ABSTRACT

The alkoxy zinc complexes (±)-[(NNOt-Bu)Zn(OCH2Ph)]2 4, (±)-[(NNOt-Bu)Zn(OCH2Ph)]2 5, and 6 (±)-[(NNOcm)Zn(OCH2Ph)]2 were prepared from the reactions of the corresponding alkyl zinc complexes (±)-(NNt-Bu)Zn(CH2CH3) 1, (±)-(NNOt-Bu)Zn(CH2CH3) 2, and (±)-(NNOcm)Zn(CH2CH3) 3, respectively, with benzyl alcohol (PhCH2OH). All zinc compounds 1-6 were characterized by 1H and 13C{1H} NMR spectroscopy. The molecular structures of 2-6 were characterized by single-crystal X-ray crystallography. The alkyl zinc complexes are mononuclear with a tridentate coordination mode and a distorted tetrahedral geometry around the zinc metal centers. The alkoxy zinc catalysts show a dimeric feature containing two zinc metal centers bridging through the benzyl alkoxy oxygen atoms with different coordination modes for all three catalysts. The solution denticities of 4-6 were further investigated through 1D and 2D NMR spectroscopy experiments. Exchange studies with pyridine and complexes 4-6 were also conducted.

The catalytic activities of alkyl and alkoxy zinc complexes 1-6 toward ring opening polymerization (ROP) of racemic lactide (rac-LA) have been studied by 1H NMR spectroscopy, Gel permeation chromatography, and MALDI-TOF mass spectrometry. Experimental results indicate that the alkyl zinc compounds 1-3 show relatively less activity toward ROP of cyclic esters than the alkoxy zinc compounds 4-6. Catalysts 5 and 6 demonstrate a better control over experimental molecular weights and dispersity values of PLA, and more stereoselective than 4. Catalyst 4 undergoes the depolymerization reactions. Different transesterification side reactions operate at low equivalency polymerization studies to a different extent for all alkoxy zinc complexes. Immortal ROP of alkyl zinc compounds 1-3 was investigated in the presence of a chain transfer agent. The obtained results reveal the controlled nature of iROP.
PREFACE

Work towards the initial synthesis and characterization of the proligands and zinc complexes 1-6 was completed by a former Ph.D. student in our group Insun Yu. The crystal structures presented in this work were obtained, run and solved by Dr. Insun Yu. Optimization of the synthesis of zinc compounds and further characterization data was completed by myself. All polymerization studies presented in Chapter 3 were completed by myself.
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% percent
(±) racemic
$^{13}\text{C}\{^1\text{H}\}$ proton decoupled carbon-13
$^1\text{H}$ proton
$^1\text{H}\{^1\text{H}\}$ homonuclear proton decoupled
$\delta$ chemical shift relative to tetramethylsilane at 0 ppm
$^\circ$ degrees
$^\circ\text{C}$ degrees Celsius
$\kappa$ denticity of a ligand
anal. analytical
Bn benzyl
BnOH benzyl alcohol
Boc\,\textit{tert}-butoxycarbonyl
br broad
C$_6$D$_6$ deuterated benzene
calc. calculated
CD$_2$Cl$_2$ deuterated dichloromethane
CDCl$_3$ deuterated chloroform
Cm cumyl (-C(CH$_3$)$_2$(C$_6$H$_5$))
conv. conversion
CTA chain transfer agent
d day(s)
Da Daltons (grams per mole)
DACH\,\textit{trans}-1,2-diaminocyclohexane
DCM dichloromethane
D-LA\,(R,R)-lactide
$\frac{dn}{dc}$ the rate of change in the refractive index of a polymer solution with a change in concentration

$D_M$ dispersity

EA elemental analysis

equiv equivalent(s)

Et ethyl

et al. and others

EtOH ethanol

g grams

GPC gel-permeation chromatography

h hour(s)

in situ in a chemical reaction

in vacuo in vacuum

iROP immortal ring opening polymerization

$J$ coupling constant

LA lactide

L-LA (S,S)-lactide

M molar (moles per liter)

MALDI-TOF matrix-assisted laser desorption time of flight

$M_{\text{BnOH}}$ molar mass of benzyl and hydroxy end group (108.14 g/mol)

Me methyl

MeOH methanol

meso-LA (R,S)-lactide

$M_{\text{EtOH}}$ molar mass of ethyl and hydroxy end group (46.07 g/mol)

mg milligrams

MHz megahertz

min. minute(s)

mL milliliters
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLA</td>
<td>molar mass of lactide (144.13 g/mol)</td>
</tr>
<tr>
<td>mM</td>
<td>millimolar</td>
</tr>
<tr>
<td>MMEOH</td>
<td>molar mass of methyl and hydroxy end group (32.04 g/mol)</td>
</tr>
<tr>
<td>mmol</td>
<td>millimoles</td>
</tr>
<tr>
<td>Mn</td>
<td>number average molecular weight</td>
</tr>
<tr>
<td>mol</td>
<td>moles</td>
</tr>
<tr>
<td>MW</td>
<td>weight average molecular weight</td>
</tr>
<tr>
<td>NMR</td>
<td>nuclear magnetic resonance</td>
</tr>
<tr>
<td>NOESY</td>
<td>nuclear overhauser enhancement spectroscopy</td>
</tr>
<tr>
<td>OBn</td>
<td>benzoxide</td>
</tr>
<tr>
<td>OEt</td>
<td>ethoxide</td>
</tr>
<tr>
<td>OMe</td>
<td>methoxide</td>
</tr>
<tr>
<td>PDLA</td>
<td>poly(D-lactic acid)</td>
</tr>
<tr>
<td>PGSE</td>
<td>pulsed gradient spin-echo</td>
</tr>
<tr>
<td>Ph</td>
<td>phenyl</td>
</tr>
<tr>
<td>PLA</td>
<td>poly(lactic acid)</td>
</tr>
<tr>
<td>PLLA</td>
<td>poly(L-lactic acid)</td>
</tr>
<tr>
<td>P_m</td>
<td>probability of meso linkages within a polymer chain</td>
</tr>
<tr>
<td>ppm</td>
<td>parts per million</td>
</tr>
<tr>
<td>P_r</td>
<td>probability of racemic linkages within a polymer chain</td>
</tr>
<tr>
<td>R.T.</td>
<td>room temperature</td>
</tr>
<tr>
<td>rac-LA</td>
<td>a 1:1 mixture of (S,S) and (R,R)-lactide</td>
</tr>
<tr>
<td>ROP</td>
<td>ring opening polymerization</td>
</tr>
<tr>
<td>t-Bu</td>
<td>tert-butyl</td>
</tr>
<tr>
<td>temp.</td>
<td>temperature</td>
</tr>
<tr>
<td>T_g</td>
<td>glass transition temperature</td>
</tr>
<tr>
<td>theo.</td>
<td>theoretical</td>
</tr>
<tr>
<td>T_m</td>
<td>melting temperature</td>
</tr>
</tbody>
</table>
Tol. toluene
vs. versus
VT variable temperature
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I would like to thank my supervisor Prof. Parisa Mehrkhodavandi for her constant support and encouragement. Her endless enthusiasm, optimism, and wisdom helped me to learn, overcome all obstacles on my way, and stay positive about the future. Especially I want to thank Prof. Mehrkhodavandi for believing in me, in my abilities to accomplish the work.

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CHAPTER 1 – LITERATURE REVIEW

1.1 Introduction to poly(lactic acid)

Plastics were developed in the twentieth century and since then they have greatly affected all aspects of the modern world.1 “Plastics” can be defined as "any of a large and varied class of materials used widely in manufacturing, which are organic polymers of high molecular weight based on synthetic materials, and may be molded, extruded, or cast when they are soft or liquid, and then set into a rigid or slightly elastic form".2 According to PlasticsEurope (the Association of Plastics Manufacturers in Europe) the annual worldwide plastics production reached 299 million tons in 2013, and global plastic consumption is expected to grow by an average of 4% each year.3 Plastics play a crucial role in everyday life, due to their unique properties: low cost, resistance to chemicals and light, lightweight, strength, toughness, and readiness to be molded into different shapes.4 On the other hand, there are drawbacks to the present consumption of plastics. One drawback is that fossil fuels, a non-renewable resource, is the major raw material for production of polymers. Furthermore, increasing waste accumulation of disposed plastic materials and their persistence for long periods of time have caused harmful environmental consequences. Therefore, increasing attention has been devoted to the usage and applications of biodegradable polymers and polymers obtained from biorenewable resources.

One example of a biodegradable and biocompatible polymer that has received considerable attention in recent years is poly(lactic acid) (PLA) (Figure 1.1).5-7 High-molecular weight PLA is a stiff thermoplastic polymer with properties similar to polystyrene.8,9 Poly(lactic acid) has multiple practical and potential applications in the biomedical area such as drug delivery, orthopedic fixation, implants, and sutures.8,10 It is also being widely used in agriculture, engineering, and for packaging materials. Poly(lactic acid) is environmentally degraded in two steps. Upon hydrolysis, high molecular weight PLA is converted to lower molecular weight oligomers.8,9 The presence of acids and bases, temperature, and moisture influence the hydrolysis reaction. Then, microorganisms carry on the degradation of the oligomers and convert them into
carbon dioxide, water, and humus. The estimated degradation time for PLA in the environment varies from 6 months to 2 years.

Figure 1.1. Molecular structure of poly(lactic acid) (PLA).

Certain limitations challenge the production of PLA on a broader scale. Poly(lactic acid) homopolymers have a glass transition temperature \( (T_g) \) of 55 °C and a melting temperature \( (T_m) \) of 175 °C. The required processing temperature window for PLA is narrow and in the range of 185-190 °C. At higher temperatures PLA tends to degrade which leads to the loss of its molecular weight and useful properties. The low glass transition temperature \( (T_g) \) and impact strength, which is "the ability of a material to resist shock loading", make PLA undergo deformation at low temperatures. Moreover, food feedstocks such as corn are not the best option to produce PLA. However, new solutions have been proposed to solve the feedstock problem by using plant parts like stems and leaves and glycerol, which is an abundant waste of biofuel production.

Sustainability is a novel contemporary concept that emphasizes the importance of understanding the relationship between humanity and the environment and the recognition that excessive consumption of natural resources and massive waste and pollution generation by human beings are threatening the sustainability of humanity and global environment. The World Commission on Environment and Development (WCED) definition of sustainable development is "maintaining the needs of the present generation without compromising the ability of future generation to meet their needs". Although sustainability still remains as an abstract concept that has many interpretations and uncertainties on how the harmony can be achieved between the needs of humanity and the environment, it is becoming more obvious that
the concept of sustainability needs improvements and tangibility that can be realized through an interdisciplinary approach. The phrase "green chemistry" was coined by the US Environmental Protection Agency (EPA) in early 1990s.\textsuperscript{17,18} Green chemistry has been recognized as a culture and a methodology to reach sustainability. The twelve principles of green chemistry were developed by P.C. Ananistas and J. C.Warner to demonstrate how to move towards sustainability. Green Chemistry faces many challenges and obstacles to become adopted in large scales. The major challenge that causes problems is the communication gaps between academia and industry and between scientists and engineers. Green chemistry is not a new branch of science, but a new philosophical approach which has technological, environmental and societal goals. Team work in minimizing waste is very important. Scientists and engineers have to work with social scientists, economists, and politicians to develop and improve the appropriate culture, infrastructure and society, and technological developments which are needed to contribute to sustainable development.\textsuperscript{18}

1.2 Synthesis of PLA
There are two major routes to produce PLA on an industrial scale.\textsuperscript{8,11} The first is the direct condensation polymerization of lactic acid, which itself is derived by the fermentation of carbohydrates.\textsuperscript{14} Lactic acid is produced from the fermentation processes is L-lactic acid.\textsuperscript{7} The step-growth polycondensation suffers, as high molecular weight polymers are only achieved at high conversions and impurities, such as ethanol and acetic acid, limit the molecular weights. Regardless, high molecular weight PLA is produced by employing pure lactic acid and removing produced water azeotropically in the presence of such solvents as diphenyl ether.\textsuperscript{14}

In the second route PLA is produced from ring opening polymerization (ROP) of lactide (LA).\textsuperscript{8,11} Lactide is formed by the following procedure. Low molecular weight PLA oligomer is produced from the condensation of lactic acid (Scheme 1.1).\textsuperscript{11} The oligomer is depolymerized into a mixture of lactide stereoisomers by a tin catalyst such as a Sn\textsuperscript{II}-carboxylate or –alkoxide compound.\textsuperscript{14} The mixture is then purified and used in the ring opening polymerization (ROP)
Scheme 1.1. Methods for production of high-molecular-weight PLA.

There are three stereoisomers of lactide: D-lactide (D-LA) (known as (R,R)-lactide), L-lactide (L-LA) (or (S,S)-lactide) and meso-lactide (or (R,S)-lactide). During the depolymerization reaction L-lactyl sites can be racemized to D-lactyl units. The racemic mixture of D- and L-lactide is also called rac-lactide (rac-LA). L- and D-lactides are optically active; however, meso-lactide is optically inactive.

There is also a petrochemical route to produce rac-LA based on lactonitrile. Ethylene obtained from petrochemical feedstock is oxidized to acetaldehyde (Scheme 1.2). Then, reaction of acetaldehyde with hydrogen cyanide in the presence of a base forms lactonitrile. The reaction is carried out in liquid phase at elevated temperatures. Formed crude lactonitrile is purified by distillation. Ammonium salt and desired lactic acid are formed from the hydrolysis of lactonitrile in concentrated HCl or H2SO4. Obtained lactic acid is a 50:50 mixture of the L and D forms, racemic lactic acid, which is further converted to rac-LA.
Scheme 1.2. Production of racemic lactide from petrochemical feedstock.

Tin (II) bis-2-ethylhexanoic acid (tin octanoate, Sn(Oct)$_2$) is a commercially available complex used in industry to prepare PLA (Figure 1.2) through ROP.$^{20-22}$ It is an active catalyst to obtain high molecular weight PLA. On an industrial scale, the polymerization is performed in the melt.$^8,11,20$ However, due to transesterification side reactions there is a low degree of control of polymerization and a large range of dispersities ($D_M$). The addition of an alcohol to Sn(Oct)$_2$ leads to a more controlled polymerization. Aluminum alkoxide, Al(O$i$-Pr)$_3$, (Figure 1.2) is also a catalyst utilized for the ROP of lactide.$^{23}$ Despite the fact that it has proved to be less active than Sn(Oct)$_2$, Al(O$i$-Pr)$_3$ has been used for the mechanistic investigation of the polymerization. Ring opening polymerization is driven by the unusual increased ring strain of LA.$^{20}$ Three- and four-membered rings are strained, and the polymerization of this type of monomers is enthalpy driven.$^{24}$ For bigger rings, including most of the six-membered rings, the ring strain decreases making enthalpy become closer to zero (or even positive) and thus harder to polymerize.$^{24}$ X-ray crystallographic data shows that D-LA has an unusual irregular skew boat conformation with $C_2$ symmetry, with two ester groups adopting a planar conformation.$^{25}$ The boat conformation is assumed to prevail in solution as well. The standard state polymerization enthalpy for lactide was determined to be $-22.9$ kJ/mol.$^{20,24,25}$
Figure 1.2. Structures of tin octanoate, Sn(Oct)₂, and aluminum alkoxide, Al(Oi-Pr)₃.

1.3 ROP mechanism of lactide using metal catalysts

Ring opening polymerization of lactide is by far the most convenient and efficient way to produce PLA due to mild reaction conditions and the elimination of the formation of byproducts. Poly(lactic acid) with controlled molecular weight is produced from ROP. Ring opening polymerization processes can be anionic, cationic, organocatalytic, and metal-mediated. The latter process has attracted the most attention lately and in most cases occurs via a coordination-insertion mechanism. Various different metals have been studied for ROP of LA: Ga, Ge, Bi, Al, Sn, Fe. The focus of this research project is Zn and some distinguished zinc complexes will be discussed in detail in the following sections.

Dittrich and Schulz described a coordination-insertion mechanism in 1971 (Scheme 1.3). The first step in the coordination-insertion mechanism is coordination of the monomer to the metal center. Subsequently, a nucleophilic initiator (for example an alkoxide) attacks the carbonyl carbon resulting in the insertion of the monomer into the metal-initiator bond. Finally, the ring opens through acyl-oxygen bond cleavage. The newly formed metal-initiator species is then ready for the next insertion. It was experimentally proved that the ring opening of lactones occurs through the cleavage of the acyl-oxygen bond and the initiator’s alkoxide group forms the corresponding alkyl ester end group supporting the coordination-insertion mechanism.

Two mechanisms, chain-end control and enantiomorphic site control, can be responsible for stereoselectivity in the ROP process. Chain-end control is prominent for hindered and achiral catalysts, where the stereogenic center of the last monomer of the propagating chain determines
which monomer is going to be inserted next. In contrast, in enantiomorphic site control the chiral catalyst itself prefers one enantiomer of the monomer over the other. The combination of two mechanisms is also possible for some systems.

