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Review

Recent developments in main group metal complexes catalyzed/initiated polymerization of lactides and related cyclic esters

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Abstract

This review describes recent development of ring-opening polymerization of lactides and related cyclic esters using main group metal complexes as catalysts/initiators. The complexes described here are classified according to metal groups. Most attention is devoted to the well-defined metal complexes.

Keywords: Lactide; Main group metal; Polymerization; Polyester; Lithium; Magnesium; Aluminum; Zinc; Tin

1. Introduction

Polyesters are among the most versatile synthetic polymers, and they have been widely used as fibers, plastics and coatings. Over the past three decades, polyesters, especially polylactide (PLA), polyglycolide (PGL), polycaprolactone (PCL) and their copolymers, have attracted considerable attention due to their new biomedical and pharmaceutical applications such as biodegradable surgical sutures and post-operative support pins and splints, or as a delivery medium for controlled release of drugs [1]. The starting materials for biodegradable and bioassimilable PLA are derived from corn, beets, and other annually renewable resources. As the depletion of petrochemical feedstock comes near, the renewable and environmentally friendly polymers are increasingly important for a sustainable future.

A particularly convenient method for the synthesis of polyesters is the ring-opening polymerization (ROP) of cyclic esters (Fig. 1). Due to the advantages of well controlled molecular weight and low polydispersity (PDI), many chemists have focused on the development of new catalysts for ring-opening polymerization. In this aspect, coordination complexes with adjustment of ligands play an important role not only in molecular weight and molecular weight distribution, but also in the production of stereoregular polyesters. Recently, some excellent review articles on polymerization of lactide have been published [2–4]. In this article, we focus on discrete main group metal complexes initiating/catalyzing ring-opening polymerization of lactide and the related cyclic esters in that most of our group's work is introduced. The zinc ion has filled d-orbitals and shares many similar properties, including a similar ionic radius to the magnesium ion [5]. In many references, complexes of these two metals were studied together, therefore, zinc complexes are also discussed in the section describing the chemistry of magnesium.

Recent studies exhibit that a good catalyst/initiator for ROP of lactide and cyclic esters requires the following conditions: (1) The metal should be redox-inactive and inert to β-hydrogen atom abstraction from the growing alkoxide

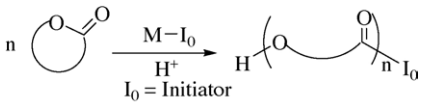


Fig. 1. General method for the ring-opening of cyclic esters by metal complexes.

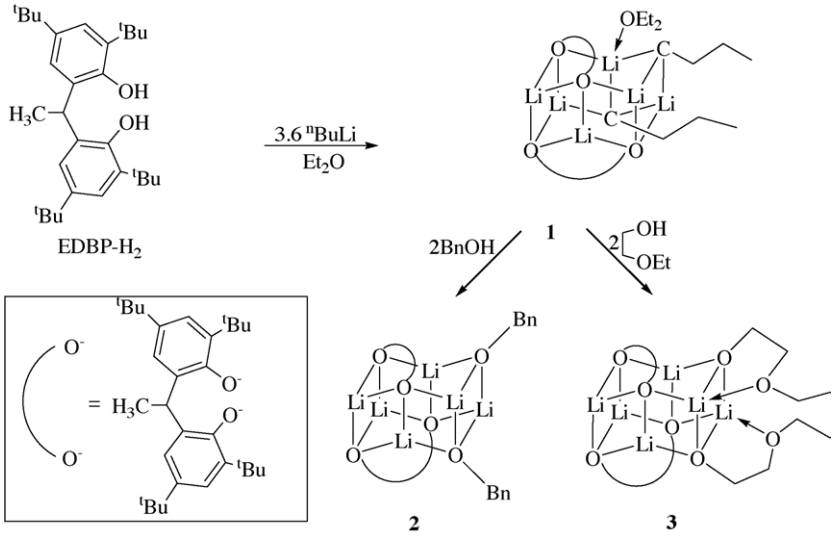
polymer chain, otherwise side reactions could lead to chain termination with the loss of catalytic activity, therefore, most main group metals agree well with this condition. (2) The inorganic template L_nM should be inert with respect to ligand scrambling, otherwise oligomeric alkoxides can be formed by intermolecular exchange. These would then no longer offer the advantages of single-site catalysis and would be akin to catalysis by simple metal alkoxides. (3) The alkoxide ligand in the L_nMOR complex should be labile to alcohol exchange and insertion reactions with C–X multiple bonds. Chain transfer and functionality can be introduced into the polymer by such reactions.

2. Group 1 metals (Li, Na, K)

Lithium chloride was found to be an active and biocompatible catalyst for the ring-opening polymerization of lactide in the presence of ethylene glycol and methyl α-D-glucopyranoside [6]. The polymerization was carried out at 128 °C in bulk with 1% (w/w) of LiCl while the PDIs were too high (>2.2). Several alkali metal compounds such as butyllithium, lithium *tert*-butoxide and potassium *tert*-butoxide, have been applied earlier to polymerize L-lactide and *rac*-lactide by Kricheldorf and Kasperczyk et al. [7–9]. These compounds are effective initiators, however, the high basicity of these ionic species results in detrimental side reactions such as epimerization of chiral centers in the PLA backbone. Back-biting reactions lead to the formation of macrocycles and thereby result in very broad or multimodal molecular weight distribution.

2.1. Polymerization with lithium alkoxides

In recent years, series of novel lithium aggregates with a bulky ligand ($EDBP–H_2$) have been synthesized. The bulky ligand was designed to provide a steric barrier around active lithium ions for minimizing the side reaction in our laboratory. From the reaction of ^{n}BuLi and $EDBP–H_2$, cage-like complex **1** can be synthesized [10] in which the ^{n}Bu groups coordinated to lithium can be replaced by almost any alkoxy group without dramatic changes in its skeleton. For instance, complexes **2** and **3** can be obtained from alcoholysis of **1** with benzyl alcohol and 2-ethoxyethanol, respectively (Scheme 1). Complex **2** is an efficient initiator for the ROP of L-lactide. Polymerization goes to completion within 6 h in dichloromethane with very low PDIs (1.06–1.12) when



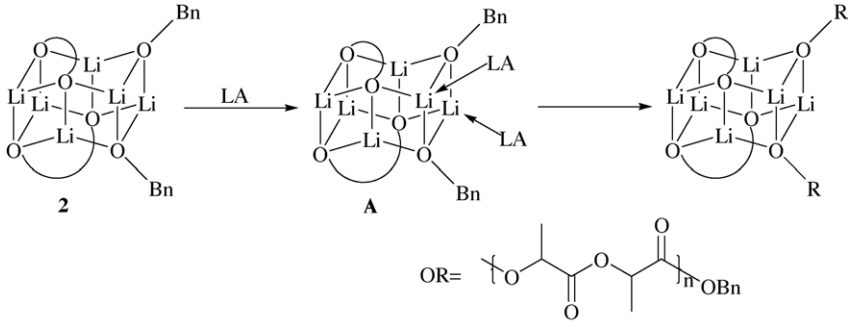
Scheme 1. Synthesis and structure of lithium aggregates **1**, **2**, and **3**.

monomer-to-initiator ratio ($[M]_0/[I]_0$) is 50–200 and a linear relationship between the number-average molecular weight (M_n) and ([M]/[I]) upon cooling the temperature to 0 °C. ^{1}H NMR spectrum of PLA also shows one benzyl ester and one hydroxy chain end with a ratio of 5:1 suggesting that the initiation occurs through the insertion of the benzyl alkoxy group from **2** into L-lactide by acyl cleavage without the back-biting reactions. Furthermore, epimerization of the chiral centers in PLA does not occur as observed by the homonuclear decoupled ^{1}H NMR studies in the methine region. The formation of **3** suggests that the ROP of L-lactide initiated by **2** may proceed with the coordination of L-lactide on the less hindered lithium atoms, leading to intermediate A, followed by the attacking of the benzyl alkoxy group on the carbonyl group of lactide, as shown in Scheme 2.

Chisholm et al. treated a similar bulky ligand (biphenolate–H_2) with 4 molar equiv. of ^{n}BuLi to achieve [(μ_3,μ_3-biphenolate)$_2$Li$_4$(^{n}BuLi)$_4$] (**4**) in high yield [11]. Further reactions of **4** with 4 molar equiv. of 2,4-dimethyl-3-pentanol in the presence of tetrahydrofuran (THF) or cyclohexene oxide (CyHO) give the lithium aggregate [(μ,μ-biphenolate)Li$_2$(μ_3-OCH(^{i}Pr)$_2$)$_2$Li$_2$(L)$_2$] (**5-THF**, L = THF; **5-CyHO**, L = CyHO) (Fig. 2). It has been found that ROP of lactide employing **5-THF** as an initiator goes to completion within 1 h at ambient temperature and the reaction rate decreases with decreasing temperature. However, there is not much difference in the PDIs of PLA obtained at 0 and 25 °C (1.70 versus 1.72).

2.2. Polymerization with lithium complexes in the presence of alcohols

Most recently, several novel lithium complexes have been developed (Fig. 3) to exhibit excellent catalytic activity toward ROP of lactide in the presence of free alcohol [12]. The reactions of EDBP–H_2 with ^{n}BuLi in THF or diethyl ether produce compounds **6** and **7**, respectively. However, EDBP–H_2 reacted with ^{n}BuLi in the presence of benzyl alcohol giving **8** in high yield. Further reaction of **8** with excess of THF produces **9**. The molecular structures showed **6** and **7** formed in monomer, and the intramolecular hydrogen bonds are observed between the phenoxy oxygen and phenol group of the EDBP^{2-}. Both **6** and **7** are active for polymerization of L-lactide in the presence of benzyl alcohol. The crystal



Scheme 2. Proposed mechanism for ring-opening polymerization of L-lactide initiated by compound **2**.

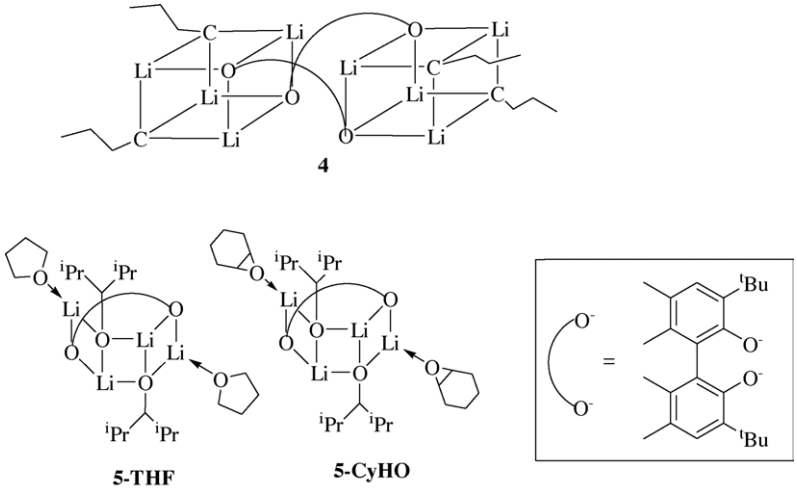


Fig. 2. Biphenolate lithium aggregates **4** and **5**.

structure of **8** consists of 2 equiv. Li atoms and each Li atom are coordinated by two bridged phenoxy oxygen atoms of two EDBP–H^- ligands and the oxygen atom of benzyl alcohol. Complex **8** was used to initiate the ROP of L-lactide at 0 °C giving polymers with narrow PDIs (1.04–1.08) up to more than 91% conversion in CH_2Cl_2. Notably compound **8** behaves in both living and immortal characters with a number of polymer molecules exceeding the number of initiator molecules. The polymerization of L-lactide was initiated with **8** in the presence of benzyl alcohol as the chain transfer agent. Preliminary results showed that as much as 31-folds excess of BnOH can be added resulting in a low PDI polymer with a M_n of only 1/32 of that without the addition of BnOH. The formation of complex **9** suggests that the ROP of L-lactide initiated by **8** may proceed with the coordination of L-lactide on lithium to give the monomeric intermediate, followed by the insertion of benzyl alkoxy group, in which benzyl alcohol is activated by the formation of a hydrogen bond through the terminal oxygen atom of EDBP–H^-, to the carbonyl group of L-lactide leads to the ring-opening polymerization as shown in Scheme 3. It is interesting to note that complex **6** is active for ROP of L-lactide in the absence of benzyl alcohol at ambient temperature ($[LA]_0/[BnOH]_0 = 100$, $M_n = 29{,}400$, PDI = 1.87). Based on the ^1H NMR studies of the polymer, the reaction may follow the process of cationic polymerization.

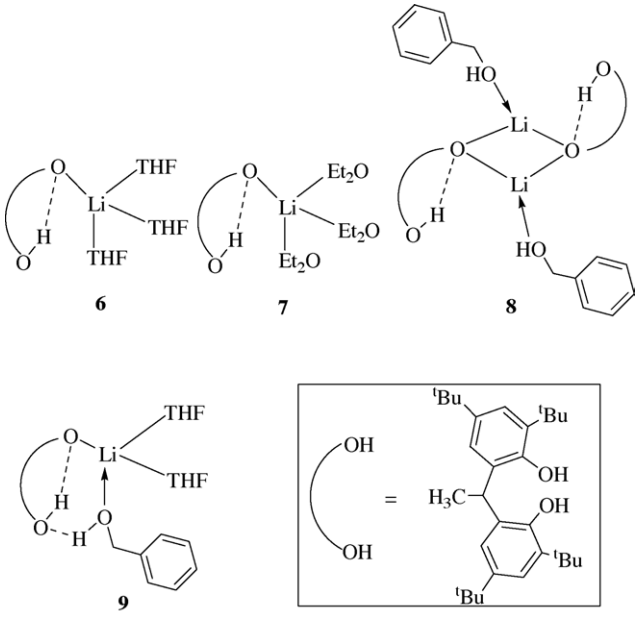


Fig. 3. EDBP–H_2 supported lithium complexes **6–9**.

2.3. Polymerization with lithium macroinitiators

Treatment of complex **1** with 4-hydroxy-TEMPO terminated polystyrene, lithium alkoxide macroinitiator can be achieved (Fig. 4). With this macroinitiator, a series of PS-*b*-PLLA copolymers (PDIs ranging from 1.11 to 1.28) with different volume ratios can be prepared. Interestingly, the copolymer appeared as a nano-helical phase structure when the ratio of PLA is 0.35 [13]. 4-Hydroxy-TEMPO terminated polystyrene ($M_w = 12{,}500$, PDI = 1.12) can work as macroinitiator in ROP of lactide with good controlled manner to synthesis of PS-*b*-PLA ($M_n = 34{,}200$, PDI = 1.12) with 100 equiv. of L-lactide in the presence of **6**.

