation was consistent with literature reports.¹²⁹a ¹H NMR (500 MHz, CDCl₃): δ 10.56 (s, 1H, CHO), 7.86 (dd, J = 7.7, 1.8 Hz, 1H, ArH), 7.53 (ddd, J = 8.4, 7.4, 1.8 Hz, 1H, ArH), 7.09 (ddd, J = 7.7, 7.4, 1.8 Hz, 1H, ArH), 6.81 (dd, J = 8.4, 1.8 Hz, 1H, ArH), 4.66 (s, 2H, OCH₂C(O)CH₃), 2.32 (s, 3H, OCH₂C(O)CH₃).

Method B

1-(2-(1,3-Dioxan-2-yl)phenoxy)propanone (1.78 g, 7.5 mmol) was dissolved in 18 mL of THF. Para-toluenesulfonic acid monohydrate (0.15 g, 0.8 mmol) in distilled water (5mL) was added to the solution. The solution was then heated to 80°C for 2 h. After 2 h, the solution was cooled to room temperature and 15 mL of CH₂Cl₂ was added. The solution was then washed with NaHCO₃(aq), dried over Na₂SO₄ and concentrated to yield 1.21 (89%) of a pale yellow solid which was purified by column chromatography (EtOAc:hexane 1:4). ¹H NMR spectroscopic analysis was consistent with previously reported data.

Synthesis of 2-(2-oxo-2-phenylethoxy)benzaldehyde: Synthesis was achieved as for Method B. Product was purified by recrystallisation from EtOAc. ¹H NMR characterisation was consistent with literature reports.¹²⁹a ¹H NMR (500 MHz, CDCl₃): δ 10.58 (s, 1H, CHO), 7.99 (dd, J = 8.4, 1.2 Hz, 2H, C(O)Ph), 7.87 (dd, J =
7.8, 1.8 Hz, 1H, ArH), 7.65 (ddd, J = 8.2, 7.5, 1.8 Hz 1H, ArH), 7.51 (m, 3H, C(O)Ph), 7.09 (ddd, J = 7.8, 7.5, 1.8 Hz 1H), 6.87 (dd, J = 8.2, 1.8 Hz, 1H, ArH), 5.43 (s, 2H, OCH₂C(O)Ph).

**Synthesis of [Rh(phosphine)]BF₄:** In a nitrogen filled glovebox, [Rh(nbd)₂]BF₄ (29 mg, 0.08 mmol) and phosphine (DTBM-SEGPHOS® or 1,3-bis(diphenylphosphino)propane, 1.1 equivalents) were dissolved in CH₂Cl₂ (3 mL), added to an ampoule and removed from the glovebox. The ampoule was degassed three times by freeze-pump-thaw cycles and refilled with one atmosphere of H₂. The ampoule was left open to H₂ for 30 minutes where a color change from orange to deep red was observed. The reaction was then concentrated and used in subsequent hydroacylation reactions without further purification.

**Synthesis of ClCr[salen]^{Rbridge-XY} complexes:** In a nitrogen filled glovebox, CrCl₂ (1.1 equivalents) was added to a stirring solution of free ligand in THF. The solution was stirred at room temperature for four hours under nitrogen. After four hours, the reaction vessel was opened to air and stirred for 18 h. After 18 h, the solution was diluted with Et₂O, washed three times with NH₄Cl (aq), twice with NaCl (aq), dried over Na₂SO₄ and concentrated. The dark solid was then recrystallised from hot acetonitrile to leave a deep red solid. The complexes were characterised by ESI mass spec.

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m/z: \text{ClCr[salen]}^{\text{BuPh}}: [\text{Cr}^+]; 590.3 \text{ (theo.)} 590.3 \text{ (exp.)} \text{ClCr[salen]}^{\text{ClPh}}: [\text{Cr}^+]; 503.9 \text{ (theo.)} 527.9 \text{ (exp., [Cr}^+ + \text{Na)} ClCr[salen]}^{\text{AdPh}}: [\text{Cr}^+]; 662.3 \text{ (theo.)} 662.3 \text{ (exp.)} ClCr[salen]}^{\text{BuEl}}: [\text{Cr}^+]; 542.3 \text{ (theo.)} 542.4 \text{ (exp.)} \text{ClCr[salen]}^{\text{BuPr}}: [\text{Cr}^+]; 556.3 \text{ (theo.)} 556.4 \text{ (exp.)} \text{ClCr[salen]}^{\text{ClEt}}: [\text{Cr}^+]; 455.9 \text{ (theo.)} 455.9 \text{ (exp.)} \text{ClCr[salen]}^{\text{ClPr}}: [\text{Cr}^+]; 469.9 \text{ (theo.)} 469.9 \text{ (exp.)} \text{ClCr[salen]}^{\text{BuPh-Cl}}: [\text{Cr}^+]; 624.3 \text{ (theo.)} 624.3 \text{ (exp.)} \text{ClCr[salen]}^{\text{BuPh-F}}: [\text{Cr}^+]; 608.3 \text{ (theo.)} 608.4 \text{ (exp.)} \text{ClCr[salen]}^{\text{BuPh-OMe}}: [\text{Cr}^+]; 620.3 \text{ (theo.)} 643.4 \text{ (exp., [Cr}^+ + \text{Na)} \text{ClCr[salen]}^{\text{BuPh-Me}}: [\text{Cr}^+]; 618.3 \text{ (theo.)} 618.4 \text{ (exp.)}
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7.4 Synthesis of monomers

Synthesis of monomers by Baeyer-Villager oxidation of ketones: According to a modified literature report,

A typical procedure for Baeyer-Villager oxidation was as follows. To a vigorously stirring suspension of sodium percarbonate (98.92 g, 630 mmol), ketone (45.8 mmol) and dry dichloromethane (400 mL) was added trifluoroacetic anhydride (25.7 mL) dropwise. This suspension was allowed to stir at room temperature for 16 hours with venting. After 16 hours, the suspension was filtered and washed with CH$_2$Cl$_2$ (~100 mL). The organic layer was washed with NaHCO$_3$(aq) until neutral. The organic layer was then dried over Na$_2$SO$_4$ and concentrated. The crude mixture was then purified by column chromatography, recrystallisation or distillation under reduced pressure.