**Scheme 1.3.** Coordination-insertion mechanism.

In the coordination-insertion ROP mechanism there are two possible transesterification side reactions: intramolecular and intermolecular (Scheme 1.4). The presence of both odd and even numbers of lactyl repeat units in polymer chains, as well as an absence of a chain end, are indications of intramolecular transesterification side reactions taking place during the polymerization leading to macrocyclic structures and shorter chains. Intermolecular transesterification side reactions lead to chain redistributions. These two side reactions lead to a large range of $D_M$ values and irreproducible polymer molecular weight.
1.4 Microstructures of PLA and tacticity

The synthesis of PLA from LA, which contains two stereogenic centers, leads to the formation of different polymer microstructures (Figure 1.3).\textsuperscript{20} Isotactic poly(D-lactic acid) (PDLA) and poly(L-lactic acid) (PLLA) are formed from the polymerization of enantiopure D-LA and L-LA, respectively, with no epimerization present. In isotactic polymers all stereogenic centers have the same absolute stereochemistry.\textsuperscript{63}

The polymerization of rac-LA results in a number of different microstructures (Figure 1.3). Isoselective systems can form isotactic stereoblock or stereogradient PLA, stereocomplex PLA, and multiblock PLA. Such factors as the degree of selectivity, chain exchange and insertion errors determine the final microstructure of polymer. Atactic PLA, which has a random distribution of stereogenic centers along a polymer chain, is produced from a non-stereoselective system. Alternating insertion of D-LA and L-LA enantiomers of rac-LA leads to heterotactic PLA. In heterotactic PLA pairs of stereogenic centers with the same stereochemistry alternate with each other along a polymer chain.
Various microstructure types influence the macroscopic properties of polymers. Isotactic PLA is a crystalline material having a melting temperature ($T_m$) of 180 °C and a glass transition temperature ($T_g$) of 50 °C. Stereoblock and stereocomplex PLAs have a similar $T_g$ to isotactic PLA and display an increased $T_m$ value of 230 °C because of higher crystallinity compared to enantiopure chains of PLLA and PDLA. Atactic and heterotactic PLAs are amorphous materials having a $T_g$ of 50 °C and no $T_m$.65

The degree of stereoregularity is expressed by $P_m$ and $P_r$ values, which are the probabilities of forming *meso* (isotactic) and *racemic* (syndiotactic) linkages in a polymer chain, respectively.32,63,66 When two adjacent stereogenic centers have the same absolute stereochemistry it is called a *meso* linkage ($m$) and when two centers have opposite stereochemistry it is a *racemic* linkage ($r$) (Figure 1.4). For the ROP of rac-LA $P_r$ and $P_m$ values of 1.00 define heterotactic and isotactic polymers, respectively. An atactic polymer is described by $P_r$ or $P_m = 0.50$ for the ROP of both rac- and meso-lactide.
Figure 1.4. Tetrad sequence (mrm) with meso and racemic linkages.

The P_r and P_m values are calculated from the homonuclear decoupled ¹H NMR spectroscopy (¹H{¹H}NMR). The methyl signal of PLA is irradiated in order to decouple the splitting between the methyl and methine protons that leads to simplified singlet series in the region of 5.15-5.25 ppm (Figure 1.5). There are five tetrad sequences of PLA formed from rac-LA according to Bernoullian statistics; mmm, mnr, rnm, rmr, mrm. The observed decoupled peaks in the methine region correspond to particular tetrad sequences. In Bernoullian statistics there is a set of equations to calculate the probability of each tetrad to appear in a polymer chain (Table 1.1). With the help of these equations and the total integration of the methine region, the P_r and P_m values are calculated in the following fashion. The region of rnr tetrad (x) is integrated as 1 and the other two regions rnm/mnr (y) and mnr/rnm, mmm, mrm (z) are integrated accordingly (Figure 1.5). The total integration (ε) is the sum of all three integrations (ε = x + y + z). Then, [rnr] = P_r²/2 = 1/ ε and therefore P_r = (2/ ε)¹/₂. [mnr/rnm] = y/ ε = P_rP_m/2 and therefore P_m = 2y/ εP_r.

Figure 1.5. Homonuclear decoupled ¹H NMR spectrtum of methine region of PLA prepared by complex 5 (P_r = 0.80).
Table 1.1. Tetrad probabilities based on Bernoullian statistics.\textsuperscript{67}

<table>
<thead>
<tr>
<th>Tetrad</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>([mmm])</td>
<td>(P_{m}^2 + P_{r}P_{m}/2)</td>
</tr>
<tr>
<td>([mmr])</td>
<td>(P_{r}P_{m}/2)</td>
</tr>
<tr>
<td>([rmm])</td>
<td>(P_{r}P_{m}/2)</td>
</tr>
<tr>
<td>([rmr])</td>
<td>(P_{r}^2/2)</td>
</tr>
<tr>
<td>([mrm])</td>
<td>((P_{r}^2 + P_{r}P_{m})/2)</td>
</tr>
</tbody>
</table>

1.5 Immortal ROP of lactide

There are a number of catalytic systems studied for ROP of cyclic esters that are considered to be living. In a living polymerization, the number of growing polymer chains equals the total number of active available sites of a catalyst (Figure 1.6). The initiation, which is the ring opening of the first cyclic monomer, is faster than the propagation in the living polymerization (\(k_{i} \gg k_{p}\)) and there are no termination and chain transfer reactions.\textsuperscript{73} The polymers produced have controlled molecular weights and a small range of dispersities. However, living polymerization has its limitations and disadvantages. The catalytic productivity is low and the produced polymer is contaminated with catalyst residues.

Immortal ROP (iROP) can be an alternative option to living ROP.\textsuperscript{74} The components of iROP are a catalyst and a chain transfer agent (CTA) that is also an initiator. Here the number of growing polymer chains exceeds the number of active catalyst’s sites, but equals to the amount of chain transfer agent (Figure 1.6). Therefore, iROP is truly catalytic and more attractive from the green chemistry perspective.\textsuperscript{75}
Figure 1.6. Living (top) and immortal (bottom) ring opening polymerizations.

There are two mechanisms of iROP involved. A metal catalyst with a nucleophilic initiator undergoes the usual steps of a coordination-insertion mechanism, where \((k_i >> k_p)\) without a termination, to form the propagating species.\(^{75}\) In the next step, the formed active polymer chain exchanges with a CTA to convert into a dormant chain with a terminal hydroxy group (Scheme 1.5). This reversible transfer reaction should be faster than propagation to form polymers with a small range of \(D_M\) values. A number of polymer chains can be formed in the presence of only one molecule of metal complex, thus making a system truly catalytic with lower catalyst amount needed for the reaction. In addition, iROP can produce end-functionalized polymers by using end-functionalized CTA. However, at the same time iROP encounters the main challenge of the utilization of a catalytic system that can be efficient in living ROP and can deal with large amounts of CTA without becoming inactive.\(^{75}\)

Scheme 1.5. Chain transfer in iROP.
The first example of iROP was reported by Inoue et al. in 1985 by using [tetrathenylporphinate]aluminium chloride-alcohol system to polymerize epoxide to obtain polyether (Figure 1.7). Polyether had a controlled molecular weight and a narrow range of dispersities, and the number of polymer chains was more than the number of aluminium porphyrin molecules. Rapid exchange between the active porphinate-aluminium alkoxide and an alcohol occurred, and the polymer grew on the new aluminium alkoxide. Even in the presence of protic compounds such as acetic acid, hydrogen chloride, carboxylic acids, alcohols and water the polymerization remained immortal. Living polymerization of epoxides mediated by visible light was found by utilizing zinc N-methylated tetrathenylporphyrin complexes. The growing species was (N-methyltetraphenylporphinate)zinc alkoxide. Immortal polymerization was also possible in the presence of 1-propanethiol or methanol giving polymers with a narrow range of $D_M$ values. It was also found that zinc N-substituted porphyrins such as zinc N-methyl and -phenyl-5,10,15,20-tetraphenylporphyrins with thiolate groups at the axial position were capable of living polymerization of propylene sulfide as well as immortal polymerization in the presence of 1-propanethiol.

![Figure 1.7. Structures of aluminum and zinc porphyrin (5,10,15,20-tetraphenylporphyrins).](image)

Zinc-based ROP catalysts are considered to be intrinsically less active compared to other metal ROP catalysts and they can withstand large amounts of protic CTA necessary for the operation of iROP. One of the first examples of a zinc catalyst in iROP of L-LA was commercially available zinc(II) lactate, Zn(Lact)$_2$ (Figure 1.8). Zn(Lact)$_2$ in combination with an alcohol, which acted as a co-initiator, increased the polymerization rate and allowed for
better control over the polymer molecular weight. The polymerization reaction proceeded via a coordination-insertion mechanism with acyl-oxygen bond cleavage, yielding polymer chains with ester and hydroxy end groups after hydrolysis of the Zn-O bond following polymerization.\(^7\)

Bioactive alcohols such as \(\alpha\)-tocopherol, stigmasterol and testosterone were incorporated into oligo- or polylactides as active endgroups (Figure 1.8).\(^7\)

![Figure 1.8. Structure of zinc(II) lactate, Zn(Lact)\(_2\), \(\alpha\)-tocopherol, stigmasterol, and testosterone.](image)

Sarazin \textit{et al.} reported the production of poly(lactide)-\textit{block}-poly(styrene) materials in a one-pot, solvent-free system by utilizing iROP.\(^8\) For the iROP of \textit{rac}-LA and L-LA such homoleptic precursors as \(\text{Zn}[\text{N(SiMe}_3\text{)}_2]_2\), \(\text{Mg}[\text{N(SiMe}_3\text{)}_2]_2\), \(\text{Ca}[\text{N(SiMe}_3\text{)}_2](\text{THF})_2\) and \{BDI-\textit{i}-\textit{Pr}\}\(\text{Zn}[\text{N(SiMe}_3\text{)}_2]_2\) (bis(diketiminate) ligand) were utilized with a functional CTA (TEMPO-OH, 2-hydroxyethyl methacrylate (HEMA), 1-hyroxy-2-phenyl-2-(2',2',6',6'-tetramethyl-1'-piperidinyloxy)ethane (AA-OH)) in styrene, which acted as both a solvent and a reagent. The catalysts were inert toward styrene, but effective and active toward iROP of LA at low monomer loadings. Only \{BDI-\textit{i}-\textit{Pr}\}\(\text{Zn}[\text{N(SiMe}_3\text{)}_2]_2\) was able to convert up to 20 000 equiv of L-LA in the presence of 100 equiv of CTA. The experimental molecular weights of the produced functionalized PLAs closely matched the expected molecular weights with a small range of dispersities confirming the controlled nature of iROP. The end-functionalized PLA
Macromolecules were used as macrorinitiators for the nitroxide-mediated polymerization of styrene.80

Carpentier and coworkers prepared homo- and heteroleptic zinc complexes with fluorinated alkoxide-imino ligands of the type \( \text{ON}^{R_1,R_2} \).81 Zinc heteroleptic complexes \([\text{ON}^{R_1,R_2} \text{Zn}(X)]\) were reported to undergo disproportionation/ligand redistribution that could be controlled by the electron-donating abilities of ligands. The electron-donating abilities of ligand could be modified by changing the substituent on imino group. Immortal ROPs of rac-LA were studied utilizing complexes \( \text{ON}^{\text{Ph},\text{Bn}} \text{ZnEt} (A1^*) \) and \( \text{ON}^{\text{Ph},\text{Bn}} \text{Zn} (A2) \) in the presence of BnOH. Compound A1 was able to convert 250 equiv of the monomer in a controlled and non-stereoselective fashion. The experimental molecular weights matched the theoretical weights and had low dispersity values. A comparison of PLA produced by A2 it was concluded that iROP was less controlled.

![Figure 1.9. Hetero- (left) and homoleptic (right) zinc complexes with \( \text{ON}^{R_1,R_2} \) ligand.](image)

Sarazin et al. reported a family of multidentate amino-ether phenolate ligands to form zinc heteroleptic complexes, which formed some of the most active catalysts for ROP (Figure 1.10).82,83 The compounds were used for iROP of L-LA and rac-LA with isopropanol as a CTA. All reported complexes (A3-A6) demonstrated great activities. Complexes A3 and A4 had the unique ability to polymerize large amounts of monomer (50 000 equiv) with as much as 1000 equiv of CTA. No monomer epimerization was observed during the polymerization reactions producing purely isotactic PLLA from L-LA. Atactic PLA was obtained from rac-LA. Efficient

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*All previously reported in literature complexes described in Chapter 1 are denoted by A.*
catalysts for controlled polymerization were formed only in the presence of an alcohol. Complex A3 was as active as complex A4, suggesting that there was no change in sterics by the presence of the second heterocyclic substituent. Complex A6 polymerized 1000 equiv of monomer in 10 min and 5000 equiv in 60 min in the presence of 25-250 equiv of isopropanol. The polymer chain end groups were studied by NMR spectroscopy and MALDI-TOF MS analyses in order to confirm the iROP nature. All complexes showed good control over the polymerization parameters, proved by low dispersity values and a good match between the experimental and the theoretical molecular weights.

Figure 1.10. Structures of heteroleptic complexes (A3-A6).

1.6 Zinc catalysts for the ROP of lactide
Zinc is considered to be a cheap, available, and non-toxic metal suitable as a potential catalyst for ROP. Zinc powder is being used industrially as a lactide polymerization catalyst. By the work of Schwach and coworkers it was proved that the true initiating species in this case was zinc lactate. The ROP was proposed to be cationic, which led to polymers with alcohol and carboxylic acid end-groups. Lactic acid and water impurities in the monomer facilitated the formation of zinc lactate catalyst.
Zinc(II) lactate, Zn(Lact)$_2$, is a commercially available compound which shows a faster polymerization rate and better control of polymer molecular weight than zinc powder.\textsuperscript{20,91,93} The combination of Zn(Lact)$_2$ with an alcohol leads to an enhancement in the rate of polymerization and control of polymer molecular weights. Many other zinc salts such as Zn(II) L-mandelate, Zn(II) stearate, Zn(II) glycolate, ZnCl$_2$, ZnBr$_2$, and ZnI$_2$ were investigated for the polymerization of L-lactide (Figure 1.11). However, the obtained molecular weights were lower than those collected with Zn(Lact)$_2$.\textsuperscript{78} Diethyl zinc (ZnEt$_2$) shows some catalytic activity, but due to its high flammability and moisture sensitivity it is not suitable for bulk polymerization.\textsuperscript{94}

![Zinc complexes]

**Figure 1.11.** Early zinc catalysts.

Chisholm and colleagues reported tripodal monoanionic tridentate trispyrazolyl- and trisindazolyl-hydroborate complexes with Zn, Mg, and Ca (Figure 1.12).\textsuperscript{95-97} Polymerization was found to be first order in both catalyst and monomer, and proceeded through a coordination-insertion mechanism. The polymerization reactions were living in nature and had dispersity values of 1.1-1.25. Zinc based catalytic systems were slower (60 d, [M]$_0$/[I]$_0$ = 500, 90 % conversion), but more tolerant than analogous magnesium catalysts (60 min, [M]$_0$/[I]$_0$ = 500, 90 % conversion). This result was explained by the polarity of M-OR bond. For M = Zn, the Zn-OR bond is more covalent in nature and less highly polarized than the Mg-OR bond. Complex A7 in solid state was stable in air for a few days. The rate of polymerization of complex A8 was faster than complex A7, because of the steric crowding of the tris-indazolyl ligand. Catalyst A9 was not active toward the polymerization of LA due to the electron-withdrawing effect of the trifluoromethyl substituents on the ligand.
Sterically bulky β-diketiminate (BDI) ligands were widely used ligands for preparation and consequent exploration of zinc and magnesium complexes for ROP of LA.\(^{85,98}\) Coates and colleagues developed a single-site zinc catalyst using a β-diiiminate ligand framework (Figure 1.13).\(^{67,99,100}\) It was found that the catalysts with –Et, -N(SiMe\(_3\))\(_2\), and –OAc (A10, A11, A13) were poor initiators. The polymers produced by those complexes had poorly matched experimental and theoretical weights and broad dispersity values. It was proposed that these groups could react with impurities such as lactic acid, hydrolyzed lactide, or water to produce new initiators. Complexes with isopropoxide and methyl lactate (A12, A14) formed polymers with predicted molecular weights and narrow dispersities. Catalyst A12, [(BDI-1)Zn(μ-O\(^{\text{i}}\)Pr)]\(_2\), was the most active initiator (\(k_{\text{obs}}= 0.22 \text{ min}^{-1}\)) among the three related catalysts, for the polymerization of rac-LA producing heterotactic PLA (\(P_r = 0.9\)) with a dispersity (\(D_M\)) of 1.10. The nature of polymerizations was living as indicated by the narrow \(D_M\) and the linear nature of the plots of the number average molecular weight versus conversions. The steric bulk of the BDI ligands was responsible for the stereochemical control of the polymerization reaction, which proceeded through a chain-end control mechanism. The stereochemical influence of the last enchainated monomer in a polymer chain was impacted by the bulky ligands and the catalyst enchained the opposite enantiomer of lactide leading to a racemic enhancement and heterotactic PLA. The substituents on the β-diiiminate ligand had an influence on the overall performance of the corresponding catalyst, particularly on the rate and stereoselectivity of the polymerization.
For example, [(BDI-2)Zn(μ-Oi-Pr)]₂ and [(BDI-3)Zn(μ-Oi-Pr)]₂ polymerized rac-LA to form polymers with decreased heterotacticity values of Pr = 0.79 and 0.76 and k_{obs} values of 0.017 min⁻¹ and 0.0066 min⁻¹, respectively. Gibson and coworkers reported unsymmetrically substituted β-diketimine zinc complexes (A15 and A16).¹⁰¹ Both complexes were active toward the polymerization of rac-LA reaching 80-90% conversion in 10-30 min. Polymer molecular weights were higher than the theoretical molecular weights with dispersity values of 1.10-1.15, and the heterotactic stereoselectivity was reduced. Surprisingly, for both complexes initiation took place via insertion into Zn-N and Zn-O bonds. It was shown that polymerizations with complexes A15 and A16 had poor initiations due to the large NR₂ and OSiPh₃ initiating groups, but the length of chains increased with monomer conversion.
Figure 1.13. Structures of single-site zinc catalyst reported by Coates and Gibson et al.