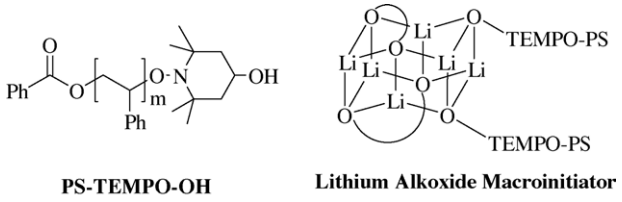
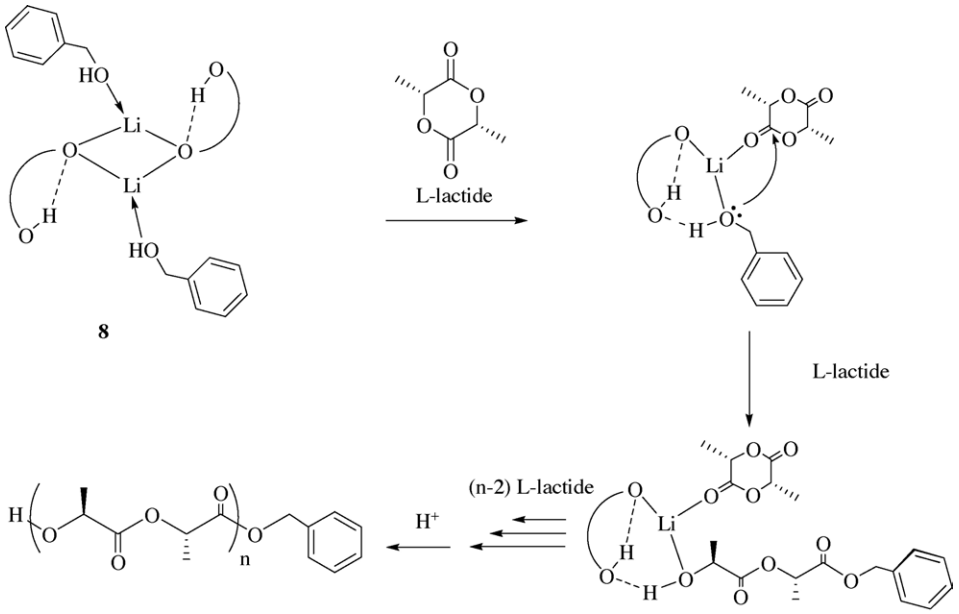


Fig. 4. Lithium alkoxide macroinitiator.



Scheme 3. Proposed mechanism for ring-opening polymerization of L-lactide initiated by compound **8**.

3. Group 2 metal complexes (Mg, Zn, Ca, Sr)

Recently, Mg(II), Zn(II), Ca(II), and Sr(II) complexes for cyclic ester polymerization have been motivated largely by advantageous features of these ions that include lack of color, low cost, and low toxicity that are important in biomedical applications of the polymer.

3.1. Magnesium and zinc complexes

The magnesium and zinc elements share many similar properties and many research groups study zinc and magnesium complexes in ROP of cyclic ester together. Therefore, some zinc complexes are included here for comparison. As for the case of lithium *tert*-butoxide, the polymerization of lactide cannot avoid side reactions when dibutyl magnesium was used as an initiator directly [14]. It is an effective initiator at 0 °C, and no epimerization of chiral centers in the PLA backbone occurs. However, the high PDIs (ca. 2) indicate the presence of trans-esterification reaction. In the past decades many well-defined magnesium and zinc complexes have been synthesized and applied in ROP of lactide and cyclic esters.

3.1.1. Tripodal tridentate ligand supported magnesium and zinc complexes

Chisholm et al. have used trispyrazolyl- and trisindazolyl-hydroborate ligands as tripodal monoanionic tridentate ligands which can confer the required steric hindrance around the metallic center to prevent aggregation. Therefore, two magnesium alkoxide complexes (**10**, **12**) and three zinc alkoxide complexes (**11**, **13**, **14**) have been synthesized (Fig. 5) [15]. Based on the monomeric structure of Zn complex **14** and molecular weight determination of **10** in benzene, all of these complexes were proposed to be mononuclear.

According to the spectroscopic analysis of PLA initiated by complex **10**, the ester OEt group was detected by ^{1}H and ^{13}C NMR spectroscopy. This proved that the ROP of lactide occurred by acyl cleavage rather than ether cleavage. Polymerizations of L-lactide employing **10** and **11** were controlled with the evidences of a linear relationship between M_n and conversion and low PDIs (1.10–1.25). The kinetic studies of

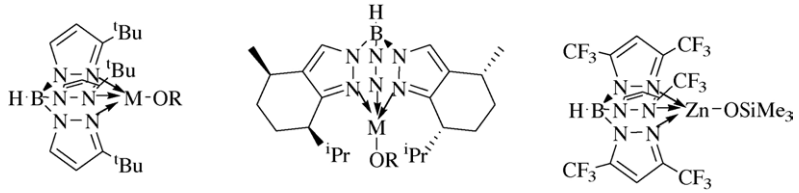


Fig. 5. Trispyrazolyl- and trisindazolyl-hydroborate ligands supported zinc and magnesium complexes **10**–**14**.

ring-opening polymerization were shown to be first-order in lactide and first-order in metal complex in CD_2Cl_2 and $CDCl_3$ solutions. The results showed the magnesium complex **10** is much more active (60 min, $[M]_0/[I]_0 = 500$, CH_2Cl_2, 25 °C, 90% conversion) than its Zn(II) analogous complex (60 days, $[M]_0/[I]_0 = 500$, CH_2Cl_2, 25 °C, 90% conversion) because of the high polarity of the Mg–OR bond relative to that of zinc complexes. Because the magnesium catalyst precursors are extremely water- and air-sensitive, the presence of water leads to deactivation of the catalyst. The zinc complexes, while slower than their related magnesium counterparts, are more tolerant. The zinc complex **11** is even inert to air in the solid state for a period of few days. Results also showed the more bulky ligand leads to higher activity. Complex **14** is nearly inactive for ROP of lactide because of electron-withdrawing effect. The achiral catalyst precursors **10** and **11** showed a significant preference for the polymerization of *meso*-lactide over L- and D-lactide in methylene chloride at 22 °C. The chiral magnesium complex **12** showed a marked preference for the polymerization of *meso*-lactide over *rac*-lactide. In CD_2Cl_2 at −40 °C *meso*-lactide was effectively polymerized, exclusively leaving only unreacted *rac*-lactide. In contrast sharply to the behavior of complex **11**, the copolymerizatioin of a 1:1 mixture of *meso*- and *rac*-lactide by the chiral zinc complex **13** in CD_2Cl_2 revealed that *meso*- and *rac*-lactide were polymerized at essentially the same rate during the initial phase of the polymerization, that is, over the first 30% of the polymerization. Then the *meso*-lactide was consumed faster. The chiral complex **13** with (*R*,*R*) stereo centers at the ^{i}Pr- and Me-substituted carbon atoms exhibits a very modest preference for the polymerization of L-lactide from *rac*-lactide.

3.1.2. β-Diketiiminate supported magnesium and zinc complexes

Due to the successful implementation of tris(pyrazolyl)borato magnesium and zinc alkoxides as single-site catalysts for lactide polymerization, sterically bulky β-diketiminate (BDI) ligands were used to access many magnesium(II) and zinc(II) complexes (**15**–**31**) (Fig. 6) for ROP of lactide in the past several years. Some of these analogous complexes have excellent stereoselective character.

Coates et al. reported complexes **18**, **21**, **25**, **28**, and **29** for polymerization with *rac*-lactide [16,17]. From the polymerization results, it is apparent that –$N(SiMe_3)_2$, –Et, and –OAc are clearly inferior initiating units, as they yield polymers with broad PDIs and molecular weights that compare poorly with theoretical values. Unlike –O^{i}Pr and –OCH(Me)CO_2Me, initiation with these three species most likely does not proceed direct insertion of the moiety into the acyl-oxygen bond. Rather, these groups likely react with monomer impurities (e.g., lactic acid, hydrolyzed lactide, water) to form a new initiating group. Consequently, the rate of initiation is slower than the propagating rate of polymer-

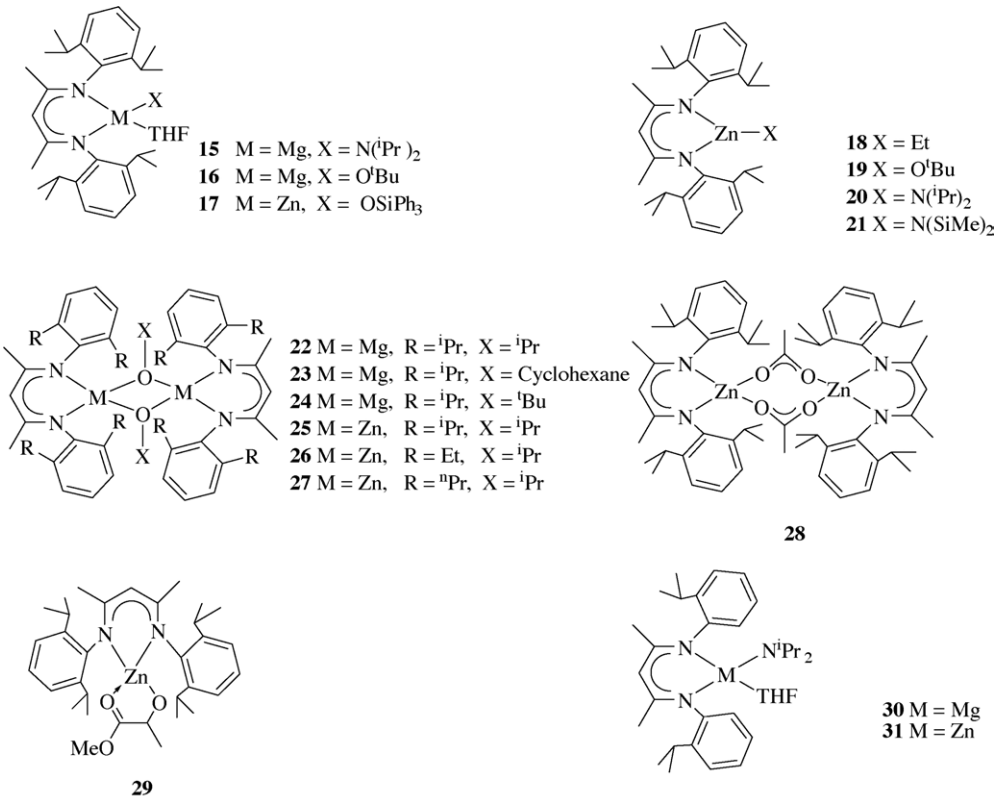


Fig. 6. β-Diiminate supported complexes **15**–**31**.

ization, resulting in polymers with broad molecular weight distributions and higher than expected molecular weights. In contrast, the isopropoxide and methyl lactate initiating groups closely mimic the putative propagating groups of the presumed active species, and complexes with these moieties produce PLA of predictable molecular weight and narrow molecular weight distribution.

Notably, complex **25** catalyzed the stereoselective ROP of *rac*-lactide yielding highly heterotactic microstructures, with stereoselectivities up to 90% at room temperature and 94% at 0 °C [16,17]. Further studies indicate that the substituted groups on the β-diketiminate ligand significantly affect its stereoselectivity. For instance, changing the ligand substituents from isopropyl to ethyl groups (**26**) results in decrease in heterotacticity (Pr = 0.79) and substituting with *n*-propyl groups (**27**) lowers the heterotacticity too (Pr = 0.76). It is interested to note that polymerization of *meso*-lactide with **25** affords syndiotactic PLA, while **26** yields moderately heterotactic PLA. The reasons for the different stereoselectivities of these two complexes are still unknown.

Polymerization of *rac*-lactide was 50% faster than that of *meso*-lactide by using complex **25** as catalyst, and seven times faster than the polymerization of L-lactide. This information consisted with the preference formation of heterotactic PLA during polymerization of *rac*-lactide. Kinetic investigation showed the polymerization of lacide in CH_2Cl_2 was first-order in monomer, while with 1.56 order in Zn(II) initiator. This non-integer dependency was attributed to the presence of multiple active species with variable polymerization reactivity.

Zinc alkoxide complexes **25**, **26**, **29** are also extremely efficient catalysts for the ring-opening polymerization of β-butylrolactone (BBL) and β-valerolactone (BVL) with unprecedented rates under mild conditions in a controlled manner [18]. When the $[BBL]_0/[Zn]_0$ ratio equals 200, polymerization with **25** surpasses 90% conversion in just over 1 h at room temperature. The number-average molecular weight (M_n) of the polymer grows linearly with very narrow PDIs (1.07–1.20), suggesting that the polymerization is living. At higher temperatures, polymerizations with **25** proceed more quickly, as expected. For instance, polymerization at [BBL]/[Zn] = 220 reached 97% conversion in 20 min at 50 °C. While at 75 °C, up to 94% conversion can be achieved in 5 min with PDIs remaining narrow within all tested temperature ranges. β-Valerolactone (BVL) is also polymerized by **25** to make poly(3-hydroxyvalerate) (PHV). Rates are somewhat slower than those for BBL, requiring 2 h to polymerize 150 equiv. of BVL to 88% conversion at 23 °C. The molecular structures show the three complexes forming as dimers in solid state, however, **25** and **29** exist primarily as monomers in solution at room temperature evidenced by analysis of the varying temperature ^{1}H NMR spectrum and mixed ligand experiments. Complex **26** is a poor initiator for the ROP of BBL at room temperature because it prefers to adopt the inactive dimeric form (40 h to reach 95% conversion when $[BBL]_0/[Zn]_0 = 200$), which inhibits coordination of the monomer and, therefore, prevents polymerization. This limitation is minimized by using higher temperature, which pushes the monomer-dimer equilibrium toward the active monomer. The presence of isopropyl ester and hydroxy end groups and no epimerization of chiral center in PRHB strongly suggest a coordination–insertion mechanism. Kinetic study of the polymerization is first order dependence on zinc and monomer concentrations.