6-methyl-ε-caprolactone (6-Me-ε-CL): From 2-methylcyclohexanone. Distilled under reduced pressure (105°C, Kugelrohr). $^1$H NMR characterisation was consistent with literature reports.$^{[185]}$ $^1$H NMR (400 MHz, CDCl$_3$): δ 4.45 (m, 1H, C(O)OC$_2$H$_5$), 2.64 (m, 2H, C(O)CH$_2$), 1.62-1.92 (m, 6H, C(O)OCHCH$_3$(CH$_2$)$_3$CH$_2$), 1.62 (m, 3H), 1.36 (d, J = 6.3 Hz, 3H, C(O)OCHCH$_3$).

2,6-dimethyl-ε-caprolactone (2,6-Me-ε-CL): From 2,6-dimethylcyclohexanone (mixture of isomers). Distilled under reduced pressure (110°C, Kugelrohr). $^1$H NMR characterisation was consistent with literature reports.$^{[186]}$ $^1$H NMR (500 MHz, C$_6$D$_6$): δ 4.16, 3.91 (m, 1H, C(O)OCHCH$_3$), 2.71, 2.22 (m, 1H, C(O)CHCH$_3$), 1.41 – 1.11 (m, 6H, C(O)OCHCH$_3$(CH$_2$)$_3$CHCH$_3$), 1.08, 1.03 (d, J = 6.7, 6.4 Hz, 3H, C(O)OCHCH$_3$), 1.02, 1.01 (d, J = 7.5, 6.5 Hz, 3H, C(O)CHCH$_3$).

1,4-dioxepin-5-one (1,4-DPO): From tetahydro-4H-pyran-4-one. Distilled under reduced pressure (120°C, Kugelrohr) to yield the desired product. $^1$H NMR characterisation was consistent with literature reports.$^{[187]}$ $^1$H NMR (500 MHz, CDCl$_3$): δ 4.31 (m, 2H, C(O)OCH$_2$CH$_2$O), 3.91 (m, 2H, C(O)CH$_2$CH$_2$O), 3.84 (m, 2H, C(O)OCH$_2$CH$_2$O), 2.91 (m, 2H, C(O)CH$_2$CH$_2$O).

(-)-Menthide (Menth): From l-menthane. Purified by column chromatography (SiO$_2$, 4:1 hexanes:EtOAc). $^1$H NMR characterisation was consistent with literature
reports.\textsuperscript{[146]} $^1$H NMR (500 MHz, CDCl$_6$): $\delta$ 4.04 (dd, $J = 9.2, 4.3$ Hz, 1H, C(O)OCHCH(CH$_3$)$_2$CH$_2$), 2.50 (m, 2H, C(O)OCHCH(CH$_3$)$_2$CH$_2$), 1.89 (m, 4H, CH$i$PrCH$_2$CH$_2$CHCH$_3$), 1.60 (m, 1H, CH$i$PrCH$_2$CH$_2$CHCH$_3$), 1.29 (m, 1H, C(O)OCHCH(CH$_3$)$_2$CH$_2$), 1.04 (d, $J = 6.7$ Hz, 3H, CH$i$PrCH$_2$CH$_2$CHCH$_3$), 0.97 (t, 6.8 Hz, 6H, C(O)OCHCH(CH$_3$)$_2$CH$_2$).

3,4-Dihydro-2H-1,5-benzodioxepin-2-one (3,4-DHB): From 4-chromanone. Purified by either recrystallisation from hot CH$_2$Cl$_2$ or column chromatography (EtOAc:hexanes = 4:1). The product was isolated as an off white solid that was only sparingly soluble in CDCl$_3$ or $d_6$-DMSO. $^1$H NMR characterisation was consistent with literature reports.\textsuperscript{[188]} $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 6.93 (m, 3H, ArH), 6.83 (m, 1H, ArH), 4.28 (t, $J = 5.9$ Hz 2H, C(O)CH$_2$CH$_2$O), 2.88 (t, $J = 5.9$ Hz 2H, C(O)CH$_2$CH$_2$O). $^{13}$C NMR (101 MHz, CDCl$_3$): 176.26, 147.00, 145.47, 123.24, 120.31, 115.56, 114.57, 65.30, 34.15. $^1$H NMR (400 MHz, DMSO-$_d_6$): $\delta$ (ppm) 6.91 (d, $J = 8.3$ Hz, 1H, ArH), 6.74 (m, 3H, ArH), 4.13 (t, $J = 6.1$ Hz, 2H, C(O)CH$_2$CH$_2$O), 2.70 (t, $J = 6.1$Hz, 2H, C(O)CH$_2$CH$_2$O). $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta$ (ppm) 172.47, 147.04, 146.59, 121.52, 119.22, 115.78, 114.41, 64.61, 34.15.

Synthesis of substituted 2,3-DHBs Synthesis of 3-methyl and 3-phenyl substituted 2,3-DHB monomers were performed under identical conditions. A typical procedure was as follows. In a nitrogen filled glovebox, 2-(2-oxo-2-phenylethoxy)benzaldehyde (108mg, 0.6mmol) was added to an 15mL oven-dried ampoule in dry CH$_2$Cl$_2$ (5mL). [Rh(phosphine)]BF$_4$ (0.03mmol) was then added and the ampoule was sealed and stirred at room temperature for 3.5 – 24 hours. After the desired amount of time, the reaction mixture was concentrated and purified by column chromatography (EtOAc:hexanes = 4:1) to yield the desired product with all yields $\geq$90%.