Complexes of zinc, aluminium, lithium, and titanium using the bulky racemic binolate ligand were described by Chisholm and colleagues (Figure 1.14). 102 Polymerization of rac-LA with the zinc catalyst was slower compared to the lithium aggregate (96% conversion within 40 h at room temperature). Once the temperature was increased to 80 °C the polymerization reached 99% conversion in 4 h. The expected end groups (H and OCH-i-Pr) were observed by NMR and mass spectrometry. Poly(lactic acid) produced by the zinc complex was found to be heterotactically enriched.
Figure 1.14. Diol supported zinc complex.

Schiff bases are an attractive choice for the ligand design due to the easy tuning of the ligand steric and electronic properties. Three-coordinate monomeric zinc amide and phenoxide complexes were prepared by utilizing a sterically demanding Schiff base ligand (Figure 1.15). Both compounds were found to undergo ligand scrambling in solution and solid state upon heating. Complexes A17 and A18 were capable of polymerizing L-LA and rac-LA to form isotactic and atactic PLA, respectively. Complex A18 was found to be less reactive than complex A17, due to the slower rate of initiation for the bulky 2,6-tert-butylphenoxide. Zinc and magnesium complexes with a more bulky monoether Salen like Schiff base ligand were synthesized by Lin et al (Figure 1.14). Complex A19 was an efficient initiator for ROP of L-LA and rac-LA. Conversion of 90% was achieved in 3.5 h at 60 °C. The polymerization reactions were well controlled with low dispersity values (1.03-1.10). Zinc complex A19 was less active than its magnesium analogue. Polymer formed by polymerizing rac-LA by complex A19 was heterotactic with a Pr value of 0.75. Polymerization proceeded with a first order dependence on monomer concentration and initiator.
Chelating nitrogen ligands can stabilize low-valent species due to their ability to form a rigid bicyclic core that leads to trigonal-monopyramidal coordination geometry around the metal center.\textsuperscript{105} Therefore, the axial position is unoccupied and ready for coordination of monomer in ROP. The triamine ligand was used to form neutral zinc and samarium complexes (Figure 1.16). Although it was expected for secondary bulky amines to form monomeric metal structures, it was found that the zinc complex A20 was a dimer in solution and in the solid state. The copolymerization of rac-LA with glycolide initiated by the zinc complex was done in 3 h at 180 °C (Figure 1.16). Longer reaction times increased the copolymer molecular weight, but the dispersity values increased as well. High molecular weight copolymers with narrow dispersity values could be achieved if the conditions of polymerization were optimized. Another set of diamine supported tetranuclear A21 and dinuclear A22 zinc complexes were reported by Chen and coworkers.\textsuperscript{106} Complex A21 had four three-coordinate planar zinc centers, two of them were bonded to two amide groups in an symmetrical fashion through intramolecular Zn-N coordination, and the other two were bonded to two amide via intermolecular Zn-N coordination. Complex A22 had a center of symmetry and a planar four-membered Zn$_2$N$_2$ core. Both complexes were able to polymerize L-LA at 70 °C, achieving 90% conversion in 2 h. The experimental molecular weights were half the theoretical molecular weights suggesting the
presence of two Zn amide initiators per molecule. Immortal ROP with 4 equiv of isopropanol resulted in a decrease of molecular weight without any increase in activity.

Figure 1.16. Structures of triamine and diamine zinc complexes and glycolide.

N-heterocyclic carbenes were studied for the organocatalytic living ROP of cyclic esters. Hillmyer et al. reported several novel zinc alkoxide catalysts supported by a N-heterocyclic carbene (Figure 1.17). It was demonstrated that in the solid state complexes A23 and A24 were dimeric and the metal centers had distorted tetrahedral geometry that were bound to a carbene and bridged by alkoxide oxygen atoms. In solution, the zinc complex A23 might have broken down into monomers or stayed as a fluxional dimer. The solution structure of complex A24 was more complicated. Both complexes could polymerize rac-LA at room temperature showing a linear relationship between conversion and the experimental molecular weights. Polymerization of LA had a first order dependence on monomer concentration. Heterotactic PLA was produced with a P_t value of 0.6. Further investigations showed that free carbenes could also polymerize LA in the presence of alcohol. However, isotactic PLA (P_m = 0.75) was produced under these circumstances. Bidentate carbene complexes A25 and A26 were also synthesized containing imidazolium salt with a pyridyl arm. Both complexes were
reported to polymerize rac-LA in the melt to form heterotactically enriched PLA (Pᵣ = 0.6) with good monomer conversion at a rapid rate.

![Structures A23, A25, A26](image)

Figure 1.17. Carbene supported zinc complexes.

Hillmyer, Tolman and coworkers first reported a new dizinc-monoalkoxide complex A27. Complex A28 and a highly active zinc ethoxide catalyst using a tridentate diamino-phenoxy ligand A29 were synthesized later (Figure 1.18). The polymerization of rac-LA initiated by complex A27 was rapid (90% conversion within 30 min) at room temperature with good molecular weight control and narrow ℃. The polymerization proceeded via a coordination-insertion mechanism as was proved by the presence of ethoxide end group by ¹H NMR spectroscopy. Atactic PLA was formed from rac-LA. Poly(L-lactic acid) (PLLA) produced from L-lactide using this catalyst was isotactic, ruling out the possibility of stereogenic epimerization. Kinetic studies showed that the rate was first order in lactide and complex A27. Complex A28 did not polymerize LA. Complex A29 was an achiral zinc catalyst that existed as a dinuclear complex in the solid state but was mononuclear in solution. The mononuclear nature of complex A29 in solution was determined by pulsed gradient spin-echo (PGSE) NMR experiments and laser desorption mass spectrometry (LDMS). Complex A29 polymerized rac-LA with good molecular weight control and ℃ values of around 1.4. The rate of LA ROP with compound A29 was showed to be much higher compared to previously well studied systems. The experimental molecular weights were lower than the theoretical values because the effective catalyst concentration deviated from the theoretical value due to impurities and/or an exchange.
agent. The catalyst showed no epimerization during polymerization as PLA formed from L-LA was isotactic, however atactic polymers were produced from the polymerization of rac-LA. Experimentally, it was proved that ethoxy groups initiated ROP via a coordination-insertion mechanism by analyzing high catalyst loadings reactions by $^1$H NMR spectroscopy.

![A27](image1.png) ![A28](image2.png) ![A29](image3.png)

**Figure 1.18.** Structures of complexes reported by Hillmyer and Tolman *et al.*

Inspired by the work of Hillmyer and Tolman, in 2008 Mehrkhodavandi group reported a chiral version of catalyst A29 (Figure 1.19). The racemic catalyst, (±)-(NNMeO$_2$-Bu)ZnOPh (A31), was synthesized and studied for ROP of rac-LA. The racemic zinc phenoxide complex A31 polymerized rac-LA with less activity than complex A29. The high reactivity of complex A29 was explained by the dissociation of the ethylene diamine arm and, thus, forming coordinatively unsaturated zinc center. In contrast, the experimental results for complex A31 did not reveal the dissociation of the terminal amine group. This observation was attributed to the rigid diaminocyclohexane backbone of the complex, which hindered the replacement of the dimethylated amine arm by added pyridine. Poly(lactic acid) produced from rac-LA was atactic. In addition, the molecular weight control of complex A31 was poor and dispersity values were broad, which may have been associated with incomplete initiation.
In the same research group, the role of secondary versus tertiary central amine donors of ligands in dinuclear indium complexes was investigated. The influence of secondary and tertiary amine donors was investigated by the polymerization of rac-LA by complexes (A32-A35). Complexes with secondary amine donors (A33 and A35) showed rates of polymerization 2 orders of magnitude higher than the rates for tertiary amine analogues (A32 and A34) (Figure 1.20). For complex A34 the conversion of 200 equiv of LA was >95% in 3 days, while for complex A35 it was >95% in just 30 min. Similar result were obtained for complexes A32 and A33. Two hypotheses were proposed to explain the polymerization results: 1) the possibility of hydrogen bonding in the system that increased the stability of the dinuclear complexes and prevented them from dissociation, and 2) the electrophilicity of the metal could be altered by secondary and tertiary amines. Further kinetic studies of polymerizations were conducted, the results suggested that H-bonding could influence the stability of complexes, but it was not the major factor in polymerization behavior. The electronic nature of the central metal was studied via DFT calculations. The calculations showed that there was not a big difference in the electronics around the metal in complexes A34 and A35. It was concluded that it was challenging to differentiate between electronic and steric factors in these catalytic systems and isolate H-bonding as a influencing factor of systems’ reactivity.
1.7 Goals of the project

Following the conclusions drawn in the previous indium studies that secondary and tertiary amine donors of the ligands affected the catalyst reactivity, it would be interesting to modify the ligand set for zinc complexes by replacing the central tertiary amine with a secondary amine and imine donor and test their polymerization abilities of cyclic esters such as LA. Therefore, the goals of this project are:

1) Develop new zinc catalysts with tridentate diaminophenolate ligands with central secondary amine and imine donors and test their polymerization abilities of rac-LA. New alkyl (1-3) and alkoxy (4-6) zinc complexes are introduced in this thesis. Initially they were synthesized and characterized (\(^1\)H and \(^{13}\)C{\(^1\)H} spectroscopy, EA, single-crystal X-ray crystallography) by a former Ph.D. student Insun Yu. The complexes have all been resynthesized and the synthetic procedures optimized by me. Further characterization of complexes (variable temperature \(^1\)H spectroscopy, 2D NOESY, pyridine studies) as well as polymerization studies were performed by me.

2) Evaluate the role of complexes with an amino backbone at the central nitrogen atom vs. complexes with an imino backbone at the central nitrogen atom in ROP of rac-LA. Bulk polymerizations as well as low equivalency polymerization studies of rac-LA catalyzed by zinc complexes (1-6) were conducted.
3) Test the ability of alkyl zinc complexes (1-3) to immortally polymerize rac-LA in the presence of different equivalents of CTA.
CHAPTER 2 – SYNTHESIS AND CHARACTERIZATION OF ZINC COMPLEXES

2.1 Introduction

One of the most studied and developed areas of LA polymerization is metal-catalyzed ROP. Various metal catalysts have been utilized for this purpose. The first metal systems studied were the previously discussed homoleptic metal catalysts, such as tin(II) octanoate and aluminium(III) isopropoxide. They are very active and used in industry, but they suffer from poor stereocontrol of rac-LA polymerization. Single-site metal catalysts, which have a general formula of \( L_nMX \) (\( L_n \) - ancillary ligand, \( M \) - Lewis acidic metal center, \( X \) - initiator group, usually an alkoxide and an amide) have attracted the most of the attention for ROP of LA. The ancillary ligands do not actively participate in the polymerization, but they impact the metal center and therefore influence the polymerization progress.

Hillmyer and Tolman used tridentate ligands to develop highly active achiral zinc complexes. The starting achiral diaminophenolate proligand was prepared by refluxing \( N,N,N \)-trimethylenediamine, para-formaldehyde, and 2,4-di-tert-butylphenol. Reacting the proligand with diethyl zinc formed alkyl zinc complex \( A28 \) (Scheme 2.1). The X-ray crystal structure of \( A28 \) demonstrated that the alkyl zinc complex was mononuclear in the solid state with a tridentate coordination mode and giving a distorted tetrahedral geometry around the Zn metal center. Next, \( A28 \) was treated with ethanol to generate the ethoxide complex \( A29 \) (Scheme 2.1). The X-ray crystal structure of \( A29 \) showed that the alkoxy zinc complex was a dimer bridged through two ethoxides having \( \kappa^3 \)-coordination of the ligand. It was found that the bridging oxygen atoms were asymmetrically placed between the two zinc atoms. The solution behavior of complex \( A29 \) was important for understanding the catalytic behavior. Laser desorption mass spectrometry (LDMS) and pulsed gradient spin-echo (PGSE) NMR experiments showed that \( A29 \) did not retain a dimeric form and existed predominantly as a monomer in solution.

Complex \( A28 \) did not show any ability to polymerize rac-LA. However, complex \( A29 \) demonstrated a high activity for the polymerization of rac-LA at low catalyst loadings (\([A29] = \))
0.7 mM) and at different monomer-to-catalyst ratios. Complex A29 exhibited good molecular weight control and relatively low dispersity values ($D_M$). Experimental molecular weights were lower than the theoretical molecular weights, as the effective concentration of the catalyst differed from the expected amount due to present impurities. It was determined by high catalyst loading polymerization studies that the ethoxide group of complex A29 started polymerization via a coordination-insertion mechanism. The produced PLA from rac-LA by complex A29 was atactic and isotactic from L-LA ruling out epimerization during the polymerization reactions. Kinetic experiments showed an overall second order rate law, with first order dependencies on both the monomer and the catalyst. The presence of low level of impurities stopped the polymerization reaction below the minimum catalyst concentration.

**Scheme 2.1.** Synthesis of Hillmyer’s zinc complexes A28 and A29.

Later, the Mehrkhodavandi group reported the chiral version of complex A29. A family of chiral tridentate proligands with trans-diaminocyclohexane as a chiral backbone was synthesized. The steric bulk of the proligands were tuned by introducing different substituents on
the aryl ring and amine groups. The proligand H(NNMeO-t-Bu) reacted with 1 equiv of diethyl zinc and formed the ethyl compound A30 (Scheme 2.2). The racemic and enantiopure (R,R) versions of alkyl zinc complex A30 were synthesized. The molecular structures of (R,R)-A30 and (±)-A30 were determined by single crystal X-ray crystallography. The complexes were mononuclear in the solid state with a tridentate coordination mode and a distorted tetrahedral geometry around the Zn metal center. The solid state structure of (±)-A30 showed two diastereomers with different chirality at the central nitrogen atom and at the zinc center. An equilibrium was also observed in solution between diastereomers generated by the central nitrogen atom. The formation of the secondary product was not observed with complex A28. Alkyl zinc complex A30 was not reactive toward alcohols such as methanol, ethanol, isopropanol, and water. However, complex A28 readily reacted with ethanol to form complex A29. Complex A30 reacted with one equiv of phenol to generate complex A31 (Scheme 2.2). Complex A31 did not form a dimer in the solid state, but aggregation was observed with excess phenol. A distorted tetrahedral geometry was seen around the zinc metal center in the X-ray crystal structure. The reactivity of complex A29 with less acidic alcohols was explained by the fact that the terminal amine arm did not dissociate, thus, the alcohols (methanol, ethanol, isopropanol) and water with pKₐ values of 30 in DMSO could not coordinate to the metal center. The coordination of an alcohol to a metal center leads to decrease of the pKₐ value, and subsequent deprotonation. However, phenol with pKₐ value of 18 in DMSO easily dissociated a proton and proceeded through a direct protonation of the zinc ethyl bond of complex A30. To further support the hypothesis regarding the lability of the terminal amine arm, complexes A28 and A30 were treated with pyridine. In complex A28 the terminal amine arm dissociated from the zinc metal center in the presence of a base, but the terminal amine arm did not dissociate in complex A30. This was explained by the rigidity of the cyclohexane ring that prevented the substitution of the terminal amine arm by a pyridine molecule. Polymerization studies of rac-LA showed that complex A31 had a slow activity and was not stereoselective. The experimental molecular
weights of the large scale polymerization samples did not match well with the theoretical molecular weights, and $D_M$ values were high. It was proposed that the reason of the observed behavior of the catalyst was the rigidity induced by the cyclohexane ring.

**Scheme 2.2.** Synthesis of Mehrkhodavandi’s zinc complexes A30 and A31.

The effect of secondary versus tertiary central amine donors of the tridentate diaminophenolate ligands of the dinuclear indium catalysts was explored. It was concluded that catalysts with the secondary central amine donor had higher activity toward the polymerisation compared to catalysts with the tertiary central amine donor. We wanted to revisit the zinc system and explore the differences in catalyst reactivity when the central tertiary amine is replaced with a secondary amine or imine donor. The steric bulk of the catalysts with the imine central donor can also be tuned by introducing different substituents on the phenolate functionality. The ancillary ligands used in this research project were racemic 2,6-di-t-butyl-(((2-(dimethylamino)cyclohexyl)amino)methyl)phenol ((±)-H(NN_{t-Bu})) and 2,6-di-alkyl-(((2-
(dimethylamino)cyclohexyl)imino)methyl)phenol ((±)-H(NNO₉₉R)), where alkyl = R = t-butyl, t-Bu, C(CH₃)₃ or R = cumyl, Cm, C(CH₃)₂Ph (Figure 2.1).

![Structures of proligands](image)

**Figure 2.1.** Structures of proligands.

### 2.2 Synthesis of proligands

Three tridentate proligands with chiral *trans*-diaminocyclohexane backbone were synthesized based on modified literature procedures reported by Finney *et al.* and the Mehrkhodavandi group for the synthesis of (±)- and (R,R)-N,N-dimethyldiaminocyclohexane (Scheme 2.3).¹¹⁴,¹¹⁷-¹²¹

The synthesis of the proligands started from commercially available (±)-*trans*-1,2-diaminocyclohexane. The diamine was protected with an equivalent of hydrochloric acid prior to its mono-functionalization with a tert-butoxycarbonyl (Boc) protecting group.¹²² Subsequently, two methyl groups were installed via reductive amination with formaldehyde and sodium cyanoborohydride to form the asymmetrically methylated intermediate after deprotection. Condensation of the amine with t-butyl (t-Bu, C(CH₃)₃) and cumyl (Cm, C(CH₃)₂Ph) substituted aldehyde afforded the imine proligands H(NNO₉₉t-Bu) and H(NNO₉₉Cm), respectively.¹²³ Reduction of H(NNO₉₉t-Bu) with sodium cyanoborohydride and recrystallization in acetonitrile produced the pure amine proligand H(NN₉₉Ht-Bu).
2.3 Synthesis and characterization of alkyl zinc complexes (1-3)

The racemic proligands H(NN₇₅O₇₅-Bu), H(NNO₇₅-Bu), and H(NNO₇₅m) react with one equiv of ZnEt₂ to form the alkyl zinc complexes (NN₇₅O₇₅-Bu)ZnEt (1), (NNO₇₅-Bu)ZnEt (2), and (NNO₇₅m)ZnEt (3) in a protonolysis reaction with the elimination of alkane (Scheme 2.4). Complexes 1-3 were isolated as colourless and yellow solids in >90% yields.
Scheme 2.4. Synthesis of alkyl zinc complexes 1-3.