Compare with zinc alkoxide complexes, magnesium alkoxide complexes are more active for the polymerization of lactide. Complex **22** completed polymerization of *rac*-lactide in 2 min at 20 °C ($[Mg]_0 = 2$ mM; $[LA]_0 = 0.4$ M; $[LA]_0/[Mg]_0 = 200$) while **25** needs 0.33 h [18]. Magnesium complex **16** (2 min) and zinc complex **19** (10 min) show the same tendency with $[LA]_0/[Metal]_0 = 100$ in CH_2Cl_2 at 20 °C [19]. The PDIs of polymers produced by magnesium complexes are broader than the related zinc complexes. Different initiating groups also affect the rate of polymerization which proved by the fact that 100 equiv. of *rac*-lactide are polymerized by **19** in 10 min at room temperature while for **17**, **20**, **21** the polymerization proceeds up to 90% completion in 40 min, 3 and 70 h in CH_2Cl_2 respectively. From the above information, a clear dependence of the rate of initiation can be obtained, which follows the order Mg > Zn and $O^tBu > N^iPr_2 > NSi_2Me_6 > OSiPh_3$. This order reflects both electronic and steric factors, while N^iPr_2 is clearly the most basic ligand, its lone pair is sterically less accessible than that of O^tBu.

Although magnesium complexes **15**, **16**, **22**, **30** show no stereoselectivity in CH_2Cl_2 or benzene, the magnesium complexes **15**, **16**, **30** have the heterotactic selectivity in THF [19,20]. Interestingly the molecular structure studies display that **16** appeared as a monomer [20], while complex **24** appeared in dimer with the oxygen atoms of two butyloxy as bridges in toluene [21]. ^{1}H NMR spectrum indicates complex **29** has four isopropyl doublets for the β-diketiminate ligand, while complex 16 reacts with L-lactide (ca. 5 equiv.) in toluene-d_8, only two isopropyl doublets appeared for the β-diketiminate ligand, even at −80 °C. The authors proposed that this arises because the magnesium compound exists in solution as dimeric molecules wherein the two magnesium atoms are united by a pair of alkoxide ligands from the growing polymer chain. This effectively creates a mirror plane of symmetry. This, of course, does not mean that the active form of the magnesium catalyst system is not monomeric in THF, and this could account for the different stereoselectivity of polymerizations in THF versus toluene and CH_2Cl_2.

For the poor initiators of complexes **30** and **31** [20], the PDIs of polymers produced by them are broad (1.6 and 1.5). Zinc complex **31** has *syn*- and *anti*-conformers, and the *syn*-conformer is much more active in the polymerization of lactide relative to the *anti*-form. So the double theoretic M_n values are observed. While *syn*- and *anti*-conformers of **30** are interconverting rapidly, **31** polymerizes *rac*-lactide (100 equiv.) to give approximately 90% heterotactic PLA

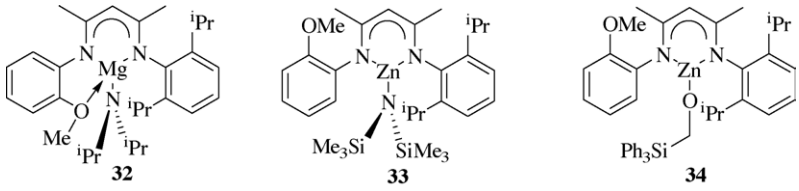


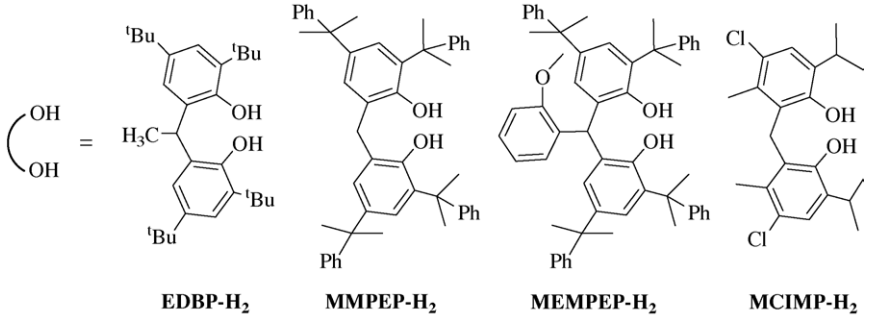
Fig. 7. Potentially tridentate-diketiminate supported magnesium and zinc complexes **32**–**34**.

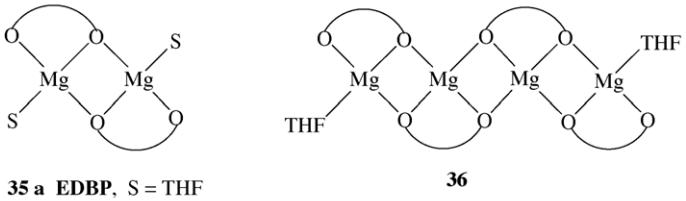
with predictable molecular weight in THF, CH_2Cl_2 and benzene.

A potentially tridentate-diketiminate supported magnesium and zinc complexes (**32**–**34**) (Fig. 7) were synthesized for ROP of lactide by Gibson and co-workers [22]. All three complexes are highly active, with complexes **32** and **33** affording >80% conversion within 10 min and complex **34** giving 90% conversion within 30 min. However, the magnesium initiator **32** is far less controlled than either of the zinc species **33** and **34**, as indicated by the broader PDIs (1.53–1.78) observed for polymers derived from **32**. A non-linear correlation between M_n and monomer conversion confirms that complex **32** does not initiate a living polymerization. The zinc complexes give rise to much lower polydispersities (1.10 and 1.15), but molecular weights are again significantly higher than the values predicted on the basis of monomer to initiator ratio. As for complex **32**, this is attributable to slow initiation (relative to propagation), a consequence of the large NR_2 and $OSiPh_3$ initiating groups. Although initiation is poor, however, the chain length increases linearly with monomer conversion initiated by **34**.

3.1.3. *Diol supported magnesium and zinc complexes*

Complexes **35a**–**35d** and **36** (Fig. 8) were synthesized by reactions of related diol ligands with Mg^nBu_2 in THF or diethyl ether in our laboratory [23]. These four complexes **35a**–**35d** are dinuclear species, while **36** are tetranuclear due to the twisted character of MCIMP–H_2 ligand. These





35 a EDBP, S = THF
35 b EDBP, S = Et_2O
35 c MMPEP, S = THF
35 d MEMPEP, S = THF

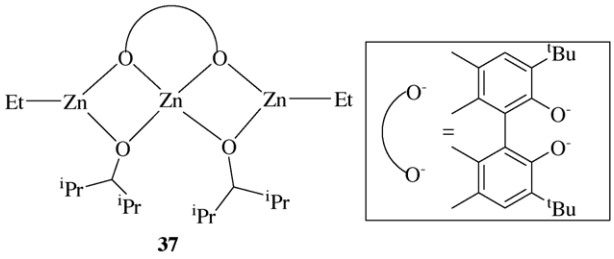
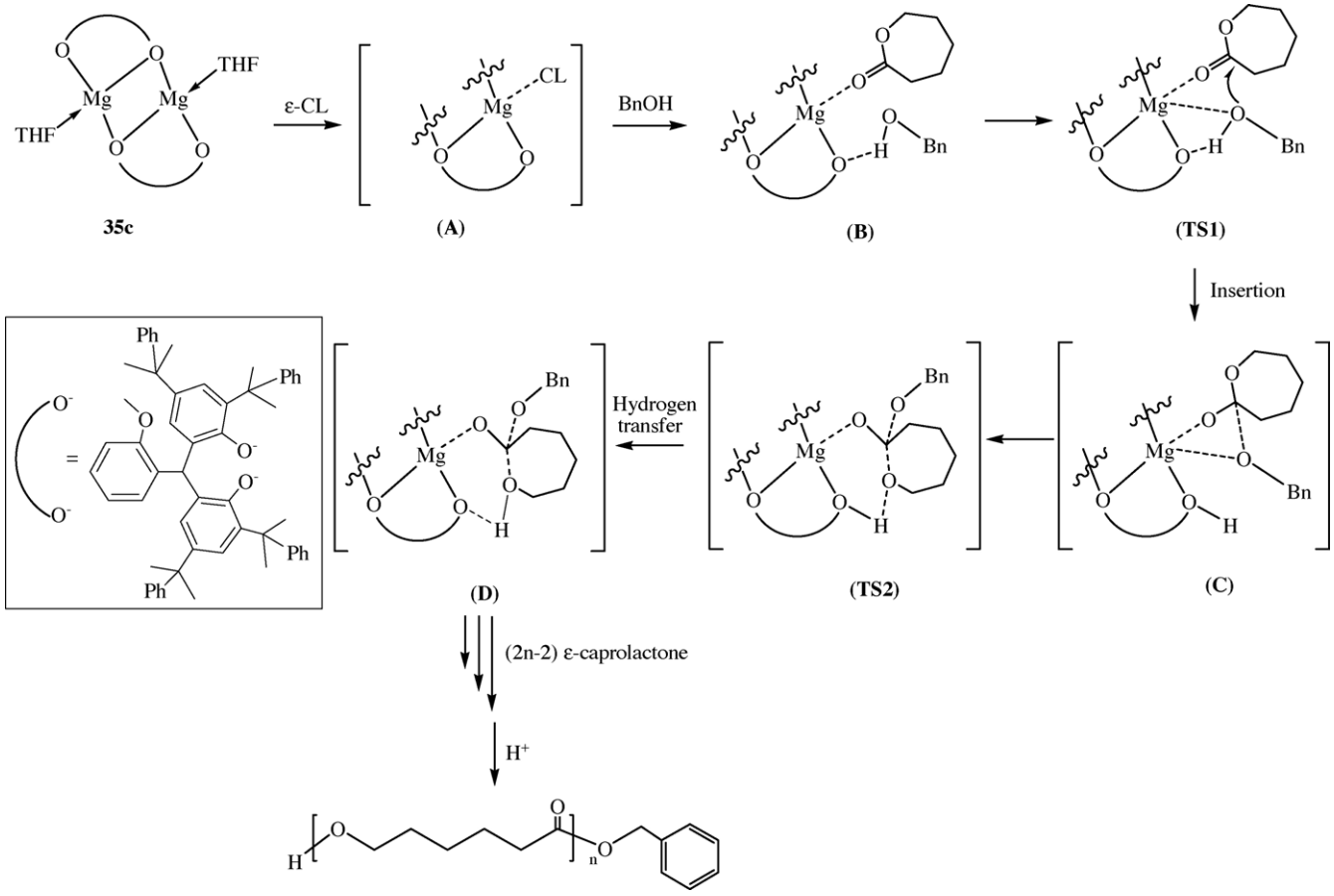


Fig. 8. Diol supported zinc and magnesium complexes **35**–**37**.

five magnesium complexes all catalyzed polymerization of ε-caprolactone in good controlled manner in toluene with low PDIs (1.06–1.30) in the presence of benzyl alcohol. It is found that **35c** is more active than the others which may result from a more sterically bulky group in bridge carbon of the MEMPEP–H_2 diol ligand. While complexes **35a**, **35b**, **35d** and **36** catalyze polymerization of ε-caprolactone to completion in several hours at high temperature (56 or 70 °C), **35c** catalyzes this polymerization to completion in several hours at room temperature. Notably, **35c** even can catalyze ROP of lactide to completion at 25 °C in 2 h when $[LA]_0/[Cat]_0/[BnOH]_0$ is 200:1:2 [23b], while **35a** needs 2 h at 83 °C [23a]. Complex **36** has also paved a way to synthesize as much as 500-fold polymer chains of poly(ε-caprolactone) with a very low PDI.

The theoretical study of the ROP mechanism of 1,5-dioxepan-2-one (DXO) and L-lactide initiated by $Sn(Oct)_2$ and methanol has been investigated by Albertsson and coworkers [24]. The calculation results exhibit that the initiator, methanol is activated by the formation of a hydrogen bond through a carboxyl ligand. The formation of a hydrogen bond between BnOH and phenoxyl oxygen of $EDBP^{2-}$ ligand has been found in complex **9**, which displays excellent activity toward ROP of L-lactide [12]. Based on the above information, theoretical study of ROP of CL catalyzed by **35c** in the presence of benzyl alcohol has been performed. On the basis of the catalytic, structural and theoretical studies of **35c**, it is believed that, during polymerization of ε-caprolactone, the initial step involves the replacement of THF by ε-caprolactone of the dimeric compound **35c** giving the dimeric intermediate (**A**) as shown in Scheme 4. When BnOH approaches intermediate **A**, formation of hydrogen bond occurs between BnOH and the terminal phenoxyl oxygen atom of MEMPEP ligand (**B**). The insertion of benzyl alkoxyl group, in which benzyl alcohol is activated by the formation of hydrogen bond and a weak interaction with Mg center (**TS1**), to the carbonyl carbon of ε-caprolactone leads to the ring-opening polymerization forming **C**. Truly ring-opening of monomer occurs between **C** and **TS2**. After dissociation of BnO···Mg bond, rotation of Mg–O=C bond gives **TS2**. Finally, followed by the transfer of H atom to the O atom of the C–O of ε-caprolactone, the C–O single bond breaks almost at the same time to give intermediate (**D**).

Employing zinc complex **37** (Fig. 8) as an initiator, lactide polymerization proceeds to 96% conversion within 40 h at room temperature (PDI = 1.41) [11]. However, polymerization is completed when the temperature is raised to 80 °C in 4 h (PDI = 2.2).



Scheme 4. Proposed mechanism for ring-opening polymerization of ε-caprolactone catalyzed by compound **35c** (half of the molecule is shown from (**A**) to (**D**) for clarity).