3-Methyl-2,3-dihydro-5H-1,4-benzodioxepin-5-one (3-Me-2,3-DHB): $^1$H NMR characterisation was consistent with literature reports.\textsuperscript{[129a]} $^1$H NMR (400 MHz, C$_6$D$_6$): $\delta$ 8.01 (dd, $J = 7.9, 1.7$ Hz, 1H, ArH), 7.03 (ddd, $J = 8.3, 7.2, 1.7$ Hz, 1H, ArH), 6.80 (dd, $J = 8.3, 0.9$ Hz, 1H, ArH), 6.74 (m, 1H, ArH), 3.90 (dqd, $J = 8.5,
6.6, 1.9 Hz, 1H, CH$_2$CHCH$_3$H$_2$O), 3.67 (dd, $J = 12.3$, 8.5 Hz, 1H, CH$_3$CHCH$_2$H$_2$O), 3.47 (dd, $J = 12.3$, 1.9 Hz, 1H, CH$_2$CHCH$_3$H$_2$O), 0.70 (d, $J = 6.6$ Hz, 3H, CH$_3$CHCH$_3$H$_2$O). $^{13}$C NMR (101 MHz, C$_6$D$_6$): $\delta$ 167.42, 155.45, 134.36, 133.80, 122.85, 121.53, 120.97, 75.41, 71.78, 16.06.

3-Phenyl-2,3-dihydro-5H-1,4-benzodioxepin-5-one (3-Ph-2,3-DHB): $^1$H NMR characterisation was consistent with literature reports.$^{[129a]}$ $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.90 (dd, $J = 7.9$, 1.8 Hz, 1H, ArH), 7.55 (m, 1H, ArH), 7.40 (m, 5H, PhCHCH$_3$H$_2$O), 7.21 (m, 1H, ArH), 7.09 (dt, $J = 10.6$, 5.3 Hz, 1H, ArH), 5.57 (dd, $J = 9.5$, 2.4 Hz, 1H, PhCHCH$_3$H$_2$O), 4.58 (dd, $J = 12.4$, 9.5 Hz, 1H, PhCHCH$_3$H$_2$O), 4.42 (dd, $J = 12.4$, 2.4 Hz, 1H, PhCHCH$_3$H$_2$O).

Synthesis of 4H-1,3-benzodioxin-4-one: Phenyl salicylate (21.4 g, 100 mmol), paraformaldehyde (15.0 g, 500 mmol) and DABCO (11.2 g, 100 mmol) were added to CHCl$_3$ (10 mL) and stirred at room temperature for 24 hours. After 24 hours, the slurry was filtered and washed with warm CHCl$_3$ (100 mL), dried over Na$_2$SO$_4$ and concentrated. The crude oil was then distilled under reduced pressure (110°C, Kugelrohr) to furnish 11.5 g (77%) of the desired product as a white solid. $^1$H NMR characterisation was consistent with literature reports.$^{[189]}$ $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 9.00 (dd, $J = 7.8$, 1.7 Hz, 1H, ArH), 7.58 (ddd, $J = 8.3$, 7.4, 1.7 Hz, 1H, ArH), 7.20 (ddd, $J = 8.3$, 7.8, 1.0 Hz, 1H, ArH), 7.07 (dd, $J = 7.4$, 1.0 Hz, 1H, ArH), 5.66 (s, 2H, C(O)OCH$_2$O). $^1$H NMR (500 MHz, C$_6$D$_6$): $\delta$ 7.92 (dd, $J = 7.8$, 1.6 Hz, 1H, ArH), 6.88 (m, 1H, ArH), 6.57 (m, 2H, ArH), 4.74 (s, 2H, C(O)OCH$_2$O).

7.5 Polymerisation procedures

Representative living homopolymerisation of $\varepsilon$-CL: In a nitrogen filled glovebox, $\varepsilon$-CL (114 mg, 1.0 mmol), 58 (5.4 mg, 0.01 mmol) and BnOH (1.0 µL, 0.01 mmol) were added to toluene (600 mg). The reaction was stirred at room temperature for a desired time interval. Once the desired time interval was reached, 0.5 mL of a 10% MeOH in CH$_2$Cl$_2$ was added to quench polymerisation. A crude sample was taken and dried before $^1$H NMR spectroscopic analysis to determine conversion. The
remainder was added dropwise to cold methanol and the precipitate was filtered and dried until constant weight. The procedure was repeated for all monomers.

**Poly(e-caprolactone) (PCL):** $^1$H NMR characterisation was consistent with literature reports.$^{[190]}$ $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 4.04 (t, $J = 6.7$ Hz, 2H, C(O)OCH$_2$(CH$_2$)$_3$CH$_2$), 2.28 (t, $J = 7.5$ Hz, 2H, C(O)OCH$_2$(CH$_2$)$_3$CH$_2$), 1.64 (m, 4H, C(O)OCH$_2$(CH$_2$)$_2$CH$_2$CH$_2$), 1.36 (m, 2H, C(O)OCH$_2$(CH$_2$)$_2$CH$_2$CH$_2$); (500 MHz, C$_6$D$_6$): $\delta$ 3.95 (t, $J = 6.7$ Hz, C(O)OCH$_2$(CH$_2$)$_3$CH$_2$), 2.09 (t, $J = 7.4$ 2H, C(O)OCH$_2$(CH$_2$)$_3$CH$_2$), 1.49 (m, 2H, C(O)OCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$), 1.40 (m, 2H, C(O)OCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$), 1.18 (m, 2H, C(O)OCH$_2$CH$_2$CH$_2$CH$_2$). 95%, $M_{n,th}$ = 10950, $M_n = 10450$, $D = 1.01$.

**Polyvalerolactone (PVL):** $^1$H NMR characterisation was consistent with literature reports.$^{[191]}$ $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 4.06 (t, $J = 6.0$ Hz, 2H, C(O)OCH$_2$(CH$_2$)$_2$CH$_2$), 2.32 (t, $J = 7.0$ Hz, 2H, C(O)OCH$_2$(CH$_2$)$_2$CH$_2$), 1.66 (m, 4H, C(O)OCH$_2$(CH$_2$)$_2$CH$_2$); (500 MHz, C$_6$D$_6$): $\delta$ 3.94 (t, $J = 6.5$ Hz, 2H, C(O)OCH$_2$(CH$_2$)$_2$CH$_2$), 2.07 (t, $J = 7.3$ Hz, 2H, C(O)OCH$_2$(CH$_2$)$_2$CH$_2$), 1.54 (m, 2H, C(O)OCH$_2$CH$_2$CH$_2$), 1.43 (m, 2H, C(O)OCH$_2$CH$_2$CH$_2$). 93%, $M_{n,th}$ = 9420, $M_n = 9300$, $D = 1.05$.