The $^1$H NMR spectra (C$_6$D$_6$, 25 °C) of complexes 1-3 confirm the formation of the desired alkyl zinc complexes. A multiplet peak corresponding to the (-CH$_2$-) protons of the ethyl ligand is observed at 0.53-0.66 ppm, 0.66-0.72 ppm, and 0.39-0.45 ppm for 1, 2, and 3, respectively. Triplet peaks corresponding to the (-CH$_3$) protons of the ethyl ligand are found at 1.80 ppm, 1.79 ppm, and 1.57 ppm in 1, 2, and 3, respectively. These two sets of peaks are shifted downfield compared to the (-CH$_2$-) and (-CH$_3$) protons of pure ZnEt$_2$. The two (-N(CH$_3$)$_2$) methyl groups of the terminal dimethylated amine appear as two singlets at 1.87 and 1.51 ppm, and 1.97 and 1.87 ppm in 1 and 3, respectively. However, for 2, the (-N(CH$_3$)$_2$) protons appear as one sharp singlet at 1.80 ppm. This suggests that the terminal dimethylated amine does not dissociate from the zinc center in 1 and 3 resulting in a $\kappa^3$-coordination mode for both complexes in solution, in contrast, it does dissociate in 2 resulting in equilibration of the methyl groups on the NMR timescale and a $\kappa^2$-coordination mode of the ligand. Previously
reported Zn complex A30 demonstrates two singlets for the terminal (-N(CH₃)₂) and adopts a κ³-coordination mode.

Single crystals of complexes 2 and 3 were grown from a solution of diethyl ether and hexane at room temperature and they were analyzed by single-crystal X-ray diffraction (Figure 2.2). The molecular structures of complexes 2 and 3 have a tridentate coordination mode with a distorted tetrahedral geometry around the Zn metal center. Complex 2 shows a κ³-coordination mode of the ligand in the solid state, but a κ²-coordination mode in solution. The difference between the angles O1-Zn1-C24 (118.9(5)°) and N1-Zn1-N2 (76.9(4)°) for complex 2, and O1-Zn1-C35 (117.4(6)°) and N1-Zn1-N2 (77.8(6)°) for complex 3 is indicative of the distortion from an ideal tetrahedral topology. The Zn1-C24 distance of 1.991(1) Å for complex 2 and the Zn1-C35 distance of 1.989(2) Å for complex 3 are marginally longer than the usually observed distance for Zn(II)-alkyl bonds (1.93-1.98 Å). Complexes 2 and 3 have similar bond distances and angles, which suggests that there is not a big electronic or steric difference between the t-butyl and cumyl substituents on the phenolate functionality.

The angles and distances of complexes 2 and 3 are significantly different from those of the previously reported alkyl Zn complex A30, that has the tertiary central amine donor in the ligand backbone (bond distances (Å): Zn-C (1.971(6)), Zn-N1 (2.152(4)), Zn-N2 (2.185(5)), Zn-O1 (1.927(3)); bond angles (deg): N1-Zn-N2 (82.2(1)), N1-Zn-O1 (95.5(1)), N1-Zn-C (124.5(2)), N2-Zn-O1 (111.6(2)). The Zn-C and the Zn-O bond lengths are slightly longer in complexes 2 and 3 than in A30. The Zn-N2 bond length is longer than the Zn-N1 distance for both complexes 2 and 3, which is evidence that N2 coordinates to the zinc ion more weakly than N1. Lin and coworkers also reported a similar result where the Zn-N bond distances of a tertiary amine group were longer than the imine group Zn-N distances in corresponding zinc alkyl complexes with NNO-tridentate Schiff base ligands. In contrast, A30 has similar Zn-N1 (2.152(4) Å) and Zn-N2 (2.185(5) Å). These results indicate that there are obvious
dissimilarities in electronic properties at the zinc metal center between the imino and amino backbone at the central nitrogen atom.

Figure 2.2. Molecular structures of complexes 2 (left) and 3 (right) with thermal ellipsoids at 50% probability and all H atoms omitted for clarity. Selected distances (Å) and angles (deg) for 2 and 3: Zn-C (2, 1.991; 3, 1.989), Zn-N1 (2, 2.042; 3, 2.000), Zn-N2 (2, 2.292; 3, 2.285), Zn-O1 (2, 1.975; 3, 1.967), N1-Zn-N2 (2, 76.87; 3, 77.84), N1-Zn-O1 (2, 89.54; 3, 90.25), N1-Zn-C (2, 139.76; 3, 135.06), N2-Zn-O1 (2, 121.52; 3, 118.89).

2.4 Synthesis and characterization of alkoxy zinc complexes (4-6)

Alkyl zinc complexes 1-3 react with one equiv of benzyl alcohol in toluene at room temperature for 4 h to form the alkoxy zinc complexes 4-6 (Scheme 2.5), which were isolated as colourless and yellow solids in >80% yields. The $^1$H NMR spectra (C$_6$D$_6$, 25 ºC) of compounds 4-6 show the distinctive broad and multiplet signals for the (-CH$_2$-) protons of the benzyl alkoxy group at 5.40-5.60 ppm, 5.24-5.38 ppm, and 4.65-5.10 ppm, respectively. These observations can be explained by the free rotation in complex 4 around the O-C bond of the alkoxide bridge resulting in an average broad signal for both CH resonances, the hindered rotation of the cyclohexyl moiety around the N-C bond in complex 5 leads to the formation of conformational isomers and multiplet signal with different intensities, and different denticities of both ligands in complex 6 influence the environment for Zn-CH$_2$-Ph. These peaks are shifted downfield compared to the (-CH$_2$-) protons of pure benzyl alcohol. According to the $^1$H NMR spectra, unsymmetrical species are present in solution for complex 6.
Single crystals of complexes 4-6 were isolated from a solution of toluene and hexane at room temperature (Figures 2.3 and 2.4). In the solid state complexes 4-6 form benzyl alkoxy-bridged dimers. Heterochiral dimers (RR/SS) are obtained for all three complexes. In contrast, the crystal structure of the previously reported alkoxy-bridged dinuclear indium catalyst synthesized from a racemic mixture of H(NN\textsubscript{t-Bu}O\textsubscript{t-Bu}) ligand, [(NNO)\textsubscript{t-Bu}InCl\textsubscript{2}(μ-OEt)(μ-Cl)], shows homochiral dimer (RR/RR) formation exclusively without any evidence for the formation of (RR/SS).

The molecular structure of complex 4 retains the κ\textsuperscript{3}-coordination mode of the (NN\textsubscript{t-Bu}O\textsubscript{t-Bu}) ligands. In contrast, the molecular structure of complex 5 shows the κ\textsuperscript{2}-coordination mode of the (NNO\textsubscript{t-Bu}) ligands, and the molecular structure of complex 6 shows both κ\textsuperscript{2}- and κ\textsuperscript{3}-coordination modes of the (NNO\textsubscript{Cm}) ligands. Alkyl zinc complex 2 has the same denticity as complex 5 in solution. The distances and angles around the alkoxy bridging ligands are varied in all three complexes. The Zn-N1 bond length in complex 4 is significantly longer than in both complexes 5 and 6. The bridging oxygen atoms are placed symmetrically between the zinc atoms in complexes 4 and 5, while in complex 6 they are placed unsymmetrically (e.g., O3 is 0.1068 Å).
and O4 is 0.0628 closer to Zn2 than to Zn1). Previously reported complex A29 also exists as a dimer bridged by two ethoxides with the retention of the $\kappa^3$-coordination mode of the corresponding ligand. The bridging oxygen atoms are placed asymmetrically between the zinc atoms, as is also observed for complex 6. Complex A31 shows no evidence for the formation of a phenoxy-bridged dimer in the solid state. Although aggregation is observed with excess phenol present in the crystal lattice. A distorted tetrahedral geometry is observed around the Zn metal center with a phenoxy ligand in close contact with second molecule of phenol -OH.

Figure 2.3. Molecular structures of complexes 4 (left) and 5 (right) with thermal ellipsoids at 50% probability and all H atoms omitted for clarity. Selected distances (Å) and angles (deg) for 4: N1-Zn1 2.2091(9), N2-Zn1 2.1845(9), O1-Zn1 1.9478(7), O2-Zn1 1.9852(8), O2$_i$-Zn1 2.0852(7), N1-Zn1-N2 79.67(3), N1-Zn1-O1 89.86(3), N1-Zn1-O2 96.47(3), N1-Zn1-O2$_i$ 173.45(3), N2-Zn1-O1 120.30(3), N2-Zn1-O2$_i$ 96.29(3), N2-Zn1-O2 115.19(3), O1-Zn1-O2 124.38(3), O1-Zn1-O2$_i$ 96.65(3), O2-Zn1-O2$_i$ 80.50(3), Zn1-O2-Zn1$_i$ 99.50(3). For 5: N1-Zn1 1.973(3), O1-Zn1 1.9213(19), O2-Zn1 1.9622(2), O2$_i$-Zn1 1.9691(19), N1-Zn1-O1 96.68(9), N1-Zn1-O2 131.31(9), N1-Zn1-O2$_i$ 126.76(9), O1-Zn1-O2 107.01(8), O1-Zn1-O2$_i$ 112.48(8), O2-Zn1-O2$_i$ 82.29(8), Zn1-O2-Zn1$_i$ 97.71(8).

Figure 2.4. Molecular structures of complexes 6 with thermal ellipsoids at 50% probability and all H atoms omitted for clarity. Selected distances (Å) and angles (deg) for 6: N1-Zn1 2.0745(14), N2-Zn1 2.1932(15), O1-Zn1 1.9539(12), O3-Zn1 2.0511(12), O4-Zn1 2.0097 (12), N3-Zn2 1.9818(16), O2-Zn2 1.9418(12), O3-Zn2 1.9443(12), O4-Zn2 1.9469(12), N1-Zn1-
The two NMe$_2$ groups are not seen as sharp peaks on the $^1$H NMR spectrum for complex 4 indicating the operation of the fluxional process, while two single peaks appear at 2.02 and 2.06 ppm for complex 5 and four single peaks show up at 2.01, 2.03, 2.08, and 2.10 ppm for complex 6. The $^1$H NMR spectrum of complex A31 shows three distinctive (-NCH$_3$) peaks at 2.02, 1.94, and 1.43 ppm.$^{113}$ Variable temperature $^1$H NMR experiments were performed for complex 4. The low temperature $^1$H NMR spectra of complex 4 were measured using CD$_2$Cl$_2$ as a solvent in the temperature range from 25 to −35 ºC (Figure 2.5). At low temperature the spectrum for complex 4 shows two methyl singlet peaks at 2.65 and 1.95 ppm. The broad multiplet protons of the benzyl alkoxy (-CH$_2$-) group appear as two doublets at 5.41 and 5.10 ppm. The high temperature $^1$H NMR spectrum of complex 4 was also recorded utilizing C$_6$D$_6$ as a solvent in the temperature range from 25 to 65 ºC. One broad singlet peak corresponding to two methyl groups appears at 2.13 ppm (Figure 2.6). Both variable temperature $^1$H NMR experiments (low and high) demonstrated the reversible nature of the processes occurring with complex 4 upon the changing of the temperature. These results suggest that complex 4 might be in dynamic equilibrium between κ$^3$- and κ$^2$-coordination mode of the (NNH$_2$Ot-Bu) ligand at room temperature (Scheme 2.6). The terminal dimethylated amine coordinates and dissociates from the zinc center at room temperature resulting in a broad signal. At lower temperatures, the existing equilibrium is shifted to the κ$^2$-coordination mode of the (NNH$_2$Ot-Bu) ligand, where the terminal dimethylated amine coordinates to the metal center and two methyl peaks appear as two singlet peaks. In contrast, at high temperatures the equilibrium is shifted to the κ$^2$-coordination mode of the (NNH$_2$Ot-Bu) ligand with the terminal dimethylated amine dissociated from the zinc center.
Scheme 2.6. Dynamic equilibrium between $\kappa^3$- and $\kappa^2$-coordination mode of the (NN$_2$OH$_2$Bu) ligand of complex 4.

Figure 2.5. Variable temperature $^1$H NMR spectra (400 MHz, CD$_2$Cl$_2$) of complex 4 (±)[(NN$_2$OH$_2$Bu)Zn(OCH$_2$Ph)]$_2$. (●) - residual toluene, (●) - (-CH$_2$), (●) - (-CH$_3$)$_2$.
In order to prove that complex 4 exists in dynamic equilibrium between \( \kappa^2 \) and \( \kappa^3 \)-coordination mode of the \((\text{NN}_{\text{H}}\text{O}_t\text{-Bu})\text{Zn(OCH}_2\text{Ph})\) ligand in solution at room temperature, 2D Nuclear Overhauser Effect Spectroscopy (NOESY) experiments were performed. The NOESY spectrum demonstrates the existence of through-space dipolar H-H interaction, and NOESY cross peaks are seen for nuclei that are close to each other in space (less than 3.5 Å apart). At \(-35 ^\circ\text{C}\), 2D NOESY spectrum of complex 4 shows that the protons of one methyl group of the terminal dimethylated amine are spatially close to the aromatic protons of the benzyl alkoxy group (Figures 2.7). However, the protons of the second methyl group of the same terminal dimethylated amine do not show the correlation suggesting that they are not in close proximity to anything. At \(65 ^\circ\text{C}\), 2D NOESY spectrum demonstrates that a broad singlet corresponding to the protons of both methyl groups of the terminal dimethylated amine are close to the aromatic protons and the \((-\text{CH}_2-)\) of the benzyl alkoxy group (Figures 2.8). The obtained results indicate that at lower temperature the terminal dimethylated amine coordinates to the zinc center, while at higher temperature it dissociates from the metal center.
In addition, a 2D NOESY spectrum of complex 5, which has the $\kappa^2$-coordination mode of the (NNO$_{t-Bu}$) ligand at room temperature, was taken. The NOESY experiment shows that all protons of the terminal dimethylated amine are close in space to (-N=CH-), aromatic protons and the (-CH$_2$-) of the benzyl alkoxy group, and (-CH-) of DACH (Figures 2.9). The NOESY spectra of complex 4 at 65 °C and of complex 5 at room temperature become similar to each other implying that both complexes adopt $\kappa^2$-coordination mode of the corresponding ligand only at different temperatures. It is interesting that complexes 4 and 5, which are only different at the central nitrogen atom (4 has an amino backbone and 5 has an imino backbone), have different coordination modes of the corresponding ligands in solid state and in solution at room temperature. Complex 4 at higher temperature has the same $\kappa^2$-coordination mode of the ligand as complex 5 at room temperature.

**Figure 2.7.** 2D NOESY spectrum (400 MHz, CD$_2$Cl$_2$, −35 °C, mixing time (d8) = 0.8 s) of complex 4 (±)-[NNH$_{t-Bu}$Zn(OCH$_2$Ph)]$_2$. 

Figure 2.8. 2D NOESY spectrum (400 MHz, C$_6$D$_6$, 65 °C, mixing time (d8) = 1.0 s) of complex 4 (±)-[(NN$_{t}$-Bu)Zn(OCH$_2$Ph)$_2$].

Figure 2.9. 2D NOESY spectrum (400 MHz, CD$_2$Cl$_2$, 25 °C, mixing time (d8) = 0.25 s) of complex 5 (±)-[(NNO$_{t}$-Bu)Zn(OCH$_2$Ph)$_2$].
2.5 Exchange studies

In an attempt to observe the dissociation of the terminal dimethylated amine from the zinc center, reactions between complexes 4-6 and pyridine were conducted. In the first set of experiments reactions of complexes 4-6 were carried out with 4 equivalents of pyridine in situ for 72 h at room temperature in C₆D₆. The proposed dissociation mechanism is depicted below, where a pyridine molecule can coordinate to the zinc center, thereby causing the desymmetrization of the complex (Scheme 2.7). The ¹H NMR spectra of the complexes were obtained before pyridine addition and 72 hours after pyridine addition.

**Scheme 2.7.** Proposed dissociation mechanism for the reaction of 5 and 6 and pyridine.

The experiment with complex 4, which has κ³⁻NN₇O₅⁻Bu chelating ligand in the solid state and the equilibrium between κ²⁻ and κ³⁻ chelating modes in solution, does not show any changes upon pyridine addition (Figure 2.10). The two N-methyl groups are not easily discernible in pure complex 4 due to the fact that the terminal dimethylated amine coordinates and dissociates from the zinc center at a fast rate on the NMR timescale. Therefore, it is challenging to observe the changes occurring with these methyl peaks in the presence of pyridine. Pyridine can compete with the terminal dimethylated amine to coordinate to the zinc center, but these changes are hard to detect due to their fast rate of coordinating and dissociating. Therefore, ¹H NMR spectra of the catalyst taken over 72 h at 25 °C showed that all the signals remain unchanged in this period.
In contrast, complexes 5 and 6, which have $\kappa^2$-NNO$_R$-Bu and both $\kappa^2$- and $\kappa^3$-NNO$_Cm$ chelating ligands, respectively, show changes in the $^1$H NMR spectra upon pyridine addition (Figure 2.10). In complexes 5 and 6 two and four singlet peaks for the methyl groups, respectively, become broader over time. This result suggests that the dinuclear species have $\kappa^2$-NNO$_R$ chelating ligands and can either breakup into mononuclear species under the influence of a donor such as pyridine or become desymmetrized upon pyridine coordination.