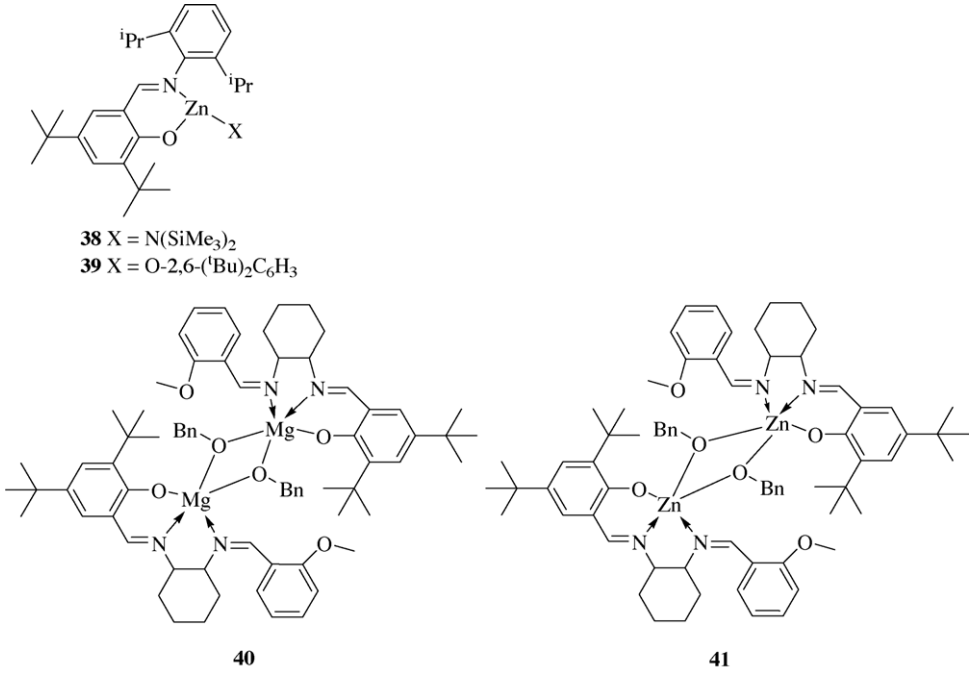


Fig. 9. Schiff base ligand supported zinc and magnesium complexes **38**–**41**.

3.1.4. Schiff base supported magnesium and zinc complexes

Schiff base ligands are particularly attractive because of their ease of preparation, which readily allows for varying their steric and electronic properties. Some groups have tried to synthesize Schiff base magnesium and zinc catalysts for ROP of lactides and related cyclic esters. Three-coordinate zinc amide and phenoxide complexes **38** and **39** supported by bulky Schiff base ligands (Fig. 9) were synthesized by Chisholm et al. [25]. Both **38** and **39** were found to catalyze ring-opening polymerization of L-lactide to produce isotactic PLA in benzene at room temperature. Similarly, **38** and **39** catalyzed polymerization of *rac*-lactide to give atactic poly(*rac*-lactide). When the ratio of $[LA]_0$ to $[Zn]_0$ was ca. 20:1, polymerization occurred slowly at 25 °C proceeding to 90% conversion in ca. 3 h for **38** and ca. 72 h for **39**. The difference in reactivity between those two compounds can be traced to the rate of initiation which is notably slower for the bulky 2,6-*tert*-butylphenoxide. The lack of stereoselectivity in the polymerization of *rac*-lactide by **38** and **39** when compared to the polymerization induced by **25**, presumably reflects the less sterically hindered metal center when coordinated by this Schiff base ligand. Trial to synthesize much more bulky monoether Salen like Schiff base ligand and its related magnesium and zinc complexes **40** and **41** (Fig. 9) was proved to be successful in our group [26]. In toluene, **40** initiates polymerization of lactide at 25 °C in 50 min with conversion up to 96%, while **41** needs 4 h at 60 °C on the ratio of $[LA]_0/[I]_0 = 100$. The experimental results showed all of the polymerizations are in good controlled manner with low PDIs (1.03–1.10). Interestingly, 40 exhibits isotactic selectivity, but **41** shows heteroatactic selectivity in polymerization of *rac*-latide in CH_2Cl_2. The molecular structure shows complex **40** appeared as dimers in solid state. Although the similar structures are assumed for zinc complex **41** in solid state, **41** might existed as a monomer in solution while magnesium complex **40** appeared mainly as a dimer based on the ^1H NMR studies.

3.1.5. Other well-defined zinc complexes

For excellent stereoselective character of sterically bulky β-diketiminate complexes, several bis(phosphinimino)methyl ligand supported complexes **42**–**44** (Fig. 10) were synthesized [27]. In these complexes only the aryloxy derivative **42d** and the triphenylmethoxy derivatives **42c** and **43b**, are active for the ROP of *rac*-lactide to effect >95% conversion of 100 equiv. of lactide monomer in toluene solution at 60 °C within 4, 5, and 2 h, respectively. The enhanced rate of monomer consumption in **43b** is most likely related to the decreased steric demands of the unsymmetrical ligand. This activity is lower than that reported for β-diketiminate zinc alkoxide systems. Unfortunately the polymerizations of lactide are not under control, which results from the strong carbanionic character of the bridge-headed carbon atom.

Dizinc–monoethyloxide complex **45** (Fig. 11) was synthesized by Hillmyer and co-workers [28]. This complex rapidly polymerized *rac*-LA in CH_2Cl_2 at room temperature; at a $[LA]_0/[I]_0$ ratio of 300 with $[LA]_0 = 1$ M, greater than 90% conversion to PLA occurred within 30 min. The level of polymerization control was high, as shown by the linear increase in M_n with conversion and the low PDIs of the produced polymers. The ^1H NMR spectrum of PLA showed ethoxide end groups (indicative of a coordination insertion mechanism) in the amount expected for initiation by every

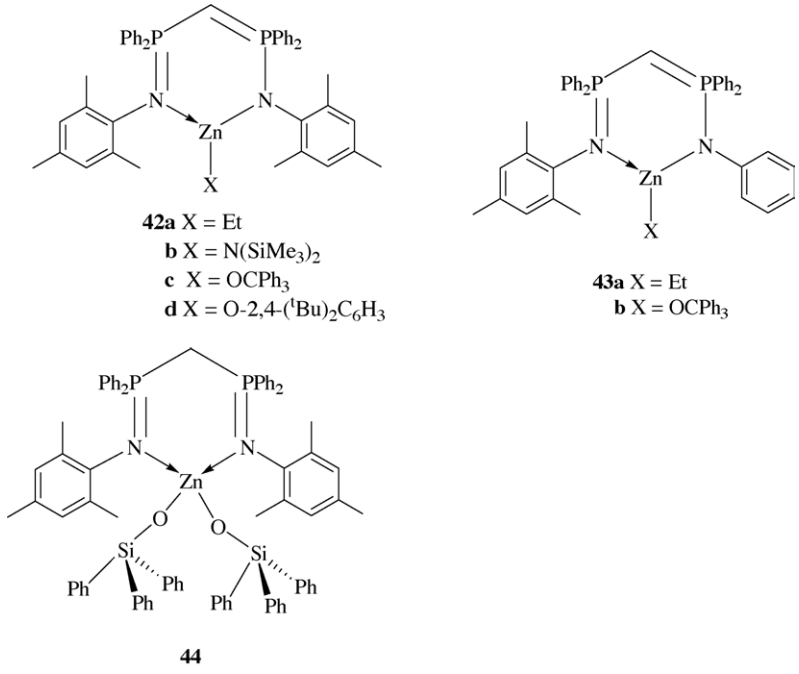


Fig. 10. Bis(phosphinimino)methyl ligand supported zinc complexes **42**–**44**.

molecule of **45**. ^{1}H NMR spectroscopic analysis also showed that *rac*-lactide yielded atactic PLA. In addition, PLA derived from L-lactide was isotactic, signifying no epimerization of stereogenic centers during the polymerization. Preliminary kinetic studies indicate a first order dependence on lactide and complex **45**. In the same research group, complexes **46** and **47** were synthesized (Fig. 11) [29]. **47a** is dimeric with two five-coordinate Zn(II) centers in the solid state proved by X-ray crystallography. **47a** and **47b** cleave into four-coordinate monomers in solution which was confirmed by pulsed gradient spin-echo (PGSE) NMR measurements and laser desorption mass spectrometry (LDMS) analysis of the mixture of **47a** and **47b**. **46a** does not polymerize *rac*-LA, consistent with a coordination insertion mechanism requiring an initiating and propagating metal alkoxide [30]. **47a** is highly active for the polymerization of *rac*-LA in CH_2Cl_2 at ambient temperature, the rate constant for ROP of lactide is 5.1 times higher than that with β-diketiminate complex **25**, 8.2 times higher than that with dinuclear zinc complex **45** and 1220 times higher than that with trispyrazolyl-hydroborate zinc ethoxy complex. Rapid reactions over a wide range of initial monomer-to-catalyst ratios, with a high conversion of LA possible even up to $[LA]_0/[\mathbf{47a}]_0$ ratios of 1500, yielding PLA with molecular weights as large as 130 kg mol^{-1} were observed. Good molecular weight control is demonstrated by a linear increase in M_n with LA conversion at $[LA]_0/[\mathbf{47a}]_0 = 1000$ and relatively narrow molecular weight distributions of the products (PDI of ca. 1.4). Despite of the linear dependence of M_n with LA conversion, the polylactide molecular weights are lower than expected, which has been attributed to the presence of impurities that maybe act as a catalyst deactivator and/or as an exchange promoter.

Complex **47a** was also applied in polymerization of α-methyl-β-pentyl-β-propiolactone(MPP) (Scheme 5) [31]. Polymerization behavior of **47a** for MPP is quite different from that for lactide. The polymerization of lactide occurs very quickly, reaching conversions of >93% after several minutes and the polydispersity also increases with time as

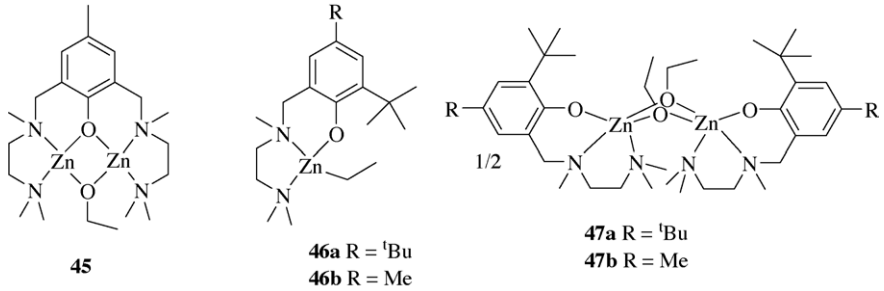
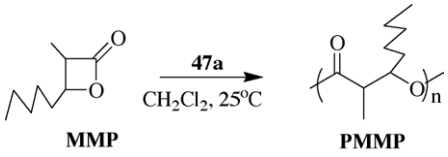
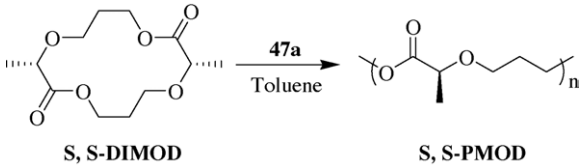


Fig. 11. Single ethylenediaminearm and double ethylenediamine arms phenolates supported zinc complexes **45**–**47**.



Scheme 5. Polymerization of MMP initiated by complex **47a**.



Scheme 6. Polymerization of *S*,*S*-DIMOD initiated by complex **47a**.

is typical for an equilibrium polymerization [28]. Meanwhile, MPP polymerization is relatively slow (up to 100 h or more until, in the ^{1}H NMR spectrum, all monomer resonances were consumed) and the polydispersity is narrow even at higher conversion (1.07–1.11). Although the molecular weights attained are consistent within the deviation between measured molecular weights and the theoretical values, and the polymerization is free of side reactions. The apparent molecular weight deviation may result from the relative SEC calibration (based on polystyrene standards) or perhaps due to the presence of an impurity that serves as a chain transfer agent. Diblock copolymers of PMPP and PLA can be obtained in a controlled manner by sequential monomer addition. Since MPP can be synthesized from renewable resources, PMPP/PLA composites may form the basis for mechanically useful materials with the desirable characteristics of complete degradability and renewable origins.

Following the above very promising results, complex **47a** was used to initiate ROP of an enantiomerically pure 14-membered cyclic diester (*S*,*S*-DMOD) for a new isotactic *S*,*S*-PMOD (poly(3-methyl-1,4-dioxan-2-one)) (Scheme 6) [32]. Polymerization of this cyclic di-ester can reach to 90% with $[Monomer]_0/[I]_0 = 100$ in 40 min at room temperature in toluene. A linear increase in molecular weight with conversion was observed, consistent with the controlled nature of the polymerization, although polydispersities are somewhat broad (1.5–1.9).

Cationic three-coordinate zinc complex **48** (Fig. 12) was synthesized for the homopolymerization of epoxides and lactones [33]. The polymerization of ε-caprolactone at room temperature was slow but accelerated on heating to 60 °C. The resulting polymer gave M_w values of up to 40,000 with polydispersities close to 1. Cationic zinc complexes **49a** and **49b** (Fig. 12) were also applied to initiate polymerization of ε-caprolactone at 60 °C in toluene in an uncontrolled manner [34].

Deprotonation of the triamine ligand precursor with 2 equiv. of ^{n}BuLi, followed by the treatment of the ensuing dilithium salt with anhydrous $ZnCl_2$ affords the neutral complex **50** in 44% yield (Fig. 13) [35]. Complex **50** initiates the bulk copolymerization of *rac*-lactide and glycolide to complete in about 3 h at 180 °C. Copolymers possessing higher molecular weight with narrow distribution and various glycolide contents could be obtained by optimizing the reaction conditions (1.7 and 1.9).

In CL polymerization, both the tetranuclear **51** and the dinuclear **52** are effective initiators (with PDIs from 1.69 to 1.80) (Fig. 13) [36], although the three-coordinate **51** is considerably more active than the four-coordinate **52**. To investigate

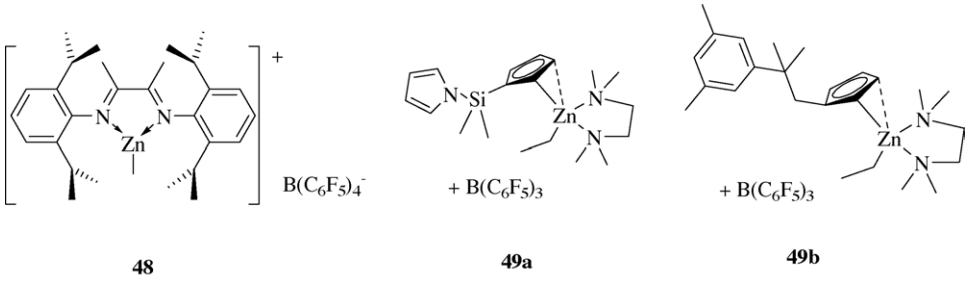


Fig. 12. Cationic zinc complexes **48** and **49**.