**Poly(7-methylcaprolactone):** $^1$H NMR characterisation was consistent with literature reports.$^{[95]}$ $^1$H NMR (500 MHz, C$_6$D$_6$): $\delta$ 4.93 (m, 1H, C(O)OCHCH$_3$), 2.13 (t, $J = 7.4$ Hz 2H, C(O)CH$_2$), 1.14 – 1.59 (m (broad), 6H C(O)CH$_2$(CH$_2$)$_3$), 1.08 (d, $J = 6.2$ Hz, 3H).

**Poly(1,4-dioxepin-5-one (1,4-DPO):** $^1$H NMR characterisation was consistent with literature reports.$^{[114g]}$ $^1$H NMR (500 MHz, C$_6$D$_6$): $\delta$ 4.06 (m, 2H, C(O)OCH$_2$), 3.50 (m, 2H, C(O)OCH$_2$CH$_2$O), 3.3 (m, 2H, C(O)CH$_2$CH$_2$O), 2.35 (m, 2H, C(O)CH$_2$CH$_2$O).

**Poly(4-(4-benzzyloxybutyl)caprolactone):** $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.32 (m, 4H, ArH), 7.26 (m, 1H, ArH), 4.48 (s, 2H, OCH$_2$Ph), 4.02 (m, 2H, CH$_2$O), 3.44 (t (broad), $J = 6.6$ Hz, 2H, CH$_2$OCH$_2$Ph), 2.22 (d (broad), $J = 6.6$ Hz, 2H, C(O)CH$_2$), 1.87 (m, 1H, C(O)CH$_2$CH$_2$), 1.59 (m, 4H, CH$_2$CH$_2$O), 1.33 (m, 6H, CH$_2$CH$_2$CH$_2$CH$_2$O).$^{[13]}$C NMR (126 MHz, CDCl$_3$): 173.27, 138.81, 128.50, 127.75, 127.64, 73.04, 70.39, 64.62, 39.04, 34.79, 33.70, 30.22, 30.11, 25.98, 23.33. $M_{n,th} = 12270$, $M_n = 14730$, $D = 1.09$. 195
Representative immortal homopolymerisation of $\varepsilon$-CL: In a nitrogen filled glovebox, $\varepsilon$-CL (114 mg, 1.0 mmol), 58 (0.2 mg, $4 \times 10^{-4}$ mmol) and BnOH (1.0 $\mu$L, 1.0 mmol) were added to C$_6$D$_6$ (600 mg). The solution was added to a Young’s tap NMR tub and removed from the glovebox. $^1$H NMR spectroscopy was used to monitor the reaction. Once the polymerisation had reached 95% monomer conversion, 0.5 mL of a 10% MeOH in CH$_2$Cl$_2$ was added to quench polymerisation. The solution was then added dropwise to cold methanol and the precipitate was filtered and dried until constant weight. $^1$H NMR spectroscopy was consistent with PCL produced in living homopolymerisation data. $M_{n,th} = 10950$, $M_n = 10470$, $Đ = 1.02$.

Representative block copolymerisation of 4-(4-BOB)-$\varepsilon$-CL and $\varepsilon$-CL: In a nitrogen filled glovebox, rac-4-(4-BOB)-$\varepsilon$-CL) (139 mg, 0.54 mmol), 58 (27.4 mg, 0.05 mmol) and BnOH (5.4 $\mu$L, 0.05 mmol) were dissolved in toluene (500 mg) and added to an ampoule. The ampoule was added to a preheated oil bath at 70°C for two hours. After two hours, the reaction was cooled to room temperature and a sample was taken for $^1$H NMR spectroscopic analysis. $\varepsilon$-CL (512 mg, 4.86 mmol) in toluene (2000 mg) was added to the reaction and stirring was continued for 15 minutes. After 15 minutes, 0.5 mL of a 10% MeOH in CH$_2$Cl$_2$ was added to quench polymerisation. The solution was then added dropwise to cold methanol and the precipitate was filtered and dried until constant weight. $^1$H NMR spectroscopy was used to determine ratio of the two polymers. $M_{n,th} = 13150$, $M_n = 13800$, $Đ = 1.18$.

Representative 2,3-DHB polymerisation: In a glovebox, 2,3-DHB (116 mg, 0.7 mmol), 58 (3.8 mg, 0.007 mmol), BnOH (0.7 $\mu$L, 0.007 mmol) were added to an ampoule with toluene (150 mg). The ampoule was sealed, removed from the glovebox and placed in a preheated oil bath at 60°C for six hours. After six hours, 0.5 mL of a 10% MeOH in CHCl$_2$ solution was added to the ampoule to quench polymerisation. The solution was then added dropwise to cold MeOH to leave a white solid. Precipitation was repeated twice to remove residual 2,3-DHB. $^1$H NMR (500 MHz, CDCl$_3$): $δ$ 7.72 (m, 1H, ArH), 7.36 (m, 1H ArH), 6.94 – 6.88 (m, 2H, ArH), 4.55 (t, $J = 5.0$ Hz, 2H, C(O)OCH$_2$CH$_2$O), 4.25 (t, $J = 5.0$ Hz, 2H,
C(O)OCCH₂). $^{13}$C NMR (126 MHz, CDCl₃) δ 166.00, 158.31, 133.70, 131.90, 121.00, 120.85, 114.40, 67.40, 63.05. $M_{n,th} = 15100$, $M_n = 13500$, $D = 1.08$.

**Representative attempted gradient copolymerisation of 2,3-DHB/l-lactide:** In a glovebox, 2,3-DHB (82 mg, 0.50 mmol), l-lactide (72 mg, 0.50 mmol), 58 (5.4 mg, 0.01 mmol) and toluene were added to an ampoule. The ampoule was sealed, removed from the glovebox and placed in a preheated oil bath at 60°C for six hours. After six hours, the reaction was quickly cooled and 0.5mL of a 10% MeOH in CH₂Cl₂ solution was added to quench polymerisation. A sample was removed for $^1$H NMR spectroscopic analysis. The remainder was added to cold MeOH and dried.