![NMR Spectra](image)

**Figure 2.10.** Addition of 4 equiv. of pyridine to complexes 4-6 (left to right) at 0 (bottom) and 72 (top) hours (400dir MHz, C$_6$D$_6$, 25 °C).

An analogous experiment was carried out with the previously reported alkyl Zn complexes A28 and A30 over 60 min and 48 h, respectively, in CD$_2$Cl$_2$. The proton NMR spectrum for complex A28 showed peaks belonging to the pyridine protons and a broad signal at 2.24 ppm corresponding to the methyl groups instead of two singlets at 2.38 ppm and 2.09 ppm seen for pure complex A28. The obtained results suggested that in the presence of pyridine the terminal dimethylated amine dissociated from the zinc center and two signals equilibrated. In the case with complex A30 the experimental results did not show the dissociation of the terminal amine group. This observation was attributed to the rigid diaminocyclohexane backbone of the
complex which hindered the replacement of the dimethylated amine arm by pyridine. However, the results obtained from the reactions of complexes 5 and 6 with excess pyridine challenge the previously reported statement regarding the rigidity of the diaminocyclohexane backbone. All tested complexes 4-6 and A30 have the diaminocyclohexane backbone in their structures, but there are distinct outcomes in the reactions with pyridine. Complexes 5 and 6 have an imino backbone at the central nitrogen atom, while complexes 4 and A30 have an amino backbone. It is likely that there are significant differences in electronic properties at the zinc metal center between the imino and amino backbone at the central nitrogen atom that causes the above mentioned complexes to react differently with pyridine, and at the same time the steric factor cannot be omitted that could be impacted by the tertiary amine in complex A30.

Attempts were made to isolate base adducts of complexes 4-6 by dissolving the compounds in neat pyridine and stirring them overnight at room temperature. In order to remove excess free pyridine from the product mixture, the solution was dried in vacuo at room temperature. The $^1$H NMR spectra of the product mixtures suggest the dissociation of complexes 4-6 into different isomers (Figures 2.11 - 2.13). Unfortunately, it was not possible to obtain the molecular structures of the corresponding adducts due to their solubility in organic solvents.

Figure 2.11. $^1$H NMR spectra (400 MHz, 25 °C, C$_6$D$_6$) of complex 4 (±)-[(NN$_4$O$_8$-Bu$_4$)Zn(OCH$_2$Ph)$_2$]$_2$ (bottom) and complex 4 stirred overnight in neat pyridine (top).
Figure 2.12. $^1$H NMR spectra (400 MHz, 25 °C, C$_6$D$_6$) of complex 5 (±)-[(NNO$_{t}$Bu)Zn(OCH$_2$Ph)]$_2$ (bottom) and complex 5 stirred in neat pyridine (top).

Figure 2.13. $^1$H NMR spectra (400 MHz, 25 °C, C$_6$D$_6$) of complex 6 (±)-[(NNO$_{Cm}$)Zn(OCH$_2$Ph)]$_2$ (bottom) and complex 6 stirred in neat pyridine (top).

2.6 Conclusion

Three tridentate proligands were synthesized using chiral trans-diaminocyclohexane backbone based on previously reported procedures. One of the proligands has a secondary amine backbone with the t-butyl substituents on the phenolate functionality and the other two
proligands have an imino central nitrogen atom with two different substituents on the phenolate functionality: \( t \)-butyl and cumyl.

Alkyl zinc complexes 1-3 were synthesized via protonolysis of ZnEt\(_2\) with the previously discussed proligands. The yields of the reactions were high >90%. The formed alkyl zinc complexes 1-3 were characterized by \(^1\)H NMR spectroscopy and single-crystal X-ray crystallography. Proton NMR spectra show that the NMe\(_2\) groups coordinate to the zinc center in complexes 1 and 3, while this analogous group dissociates in 2. Molecular structures of 2 and 3 show that they are mononuclear in solid state adopting a tridentate coordination mode with a distorted tetrahedral geometry around the zinc centers.

Alkoxy zinc complexes 4-6 were synthesized by reacting complexes 1-3 with benzyl alcohol. The yields of the reactions were over >80%. Complexes 4-6 exist as benzyl alkoxy-bridged dimers in solid state. They all have different coordination modes in solid state: 4 has \( \kappa^3 \)-coordination mode, 5 has \( \kappa^2 \)-coordination mode, and 6 has both \( \kappa^2 \) - and \( \kappa^3 \)-coordination modes. High and low variable temperature \(^1\)H NMR spectroscopy and 2D NOESY prove that at room temperature complex 4 exists in dynamic equilibrium between \( \kappa^2 \) - and \( \kappa^3 \)-coordination modes, where the terminal dimethylated amine coordinates and dissociates from the zinc metal center at a fast rate on the NMR timescale. It is an interesting finding how the change from an amino to imino backbone of the central nitrogen atom in the proligands can alter the coordination modes of complexes 4 and 5 both in the solid and solution states.

Exchange studies were also performed with complexes 4-6 in the presence of excess of pyridine \emph{in situ}. It is demonstrated that for complex 4 there are no obvious changes upon pyridine addition. However, for complexes 5 and 6 the changes are visible; the peaks corresponding to the methyl groups of the terminal dimethylated amine become broader in the presence of pyridine over 72 h at room temperature suggesting that pyridine molecules can coordinate to the metal center, thereby causing the desymmetrization of complexes. All three
complexes 4-6 dissolved in neat pyridine dissociate into their respective isomers as is showed via $^1$H NMR spectroscopy.
CHAPTER 3 – POLYMERIZATION OF RAC-LACTIDE WITH ALKOXY AND ALKYL ZINC COMPLEXES VIA RING OPENING POLYMERIZATION AND IMMORTAL RING OPENING POLYMERIZATION

3.1 Introduction

A major target of lactide (LA) polymerization is developing an ideal catalyst that exhibits high activity, good control of the molecular weight with a small range of dispersities, and is very stereoselective in the polymerization of rac-LA. It is hard to achieve all these listed requirements, but single site metal alkoxides give promising results.\textsuperscript{20,63} Stereocontrol influences tacticity, which in turn affects polymer physical properties, such as crystallinity, melting temperature, and the rate of degradation.

Stereocontrol of a polymerization can be realized by two different mechanisms, enantiomorphic site control and chain-end control.\textsuperscript{63} A chain-end control mechanism is usually associated with hindered and achiral catalysts, where the chirality of the last incorporated monomer in the propagating chain determines the chirality of the next monomer to be enchained. In an enantiomorphic site control mechanism, the chirality of the catalyst, not of the chain end, determines the chirality of the next insertion, one enantiomer of a monomer is preferred over the other enantiomer.\textsuperscript{63} Metal-based catalysts are the most widely explored and studied and have many examples of stereocontrolled ROP.

Two different chiral salen aluminium complexes were reported for the kinetic resolution of rac-LA producing isotactic stereoblock PLA via enantiomorphic site control. Spassky and coworkers used (+)-enantiomer of a chiral BINAP-derived salen-aluminium complex \textit{A36} (Figure 3.1). Complex \textit{A36} was used for the stereoselective polymerization of rac-LA. Complex \textit{A36} demonstrated a preference for the polymerization of D-LA over L-LA. At 19\% conversion, a growing polymer was made of exclusively D-LA (88\% enantiomeric enrichment). At higher conversions both enantiomers of the monomer were incorporated in a polymer chain. Stereocomplexation was proved to occur by the increased melting point of the obtained polymer at high conversions.\textsuperscript{35,130} Feijen and coworkers reported new salen aluminium alkoxides (both
enantiopure and racemic) \textbf{A37} by utilizing the cyclohexyl backboned, commercially available, Jacobsen ligand (Figure 3.1).\textsuperscript{31,34} These catalysts showed high isospecificity and excellent control in solution and melt polymerization of LA. It was the first example of high level of stereocontrol achieved under melt polymerization conditions. Kinetic studies demonstrated that \((R,R)-\textbf{A37}\) preferred L-LA over D-LA.

Achiral catalysts are more attractive to use for polymerization due to their ease of synthesis and low costs compared to their chiral counterparts. Coate’s bulky \(\beta\)-diketiminate zinc complexes \textbf{A12} formed highly heterotactic PLA from rac-LA through a chain-end control mechanism (Figure 3.1).\textsuperscript{99} The highly active achiral zinc catalyst \textbf{A29} reported by Hillmyer, Tolman and coworkers formed atactic PLA demonstrating the absence of a chain-end control mechanism.\textsuperscript{111} This work inspired Merhkhodavandi group to explore the chiral version of that catalyst \textbf{A31} that showed a low activity toward the polymerization of rac-LA and no stereoselectivity (Figure 3.1).\textsuperscript{113} 

\textbf{Figure 3.1.} Various metal complexes used for the polymerization of lactide.
In this research project, alkyl 1-3 and alkoxy 4-6 zinc complexes were studied to investigate their reactivity towards ROP of rac-LA and differentiate between complexes with an amino backbone at the central nitrogen atom and complexes with an imino backbone at the central nitrogen atom (Figure 3.2). In addition, alkyl zinc complexes 1-3 were used for immortal ring opening polymerization of rac-LA in the presence of chain transfer agents (CTAs) such as benzyl alcohol.

Figure 3.2. Alkyl (1-3) and alkoxy (4-6) zinc complexes studied in this research project.

3.2 ROP of rac-lactide with alkoxy zinc complexes 4-6
Polymerization of rac-lactide catalyzed by the zinc complexes 4-6 was carried out in solution (DCM) under dry and anaerobic conditions in a glovebox with a fixed catalyst
concentration of 0.7 mM at room temperature for 30 min. Conversions were monitored by \(^1\)H NMR spectroscopy, and molecular weights and dispersity values were obtained by multi-detector gel permeation chromatography (GPC).

It showed that complexes are highly active toward ROP of rac-LA at room temperature reaching >90% conversion for 1000 equiv of the monomer in 5 min. In order to fully convert the monomer into the desired product bulk polymerizations were left for 30 min showing >96% conversion over a wide range of initial monomer-to-catalyst ratios. The complexes are as active as complex \textbf{A29} reported by Hillmyer and Tolman at low catalyst concentration (0.7 mM). Complexes \textbf{4-6} are much more reactive than \textbf{A31} previously reported by Mehrkhodavandi group. Complex \textbf{A31} is significantly less active reaching a full conversion of 200 equiv of rac-LA in 40 h at catalyst concentration of 1.6 mM. The conversion is 96% in 25 h if the concentration is increased to 2.4 mM. The molecular weights of polymers catalyzed by complex \textbf{A31} do not match the theoretically calculated molecular weights with \(D_M\) values in the range of 1.80 - 2.15.\(^{113}\) The experimental molecular weights of the obtained polymers for complex \textbf{4} are lower than the theoretical values with a large range of \(D_M\) values (1.04 - 1.61). Complex \textbf{5} produces polymers with molecular weights lower than expected with \(D_M\) values between 1.14 - 1.32. However, catalyst \textbf{6} demonstrates better molecular weight control and produces PLA with molecular weights close to theoretical values within a smaller range of \(D_M\) values (1.07 - 1.27) (Figure 3.3).
Figure 3.3. Plot of observed PLA $M_n$ and $D_M$ as functions of added rac-LA for catalysts 4-6. The black solid line indicates the expected theoretical $M_n$ values based on the LA:initiator ratio and 100% conversion. All reactions carried out in CH$_2$Cl$_2$ at 25 °C in 30 min with rac-lactide and [Zn] = 0.7 mM, and polymer samples were obtained at >96% conversion. (■ - $M_n$ and ○ - $D_M$ in 30 min, ■ - $M_n$ and • - $D_M$ in 5 min).

Complex 4 produces polymers with consistently lower experimental molecular weights and broader dispersity values compared to 5 and 6. It was suspected that 4 can promote the depolymerization reaction of formed PLA at longer times, thereby lowering the molecular weight and broadening the dispersity values. In an attempt to test this hypothesis the polymerization of 1000 equiv of rac-LA catalyzed by complex 4 was left for 5 min instead of 30
min (Figure 3.3). As it can be seen from the plot of LA/Initiator vs. \( M_n \) the experimental molecular weights of the products are higher and the dispersity values are lower than those obtained after 30 min. To provide further evidence that complex 4 depolymerizes polymers, a sample of PLA was synthesized by the chiral dinuclear indium complex, \([\{(NNO)\text{InCl}\}_2(\mu-\text{OEt})(\mu-\text{Cl})]\). The produced PLA had a molecular weight of 123 kDa with the \( D_M = 1.00 \). The PLA was stirred with complex 4 in CD\(_2\)Cl\(_2\) at room temperature for 1 h and 24 h. The PLA samples were analyzed afterwards by GPC. A significant molecular weight decrease from 123 kDa to 25.3 kDa and broadening of the \( D_M \) value from 1.00 to 1.25 after 1 h was observed. The molecular weight further decreased to 11.9 kDa with a \( D_M \) value of 1.30 after 24 h (Figure 3.4).

![Depolymerization studies with 4](image)

**Figure 3.4.** Overlap of GPC traces for PLA samples. Black solid (\( M_n = 123 \) kDa, \( D_M = 1.00 \)). Blue dashed (\( M_n = 25.3 \) kDa, \( D_M = 1.25 \)). Red dashed (\( M_n = 11.9 \) kDa, \( D_M = 1.30 \)).

In order to characterize the polymers generated with complexes 4-6 and \( \text{rac-LA} \), polymerizations with 50 equiv of monomer were performed. Although this low equivalency polymerization is not always representative of the bulk polymerization, it is a convenient method to determine the polymer chain end and confirm a coordination-insertion mechanism. The reactions of complexes 4-6 were quenched after 30 min (over 95% conversion) and the resulting
oligomers (Mn~6800 g/mol) were analyzed by $^1$H NMR spectroscopy and matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry.

For complex 4, the $^1$H NMR spectrum clearly shows peaks corresponding to the hydroxy and benzyl alkoxy ester chain ends at 2.71 and 7.36 ppm, respectively (Figure 3.5). There are also extra peaks corresponding to the methoxy ester chain end. It is suspected that the methoxy group replaces the benzyl alkoxy group upon the precipitation of the oligomers in cold wet methanol. In order to prove the point, the next batch of the oligomers was precipitated in cold wet ethanol. The $^1$H NMR spectrum shows no peaks corresponding to the methoxy ester chain end, but rather peaks for the ethoxy ester chain end (Figure 3.6). Interestingly, in this polymerization reaction the benzyl alkoxy group can be substituted by either methoxy or ethoxy groups.

![Figure 3.5. $^1$H NMR spectrum of PLA generated by 4 and precipitated in MeOH (400 MHz, CDCl$_3$, 25 °C).](image)

![Figure 3.6. $^1$H NMR spectrum of PLA generated by 4 and precipitated in EtOH (400 MHz, CDCl$_3$, 25 °C).](image)
The MALDI-TOF mass spectrum for the same polymer sample generated with catalyst 4 and precipitated in cold wet methanol does not show the chain ends of the polymers, which contradicts the result obtained by $^1$H NMR spectrum of the oligomers. The most intense peaks are separated by 72 mass units, which is half of the molecular weight of LA (Figure 3.7).\textsuperscript{131,132} This is an indication that there are odd and even numbers of lactyl repeat units in polymer chains. Presence of odd and even lactyl units, as well as the absence of a chain end are the characteristics of an intramolecular transesterification side reaction taking place during low equivalency polymerization, leading to the formation of macrocycles.

There is a second set of less intense peaks observed on the spectrum that are separated from the major peaks by 32 mass units. These signals are also separated by 72 mass units. This information shows that the benzyl alkoxy ester chain end of the polymer can be replaced by the methoxy group after the quenching of the polymer with cold methanol. This side reaction can be catalyzed by the presence of carbonic acid in wet methanol solution.\textsuperscript{133} A similar result was obtained from the MALDI-TOF mass spectrum for the polymer sample precipitated in cold wet ethanol. The most intense peaks correspond to the macrocyclic oligomers without any chain ends confirming the operation of an intramolecular transesterification reaction as well. In addition, no peaks corresponding to the methoxy ester chain ends are observed (Figure 3.8).
Figure 3.7. MALDI-TOF mass spectrum of PLA produced by complex 4 and precipitated in MeOH (2,5-dihydroxybenzoic acid with NaTFA).

Figure 3.8. MALDI-TOF mass spectrum of PLA produced by complex 4 and precipitated in EtOH (2,5-dihydroxybenzoic acid with NaTFA).

In contrast, for both complexes 5 and 6 both the $^1$H NMR and mass spectra show the expected hydroxy and benzyl alkoxy ester chain ends of the oligomers at 2.71 and 7.36 ppm, and 2.71 and 7.35 ppm, respectively (Figures 3.9, 3.10). The benzyl alkoxy ester chain ends for
complexes 5 and 6 are visible in the spectra leading to the conclusion that both catalysts initiate the growth of the polymer chains through a coordination-insertion mechanism. The methoxy ester chain ends are also observed on the $^1$H NMR spectra if the oligomers are precipitated in cold wet methanol. However, if oligomers are precipitated in cold wet ethanol the ethoxy ester chain ends appear instead of the methoxy ester chain ends (Figure 3.11, 3.12).

Figure 3.9. $^1$H NMR spectrum of PLA generated by 5 and precipitated in MeOH (400 MHz, CDCl$_3$, 25 °C).