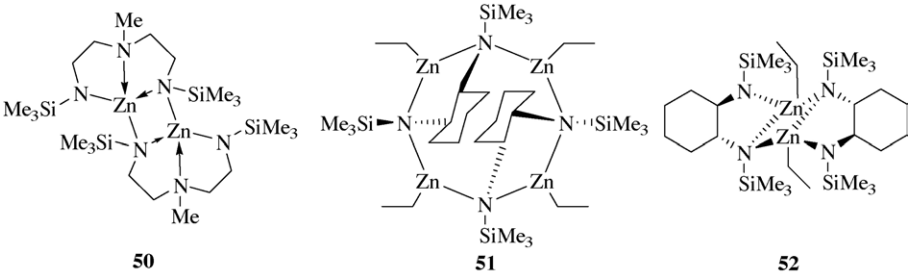
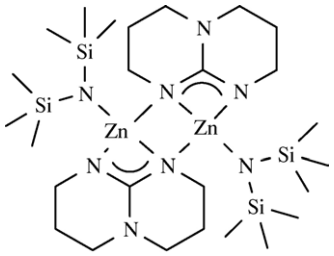
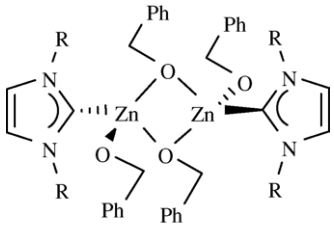


Fig. 13. Triamine and diamine supported zinc complexes **50**–**52**.



53

Fig. 14. Guanidinate amide zinc complex **53**.



54 R= 2,4,6-trimethylphenyl

Fig. 15. Carbene supported zinc alkoxide complex **54**.

the effect of chain-transfer reagents on the polymerization, an addition of 4 equiv. of ^{i}PrOH drastically decreases polymerization activity, presumably due to decomposition of the zinc complex. Complexes **51** and **52** have comparable activities for polymerization of LA at 70 °C. In a ratio of $[LA]_0/[Zn]_0 = 200{:}1$, about 90% monomer conversion was achieved for both complexes within 2 h in toluene. However, the M_n obtained against polystyrene standards is approximately half of the calculated value, suggesting that there are two Zn amide initiating groups per Zn molecule (i.e., $[LA]_0/2[Zn]_0$). An addition of 4 equiv. of ^{i}PrOH did not result in a noticeable increase of activity but a decrease of molecular weight of polylactide.

The amine-elimination reaction between [Zn{N(SiMe$_3$)$_2$}$_2$] and 1 equiv. of 1,3,4,6,7,8-hexahydro-2-hpyrimido[1,2-α-]pyrimidine (hppH) proceeds smoothly to afford the mixed (guanidinate)(amide) complex [Zn(hpp)-{N(SiMe$_3$)$_2$}]$_2$ **53** (Fig. 14) [37], which forms in a dimeric figure in the solid state. Preliminary NMR investigations of the catalytic activity of **53** towards the ring-opening of *rac*-lactide were performed in CD_2Cl_2 and toluene-d_8. In contrast to many zinc complexes incorporating the relatively bulky N(SiMe$_3$)$_2$ group, where initiation is reported as being slow, the immediate reaction of **53** to generate a new species (up to 98% in ca. 2 min) was observed, as judged by a shift of the N(SiMe$_3$)$_2$ resonance. The progress of the reaction was monitored by ^{1}H NMR spectroscopy, clearly indicating that 45–85 equiv. of LA were polymerized to polylactide (PLA) with more than 95% conversion in less than 2 h. The straight-line relationships between molecular weight and conversion generated from different monomer concentrations and solvents present good evidence that the polymerization proceeds in a "well-behaved" fashion. In addition, a sample of **53** and LA (45 equiv.) that had progressed to more than 98% conversion was able to initiate the polymerization of a further 50 equiv. of LA in CD_2Cl_2 after 18 h at room temperature. The fresh monomer was converted into PLA over a period of 2 h, demonstrating the stability of the propagating species over time and providing further indication of the controlled nature of the polymerization. There was no evidence for a tacticity bias in the ^{1}H NMR spectrum of the PLA produced by **53**, as indicated by selective decoupling of the methine protons.

In the past several years, some more active N-heterocyclic carbenes have been used to catalyze ROP of cyclic esters in living manner with narrow PDIs [38,39]. Encouraged by this information, Hillmyer and co-workers synthesized one *N*-heterocyclic carbene based zinc complex (**54**) (Fig. 15) for initiating ROP of lactide [40]. The X-ray structure of **54** shows each zinc in a distorted tetrahedral geometry bound to a carbene and three benzyloxides, two bridging and one terminal, while in solution **54** maybe exist as monomer or remains dimer but is highly fluxional via quick exchange between terminal and bridging benzyloxide ligand from analyses of ^{1}H NMR spectrum. From kinetic studies, **54** is an efficient and highly active catalyst for the polymerization of lactide with first order dependence on [*rac*-lactide]. Heteroatactic PLA (Pr = 0.6) can be obtained with predicted molecular weight. However, experiments showed that free carbene can catalyze polymerization of lactide in presence of benzyl alcohol and even is slightly more active than **54**, none can rule out the polymerization is partly catalyzed by some pure carbene ligand which was produced from the dissociation of complex **54**. In contrast to **54**, isotactic PLA were obtained when using pure carbenes in presence of benzyl alcohol (Pm = 0.75, BnOH/carbene = 0.67 equiv., temperature = −20 °C, CH_2Cl_2).

3.2. Calcium complexes

Various discrete metal complexes have been employed in lactide and cyclic esters polymerizations, while it is surprising that calcium has not been widely exploited. Calcium is significantly larger than magnesium and zinc [41]. This makes its coordination chemistry different from magnesium and zinc even though they all have +2 charge upon complex formation. Calcium has many attractive features for polyesters production. It is biocompatible and essential for life [42]. This is important for the production of biocompatible polymers where small amount of catalysts may inevitably be incorporated into the polymers. Recently a few examples of discrete calcium complexes have been reported in the polymerization of lactides and cyclic esters especially by Chisholm and Feijen groups.

Calcium isopropyloxide generated in situ from the reaction of bis(tetrahydrofuran) calcium bis[bis(trimethylsilyl)amide] and isopropanol, is highly active for the living and controlled ring-opening polymerization of

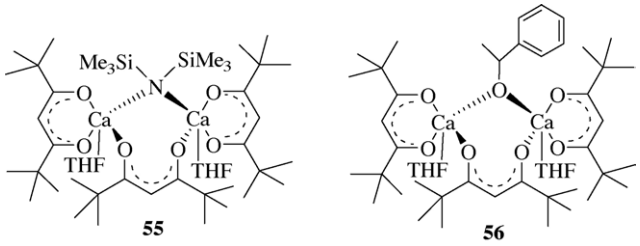


Fig. 16. Diketone supported calcium complexes **55** and **56**.

cyclic esters in THF using mild condition (18 °C) [43]. Promoted by this fact, Feijin et al. synthesized two single-site calcium initiators containing chelating tmhd (H-tmhd = 2,2,6,6-tetramethylheptane-33-dione) ligands [(THF)Ca(tmhd)]$_2$[*p*-N(SiMe$_3$)$_2$](*p*-tmhd) (**55**) and [(THF)Ca(tmhd)]$_2$[*p*-OCH(Me)Ph](*p*-tmhd) (**56**) (Fig. 16) and applied them for the ring-opening polymerization of L-lactide and ε-caprolactone [44]. Complex **55** mostly acts just as a catalyst in polymerization of cyclic esters, and the isolated polymers had high PDIs and much higher molecular weights as compared to the calculated values. Complex **56** was highly reactive and promoted a fast polymerization of L-lactide (120 min) and ε-caprolactone (30 min) to high monomer conversions under mild conditions (THF as a solvent, room temperature) with narrow PDIs (1.13–1.19) and controlled molecular weight with $[M]_0/[I]_0 = 150$. The in situ initiating system **55**/2-propanol, in which 2-propanol probably replaces the bridging (trimethylsilyl)amido ligand, shows much faster polymerization kinetics as compared to **56**. First order kinetics in monomer was observed in polymerization with **56** or **55**/2-propanol.

Based on the success with magnesium and zinc catalyst systems, syntheses of some calcium complexes (**57**–**64**) (Fig. 17) supported by tris(pyrazolyl)borate ([HB(3-Rpz)$_3$]$^-$) and β-diketiminate (BDI-H) ligands with amide or alkoxide capable of initiating the ring-opening polymerization of lactides have been reported along with a comparison with magnesium and zinc chemistry by Chisholm et al. [45]. After treatment of these ligands with KN(SiMe$_3$)$_2$ or TlN(SiMe$_3$)$_2$, calcium-amide or alkoxide complexes can been synthesized by metathetic reactions employing CaI_2 which is sparingly soluble in THF and has the lowest lattice energy of any calcium halide and Ca(N(SiMe$_3$)$_2$)$_2$. When tris(3-phenylpyrazolyl)borate with less sufficient bulk was used as ligand, only an inactive L_2Ca complex was obtained. So the steric hindrance of the ligand is necessary to stabilize the metal complex to exist as a monomeric form by shutting down the Schlenk equilibrium, which otherwise will lead to an inactive complex L_2M.

The reactivity of the M–N bonds toward ring-opening of lactide is confirmed to be Ca > Mg > Zn by a direct comparison of the reactivity of the metal amide bonds of (BDI)ZnN(SiMe$_3$)$_2$, (**21**), (BDI)MgN(SiMe$_3$)$_2$, and (BDI)CaN(SiMe$_3$)$_2$THF, (**62**) in the ring-opening of lactide using competition experiments in ^{1}H NMR. While the complex (BDI)CaN(SiMe$_3$)$_2$THF, (**62**), was allowed to react with *rac*-LA, 200 equiv., in THF at room temperature, conversion up to >90% was achieved in 2 h yielding atactic PLA. In contrast, (BDI)MgN(SiMe$_3$)$_2$ gives ca. 90% heterotactic PLA within 5 min. This reactivity order Mg > Ca is the opposite of that in the competition experiments, and probably results from the fact that a complex of the form (BDI)CaOP, where OP represents the growing polymer chain, is not monomeric or well-defined. Because Ca is bigger than

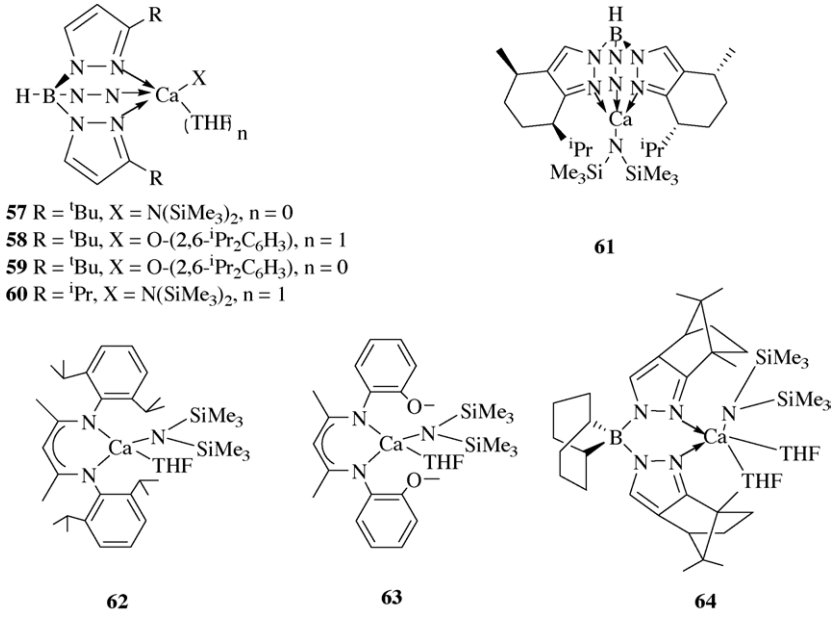


Fig. 17. Structure of calcium complexes **57**–**64** supported by β-diketiminate and tris(pyrazolyl)borate ligands.

Mg, the BDI ligand is not sufficiently steric demanding to prevent aggregation or ligand scrambling and the formation of atactic-PLA implies that the reactive site for ring-opening is not sufficiently crowded to impart any stereoselectivity in the ring-opening event. A supporting experiment to this explanation is the fact that when (BDI)CaN(SiMe$_3$)$_2$, (**62**) was allowed to react with 1 equiv. of HO^{i}Pr even at −78 °C, (BDI)$_2$Ca was obtained (probably through a rearrangement of (BDI)CaO^{i}Pr) as a major product rather than (BDI)CaO^{i}Pr, suggesting that (BDI)CaO^{i}Pr (a mimic of the growing polymer species) is not a stable monomeric unit.

The amide complexes with the bulkier Tp ligand, complexes **57**, **60**, and **61**, were also allowed to react with 200 equiv. of *rac*-LA in THF. A similar reaction was carried out with compound **64** which has the chiral 9-BBN-Bp(+)-Cam ligand. In all cases, polymerization of *rac*-LA was very rapid (90% conversion within 5 min) and the Tp^{t}Bu-bearing complex **57** was extremely rapid (polymerization to >90% in less than 1 min) and stereoselective in producing ca. 90% heterotactic PLA with a PDI of 1.74 (M_n = 37.8 kg mol^{-1}). The complex (Tp^{t}Bu)Ca(OC$_6$H$_3$-2,6-^{i}Pr$_2$) THF, 59, is also very active in the polymerization of *rac*-LA. In THF, the stereoselectivity and rate of polymerization is similar to that seen for the amide precursor complex **57**. A PDI of 1.68 (M_n = 40.1 kg mol^{-1}) was observed and is believed to reflect the relative rate of insertion into the Ca–OAr bond being slower than the subsequent rate of propagation and transesterification. The Ca–OC$_6$H$_3$-2,6-^{i}Pr$_2$ bond in **59**, unlike the Ca–N amide bond in **57**, is inert to CH_2Cl_2 solvent. Therefore, CH_2Cl_2 or CD_2Cl_2 can be used in studies of the polymerization of LA for complex **59**, but not for **57**. In CH_2Cl_2, less stereoselectivity in polymerization was observed, although the reaction was extremely rapid up to >90% conversion within 1 min for polymerization of 200 equiv. *rac*-LA. Since the Ca–O bond was unreactive toward propylene oxide (PO) and cyclohexeneoxide (CyHO), these oxiranes were also employed as solvents in the polymerization of *rac*-LA. The percentage of heterotactic tetrads was less than that for THF which leads us to suggest that the degree of heterotacticity in the PLA correlates with the coordinating ability of the solvent as a ligand to calcium: THF > PO ∼ CyHO > CH_2Cl_2.