**Representative AB block copolymerization of 2,3-DHB/l-lactide:** In a glovebox, 2,3-DHB (164 mg, 1.00 mmol), 58 (5.4 mg, 0.01 mmol), 1,3-propanediol (1.0 µL, 0.01 mmol) and toluene (265 mg) were added to an ampoule. The ampoule was sealed, removed from the glovebox and placed in a preheated oil bath at 60°C for six hours. After six hours, 0.5 mL of a 10% MeOH in CHCl₂ solution was added to the ampoule to quench polymerization. The solution was then added dropwise to cold MeOH to leave a white solid. Precipitation was repeated twice to remove residual 2,3-DHB. The isolated polymer was then dried under vacuum for 18 h. To P2HEB (0.005 mmol) was added l-lactide (72 mg, 0.50 mmol) in toluene (0.6 mL) at 70°C. The reaction was stirred for three hours followed by addition on 0.5 mL of a 10% MeOH in CH₂Cl₂ solution was added to the ampoule to quench polymerisation. The solution was then added dropwise to cold MeOH to leave the desired copolymer. $M_{n,th} = 20830$, $M_n = 12380$, $D = 1.13$.

**Representative ABA block copolymerisation of 2,3-DHB/l-lactide:** In a glovebox, 2,3-DHB (323 mg, 2.00 mmol), 58 (10.8 mg, 0.02 mmol), 1,3-propanediol (0.7 mg, 0.01 mmol) and toluene (265 mg) were added to an ampoule. The ampoule was sealed, removed from the glovebox and placed in a preheated oil bath at 60°C for six hours. After six hours, 0.5 mL of a 10% MeOH in CHCl₂ solution was added to the ampoule to quench polymerization. The solution was then added dropwise to cold MeOH to leave a white solid. Precipitation was repeated twice to remove
residual 2,3-DHB. The isolated polymer was then dried under vacuum for 18 h. To P2HEB (0.01 mmol) was added \( \varepsilon \)-lactide (72 mg, 0.5 mmol) in toluene (0.3 mL) at 70°C. The reaction was stirred for three hours followed by addition of 0.5 mL of a 10% MeOH in \( \text{CH}_2\text{Cl}_2 \) solution was added to the ampoule to quench polymerisation. The solution was then added dropwise to cold MeOH to leave the desired copolymer. 

\[ M_{n,\text{th}} = 28440, \quad M_n = 22400, \quad D = 1.13. \]

**Representative gradient copolymerisation of 2,3-DHB/rac-\( \beta \)-butyrolactone:** In a glovebox, rac-\( \beta \)-butyrolactone (50 mg, 0.66 mmol), 2,3-DHB (107 mg, 0.66 mmol), \textit{58} (7.2 mg, 0.014 mmol), BnOH (1.4 \( \mu \)L, 0.014 mmol) were added to an ampoule with toluene (100 mg). The ampoule was removed from the glovebox and placed in a preheated oil bath at 70°C for six hours. After six hours, 0.5 mL of a 10% MeOH in \( \text{CH}_2\text{Cl}_2 \) was added to quench polymerisation. A sample was removed for \(^1\text{H} \) NMR spectroscopic and GPC analysis. 

\[ M_{n,\text{th}} = 9360, \quad M_n = 12070, \quad D = 1.39. \]

**Representative AB block copolymerisation of 2,3-DHB/rac-\( \beta \)-butyrolactone:** In a glovebox, rac-\( \beta \)-butyrolactone (100 mg, 1.3 mmol), \textit{58} (14.4 mg, 0.026 mmol), BnOH (2.7 \( \mu \)L, 0.026 mmol) and toluene (250 mg) were added to an ampoule. The ampoule was sealed, removed from the glovebox and placed in a preheated oil bath at 85°C for two hours. After two hours, the ampoule was degassed three times and returned to a glovebox, where 2,3-DHB (215 mg, 1.31 mmol) was added. The ampoule was then sealed, removed from the glovebox and placed in preheated oil bath at 60°C for two hours, followed by addition of 0.5 mL of a 10% MeOH in \( \text{CH}_2\text{Cl}_2 \) to the ampoule to quench polymerisation. The solution was then added dropwise to cold MeOH and filtered to yield the desired copolymer. 

\[ M_{n,\text{th}} = 10780, \quad M_n = 9360, \quad D = 1.15. \]

**Temperature dependence on monomer-polymer equilibrium:** In a glovebox, \textit{58} (9.3 mg, 0.018 mmol), 2,3-DHB (140 mg, 0.85 mmol), benzyl alcohol (1.8 \( \mu \)L, 0.018 mmol) and toluene-d\(_8\) (300 mg) were added to a Young’s tap NMR tube. The NMR tube was then left at room temperature for six hours. \(^1\text{H} \) NMR spectroscopy revealed that the polymerisation had reached 88% conversion (n = 44). The NMR tube was
then heated to 90°C for 10 hours. 1H NMR spectroscopy revealed that polymer conversion had decreased to 70% (n = 35).

**Determination of 2,3-DHB equilibrium concentration:** In a glovebox, P2HEB solutions with 58 (1.4 mol%) were set up at three different apparent [2,3-DHB] in C₆D₆. The solutions were heated to 60°C for 12 hours and cooled. 1H NMR spectroscopy was used to calculate resulting ratio of 2,3-DHB:P2HEB and consequently [2,3-DHB].

**Depolymerisation of P2HEB:** In a glovebox, P2HEB (41 mg, 0.005 mmol) and 58 (2.7 mg, 0.005 mmol) in C₆D₆ (0.4 mL) were added to a Young’s tap NMR tube. The NMR tube was sealed and heated at 70°C for 12 hours. After 12 hours, the NMR tube was cooled to room temperature and 1H NMR analysis indicated the solution contained a mixture of 2,3-DHB:P2HEB = 92:8.