Figure 3.10. $^1$H NMR spectrum of PLA generated by 6 and precipitated in MeOH (400 MHz, CDCl$_3$, 25 °C).

Figure 3.11. $^1$H NMR spectrum of PLA generated by 5 and precipitated in EtOH (400 MHz, CDCl$_3$, 25 °C).
The mass spectra for the low equivalency polymerizations catalyzed by complexes 5 and 6 show the benzyl alkoxyl ester chain ends. The peaks are separated by 144.13 mass units, which is the molecular weight of LA (Figures 3.13, 3.16). This is evidence of linear structures with the corresponding chain ends. Undesirable intermolecular transesterification side reactions are evidenced by broadening of dispersity values and the appearance of less intense peaks separated by 72 mass units from more intense peaks. Unidentified less intense peaks were also visible on the spectra. It can be concluded that mass spectrum shows the presence of different speciation occurring during the low equivalency polymerization of rac-LA.

Figure 3.13. MALDI-TOF mass spectrum of PLA produced by complex 5 and precipitated in MeOH (2,5-dihydroxybenzoic acid with NaTFA).
Figure 3.14. MALDI-TOF mass spectrum of PLA produced by complex 6 and precipitated in MeOH (2,5-dihydroxybenzoic acid with NaTFA).

Figure 3.15. MALDI-TOF mass spectrum of PLA produced by complex 5 and precipitated in EtOH (2,5-dihydroxybenzoic acid with NaTFA).
The previous discussion shows that the different species detected using MALDI-TOF depend on catalysts. Complexes 4-6 promote different types of transesterification side reactions. The obtained results can be related to the nature of the central nitrogen atom in the complexes. Low equivalency polymerizations of rac-LA catalyzed by complex 4 with an amino central nitrogen atom have intramolecular transesterification side reactions, described as backbiting, leading to the production of macrocyclic oligomers. For complex 4 intramolecular transesterification is the major operating side reaction. However, low equivalency polymerizations of rac-LA catalyzed by complexes 5 and 6, which both have an imino central nitrogen atom, have intermolecular transesterification side reactions, which tend to redistribute the chains causing to broaden dispersity values, and the appearance of varying speciation. Intermolecular transesterification is a minor side reaction for complexes 5 and 6, as the major peaks observed by MALDI are separated by 144 mass units that correspond to the linear oligomers with the expected chain ends.
Cyclic oligomers are formed via the low equivalency polymerization studies catalyzed by complex 4, therefore, it might be possible that high molecular weight cyclic PLAs could be generated by 4 during the bulk polymerizations. This possibility was investigated by comparing the polymers’ intrinsic viscosities produced by complexes 4-6. Intrinsic viscosity \([\eta]\) is a measure of a polymer’s ability to increase the viscosity of a solvent, it is one of the most important properties of polymers in dilute solution, and it is a widely utilized measure to determine molecular weight, size, and topological structure of polymers.\(^{134-136}\) For linear monodisperse polymers the intrinsic viscosity is related to the molecular weight by the Mark-Houwink-Sakurada equation as follows:

\[
[\eta] = KM^a
\]

where \(K\) and \(a\) are constants for a given polymer/solvent/temperature system. The exponent \(a\) for linear polymers is between 0.5 and 1. As it can be seen the intrinsic viscosity is directly proportional to the molecular weight. It is a known fact that linear materials have higher intrinsic viscosities and shorter elution times compared to the cyclic structures.\(^{131,137,138}\) The classic approach to produce cyclic polymers includes the intramolecular cyclization of linear precursors at high dilution. In the overlaid Mark-Houwink-Sakurada plots of all polymers formed by three complexes it can be observed that for given number average molecular weights \((M_n)\) all polymers generated by complexes 4-6 display very similar intrinsic viscosities (Figure 3.17). There is no evidence of formation of cyclic PLAs from rac-LA by complex 4 during the bulk polymerization studies. This observation provides evidence that the mechanisms dominating in low equivalency polymerizations of a monomer are not quite the same as the mechanisms existing in the bulk polymerizations and produce different polymer structures due to the fact that low equivalency polymerizations are in fact more dilute than the bulk polymerization reactions.
Figure 3.17. Mark-Houwink-Sakurada plots of PLAs produced by 4 (♦), 5 (●), 6 (■).

$^1$H-$^1$H NMR spectrum of PLA produced from the rac-lactide and complex 4 shows an heterotactically enriched microstructure with $P_r$ values in the range of 0.53-0.58 (Figure 3.18). Catalyst 5 shows a larger degree of stereochemical control in the polymerization of rac-LA producing heterotactically enriched PLA ($P_r = 0.80$) (Figure 3.19). At decreased temperatures the stereochemical control is better giving a $P_r$ value of 0.85 (Figure 3.19). Catalyst 6 demonstrates a production of heterotactically enriched PLA with $P_r$ value of 0.68-0.69 (Figure 3.20). Isotactic PLLA is derived from the polymerization of L-LA by complexes 4-6 under the same experimental conditions suggesting the absence of any epimerization during the polymerization reactions. From the collected $P_r$ values it is seen that complexes 5 and 6 demonstrate a better stereoselectivity during the course of polymerization reactions than complex 4. Especially complex 5, which shows the highest heteroselectivity among the three complexes with $P_r$ values > 0.80.

The hypothesis can be made that complex 5 can be the bulkiest compound among the three complexes, thus, undergoing a chain-end control mechanism. It was discussed in the
previous section than complex 5 has \( \kappa^2 \)-coordination mode of both ligands with the dissociated terminal dimethylated amines both in the solid state and in solution. In solution, the terminal dimethylated amine arm is dissociated from the zinc metal center and can rotate freely around the N-C bond. These two factors can enhance the bulkiness of the complex. Previously reported zinc complexes A29 and A31 do not show any stereoselectivity forming completely atactic PLA microstructures even at lower temperatures.

![Figure 3.18. Homonuclear decoupled \( ^1 \text{H} \) NMR spectrum of methine region of PLA prepared by complex 4 (\( P_r = 0.63 \)) (600 MHz, 25 °C, CDCl\(_3\)).](image1)

![Figure 3.19. Homonuclear decoupled \( ^1 \text{H} \) NMR spectrum of methine region of PLA prepared by complex 5 at room temperature (left) (\( P_r = 0.80 \)) and at 0°C (right) (\( P_r = 0.85 \)) (600 MHz, CDCl\(_3\)).](image2)
Comparing above discussed polymerization results of complexes 4-6 it can be concluded that amino and imino central nitrogen atoms affect the polymerization outcomes. Complex 4 with an amino central nitrogen atom produces slightly heterotactically enriched polymers with a poor match between the experimental molecular weights and the theoretical molecular weights. Moreover, it depolymerizes the formed polymer. Cyclic oligomers are mostly produced by complex 4 in low equivalency polymerization studies via intramolecular transesterification side reactions. In contrast, complexes 5 and 6 with an imino central nitrogen atom polymerize LA in a more controlled fashion generating more heterotactically enriched PLA. They form linear oligomers with expected chain ends in low equivalency polymerizations, but minor intermolecular transesterification side reactions are also present.

### 3.3 ROP of rac-lactide with alkyl zinc complexes 1-3

Alkyl zinc complexes 1-3 were tested to determine whether they are capable of polymerizing rac-LA. Alkyl groups are not known to be good initiators of ring opening polymerizations of cyclic esters, because a Zn-alkyl(ethyl) bond is not as nucleophilic as alkoxides, the initiation step is slower than the propagation step, and backbiting or transesterification side reactions can occur during the polymerization.\(^ {67,84}\) Ring opening polymerization of rac-LA catalyzed by alkyl zinc complexes reach around 80% for 1000 equiv of the monomer in 20 h for complex 2 and 44 h for complexes 1 and 3 (Table 3.1). The
experimental molecular weights of the obtained polymers by complexes 1-3 are not reproducible and much higher than the theoretical values with broad $D_M$ values. These results are completely different from the results obtained by complexes 4-6 indicating that ROP of rac-LA catalyzed by complexes 1-3 has a distinct mechanism that does not involve the direct insertion of alkyl groups into the acyl-oxygen bond.

Alkyl zinc complexes can get activated by present impurities and form new initiating groups. Lactic acid, trace amounts of water, and hydrolyzed lactide are possible impurities present in the monomer. Production of polymers with high molecular weights and broad molecular weight distributions is explained by the fact that the initiation rate is slower than the propagation rate. Long PLA chains cause the reaction solution get viscous over time and eventually after certain hours form gels (Figure 3.21). Therefore, it is concluded that the nature of the initiating groups is important for the polymerization behavior.

**Table 3.1.** Ring opening polymerization of rac-lactide catalyzed by complexes 1-3.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat</th>
<th>[M]₀/[I]</th>
<th>Conv. a (%)</th>
<th>$M_{\text{tho}}^b$ (g/mol)</th>
<th>$M_{\text{exp}}^c$ (g/mol)</th>
<th>$M_{\text{w,exp}}^c$ (g/mol)</th>
<th>$D_M^c$</th>
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<tr>
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<td>118210</td>
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<td>2</td>
<td>200</td>
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<tr>
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<tr>
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<td>112450</td>
<td>2.999×10^5</td>
<td>3.726×10^5</td>
<td>1.24</td>
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</table>

All reactions carried out in CH₂Cl₂ at 25 °C in 20 h with rac-lactide and [Zn] = 0.7 mM.

*Monomer conversion is determined by $^1$H NMR spectroscopy. *bCalculated from [M]₀/[I] x monomer conversion $\times M_{\text{LA}} + M_{\text{C2H6}}$ ($M_{\text{LA}} = 144.13$ g/mol, $M_{\text{C2H6}} = 30.07$ g/mol). *cDetermined by GPC-LALLS (gel permeation chromatography-low angle laser light scattering) (dn/dc =0.044 for PLA in THF). *dReactions carried out in CH₂Cl₂ at 25 °C in 44 h with rac-lactide and [Zn] = 0.7 mM.
Figure 3.21. Gelation formation during the polymerization reactions of *rac*-lactide catalyzed by complexes 1-3.

3.4 Immortal ROP of *rac*-lactide with alkyl zinc complexes 1-3

Immortal ROP (iROP) is a truly catalytic method where each active species can produce hundreds of polymer chains from large equiv of a monomer. External protic agents such as alcohol are crucial for iROP, because they promote chain transfer during the polymerization reaction. In this research project iROP of *rac*-LA utilizing alkyl zinc complexes 1-3 in combination with benzyl alcohol (BnOH) as a transfer agent was studied (Table 3.2). In the previous section it was showed than alkyl zinc complexes 1-3 themselves only slowly promote the ROP of *rac*-LA in DCM at room temperature and produce polymers with very high molecular weights. However, upon the addition of 5 or 10 equiv of BnOH the polymerization reactions speed up reaching >90% conversion of 500 equiv of the monomer in 5 min. Most likely that complexes 1-3 react with BnOH and produce immediate \{((\text{NNO}_R)\text{ZnOBn})_n\} species *in situ* that can start the polymerization of a monomer (Scheme 3.1).
Scheme 3.1. Immortal ROP of rac-LA catalyzed by complexes 1-3/BnOH.

As expected the molecular weights of the obtained polymers decrease as more BnOH is added. This is explained by the fact that the molecular weights of the polymers are inversely related to the amount of the initiating species, in this case alcohol. Experimental molecular weights of produced PLA samples match well the theoretical molecular weights. The dispersities in all cases are in the range of 1.02-1.12. These results suggest that the polymerization reactions proceed in a well-controlled fashion, and the rate constant for the transfer between active PLA chains and dormant hydroxy terminated chains ($k_\alpha$) is greater than the chain propagation constant ($k_p$) as it was discussed previously (Scheme 3.1).

Table 3.2. Immortal ring opening polymerization of rac-lactide catalyzed by complexes 1-3 in the presence of benzyl alcohol.

<table>
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<tr>
<th>Entry</th>
<th>Cat</th>
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<th>$M_n, \text{exp}^b$ (g/mol)</th>
<th>$M_w, \text{exp}^b$ (g/mol)</th>
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<td>500/1/5</td>
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All reactions carried out in CH₂Cl₂ at 25 ºC in 30 min with rac-lactide and [Zn] = 1.7 mM. Polymer samples are obtained at >92% conversion determined by ¹H NMR spectroscopy. $^a$Calculated from [M]₀/[BnOH] × monomer conversion × $M_{LA}$ + $M_{BnOH}$ ($M_{LA} = 144.13$ g/mol,
Determined by GPC-LALLS (gel permeation chromatography-low angle laser light scattering) (dn/dc = 0.044 for PLA in THF).\textsuperscript{65}

Produced PLA samples were examined by \textsuperscript{1}H NMR spectroscopy and MALDI-TOF in order to determine the polymer end groups and establish the initiating group. The hydroxy and benzyl alkoxy ester chain ends for complexes 1-3/BnOH are identified at 2.71 and 7.35 ppm, confirming that the polymerization reactions of rac-LA proceed through a coordination-insertion mechanism (Figures 3.22-3.24). In addition, the methoxy ester chain ends are also visible on the \textsuperscript{1}H NMR spectra of the polymers precipitated in cold wet methanol. The same methoxy ester chain ends are observed for the above discussed PLA oligomers generated by complexes 4-6.

**Figure 3.22.** \textsuperscript{1}H NMR spectrum of PLA generated by 1/BnOH and precipitated in MeOH(300 MHz, CDCl\textsubscript{3}, 25 °C).

**Figure 3.23.** \textsuperscript{1}H NMR spectrum of PLA generated by 2/BnOH and precipitated in MeOH(300 MHz, CDCl\textsubscript{3}, 25 °C).
Analysis by MALDI-TOF mass spectrometry of low molecular weight samples further confirmed the existence of the expected polymer chain ends (Figures 3.25-3.27). The major species present in all three mass spectra are of the same family of polymers with hydroxy and benzyl alkoxy ester chain ends. The most intense peaks are separated by increments of 144 mass units. However, undesirable transesterification reactions are also identified on the spectra due to the presence of the minor distribution with the peaks separated from the most intense peaks by 72 mass units. At the same time, the transesterification reactions cannot be detrimental to the overall polymerization reaction, because the dispersity values of the polymers are narrow. By comparing the mass spectra of the PLA oligomers formed by complexes 4-6 to the mass spectra of low molecular weight PLA samples generated by complexes 1-3/BnOH via iROP, it can be concluded that complexes with an imino central nitrogen atom (5, 6, 2/BnOH, 3/BnOH) form the same linear PLA chains with the presence of minor intermolecular transesterification side reactions. The outcomes are completely different for the complexes with an amino central nitrogen atom (4, 1/BnOH) suggesting they are more influenced by the concentration factor. An intramolecular transesterification side reaction is the major reaction operating in more diluted low equivalency polymerization reactions catalyzed by complex 4 that produces oligomeric PLA macrocycles. However, in more concentrated polymerization reactions catalyzed by complex 1/BnOH an intramolecular transesterification side reaction is absent, the major species formed are linear PLA chains, and only minor intermolecular transesterification is observed.

Figure 3.24. 1H NMR spectrum of PLA generated by 3/BnOH and precipitated in MeOH (300 MHz, CDCl₃, 25 °C).
Figure 3.25. MALDI-TOF mass spectrum of PLA produced by complex 1/BnOH from iROP of \textit{rac}-lactide (2,5-dihydroxybenzoic acid with NaTFA).

Figure 3.26. MALDI-TOF mass spectrum of PLA produced by complex 2/BnOH from iROP of \textit{rac}-lactide (2,5-dihydroxybenzoic acid with NaTFA).
Figure 3.27. MALDI-TOF mass spectrum of PLA produced by complex 3/BnOH from iROP of rac-lactide (2,5-dihydroxybenzoic acid with NaTFA).

Produced polymers were characterized by homonuclear $^1$H/$^1$H NMR spectroscopy. PLA produced from the rac-lactide and complex 1/BnOH shows a heterotactically enriched microstructure with a $P_r$ value of 0.66. Catalyst 2/BnOH shows a larger degree of stereochemical control in the polymerization of rac-lactide producing heterotactically enriched PLA ($P_r = 0.82$). Catalyst 3/BnOH demonstrates a production of heterotactically enriched PLA with a $P_r$ value of 0.68. Those results closely match the results obtained by ROP of rac-LA by complexes 4-6, suggesting that complexes 4-6 are actually generated in situ upon the addition of an alcohol to the alkyl zinc complexes 1-3 that can initiate the ROP of the monomer.

3.5 Conclusion

Polymerization studies were carried out using complexes 4-6 with rac-lactide. Unlike previously reported A31, catalysts 4-6 demonstrate high activity toward the polymerization of rac-lactide. The activity of 4-6 are compared to the activity of the complex A29 reaching a complete conversion of 1000 equiv of the monomer in 5 min. Compound 4 produces polymers with lower experimental molecular weights with broad dispersity values. However, compounds 5
and 6 show a better control over the polymer molecular weights with narrower dispersity values, particularly compound 6. Catalyst 4 was showed to undergo the depolymerization reactions. The polymerization parameters including experimental molecular weights and dispersity values are more controlled after 5 min. In the presence of complex 4 formed PLA samples of high molecular weight depolymerize thereby decreasing the molecular weight and broadening the $D_M$ values over time.