3.3. Strontium complexes

To the best of our knowledge, only a few simple strontium complexes have been used to catalyze/initiate ring-opening of cyclic esters. For example, an amino isopropoxyl strontium (Sr-PO) initiator [46], which was prepared by the reaction of propylene oxide with liquid strontium ammoniate solution, was used to carry out ROP of cyclic esters. The Sr-PO initiator demonstrated an effective initiating activity for the ROP of ε-caprolactone and L-lactide under mild conditions and the molecular weight can be adjusted by the ratio of monomer to Sr-PO initiator. Block copolymer PCL-*b*-PLLA was prepared as well. A coordination–insertion mechanism was confirmed by the hydroxyl and isopropoxycarbonyl end groups of PCL and by the coordination between Sr-PO initiator and model monomer γ-butyrolactone.

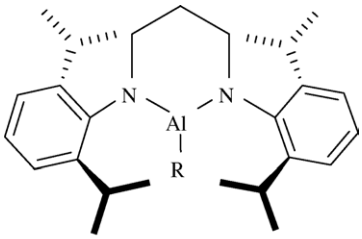
4. Group 13 metal complexes

Gallium(III) complexes supported by the BDI ligand for ring-opening polymerization of lactide have been synthesized by Chisholm's group, but experimental results showed they are poor catalysts [47]. In group 13, only aluminum complexes have displayed good catalytic activity toward ring-opening polymerization of lactide and cyclic esters, most of them are aluminum alkoxide and alkyl complexes, including diamide aluminum complexes, porphyrin aluminum alkoxides, ketiminate or diketiminate aluminum complexes, alkylaluminum complexes, diol-aluminum alkoxides, and aluminum thiolates, Salen-aluminum alkoxide, featuring Salen-aluminum complexes, diamidoamino aluminum, amine bisphenolate aluminum complexes, etc.

4.1. Polymerization initiated with aluminum alkyl, amide and thiolate

4.1.1. Initiating with amide groups

Diamine complexes **65a** and **65b** (Fig. 18) were synthesized by the reactions of diamine with trimethylaluminum and triisobutylaluminum, respectively. Refluxion of **65a** with B(C$_6$F$_5$)$_3$ in toluene can yield complex **65c** (Fig. 18) [48]. X-ray structure of **65a** showed aluminum was three-coordinated. After polymerization of lactone, the methyl group still attached to Al in complexes **65a** demonstrating polymerization was initiated by amide group, and result also showed monomer insertions favor the nucleophilic attack onto a monomer by the alkoxy group generated in the initiation step rather than attack by the second bulky amide group. The isobutyl derivative **65b** exhibits the higher activity than **65a**, polymerization of 200 equiv. of lactone at room temperature needs 1.5 h with 74% isolated polymer yield. The C$_6$F$_5$-substituted derivative **65c** exhibits the low activity, and only broad PDI molecular weight distribution polymers (2.55–7.83) were produced with these three complexes.



65a R = Me
65b R = ^{i}Bu
65c R = C$_6$F$_5$

Fig. 18. Complexes **65a**–**65c**.

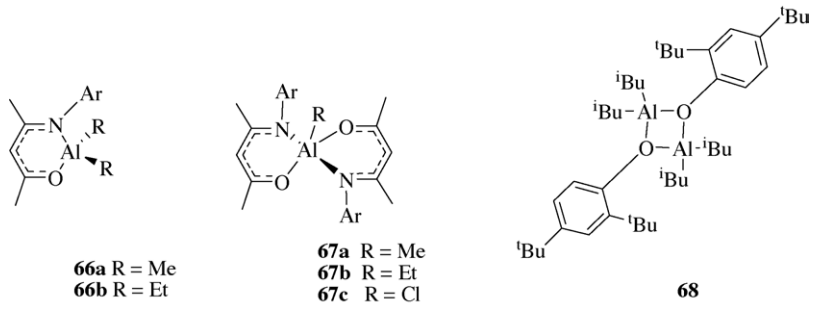


Fig. 19. Complexes **66–68**.

4.1.2. Initiating with alkyl groups

An anionic coordination mechanism can be observed using ketiminate and diketiminate aluminum complexes (**66a–67c**) (Fig. 19) to initiate the ring-opening polymerization of ε-caprolactone [49]. Analysis of polymers showed insertion of monomer into Al-alkyl bond. At room temperature or 60 °C, the lactone was added to the catalyst/toluene solution, broad PDIs (1.29–2.80) polymers can be obtained after 2.4 or 3.5 h. The more reactive Al-alkyl complexes were used as catalysts yielding polymers with higher molecular weight. When the Al-chloride complex (**67c**) was used as a catalyst, a low molecular weight oligomer was obtained, indicating the inert Al-chloride bond. Complex **68** is another example of using alkyl group (*iso*-butyl) to initiate polymerization of ε-caprolactone at 25 °C with narrow PDIs (1.07–1.31) in controlled condition [50].

4.1.3. Initiating with thiolate groups

Thiolate complexes **69–70** (Fig. 20) were synthesized in our laboratory for producing thiolate end groups polyesters [51]. X-ray crystallographic studies showed **69a** and **69b** are monomeric while **70a** and **70b** are dimeric. All of these four complexes are active for polymerizing ε-caprolactone at 25 °C in toluene with controlled character of the polymerization process and a thioester end group can be observed in ^{1}H NMR spectrum. The "controlled" character was further confirmed from the polymerization resumption experiment. Complex **69a** is also active for ring-opening of L-lactide in refluxed toluene or xylene with narrow PDIs (1.15–1.25).

4.2. Polymerization initiated with aluminum alkoxides

To the best of our knowledge, aluminum alkoxide complexes are more active than other aluminum initiators, and most of them can initiate ring-opening of ε-caprolactone, even lactide at moderate condition.

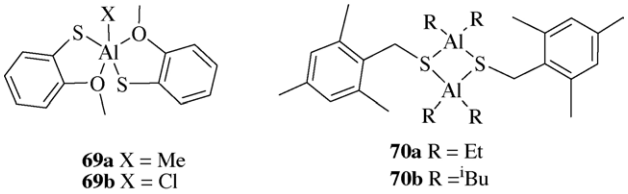


Fig. 20. Structure of complexes **69–70** initiating polymerization of lactide with thiolate groups.

4.2.1. Porphyrin supported aluminum alkoxides

Porphyrin aluminum complexes **71a** and **71b** (Fig. 21) were synthesized for ROP of lactide by Inoue and co-workers [52]. Controlled molecular weights and narrow PDIs (<1.25) PLA can be gotten at 100 °C in dichloromethane. Notably, 1 equiv. lactide inserted complex could be characterized by ^{1}H NMR with aluminum methoxide **71b**, thereby, demonstrating that polymerization proceeds at the acyl-oxygen bond. Studies of kinetics on related systems revealed that the polymerization is second order with respect to aluminum complex, suggesting that the propagation involves two molecules of initiator, one as a nucleophilic species involved in chain growth and the other as a Lewis-acidic monomer activator.

4.2.2. Salen and featuring Salen supported aluminum complexes

The best character of Salen-aluminum complexes is the excellent selective polymerization of *rac*-lactide, while they suffer from inherently low activity; reasonable conversions are generally attained only at high temperatures (>70 °C) over a long period of time (h). The Salen ligands are easily achieved by condensation of salicyl carbonyl derivatives and diamines, and it is easy to adjust groups of Salen ligands. Aluminum alkyl complexes can be prepared by treatment of ligand with trialkyl aluminum. The aluminum alkoxide complexes can be obtained by alcoholysis of aluminum alkyl

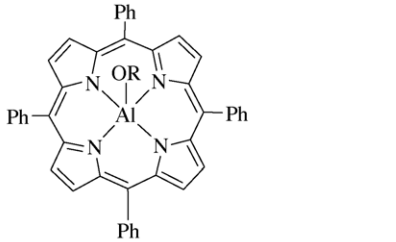


Fig. 21. Porphyrin supported aluminum alkoxides **71a** and **71b**.

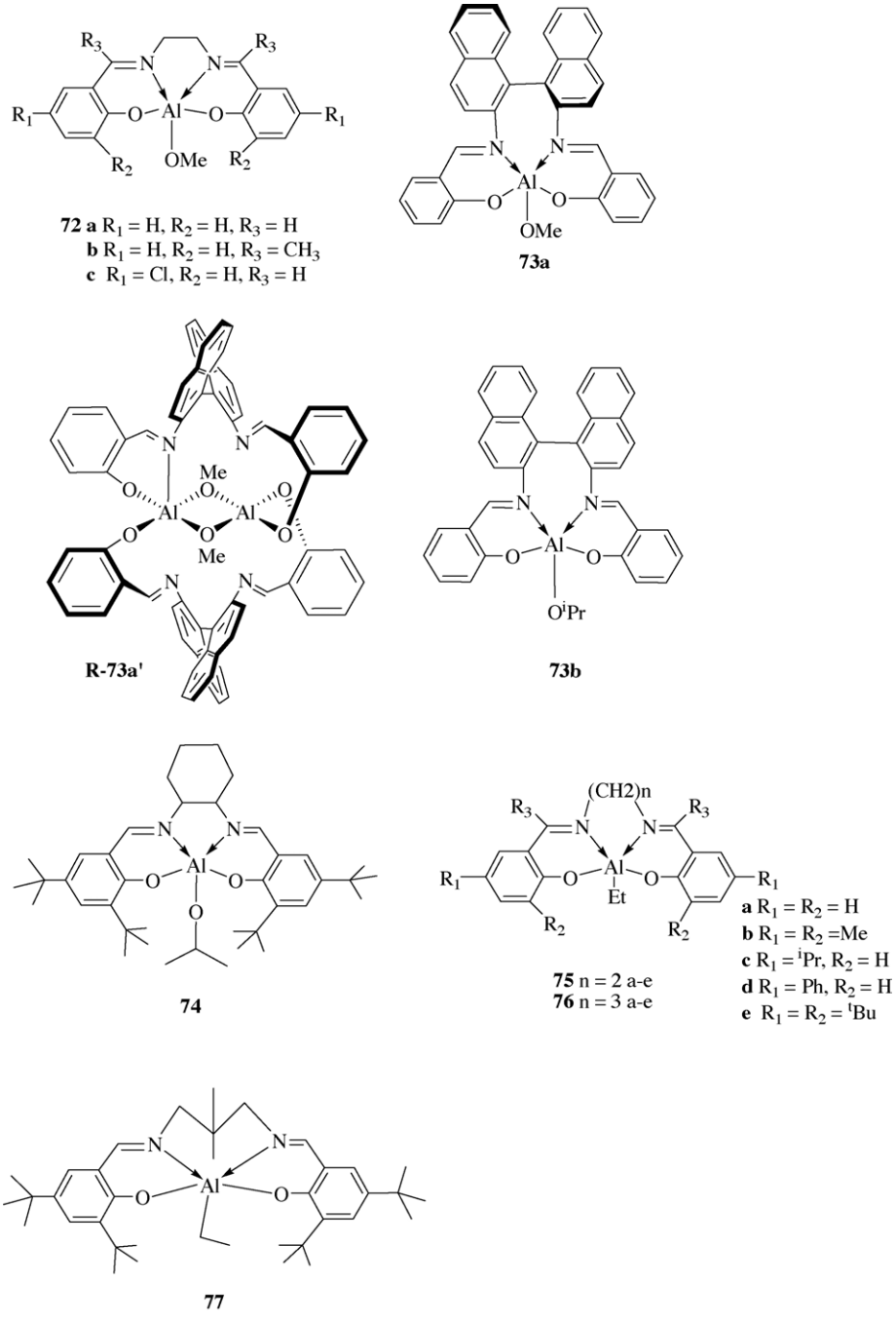
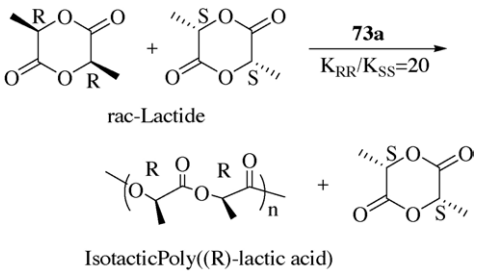


Fig. 22. Salen supported aluminum alkoxides **73**–**77**.

complexes or by ligand exchange with trialkoxy aluminum precursors. X-ray structures showed the geometry at aluminum in these complexes is either distorted square pyramidal or trigonal bipyamidal.

Spassky and co-workers synthesized complexes **72a**–**72c** (Fig. 22) and applied them in ROP of lactide [53], experimental results showed **72c** with electron-withdrawing substituents on the Schiff-base ligand backbone can more efficiently catalyze ROP of lactide at ambient temperature with less transesterification than **72a**, which may result from an enhancement of the aluminum electrophilicity and/or an increase of the polarization of the initiating/propagating Al-X bond. When **72a** was used to initiate polymerization of lactide [54], both inter- and intramolecular transesterification reactions were observed, while the side reaction can be significantly decreased with bulky at Salen ligand backbone such as **75c**–**75e** and **76c**–**76e**.