**Concentration dependent reversible polymerisation of 2,3-DHB:** In a glovebox, 2,3-DHB (116 mg, 0.71 mmol), 58 (3.8 mg, 0.01 mmol), BnOH (0.7 µL, 0.01 mmol) and toluene (150 mg) were added to an ampoule. The ampoule was sealed and heated to 60°C for six hours. A sample was removed via syringe under nitrogen. GPC and 1H NMR spectroscopy analysis of the crude sample indicated 82% conversion to polymer. Dry toluene (3 mL) was then added to the ampoule and the reaction was stirred at 60°C for 16 hours. A sample was removed via syringe under nitrogen. GPC and 1H NMR spectroscopy analysis of the crude sample indicated conversion of 2,3-DHB to polymer had decreased to 6%. The reaction was then concentrated under reduced pressure and toluene (120 µL) was then added. The reaction was stirred at 60°C for six hours. A sample was removed via syringe under nitrogen. GPC and 1H NMR spectroscopy analysis of the crude sample indicated 84% conversion to polymer.

**Depolymerisation of P2HEB/P(L-LA) copolymers:** P2HEB/P(L-LA) copolymer (30 mg), 58 (1.0 mg, 0.002 mmol) were dissolved in C₆D₆ and added to a Young’s tap NMR tube. The NMR tube was then heated to 60°C for 72 hours. After 72 h, 1H NMR spectroscopy was used to determine degree of P2HEB depolymerisation. The
reactions were then precipitated into cold MeOH, filtered and dried to constant weight.

**Depolymerisation of P(3HB-b-2HEB):** Toluene (6 mL) was added to a solution of P(3HB-b-2HEB) in toluene and stirred at 60°C for 12 hours. After 12 hours, 0.5 mL of a 10% MeOH in CH₂Cl₂ was added to quench polymerisation/depolymerisation. A crude sample was removed for ¹H NMR spectroscopic and GPC analysis. The remainder was added to cold MeOH and cooled at -35°C overnight. MeOH was decanted and the pale oil was dried to constant weight.

**Representative homopolymerisation of β-lactones:** MeAl[salen] (58, 23 mg, 0.042 mmol) BnOH (4.4 µL, 0.042 mmol) and β-valerolactone (430 mg, 4.20 mmol) in toluene (4 mL) was added to an oven dried ampoule. The ampoule was then sealed and heated to 85°C for 6 h. The reaction was then quenched by addition of two drops of MeOH and samples were taken for ¹H NMR and GPC analysis. The remainder was added dropwise to cold methanol and upon cooling to -35°C for two days a colorless solid was separated and dried under vacuum until constant weight.

**Poly(3-hydroxypentanoate) (P3HP):** (500 MHz, CDCl₃): δ (ppm) 5.20 (m, 1H, COCH₂CH), 2.56 (m, 2H, COCH₂CH), 1.68 (m, 2H, CHCH₂CH₃), 0.95 (m, 3H, CHCH₂CH₃). Mₙ,th = 10120, Mₙ = 10080, Đ = 1.08.

**Poly(3-hydroxyheptanoate) (P3HH):** (500 MHz, CDCl₃): δ (ppm) 5.20 (m, 1H, COCH₂CH), 2.40 – 2.70 (m, 2H, COCH₂CH), 1.60 (m, 2H, CHCH₂CH₂CH₂CH₃), 1.31 (m, 4H, CHCH₂CH₂CH₂CH₃), 0.90 (m, 3H, CHCH₂CH₂CH₂CH₃). Mₙ,th = 12800, Mₙ = 12030, Đ = 1.08.

**Poly(3-hydroxytridecanoate) (P3HTD):** (500 MHz, C₆D₆): δ (ppm) 5.47 (m, 1H, COCH₂CH), 2.45 – 2.75 (m, 2H, COCH₂CH), 1.31 (m, 18H, (CH₂)₉CH₃), 0.92 (m, 3H, (CH₂)₉CH₃). Mₙ,th = 21340, Mₙ = 23700, Đ = 1.06.

**Representative random/gradient copolymerisation of β-lactone/l-lactide:** MeAl[salen] (58, 13 mg, 0.025 mmol), BnOH (2.5 µL, 0.025 mmol), l-lactide (171 mg, 1.2 mmol) and β-heptanolactone (306 mg, 2.38 mmol) in toluene (2.5 mL) was added to an oven dried ampoule. The ampoule was then heated to 85°C for 18 h. The
reaction was then quenched by addition of two drops of MeOH and samples were taken for $^1$H NMR and GPC analysis. The remainder was added dropwise to cold methanol and left in a freezer overnight, filtered and dried under vacuum to constant weight. $M_{n,th} = 20130, M_n = 18280, D = 1.10$.

**Representative ABA block copolymerisation of $\beta$-lactone/1-lactide:** MeAl[salen] (58, 38 mg, 0.07 mmol), BnOH (7.2 µL, 0.07 mmol) and 1-lactide (100 mg, 0.7 mmol) in toluene (3 mL) was added to an oven dried ampoule. The ampoule was then heated to 85°C for 3 h. $\beta$-Valerolactone (700 mg, 7 mmol) was then added under $N_2$ and the solution was continued to heat for 18 h. 1-lactide (100 mg, 0.7 mmol) in toluene (1 mL) was then added under $N_2$ and stirred for 3 h. The reaction was then quenched by addition of two drops of MeOH and samples were taken for $^1$H NMR and GPC analysis. The remainder was added dropwise to cold methanol and left in a freezer overnight, filtered and dried under vacuum to constant weight. $M_{n,th} = 18720, M_n = 18200, D = 1.16$.

**Polymerisation of 4-Cl-$\beta$-BL:** In a nitrogen filled glovebox, 4-Cl-$\beta$-BL (120 mg, 1.0 mmol), 84 (6.3 mg, 0.01 mmol) and BnOH (1.0 µL, 0.01 mmol) were added to an ampoule with toluene (0.6 mL). The ampoule was sealed, removed from the glovebox and placed in a preheated oil bath at the desired temperature and time. Once the desired time was reached, 0.5 mL of a 10% MeOH in CH$_2$Cl$_2$ solution was added to quench polymerisation. A crude sample was taken for $^1$H NMR spectroscopic analysis. The remainder was added to cold MeOH. MeOH was decanted and the remaining oil was dried until constant weight. $^1$H NMR characterisation was consistent with literature reports.$^{[152a]}$ $^1$H NMR (500 MHz, CDCl$_3$): δ 5.43 (m, 1H, CH$_2$CHO), 3.74 (m, 2H, CH$_2$CHO), 2.82 (d (broad), J = 5.8 Hz, CH$_2$Cl). $M_{n,th} = 11680, M_n = 9540, D = 1.02$.