Low equivalency polymerization reactions were set up to study the polymer chain end groups through $^1$H NMR spectroscopy and MALDI-TOF. Proton spectra of formed oligomers show the expected hydroxy and benzyl alkoxy ester chain ends confirming that catalysts 4-6 polymerize the monomer through a coordination-insertion mechanism. In addition, extra peaks corresponding to different chain ends (methoxy and ethoxy) are observed suggesting that some of benzyl alkoxy chain ends can be replaced during the precipitation of polymers in cold wet solvents. Different transesterification side reactions are detected for complexes 4-6 via MALDI-TOF. The polymerizations with complex 4 undergo intramolecular transesterification and form oligomeric macrocycles without any chain ends, while both complexes 5 and 6 have only minor intermolecular transesterification producing linear redistributed oligomers with the expected chain ends. Through the careful investigation of the intrinsic viscosities of the produced PLAs it is concluded that catalyst 4 does not form high-molecular weight cyclic PLAs.

Catalysts 4-6 are more stereoselective compared to both complexes A29 and A31. Compound 4 forms slightly heterotactic polymers. However, 5 and 6 form more heterotactically enriched PLA. Complex 5 shows the highest stereoselectivity that can be raised by decreasing the temperatures. The dissociated terminal dimethyl amine arm of compound 5 could be the reason of enhanced heteroselectivity, as it can increase the steric bulk of 5 in solution. Examination of all these results strongly suggests that amino and imino central nitrogen donors in complexes play the crucial role in the polymerization behavior of the catalysts.
Alkyl zinc complexes 1-3 were also examined to determine if they can polymerize rac-LA at ambient conditions. They are very inactive producing irreproducible, uncontrolled, and very high molecular weight polymers. High molecular weight chains of PLA in solution cause the increase in viscosity over time and eventually form gel-looking materials, which are hard to dissolve and precipitate. These results are not surprising due to the previously reported works that claimed that alkyls are not as sufficient initiators as alkoxides.

Immortal ROP of complexes 1-3 in the presence of CTA was studied. The systems 1-3/CTA are very active reaching almost a complete conversion of the monomer in 5 min. The experimental molecular weights closely match the theoretical molecular weights with very narrow $D_M$ values suggesting that the nature of iROP is well controlled. The $^1$H NMR and mass spectra of polymers confirmed the presence of the expected chain ends.
CONCLUSION AND FUTURE WORK

New active zinc complexes (1-6) supported by tridentate diaminophenolate ligands with a central secondary amine and imine donors were developed. Zinc compounds were synthesized and characterized by $^1$H and $^{13}$C{$^1$H} spectroscopy, EA, single-crystal X-ray crystallography, variable temperature $^1$H NMR spectroscopy, and 2D NOESY. The alkyl zinc complexes 1-3 were synthesized by reacting the corresponding proligands with ZnEt$_2$. Compounds 1-3 are mononuclear in solid state with a tridentate coordination mode and a distorted tetrahedral geometry around the zinc centers. Alkoxy zinc complexes 4-6 were synthesized by reacting alkyl zinc compounds with benzyl alcohol. In solid state and in solution 4-6 are benzyl alkoxy-bridged dimers adopting different coordination modes. The nature of the central nitrogen atom (amino vs. imino) of the proligands can impact the coordination modes of the alkoxy zinc complexes in solid and solution states. Pyridine exchange studies with compounds 4-6 were studied.

Polymerization studies were carried out using complexes 1-6 with rac-lactide. Alkyl zinc catalysts 1-3 are inactive towards the polymerization forming irreproducible, uncontrolled, and very high molecular weight gel-looking polymers. Alkyls are not efficient initiators as alkoxides. In contrast, catalysts 4-6 demonstrate high activity towards the polymerization of rac-lactide. Complex 4 produces polymers with lower experimental molecular weights with broad dispersity values, and promotes the depolymerization reactions. Catalysts 5 and 6 show a better control over the polymer molecular weights with narrower dispersity values, and produce heterotactically enriched PLA. Complex 5 shows the highest stereoselectivity possibly due to the dissociated terminal dimethyl amine arm contributing to the bulkiness of the complex. Low equivalency polymerization reactions were performed and studied via $^1$H NMR spectroscopy and MALDI-TOF. PLA oligomers are cyclic formed by complex 4 via the major existing intramolecular transesterification side reactions. However, both complexes 5 and 6 form linear oligomers, and minor intermolecular transesterification side reactions take place during the polymerization reactions. All obtained results suggest that amino and imino central nitrogen
donors impact the coordination modes of the complexes in solution and consequently influence the polymerization behavior of the catalysts. Compounds 1-3 are capable of immortal ROP of LA in the presence of CTA. The systems 1-3/CTA are very active producing polymers with the experimental molecular weights similar to the theoretical molecular weights with very narrow dispersity values.

Future work includes the redesigning the proligands by introducing other substituents on the phenolate functionality in order to increase the bulkiness of the catalysts. These changes could slow down the polymerization reaction rates, therefore, increase the control over the experimental molecular weights and dispersity values, and also increase the stereoselectivity of the systems. It would be interesting to study the influence of amino vs. imino central nitrogen donors on the polymerization of other cyclic esters. Preliminary results of iROP reactions are promising. It could be useful to extend these studies and try the polymerizations with high loading of monomers and alcohols. In addition, functionalized alcohols can be utilized in order to create new topologies and/or obtain new useful properties of the resulting materials.
EXPERIMENTAL SECTION

General methods: Unless otherwise specified all procedures were carried out using standard Schlenk techniques or in an MBraun glovebox. A Bruker Advance 300 MHz, Bruker Advance 400dir MHz and Bruker Advance 600 MHz spectrometers were used to record NMR spectra. \(^1\)H NMR chemical shifts are given in ppm versus residual protons in deuterated solvents as follows: δ 7.16 for C\(_6\)D\(_6\), δ 7.27 for CDCl\(_3\), δ 5.32 for CD\(_2\)Cl\(_2\). \(^{13}\)C{\(^1\)H} NMR chemical shifts are given in ppm versus residual \(^{13}\)C in solvents as follows: δ 128.00 for C\(_6\)D\(_6\), and δ 77.23 for CDCl\(_3\). Homonuclear decoupled \(^1\)H NMR (\(^1\)H{\(^1\)H}NMR) experiments were performed on Bruker Advance 600 MHz spectrometer. Diffraction measurements for X-ray crystallography were made on a Bruker X8 DUO diffraction with graphite monochromated Mo-K\(\alpha\) radiation. The structure was solved by direct methods and refined by full-matrix least-squares using the SHELXTL crystallographic software of the Bruker-AXS. Unless specified, all non-hydrogen were refined with anisotropic displacement parameters, and all hydrogen atoms were constrained to geometrically calculated positions but were not refined. The elemental composition of an unknown sample is determined by using a calibration factor. The calibration factor is determined by analyzing a suitable certified organic standard (OAS) of a known elemental composition. Mass spectra were recorded on Bruker Autoflex MALDI-TOF (time-of-flight mass (TOF) spectrometer equipped with MALDI ion source) operated in either linear or reflection mode. For MALDI-TOF measurement, the sample was dissolved in dichloromethane (0.6 mg/μL); 2,5-dihydroxybenzoic acid (DHB) (0.02 mg/μL) was used as the matrix (10:1) and 1 μL of sodium trifluoroacetate (100 mM) was added as the cation source. Molecular weights were determined by GPC-LLS using a Agilent liquid chromatograph equipped with a Agilent 1200 series pump and autosampler, three Phenogel 5 μm Narrow Bore columns (4.6 × 300 mm with 500 Å, 10^3 Å and 10^4 Å pore size), a Wyatt Optilab differential refractometer, Wyatt tristar miniDAWN (laser light scattering detector) and a Wyatt ViscoStar viscometer. The column temperature was set at 40 °C. A flow rate of 0.5 mL/min was used and samples were dissolved in THF (ca. 4 mg/mL).
Et$_2$O and toluene were degassed and dried using activated alumina in a Solvent Purification System from Innovation Technology, Inc. C$_6$H$_6$ (C$_6$D$_6$) and tetrahydrofuran were further dried over Na/benzophenone and distilled under N$_2$. CDCl$_3$ was dried over CaH$_2$ and vacuum-transferred to a Strauss flask and then degassed through a series of freeze-pump-thaw cycles. Deuterium-labeled NMR solvents were purchased from Cambridge Isotope Laboratory. Racemic LA was obtained from PURAC America Inc. and recrystallized from hot toluene three times and was dried under vacuum. Other chemicals and solvents were purchased from Aldrich, Fisher, or Alfa Aesar, and were used without further purification.

**Synthesis of complex 1.** The preparation of complex 1 is a modification of a literature procedure.$^{111,113}$ A 2,6-di-t-butyl-(((2-(dimethylamino)cyclohexyl)amino)methyl)phenol proligand (±)-H(NN$_{tBu}$O)$_2$ (234 mg, 0.649 mmol) was dissolved in Et$_2$O (5 mL). Then, Zn(CH$_2$CH$_3$)$_2$ (0.0665 mL, 0.649 mmol) was added dropwise. The solution was stirred at room temperature for 5 min. The solvent was removed *in vacuo* to dryness. The desired product 1 was isolated as a white crystalline solid without further purification. Yield 289 mg 98%. $^1$H NMR (C$_6$D$_6$, 600MHz): δ 7.59 (1H, d, $^4$J$_{H-H} = 2.7$ Hz, Ar H), 6.86 (1H, d, $^4$J$_{H-H} = 2.7$ Hz, Ar H), 3.96 (1H, dd, $^3$J$_{H-H} = 12.4$ Hz, $^2$J$_{H-H} = 2.2$ Hz, -HN-CH$_2$-Ar), 3.16 (1H, dd, $^3$J$_{H-H} = 12.4$ Hz, $^2$J$_{H-H} = 2.2$ Hz, -HN-CH$_2$-Ar), 2.17 (1H, td, $^3$J$_{H-H} = 4.4$ Hz, 10.9 Hz, -CH- of DACH), 1.87 (3H, s, -N(C$_3$H$_3$)$_2$), 1.89 (9H, s, Ar-C(CH$_3$)$_3$), 1.72 – 1.83 (4H, m, -CH$_2$- of DACH and -CH$_3$ of ethyl), 1.51 (3H, s, -N(CH$_3$)$_2$), 1.38 – 1.49 (10H, m, -CH- of DACH and Ar-C(CH$_3$)$_3$), 1.21 – 1.30 (2H, m, -CH$_2$- of DACH), 1.02 (1H, br. m, -CH$_2$- of DACH), 0.78 (1H, d, $^3$J$_{H-H} = 10.3$ Hz, -NH-), 0.53 – 0.66 (4H, m, -CH$_2$- of ethyl and -CH$_2$- of DACH), 0.19 – 0.29 (1H, m, -CH$_2$- of DACH), 0.07 – 0.19 (1H, m, -CH$_2$- of DACH); $^{13}$C{$^1$H} NMR (C$_6$D$_6$, 151MHz): δ 166.5 (Ar C), 138.2 (Ar C), 134.1 (Ar C), 126.6 (Ar C-H), 124.6 (Ar C-H), 120.9 (Ar C), 68.6 (-CH- of DACH), 53.2 (-CH- of DACH), 51.0 (-NH-CH$_2$-Ar), 45.5 (-N(CH$_3$)$_2$), 38.3 (-N(CH$_3$)$_2$), 36.4 (Ar-C(CH$_3$)$_3$), 32.8 (Ar-C(CH$_3$)$_3$), 31.6 (-CH$_2$- of DACH), 30.8 (Ar-C(CH$_3$)$_3$), 25.0 (-CH$_2$- of DACH), 25.0 (-

**Synthesis of complex 2.** Complex 2 was prepared in a similar manner to complex 1. A 2,6-di-t-butyl-((2-(dimethylamino)cyclohexyl)imino)methyl)phenol proligand (±)-H(NNO$_{tBu}$) (393 mg, 1.10 mmol) was dissolved in Et$_2$O (5 mL). Then, Zn(CH$_2$CH$_3$)$_2$ (0.112 mL, 1.10 mmol) was added dropwise. The solution was stirred at room temperature for 1 h. The solvent was removed *in vacuo* to dryness. Complex 2 was obtained as a yellow crystalline solid without further purification. Yield 442 mg 89%. $^1$H NMR (C$_6$D$_6$, 600MHz): $\delta$ 7.69 (1H, d, $^4$J$_{H-H} = 2.7$ Hz, Ar H), 7.65 (1H, s, -N=CH-Ar), 6.99 (1H, d, $^4$J$_{H-H} = 2.6$ Hz, Ar H), 2.45 (1H, td, $^3$J$_{H-H} = 3.6$ Hz, 10.9 Hz, -CH$_2$- of DACH), 2.16 – 2.25 (1H, m, -CH$_2$- of DACH), 1.82 (9H, s, Ar-C(CH$_3$)$_3$), 1.75 – 1.81 (m, 9H, -CH$_3$ of ethyl and -N(CH$_3$)$_2$), 1.45 (9H, s, Ar-C(CH$_3$)$_3$), 1.35 – 1.44 (3H, m, -CH$_2$- of DACH), 1.24 – 1.32 (1H, m, -CH$_2$- of DACH), 0.98 – 1.10 (1H, m, -CH$_2$- of DACH), 0.85 (1H, m, -CH$_2$- of DACH), 0.76 (1H, m, -CH$_2$- of DACH), 0.69 (2H, q, $^3$J$_{H-H} = 8.1$ Hz, -CH$_2$- of ethyl), 0.55 (1H, m, -CH$_2$- of DACH); $^{13}$C{$^1$H} NMR (C$_6$D$_6$, 151MHz): $\delta$ 168.9 (Ar C), 168.2 (-N=CH-Ar), 142.2 (Ar C), 134.8 (Ar C), 129.5 (Ar C-H), 128.7 (Ar C-H), 119.6 (Ar C), 68.7 (-CH- of DACH), 66.0 (-CH- of DACH), 40.2 (-N(CH$_3$)$_2$), 36.5 (Ar-C(CH$_3$)$_3$), 34.4 (Ar-C(CH$_3$)$_3$), 32.9 (-CH$_2$- of DACH), 32.2 (Ar-C(CH$_3$)$_3$), 30.3 (Ar-C(CH$_3$)$_3$), 25.5 (-CH$_2$- of DACH), 25.3 (-CH$_2$- of DACH), 21.0 (-CH$_2$- of DACH), 14.2 (Zn-CH$_2$-CH$_3$), -1.1 (Zn-CH$_2$-CH$_3$). Anal. Calcd. For C$_{25}$H$_{42}$N$_2$OZn: C 66.43; H 9.37; N 6.19. Found: C 66.44; H 9.45; N 6.13.

**Synthesis of complex 3.** Complex 3 was prepared in a similar manner to complex 1. A 2,6-bis-(dimethylphenyl)-((2-(dimethylamino)cyclohexyl)imino)methyl)phenol proligand (±)-H(NNO$_{cm}$) (320 mg, 0.663 mmol) was dissolved in Et$_2$O (5 mL). Then, Zn(CH$_2$CH$_3$)$_2$ (0.0679 mL, 0.663 mmol) was added dropwise. The solution was stirred at room temperature for 1 hour. The solvent was removed *in vacuo* to dryness. Complex 3 was obtained as a dark yellow crystalline solid without further purification. Yield 377 mg 99%. $^1$H NMR (C$_6$D$_6$, 600MHz): $\delta$ 7.64 (1H, d, $^4$J$_{H-H} = 2.7$ Hz, Ar H), 7.35 – 7.45 (5H, m, 4 Ar-H and -N=CH-Ar), 7.19 – 7.27 (4H,
m, 4 Ar-H), 7.08 – 7.12 (2H, m, 2 Ar-H), 6.95 (1H, d, $^4J_{H-H} = 2.6$ Hz, Ar-H), 2.32 (1H, td, $^3J_{H-H} = 3.7$ Hz, 10.8 Hz, -CH- of DACH), 1.98 – 2.03 (1H, m, -CH- of DACH), 1.97 (3H, s, -N(CH$_3$)$_2$), 1.87 (3H, s, -N(CH$_3$)$_2$), 1.79 (6H, s, Ar-C(CH$_3$)$_2$(C$_6$H$_5$)), 1.65 (6H, s, Ar-C(CH$_3$)$_2$(C$_6$H$_5$)), 1.57 (3H, t, $^3J_{H-H} = 8.1$ Hz, -CH$_3$ of ethyl), 1.27 – 1.39 (2H, m, -CH$_2$- of DACH), 1.17 – 1.27 (2H, m, -CH$_2$- of DACH), 0.81 - 0.92 (1H, m, -CH$_2$- of DACH), 0.76 (1H, m, -CH$_2$- of DACH), 0.63 – 0.72 (1H, m, -CH$_2$- of DACH), 0.39 – 0.54 (3H, m, -CH$_2$- of DACH and -CH$_2$- of ethyl); $^{13}$C[$^1$H] NMR (C$_6$D$_6$, 151MHz): δ 167.9 (Ar C), 167.4 (-N=CH-Ar), 152.9 (Ar C), 152.2 (Ar C), 142.3 (Ar C), 134.4 (Ar C), 131.2 (Ar C-H), 131.1 (Ar C-H), 128.7 (Ar C-H), 128.2 (Ar C-H), 127.7 (Ar C-H), 126.6 (Ar C-H), 126.2 (Ar C-H), 125.0 (Ar C-H), 119.8 (Ar C), 68.6 (-CH- of DACH), 65.9 (-CH- of DACH), 43.5 (Ar-C(CH$_3$)$_2$(C$_6$H$_5$)), 42.9 (Ar-C(CH$_3$)$_2$(C$_6$H$_5$)), 40.2 (Ar-C(CH$_3$)$_2$(C$_6$H$_5$)), 32.4 (-CH$_2$- of DACH), 31.8 (Ar-C(CH$_3$)$_2$(C$_6$H$_5$)), 31.8 (Ar-C(CH$_3$)$_2$(C$_6$H$_5$)), 30.9 (-N(CH$_3$)$_2$), 29.2 (-N(CH$_3$)$_2$), 25.4 (-CH$_2$- of DACH), 25.2 (-CH$_2$- of DACH), 21.1 (-CH$_2$- of DACH), 14.0 (Zn-CH$_2$-CH$_3$), −1.3 (Zn-CH$_2$-CH$_3$). Anal. Calcd. For C$_{35}$H$_{46}$N$_2$OZn: C 72.97; H 8.05; N 4.86. Found: C 73.08; H 8.08; N 4.70.