Polylactides can bear different microstructures and their mechanical properties strongly depend on their stereochemical compositions. To develop efficient and inexpensive

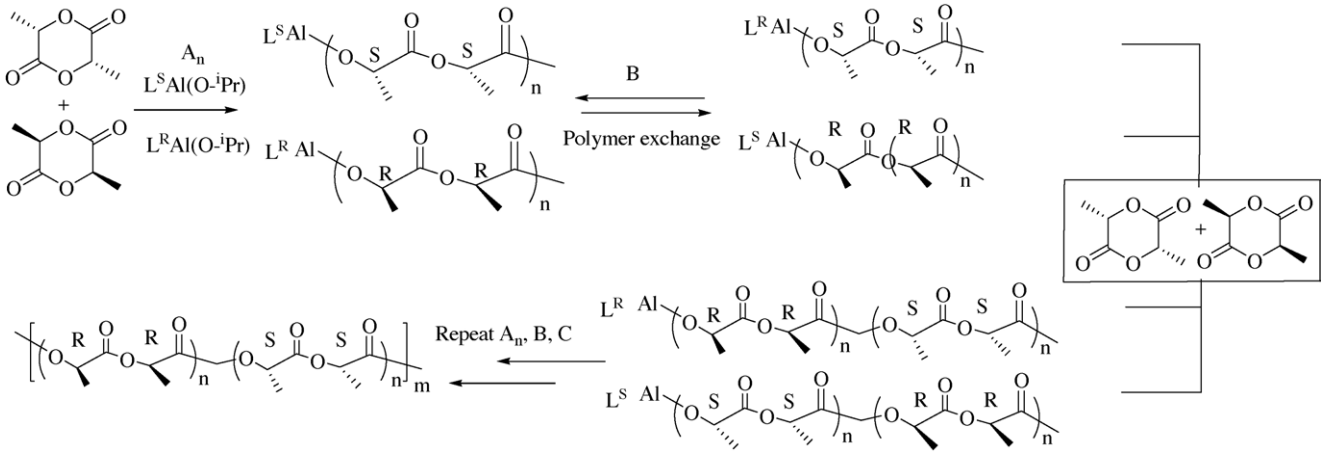


Scheme 7. Highly selective polymerization of (*R*,*R*)-lactide over (*S*,*S*)-lactide using complex **73a**.

processes for stereocontrolled polymerization of *rac*-lactide is a main task of many groups. Indubitably, the most important breakthrough was the discovery of stereoelective lactide polymerization by Spassky et al. An enantiomerically pure complex (*R*)-**73a** (Fig. 22), afforded by the reaction of (*R*)-(SalBinap)AlEt with dry ethanol, exhibited high selectivity in the kinetic resolution of *rac*-lactide [55]. At 70 °C, the catalyst exhibited a 20:1 preference for the polymerization of (*R*,*R*)-lactide over (*S*,*S*)-lactide (Scheme 7). The polymerization proceeded in a living mechanism, as shown by the narrow PDIs and control of the resultant polymer molecular weight by the monomer/catalyst ratio. At conversions less than 50%, the polymer microstructure was predominantly isotactic poly[(*R*)-lactide]. At conversions greater than 60%, only (*S*,*S*)-lactide remained. The reaction reached 100% conversion very slowly due to the kinetic preference for the (*R*)-enantiomer. The polymer formed presumably had a tapered stereoblock microstructure, where the monomer composition varied from all *R*-units to all *S*-units over the length of the polymer chain. This material exhibited a high melting temperature, T_m = 187 °C, relative to enantiopure isotactic material, which melts between 170 and 180 °C. Coates et al. repeated this preparation and found that the methanol mother liquor produced large colorless crystals of a bimetallic complex (*R*)-**73a**′ upon standing (Fig. 22), which accounts for approximately 30% of the total reaction product. (*R*)-**73a**′ was found to be a catalytically inactive by-product. More interestingly, a remarkable preference for L-lactide over D-lactide isomer was imposed by enantiopure (*R*,*R*)-**74** (Fig. 22) [56], which contrasts to (*R*)-**73a**. The polymerization obeyed first-order kinetics in monomer with instantaneous initiation with different combination of **74** and lactide stereoisomers. Feijen and co-workers demonstrated complex **74** exerted excellent molecular-weight control as well as stereochemical control in lactide polymerization in the absence of solvent [57].

Aluminum complex (*R*)-**73b** (Fig. 22) was applied to the synthesis of syndiotactic PLA from *meso*-LA by Coate's group [58,59]. The results showed the selectivity of the reaction is Pr = 0.96 when the polymer is produced at 70 °C in toluene for 40 h. Interestingly, *rac*-**73b** polymerized *meso*-lactide to heterotactic PLA. On the basis of the absolute stereochemistry of ring-opening of *meso*-lactide, a polymer exchange mechanism is proposed to account for the tacticity of the polymer by using (*R*)-**73b**. Furthermore, they re-investigated the polymer made from *rac*-lactide using (*R*)-**73b**. Instead of producing the expected stereocomplex PLA consisting of enantiomerically pure strands of isotactic polymer, an isotactic stereoblock PLA was produced. They proposed this novel microstructure again results from a polymer exchange mechanism, where runs of enantiomerically pure lactide are interrupted by periodic changes in stereochemistry due to interchange between enantiomeric catalyst species (Scheme 8). In contrast to kinetic resolution of *rac*-lactide with **R-73a**, Baker et al. used *rac*-**73b** to polymerize *rac*-lactide producing highly enantiopure isotactic PLA [60].

Nomura et al. recently reported the living polymerization of *rac*-LA using complexes **75a**–**e** and **76a**–**e** (Fig. 22) as catalysts in the presence of benzyl alcohol without any chiral auxiliaries. The reaction proceeded via chain end controlled mechanism (CEM) and the highest selectivities (Pm = 0.91) were obtained for ^{t}Bu group at the aromatic rings (**76e**) [61]. Complex **77** also showed highly isotactic selectivity for the polymerization of *rac*-lactide to get stereoblock poly(*rac*-LA) in the presence of 2-propanol with Pm = 0.9 [62].



Scheme 8. Proposed polymer exchange mechanism for isotactic stereoblock PLA initiated by **73b**.

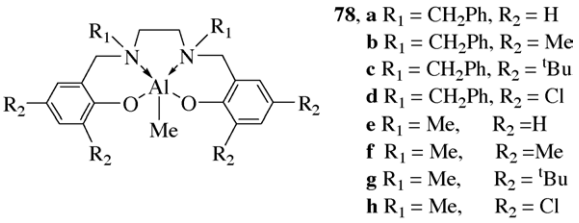
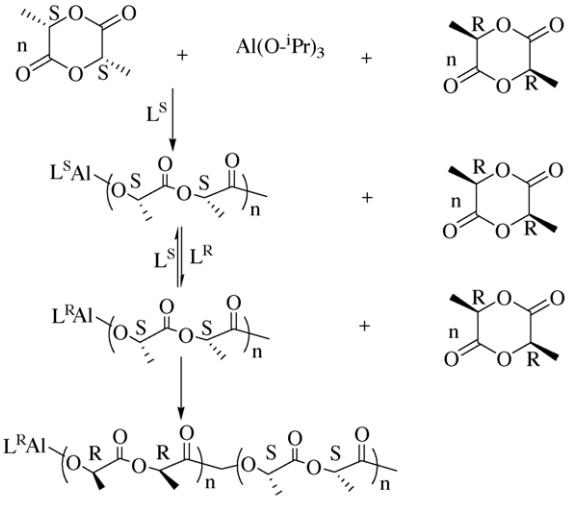


Fig. 23. Featuring Salen ligands supported aluminum complexes **78a**–**78h**.

It must be emphasized that Gibson et al. have found quite remarkable stereocontrol in the polymerization of *rac*-lactide by aluminum complexes **78a**–**h** (Fig. 23) supported by tetradentate aminophenoxide ligands [63]. The polymerizations are well-controlled and living, affording PLA materials that range from highly isotactic (**78e**, Pm = 0.79 in toluene 21 h at 70 °C) to highly heterotactic (**78h**, Pr = 0.96, in toluene 21 h at 70 °C), depending upon the ligand substitution pattern. This is the first time aluminum-based systems have been found to give heterotactic PLA and the first time a dramatic switch in tacticity has been observed for a lactide polymerization system upon small changes to the remote ligand substituents.

Duda et al. designed a two-step polymerization method, a combination of stereoselection and chiral ligand exchange (Scheme 9) to provide isotactic stereocopolymers (*S*)-PLA-*b*-(*R*)-PLA [64]. The initiator (SBO_2Al–O^iPr) for two-step polymerization of *rac*-lactide was prepared in situ by the mixing of 2,2′-[1,1′-binaphthyl-2,2′-diyl-bis-(nitrylomethilidyne)]diphenol ($SB(OH)_2$) with $Al(O^iPr)_3$ in THF at 80 °C for 24 h. Followed by the addition of *rac*-lactide, the polymerization goes to approximately 47% consumption of lactide after 12.5 h. PLA obtained almost is *R*-lactide. In the second step, an equimolar quantity of *R*-$SB(OH)_2$, with regard to *S*-$SB(OH)_2$, was introduced to polymerize further lactide. Further polymerization was accompanied by a gradual decrease of optical rotation readings, and finally (conversion >90 mol%) the polymerization product precipitated out after another 12.5 h. The resulting polylactides has very high melting point (T_m reached 210 °C), and are highly crystalline (about 70% according to the melting enthalpies). All these data support the consecutive site-controlled polymerization of both enantiomers of *rac*-lactide, the homochiral ancillary ligand rapidly exchanging with its enantiomer after half conversion. According to kinetic study, a given homochiral catalyst exhibits a 28:1 preference for the polymerization of one enantiomer for the monomer over the other. Therefore, the resulting polymers are gradient stereocopolymers rather than pure block stereocopolymers.



Scheme 9. Two-step polymerization of *rac*-lactide from exchange chiral Salen ligand.

4.2.3. Diol supported aluminum alkoxide complexes

A series of diol ligands including EDBP–H_2, MCIMP–H_2, MMPEP–H_2, MEBBP–H_2, and Biphenol (Fig. 24) supported aluminum alkoxides have been studied widely to polymerize lactide and cyclic esters. Complexes **79**–**85** (Fig. 24) all exist as dimer with the oxygen atoms of benzyloxide as bridges. Complex **79a** can initiate ROP of ε-caprolactone and γ-valerolactone in toluene at 25 °C in good controlled manner (PDIs = 1.04–1.19) [65]. Complex **84** was synthesized by treatment **79a** with benzylaldehyde, and was proposed to be a model for an intermediate in the polymerization of lactones. During the ROP of lactones, a lactone molecule coordinates to an aluminum center, forming a penta-coordinated intermediate, followed by the attack of a benzylalkoxy group on lactone. **84** also shows great catalytic activity toward the ROP of ε-CL, the reaction rate, however, is much slower than that of compound **79a**, probably due to the existence of PhCHO inhibiting the coordination of lactone to the Al atom, thereby retarding the polymerization. The more sterically encumbered complexes **80** and **81** are more active than **79a** [66–68], when the ratio of monomer to initiator is 100, the completion of polymerization can be achieved in 32, 3, and 1 h for complexes **79a**, **81**, and **80** respectively at room temperature. **79b**–**79d**, **85** and **82** were also applied to initiate polymerization of ε-lactone and completed polymerization can be achieved in 15 h at 60 °C or 2 h at 50 °C in toluene in good controlled manner [68,69]. Although **79**, **81**, **82** and **85** are less active toward polymerization of lactide, **80** can initiate ROP of lactide in refluxed toluene under good controlled manner. The polymerization of 20–50 equiv. lactide can be completed after a few days when the monomer concentration is 1 M. It is worthwhile to note that compounds **79a**–**82** initiate the ROP of lactones not only in a living manner but also in an immortal manner in which a narrow PDIs polymers are obtained with a number of polymer molecules exceeding the number of initiator molecules. Especially, complex **80** can bear 160 equiv. BnOH in ROP of ε-caprolactone. The "immortal" character of these complexes has paved a way to synthesize many-fold polymer chains with very narrow PDIs in the presence of a small amount of initiator. Although

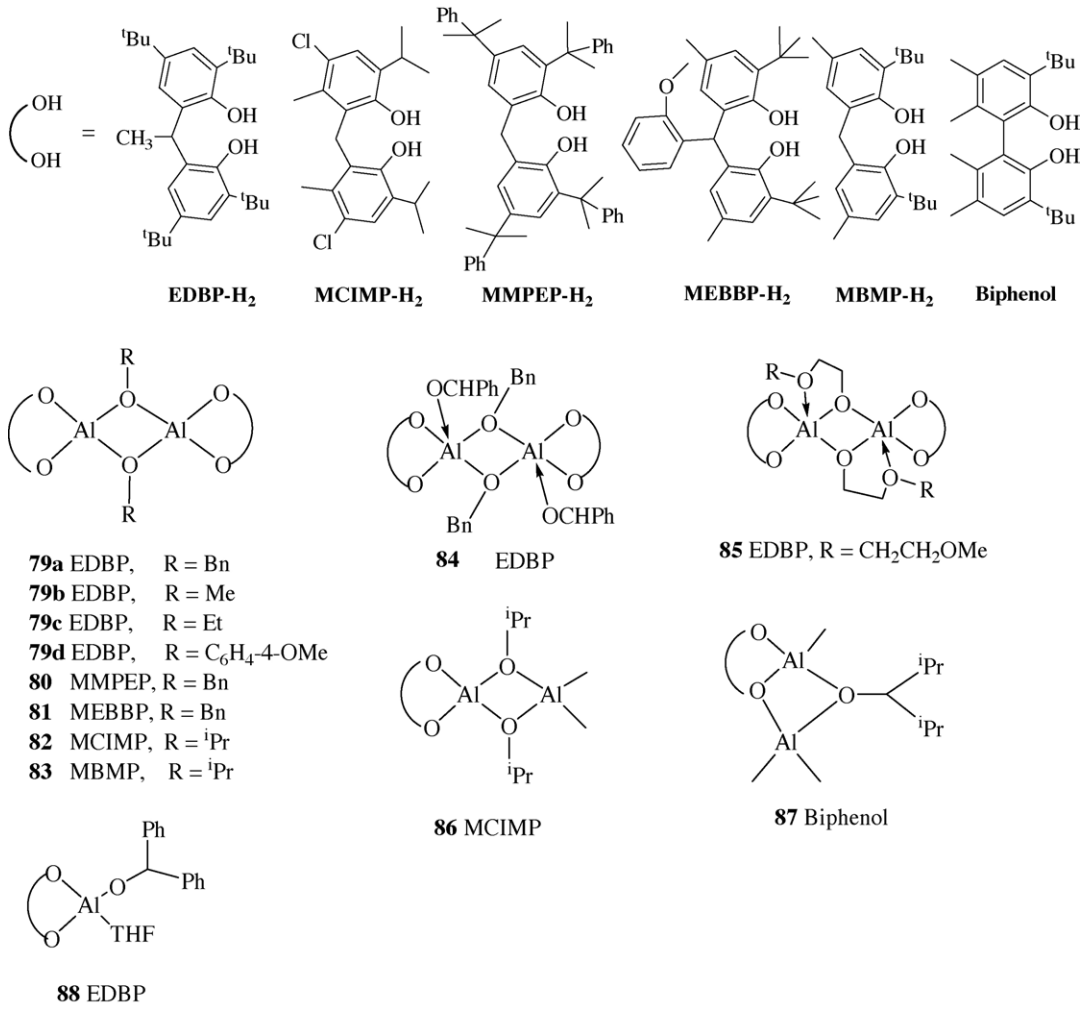


Fig. 24. Diol ligand supported aluminum complexes **79**–**88**.

complex **83** showed good control in polymerization of ε-caprolactone too [70], the efficiency, reflecting the number of chains started per aluminum, has a value of about 0.36, which might result from the equilibrium between a dimer and a monomer Al(mbmp)(μ-O^{i}Pr) is not completely on the side of the monomer, and monomer is more active than dimer.