**Polymerisation of $\beta$-6-HEL:** In a nitrogen filled glovebox, $\beta$-6-HEL (125 mg, 1.0 mmol), 58 (5.4 mg, 0.01 mmol) and BnOH (1.0 µL, 0.01 mmol) were added to an ampoule with toluene (0.6 mL). The ampoule was sealed, removed from the glovebox and placed in a preheated oil bath at the desired temperature and time.
Once the desired time was reached, 0.5 mL of a 10% MeOH in CH₂Cl₂ solution was added to quench polymerisation. A crude sample was taken for ¹H NMR spectroscopic analysis. The remainder was added to cold MeOH. MeOH was decanted and the remaining oil was dried until constant weight. ¹H NMR characterisation was consistent with literature reports.¹¹⁷⁴ ¹H NMR (500 MHz, CDCl₃): δ 5.73 (m, 1H, CH₂CH=CH₂), 5.20 (m, 1H, CH₂CHO), 4.96 (m, 2H, CH₂CH=CH₂), 2.51 (m, 2H, C(O)CH₂CH₂), 2.04 (m, 2H, CHCH₂CH₂CH₂), 1.69 (m, 2H, CHCH₂CH₂CH₂). Mₙ,th = 12620, Mₙ = 11800, D = 1.07.

Synthesis of P(EG₄₅-b-3HHeneₙ): In a nitrogen filled glovebox, β-6-HEL (125 mg, 1.0 mmol), 58 (5.4 mg, 0.01 mmol) and mPEG (77 mg, 0.004 mmol) were added to an ampoule with toluene (0.6 mL). The ampoule was sealed, removed from the glovebox and placed in a preheated oil bath at the desired temperature and time. Once the desired time was reached, 0.5 mL of a 10% MeOH in CH₂Cl₂ solution was added to quench polymerisation. A crude sample was taken for ¹H NMR spectroscopic analysis. The remainder was added to cold MeOH. MeOH was decanted and the remaining oil was dried until constant weight. Mₙ,th = 8180, Mₙ = 7930, D = 1.35.

Synthesis of P(EG₄₅-b-(3HHeneₙ-co-3HHₙ₉ₙ)): In a nitrogen filled glovebox, β-6-HEL (62 mg, 0.5 mmol), β-HL (62 mg, 0.5 mmol) 58 (5.4 mg, 0.01 mmol) and mPEG (77 mg, 0.004 mmol) were added to an ampoule with toluene (0.6 mL). The ampoule was sealed, removed from the glovebox and placed in a preheated oil bath at the desired temperature and time. Once the desired time was reached, 0.5 mL of a 10% MeOH in CH₂Cl₂ solution was added to quench polymerisation. A crude sample was taken for ¹H NMR spectroscopic analysis. The remainder was added to cold MeOH. MeOH was decanted and the remaining oil was dried until constant weight. Mₙ,th = 8360, Mₙ = 8040, D = 1.11.
7.6 Carbonylation procedures and synthesis of β-lactones

**General carbonylation considerations:** All carbonylation reactions were performed in either a 100 mL or 45 mL pressure reactor (Figure 8.1). All manipulations of equipment were performed in a well-ventilated fumehood with a carbon monoxide detector. The cylinder of carbon monoxide was kept closed at all times when not in use.

![100 mL and 45 mL pressure reactors used in carbonylation](image)

**General carbonylation procedure with 100 mL pressure reactor:** The pressure chamber was heated prior to use. While still hot, pressure reactor was assembled and gas inlets were connected to a Schlenk line and a cylinder of carbon monoxide. The vessel was then evacuated for 30 minutes. The reactor was then refilled with nitrogen, and the reaction mixture was transferred under inert atmosphere through the injection port. The reactor was then sealed, pressurised with ~20 psi of carbon monoxide and stirred for five minutes. The reactor was carefully vented and then repressurised to the desired pressure. Heating was performed by placing the reactor in a pre-heated oil bath. Once the reaction was complete, the vessel was cooled to
room temperature and carefully vented in a well-ventilated fume hood with a carbon monoxide detector.

**General carbyonylation procedure with 45 mL pressure reactor:** The pressure chamber was heated prior to use. While still hot, pressure reactor was assembled and the gas inlet was connected to a Schlenk line. The vessel was then evacuated for 30 minutes. The reactor was then refilled with nitrogen, and the reaction mixture was transferred under inert atmosphere through the injection port. The reactor was then sealed and the gas inlet was attached to a cylinder of carbon monoxide. The reactor was pressurised with ~20 psi of carbon monoxide and stirred for five minutes. The reactor was then carefully vented and then repressurised to the desired pressure. Heating was performed by placing the reactor in a pre-heated aluminium block. Once the reaction was complete, the vessel was cooled to room temperature and carefully vented in a well-ventilated fume hood with a carbon monoxide detector.

**Carbonylation with ClCr[TPP]/Co$_2$(CO)$_8$:** In a nitrogen filled glovebox, ClCr[TPP] (7 mg, 0.010 mmol), Co$_2$(CO)$_8$ (5 mg, 0.015 mmol) and 1,2-epoxybutane (2.9 g, 40 mmol) and THF (5 mL) were added to an ampoule. The ampoule was sealed, removed from the glovebox and the contents were transferred to a nitrogen flushed 100 mL pressure reactor under nitrogen. The pressure reactor was pressurised to ~20 psi with carbon monoxide and stirred for five minutes at room temperature. The vessel was then placed in an oil bath preheated to 70°C. The reaction was then continued until carbon monoxide pressure ceased decreasing. The vessel was carefully vented and a sample was taken for analysis by $^1$H NMR spectroscopy.