**Synthesis of complex 4.** The equimolar amount of benzyl alcohol (48.3 mg, 0.446 mmol) in toluene (0.5 mL) was added to a solution of complex 1 (203 mg, 0.446 mmol) in toluene (5 mL) at room temperature. The reaction mixture was stirred for 4 h, and a white solid was precipitated which was not purified further. The solvent was removed *in vacuo* to dryness. Yield 190 mg 80%. $^1$H NMR (600 MHz, C$_6$D$_6$): δ 7.78 (2H, d, $^3J_{H-H} = 6.6$ Hz, Ar H of benzyl alkoxide), 7.63 (1H, d, $^4J_{H-H} = 2.3$ Hz, Ar H), 7.26 (2H, t, $^3J_{H-H} = 7.2$ Hz, Ar H of benzyl alkoxide), 7.08 – 7.14 (1H, m, Ar H of benzyl alkoxide), 6.88 (1H, d, $^4J_{H-H} = 2.2$ Hz, Ar H), 5.49 (2H, br. s., -CH$_2$- of benzyl alkoxide), 4.30 (1H, d, $^2J_{H-H} = 11.9$ Hz, -HN-CH$_2$-Ar), 3.35 (1H, d, $^2J_{H-H} = 10.3$ Hz, -HN-CH$_2$-Ar), 2.12 – 2.19 (1H, m, -CH- of DACH), 1.87 – 1.96 (1H, m, -CH- of DACH), 1.85 (9H, br. s., Ar-C(CH$_3$)$_3$), 1.66 (1H, t, $^3J_{H-H} = 10.2$ Hz, -NH-), 1.46 (9H, s, Ar-C(CH$_3$)$_3$), 1.17 – 1.31 (4H, m, -CH$_2$- of DACH), 0.52 – 0.71 (2H, m, -CH$_2$- of DACH), 0.11 – 0.30 (2H, m, -CH$_2$- of DACH); $^{13}$C[$^1$H] NMR (C$_6$D$_6$, 151MHz): δ 165.8 (Ar C), 148.3 (Ar C of
benzyl alkoxide), 138.0 (Ar C), 133.9 (Ar C), 126.6 (Ar C-H of benzyl alkoxide), 127.3 (Ar C-H of benzyl alkoxide), 127.2 (Ar C-H of benzyl alkoxide), 126.1 (Ar C-H), 124.4 (Ar C-H), 121.2 (Ar C), 69.5 (-CH$_2$- of benzyl alkoxide), 68.4 (-CH- of DACH), 51.9 (-CH- of DACH), 50.7 (-NH-CH$_2$-Ar), 36.2 (Ar-C(CH$_3$)$_3$), 34.4 (Ar-C(CH$_3$)$_3$), 32.7 (Ar-C(CH$_3$)$_3$), 31.3 (-CH$_2$- of DACH), 30.9 (Ar-C(CH$_3$)$_3$), 25.4 (-CH$_2$- of DACH), 24.9 (-CH$_2$- of DACH), 21.4 (-CH$_2$- of DACH). Anal. Calcd. For C$_{35}$H$_{46}$N$_2$OZn: C 67.72; H 8.71; N 5.26. Found: C 67.63; H 8.59; N 5.11.

**Synthesis of complex 5.** Complex 5 was prepared in a similar manner to complex 4 with the corresponding zinc alkyl complex 2, (±)-(NNO$_2$-Bu)Zn(CH$_2$CH$_3$), (209 mg, 0.463 mmol). Complex 5 was obtained as a yellow crystalline solid without further purification. Yield 198 mg 80%. $^1$H NMR (600 MHz, C$_6$D$_6$): $\delta$ 7.74 – 7.79 (2H, m, Ar H), 7.70 (1H, s, -N=CH-Ar), 7.71 (1H, s, -N=CH-Ar), 7.56 (4H, br. s., Ar H of benzyl alkoxide), 7.06 (4H, t, $^3$J$_{H-H}$ = 6.5 Hz, Ar H of benzyl alkoxide), 7.00 (2H, d, $^3$J$_{H-H}$ = 2.6 Hz, Ar H), 6.89 – 6.99 (2H, m, Ar H of benzyl alkoxide), 5.24 – 5.38 (4H, br. m, -CH$_2$- of benzyl alkoxide), 2.54 – 2.71 (2H, m, -CH- of DACH), 2.29 (1H, td, $^3$J$_{H-H}$ = 3.3, 11.2 Hz, -CH- of DACH), 2.15 (1H, td, $^3$J$_{H-H}$ = 3.2, 11.2 Hz, -CH- of DACH), 2.06 (6H, s, -N(CH$_3$)$_2$), 2.02 (6H, s, -N(CH$_3$)$_2$), 1.92 (18H, 2 s, Ar-C(CH$_3$)$_3$), 1.48 – 1.64 (8H, m, -CH$_2$- of DACH), 1.45 (18H, 2 s, Ar-C(CH$_3$)$_3$), 1.31 – 1.39 (1H, m, -CH$_2$- of DACH), 1.27 (1H, m, -CH$_2$- of DACH), 1.03 – 1.14 (1H, m, -CH$_2$- of DACH), 0.95 – 1.03 (1H, m, -CH$_2$- of DACH), 0.83 – 0.95 (2H, m, -CH$_2$- of DACH), 0.78 (2H, q, $^3$J$_{H-H}$ = 11.7 Hz, -CH$_2$- of DACH); $^{13}$C($^1$H) NMR (C$_6$D$_6$, 151MHz): $\delta$ 170.6 (-N=CH-Ar), 170.2 (Ar C), 170.1 (Ar C), 170.0 (-N=CH-), 146.7 (Ar C of benzyl alkoxide), 146.5 (Ar C of benzyl alkoxide), 141.5 (Ar C), 141.4 (Ar C), 134.8 (Ar C), 134.7 (Ar C), 130.5 (Ar C-H), 129.3 (Ar C-H), 129.2 (Ar C-H), 128.7 (Ar C-H of benzyl alkoxide), 127.3 (Ar C-H of benzyl alkoxide), 127.1 (Ar C-H of benzyl alkoxide), 126.6 (Ar C-H of benzyl alkoxide), 118.9 (Ar C-H of benzyl alkoxide), 118.8 (Ar C-H of benzyl alkoxide), 69.8 (-CH$_2$- of benzyl alkoxide), 69.6 (-CH$_2$- of benzyl alkoxide), 67.4 (-CH- of DACH), 67.2 (-CH- of DACH), 67.0 (-CH- of DACH), 66.5 (-CH- of DACH), 41.2 (-
N(CH₃)₂), 41.0 (-N(CH₃)₂), 36.4 (Ar-C(CH₃)₃), 34.4 (Ar-C(CH₃)₃), 32.9 (-CH₂- of DACH), 32.6 (-CH₂- of DACH), 32.2 (Ar-C(CH₃)₃), 32.2 (Ar-C(CH₃)₃), 30.6 (Ar-C(CH₃)₃), 30.6 (Ar-C(CH₃)₃), 25.5 (-CH₂- of DACH), 25.5 (-CH₂- of DACH), 25.4 (-CH₂- of DACH), 25.4 (-CH₂- of DACH), 22.0 (-CH₂- of DACH), 21.9 (-CH₂- of DACH). Anal. Calcd. For C₆₀H₈₈N₄O₄Zn₂: C 67.98; H 8.37; N 5.28. Found C 67.86; H 8.37; N 5.30.

**Synthesis of complex 6.** Complex 6 was prepared in a similar manner to complex 4 with the corresponding zinc alkyl complex 3, (±)-(NNO₃m)Zn(CH₂CH₃), (196 mg, 0.340 mmol). Complex 6 was obtained as a pale yellow crystalline solid without further purification. Yield 208 mg 93%. ¹H NMR (600 MHz, C₆D₆): δ 7.56 – 7.59 (3H, m, Ar H and -N=CH-Ar), 7.56 – 7.59 (5H, m, -N=CH-Ar and Ar H), 7.42 – 7.46 (4H, m, Ar H), 7.33 – 7.39 (2H, m, Ar H), 7.27 – 7.33 (1H, m, Ar H), 7.21 – 7.24 (4H, m, Ar H), 7.19 (4H, t, 3J_H-H = 7.7 Hz, Ar H), 7.07 – 7.12 (5H, m, Ar H), 7.02 – 7.07 (4H, m, Ar H), 6.97 (2H, m, Ar H), 5.10 (1H, br. s., -CH₂- of benzyl alkoxide), 4.92 (1H, br. d, -CH₂- of benzyl alkoxide), 4.65 – 4.85 (2H, m, -CH₂- of benzyl alkoxide), 2.47 – 2.62 (2H, m, -CH- of DACH), 2.10 (3H, s, -N(CH₃)₂), 2.08 (3H, s, -N(CH₃)₂), 2.03 (3H, s, -N(CH₃)₂), 2.01 (3H, s, -N(CH₃)₂), 1.92 – 2.00 (1H, m, -CH- of DACH), 1.86 – 1.92 (1H, m, -CH- of DACH), 1.85 (6H, s, Ar-C(CH₃)₂Ph), 1.81 (6H, s, Ar-C(CH₃)₂Ph), 1.73 – 1.78 (12H, s, Ar-C(CH₃)₂Ph), 1.41 – 1.57 (8H, m, -CH₂- of DACH), 0.95 – 1.09 (1H, m, -CH₂- of DACH), 0.86 – 0.95 (2H, m, -CH₂- of DACH), 0.73 – 0.84 (1H, m, -CH₂- of DACH); ¹³C(¹H) NMR (C₆D₆, 151MHz): δ 169.6 (-N=CH-Ar), 168.9 (-N=CH-Ar), 152.6 (Ar C), 152.6 (Ar C), 152.3 (Ar C), 152.2 (Ar C), 146.7 (Ar C of benzyl alkoxide), 140.8 (Ar C), 140.8 (Ar C), 134.3 (Ar C), 134.2 (Ar C), 132.8 (Ar C-H), 132.8 (Ar C-H), 132.1 (Ar C-H), 132.0 (Ar C-H), 128.7 (Ar C-H), 128.6 (Ar C-H), 128.3 (Ar C-H), 128.3 (Ar C-H), 127.6 (Ar C-H), 127.3 (Ar C-H), 127.2 (Ar C-H), 127.0 (Ar C-H), 127.0 (Ar C-H), 126.4 (Ar C-H), 126.2 (Ar C-H), 125.3 (Ar C-H), 119.2 (Ar C), 119.1 (Ar C), 69.1 (-CH₂- of benzyl alkoxide), 68.9 (-CH₂- of benzyl alkoxide), 67.3 (-CH- of DACH), 67.0 (-CH- of DACH), 65.6 (-CH- of DACH), 65.6 (-CH- of DACH), 43.9 (Ar-C(CH₃)₂Ph), 42.8 (Ar-C(CH₃)₂Ph), 41.1 (Ar-C(CH₃)₂Ph), 40.9 (Ar-
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of DACH), 22.1 (-CH$_2$- of DACH). Anal. Calcd. For C$_{80}$H$_{96}$N$_4$O$_4$Zn$_2$: C 73.44; H 7.40; N 4.28.

Representative ring opening polymerization of rac-lactide catalyzed by 4. A solution of 4
(3.0 mg, 0.0028 mmol) in CH$_2$Cl$_2$ (1 mL) was added to a solution of rac-lactide (81.3 mg, 0.564
mmol) in CH$_2$Cl$_2$ (2 mL) at room temperature. Another 1 mL of CH$_2$Cl$_2$ was used to rinse vials.
The reaction mixture was stirred for 30 min. A sample of the reaction mixture was dissolved in
CDCl$_3$ to be analyzed by $^1$H NMR spectroscopy to determine conversion. The resulting mixture
was concentrated under vacuum. The polymeric material was dissolved in minimum amount of
CH$_2$Cl$_2$ and added to cold wet methanol or ethanol (for low equivalency polymerizations). The
polymer precipitated from solution and quickly solidified in liquid N$_2$. The supernatant was
decanted off and the polymer was dried under vacuum.

Representative ring opening polymerization of rac-lactide catalyzed by 2. A solution of 1
(3.0 mg, 0.0066 mmol) in CH$_2$Cl$_2$ (4 mL) was added to a solution of rac-LA (956.6 mg, 6.637
mmol) in CH$_2$Cl$_2$ (5 mL) at room temperature. The reaction mixture was then stirred for 20 h. A
sample of the reaction mixture was dissolved in CDCl$_3$ to be analyzed by $^1$H NMR spectroscopy
to determine conversion. The resulting mixture was concentrated under vacuum. The polymeric
material was dissolved in minimum amount of CH$_2$Cl$_2$ and added to cold wet methanol. The
polymer precipitated from solution and quickly solidified in liquid N$_2$. The supernatant was
decanted off and the polymer was dried under vacuum.

Representative immortal ring opening polymerization of rac-lactide catalyzed by 2/BnOH. A solution of 2 (3.0 mg, 0.0066 mmol) and BnOH (3.6 mg, 0.033 mmol) in CH$_2$Cl$_2$ (2
mL) was added to a solution of rac-LA (478.3 mg, 3.319 mmol) in CH$_2$Cl$_2$ (2 mL) at room
temperature. The reaction mixture was then stirred for 30 min. A sample of the reaction mixture
was dissolved in CDCl₃ to be analyzed by ¹H NMR spectroscopy to determine conversion. The resulting mixture was concentrated under vacuum. The polymeric material was dissolved in minimum amount of CH₂Cl₂ and added to cold wet methanol. The polymer precipitated from solution and quickly solidified in liquid N₂. The supernatant was decanted off and the polymer was dried under vacuum.
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APPENDICES

Characterization of compounds 1-6 in solution by $^1$H NMR

Figure A1. $^1$H NMR spectrum (400 MHz, 25 °C, C$_6$D$_6$) of complex 1 (±)-(NN$_2$O$_2$t-Bu)Zn(CH$_2$CH$_3$).
Figure A2. $^1$H NMR spectrum (400 MHz, 25 °C, C₆D₆) of complex 2 (±)-(NNO-t-Bu)Zn(CH₂CH₃).
Figure A3. $^1$H NMR spectrum (400 MHz, 25 °C, C$_6$D$_6$) of complex 3 (±)-(NNO$_{Cm}$)Zn(CH$_2$CH$_3$).
Figure A4. $^1$H NMR spectrum (400 MHz, 25 °C, C₆D₆) of complex 4 (±)-[(NNH₂-Ot-Bu)Zn(OCH₂Ph)]₂.

4 (±)-[(NNH₂-Ot-Bu)Zn(OCH₂Ph)]₂
Figure A5. $^1$H NMR spectrum (400 MHz, 25 °C, C$_6$D$_6$) of complex 5 (±)-[(NNO$_{t-Bu}$)Zn(OCH$_2$Ph)]$_2$. 
Figure A6. $^1$H NMR spectrum (400 MHz, 25 °C, C$_6$D$_6$) of complex 6 ($\pm$)-[(NNO$_{cm}$)Zn(OCH$_2$Ph)]$_2$. 
2 D NOESY spectra of complexes 4 and 5

Figure A7. 2D NOESY full spectrum (400 MHz, CD$_2$Cl$_2$, −35 °C, mixing time (d8) = 0.8 s) of complex 4 (±)-[(NN$_2$O$_2$-Bu)Zn(OCH$_2$Ph)]$_2$. 
Figure A8. 2D NOESY full spectrum (400 MHz, C₆D₆, 65 °C, mixing time (d8) = 1.0 s) of complex 4 (±)-[(NN₃O-Bu)Zn(OCH₂Ph)]₂.
Figure A9. 2D NOESY full spectrum (400 MHz, CD$_2$Cl$_2$, 25 °C, mixing time (d8) = 0.25 s) of complex 5 (±)-[(NNO$_{2-Bu}$)Zn(OCH$_2$Ph)]$_2$. 
Ring opening polymerization of \textit{rac}-lactide catalyzed by complexes 4-6

Table A1. Ring opening polymerization of \textit{rac}-lactide catalyzed by complexes 4-6.

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All reactions carried out in CH\textsubscript{2}Cl\textsubscript{2} at 25 °C in 30 min with \textit{rac}-lactide and [Zn] = 0.7 mM. Polymer samples are obtained at >96% conversion determined by \textit{\textsuperscript{1}H} NMR spectroscopy. \textsuperscript{a}Calculated from [M]o/[I] × monomer conversion × M\textsubscript{LA} + M\textsubscript{BnOH} (M\textsubscript{LA} = 144.13 g/mol, M\textsubscript{BnOH} = 108.14 g/mol). \textsuperscript{b}Determined by GPC-LALLS (gel permeation chromatography-low angle laser light scattering) (dn/dc = 0.044 for PLA in THF). \textsuperscript{c}Reactions carried out in 5 min with \textit{rac}-lactide and [Zn] = 0.7 mM.
$^1$H NMR spectra of PLLA formed by complexes 4-6

**Figure A10.** $^1$H NMR spectrum of PLLA formed by complex 4 (300 MHz, 25 °C, CDCl$_3$).

**Figure A11.** $^1$H NMR spectrum of PLLA formed by complex 5 (300 MHz, 25 °C, CDCl$_3$).
Figure A12. $^1$H NMR spectrum of PLLA formed by complex 6 (300 MHz, 25 °C, CDCl$_3$).