**Carbonylation with ClCr[salen]/Co$_2$(CO)$_8$:** In a nitrogen filled glovebox, ClCr[salen]$^{t}$BuPh (156 mg, 0.25 mmol), Co$_2$(CO)$_8$ (128 mg, 0.38 mmol) and 1,2-epoxyhexane (2.5 g, 25 mmol) and THF (15 mL) were added to an ampoule. The ampoule was sealed, removed from the glovebox and the contents were transferred to a nitrogen flushed 100 mL pressure reactor under nitrogen. The pressure reactor was pressurised to ~20 psi with carbon monoxide and stirred for five minutes at room temperature.
temperature. The vessel was carefully vented and then repressurised to 200 psi. The reaction was then placed in a preheated oil bath at 30°C. The reaction was continued until carbon monoxide pressure ceased decreasing. The vessel was carefully vented and a sample was taken for analysis by $^1$H NMR spectroscopy.

**Measurement of carbonylation kinetics:** A reaction was set up as for the carbonylation with ClCr[salen]/Co$_2$(CO)$_8$. At the desired time interval, the vessel was quickly and carefully vented and a crude sample was removed via syringe under nitrogen. The vessel was refilled with carbon monoxide until the next desired time interval. The crude sample was analysed by $^1$H NMR spectroscopy to determine conversion.

**Synthesis of alkyl-substituted β-lactones:** The procedure for carbonylation with ClCr[TPP]/Co$_2$(CO)$_8$ was employed. Purification of the product was achieved by distillation under reduced pressure (β-VL, β-HL) or by column chromatography (SiO$_2$, hexanes, β-TDL).

**β-Valerolactone:** $^1$H NMR characterisation was consistent with literature reports.$^{[192]}$ (400 MHz, CDCl$_3$): d 4.40 (m, 1H, CH$_A$CH$_B$CHO), 3.43 (dd, $J$ = 16.3, 5.8 Hz, 1H CH$_A$CH$_B$CHO), 2.99 (dd, $J$ = 16.3, 4.3 Hz, 1H, CH$_A$CH$_B$CHO), 1.75 (m, 2H, CH$_2$CH$_3$), 0.94 (t, $J$ = 7.4 Hz, 3H, CH$_2$CH$_3$).

**β-Heptanolactone:** $^1$H NMR characterisation was consistent with literature reports.$^{[193]}$ (500 MHz, C$_6$D$_6$): δ 3.61 (m, 1H, CH$_A$H$_b$CHO), 2.56 (dd, $J$ = 16.0, 5.8 Hz, 1H, CH$_A$H$_b$CHO), 2.20 (dd, $J$ = 16.0, 4.3 Hz, 1H, CH$_A$H$_b$CHO), 1.22 (m, 1H, CHCH$_2$H$_b$(CH$_2$)$_2$CH$_3$), 0.99 (m, 4H, CHCH$_2$H$_b$(CH$_2$)$_2$CH$_3$), 0.85 (m, 1H, CHCH$_2$H$_b$(CH$_2$)$_2$CH$_3$), 0.72 (t, $J$ = 7.1 Hz, 3H, CHCH$_2$H$_b$(CH$_2$)$_2$CH$_3$).

**β-Tridecalactone:** $^1$H NMR characterisation was consistent with literature reports.$^{[193]}$ (500 MHz, CDCl$_3$): δ 4.48 (m, 1H, CH$_A$H$_b$CHO), 3.48 (dd, $J$ = 16.2, 5.8 Hz, 1H, CH$_A$H$_b$CHO), 3.03 (dd, $J$ = 16.2, 4.3 Hz, 1H, CH$_A$H$_b$CHO), 1.82 (m, 2H, CHCH$_2$(CH$_2$)$_2$CH$_3$), 1.38 (m, 4H, CHCH$_2$(CH$_2$)$_2$CH$_3$), 0.90 (t, $J$ = 7.0 Hz, 3H, CHCH$_2$(CH$_2$)$_2$CH$_3$).
CHCH₆(CH₂)₆CH₃, 1.77 (m, 1H, 1H, CHCH₆CH₆(CH₂)₆CH₃), 1.39 (m, 16H, CHCH₆(CH₂)₆CH₃), 0.90 (t, J = 6.9 Hz, CHCH₆CH₆(CH₂)₆CH₃).

**Synthesis of 4-chloro-β-butyrolactone:** The procedure for carbonylation with ClCr[salen]/Co₂(CO)₈ was employed on a 5 mmol scale. Purification of the product was achieved by distillation under reduced pressure. ¹H NMR characterisation was consistent with literature reports.[152a] ¹H NMR (500 MHz, CDCl₃): δ 4.74 (dtd, J = 5.8, 4.9, 4.2 Hz, 1H, CH₆CH₆CHO), 3.83 (dd, J = 4.9, 0.9 Hz, 2H, CH₂Cl), 3.59 (dd, J = 16.6, 5.8 Hz, 1H, CH₆CH₆CHO), 3.39 (dd, J = 16.6, 4.2 Hz, 1H, CH₆CH₆CHO).

**Synthesis of β-6-heptenolactone:** The procedure for carbonylation with ClCr[TPP]/Co₂(CO)₈ was employed. Purification of the product was achieved by distillation under reduced pressure. ¹H NMR characterisation was consistent with literature reports.[162] ¹H NMR (500 MHz, C₆D₆): δ 5.49 (m, 1H, CH₂CH=CH₂), 4.88 (m, 2H, CH₂CH=CH₂), 3.72 (m, 1H, CH₂CHO), 2.65 (dd, J = 16.1, 5.8 Hz, 1H, C(O)CH₆CH₆CH), 2.28 (dd, J = 16.1, 4.3 Hz, 1H, CH₆CH₆CH), 1.73 (m, 2H, CH₆CH₆CH=CH₂), 1.35 (CH₆CH₆CH=CH₂), 1.13 (m, 1H CH₆CH₆CH=CH₂).
Chapter Eight

References


[40] K. F. Lindsay, Mod. Plast. Int. 1992, 22, 62.