Complex **86** (Fig. 24) can be synthesized by treatment of [(MCIMP)AlMe(THF)] with 1 equiv. $AlMe_3$, this complex has similar characters with complex **82** in initiation of ROP of ε-CL with narrow PDIs (1.11 and 1.12) and expected molecular weight too [69]. The compound [(μ-biphenolate)-AlMe(μ-OCH(^{i}Pr)$_2$)$AlMe_2$] **87** (Fig. 24) is prepared from the reaction of biphenolate–H_2 with 2 molar equiv. of $AlMe_3$ in the presence of a stoichiometric amount of 2,4-dimethyl-3-pentanol [11]. As expected, this complex is less active than lithium or zinc analogous complexes (**5** and **37**) toward polymerization of lactide, and a higher temperature is necessary to effect polymerization. Only 40% conversion of lactide is achieved after 40 h at 80 °C with $[M]_0/[I]_0 = 200$. When the reaction is carried out in refluxed toluene for 20 h, the conversion increases to 82% and a higher molecular weight polymer is obtained (1.41 and 1.53). Complex **88** (Fig. 24) has similar but less active polymerization character to **79b**–**79d**, completed polymerization of ε-caprolactone can be reached in 15 h with narrow PDIs (1.03–1.09) at 50 °C in controlled manner [68].

4.2.4. Amine bisphenolate supported aluminum complexes

Several amine bisphenolate supported aluminum complexes **89a**–**89e** have been synthesized (Fig. 25) [71,72]. X-ray structures show these complexes are monomeric with a penta-coordinated aluminum center. The complexes **89a**–**89e** were found to catalyze the polymerization of ε-caprolactone with very narrow PDIs in living manner at 25 or 50 °C in toluene. Among them **89a** and **89b** were also found to have "immortal" character. Through a comparative study of the polymerization behavior of complexes **89c**–**89e**, which are structurally well-defined aluminum catalysts supported by ligands with essentially identical steric profiles but differing only in electron donating abilities, authors found that both decreasing and increasing the electron density around the

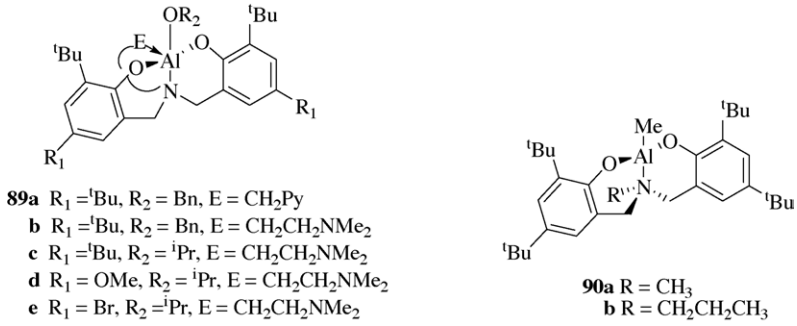


Fig. 25. Amine bisphenolate aluminum complexes **89** and **90**.

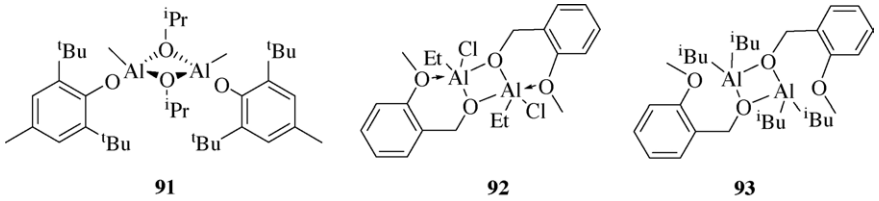


Fig. 26. Structure of aluminum alkoxide complexes **91**–**93**.

metal (relative to **89c**, R_1 = *tert*-butyl) actually decreased the propagation rate constant for the ring-opening polymerization of ε-caprolactone, with the effect of R_1 = Br being the most significant. The changes of the electron-donating ability of the supporting ligand have a more complicated effect on the mechanism of the polymerization reaction. Chen et al. found that aluminum complexes (**90a**–**90b**) supported by the bulky amine bisphenolate ligands without bearing a dative arm can catalyze the polymerization of ε-caprolactone more actively than complexes **89a**–**89b** in the presence of benzyl alcohol [73]. **90a**–**90b** can complete polymerization of ε-caprolactone in 20 min, while **89a** and **89b** need 3 and 1 h respectively with $[M]_0/[Al]_0 = 100$ at 50 °C in toluene. It seems presumable that lack of the dative pendant groups makes a better tuning of the Lewis acidity and steric hindrance of the metal center that gives a better combination of monomer binding and alkoxide nuleophilicity in this system.

4.2.5. Other aluminum complexes

Polymerization of ε-caprolactone initiated by complex **91** (Fig. 26) is noticeably less controlled [70], as can be judged by the higher molecular weight distribution values as well as by the rather erratic efficiencies, the initiation maybe occur both at the Al–Me and Al–O^{i}Pr function, so complex **57** is not a good initiator. Complexes **92** and **93** (Fig. 26) were found to initiate polymerization of ε-caprolactone in controlled manner with narrow PDIs (1.07–1.31) at 25 °C in toluene within 2 and 6 h respectively [50]. ^{1}H NMR spectrum of PCL confirmed that the polymer chain end was capped with one 2-methoxybenzyl ester and one hydroxy chain end suggesting that the initiation occurs through the insertion of the benzyl alkoxy group from compound **92** and **93** into ε-caprolactone by acyl cleavage.

A variety cationic aluminum alkoxides **95a**, **95b** and **95c** have been synthesized through exposure of the methylene chloride solution of **94a** and **94b** to an excess of dry O_2 at 0 °C for several hours (Fig. 27) [74]. **95a** and **95b** appeared to be highly reactive in the polymerization of ε-CL. The polymerization took place rapidly ([ε-CL]/[Al] = 50, temperature = 40 °C) and polymerization completed up to 95% conversion after 1 h with narrow PDIs (1.24 and 1.30). From analysis of the MALDI TOF spectrum of PCL obtained with cationic alkoxides **95a** and **95b** generated in situ, a hydroxyl group and two ester chain end, methyl ester and phenyl ester, was found, indicating the existence of two types of polymer chains, While for **95c** only one type polymer chain was found, which agreed with only one initiating group in **95c**.

A series of neutral and cationic aluminum complexes have been synthesized with different triamines (Fig. 28) [75]. X-ray analyses revealed that **96a**–**96c** adopted monomeric structures. Due to the formation of a rather rigid bicyclic core, the tridentate ligand enforced an approximately trigonal-monopyramidal coordination geometry around the metal center. The empty axial coordination site may act as reactive site during polymerization. In all of the complexes, only methyl- and hydridoaluminum derivatives **96a** and **96b** can initiate

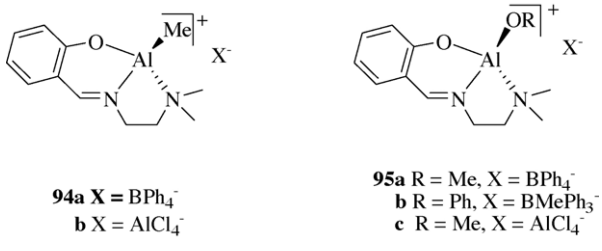


Fig. 27. Aluminum cationic complexes **94** and **95**.

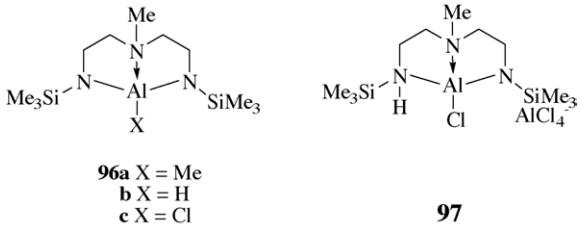


Fig. 28. Triamine supported neutral and cationic aluminum complexes **96** and **97**.

the polymerization reaction of *rac*-lactide in benzene at 80 °C with high PDIs (1.79 and 1.61). Hydride complex **96b** is about twice as active as the methylaluminum derivative **96a**. Under the same reaction conditions, an aluminum alkoxide prepared in situ by reacting **97** with propylene oxide at 80 °C, can initiate the polymerization of *rac*-lactide. However, only a low molecular weight polymer with a narrow molecular weight distribution was obtained in 46% yield after 5 days.

Similar to complex **97**, dimeric aluminum complexes **98a**, **98b** and **98d** (Fig. 29) can be activated with propylene oxide or cyclohexene oxide to form efficient lactide polymerization catalysts [76]. Lewis acid complexes **98a**, **98b** and **98d** are poor initiators for the polymerization of *rac*-lactide in toluene at 70 °C and give low conversions (5, 2 and 11%) even after 7 days. After the addition of stoichiometric quantity propylene oxide, the corresponding chloroalkoxide species can be achieved from propylene oxide ring-opening insertion into the [Al]–Cl bond and the catalyzed polymerization of lactide can reach to completion in 18 h at 70 °C with 2% mol complexes using toluene as solvent with excepted molecular weights and narrow PDIs (1.13–1.27). It is notable that examination of the ^{1}H NMR spectra of these polymers reveals that after initiation with PO there is no further incorporation of PO into polymer even in the presence of excess propylene oxide. In a comparative study authors found that [Al]–Me complex **98c** is a poor initiator for polymerization of *rac*-lactide and requires 168 h to reach 58% conversion whereas catalysts generated by alcoholysis of **98c** with chloroethanol are considerably more active and reach levels of conversion comparable to those obtained with **98a**, **98b**, **98d**/PO after only 18 h. The molecular weight and PDI of the resulting polymer is similar to that obtained with catalysts formed by activation of **98a**, **98b** and **98d** with PO. This experiment confirmed the formation of the proposed chloroalkoxide species when **98a**, **98b** and **98d** were activated by PO.

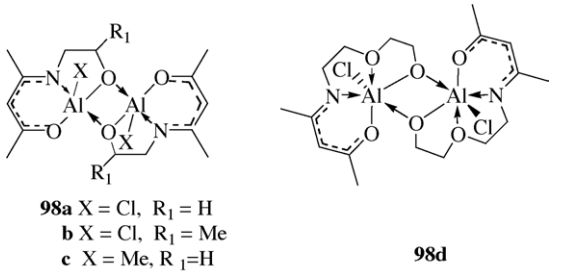


Fig. 29. Dimeric *N*-alkoxyalkyl-β-ketoimines supported aluminum complexes **98a**–**98d**.

5. Group 14 metal: Sn

Bismuth(III) 2-ethylhexanoate ($BiOct_3$) with alcohol as co-initiator have been applied to catalyze ROP of ε-caprolactone [77], however, no other bismuth complex has been reported to catalyze/initiate ROP of cyclic esters. Many simple tin complexes such as Sn(II) carboxylates and Sn(IV) dialkyl dialkoxide complexes have been widely used in ROP of cyclic esters, and recently some well-defined single site tin complexes (**99**–**103**) have been synthesized. Treatment of $SnCl_2$ with $[HC\{C(Me)NAr\}_2]Li$, followed by transmetalation with LiO^iPr, **99** can be made (Fig. 30) [78]. In the polymerization of *rac*-lactide, it was found that 100 equiv. of monomer required 96 h to complete conversion in CH_2Cl_2 at ambient temperature. The resultant polymer exhibits a narrow polydispersity (PDI = 1.11) and has a molecular weight close to the expected value. When the reaction was performed at 60 °C in toluene affording 85% conversion after 4 h. The activity of the tin complex is low than that observed for the related zinc system which may be in part due to the lower electrophilicity of the tin center, and partly a consequence of the stereochemically active lone pair which may disfavor monomer coordination. The living characteristics of the polymerization are verified by the linear increase in M_n with conversion together with narrow PDIs (1.04–1.11). The preference for heterotacticity is not as strong as the zinc complex **25**.

Complex **100** can be obtained in good yield when the related iminophenols were treated with $Sn(NMe_2)_2$ (Fig. 31) [79]. It is surprised that amide group $–NMe_2$ can reversibly migrate in Schiff base ligand in **100**, and the postulated potential terminal amide species (**100′**) can initiate polymerization

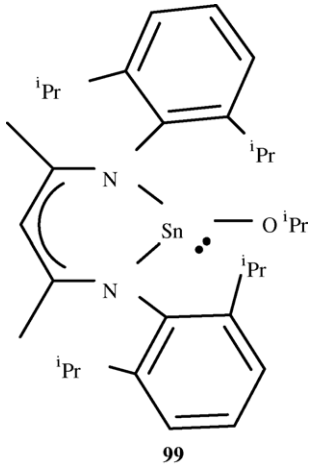
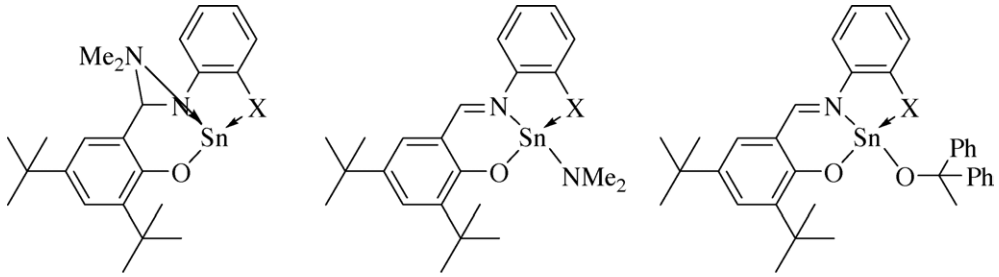


Fig. 30. β-Diketiminato tin alkoxide complex **99**.

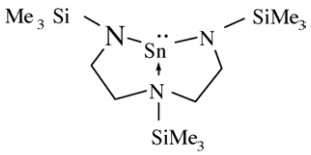


100a X = OMe
b X = SPh
c X = PPh_2

100'

101a X = OMe
b X = SPh
c X = PPh_2

Fig. 31. Iminophenol supported tin complexes **100** and **101**.



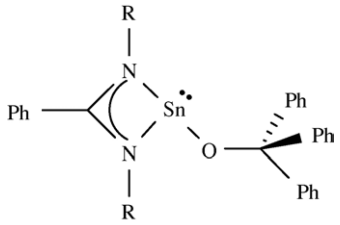
102

Fig. 32. Triamino tin complexes **102**.

of lactide with good control. A sample of PLA prepared with **100a** and 20 equiv. of *rac*-lactide revealed PLA chains bearing Me_2N end-groups. In all cases, a linear increase in molecular weight (M_n) with conversion was observed as well as a linear relationship between M_n and monomer/initiator ratio. Although complexes **101** (Fig. 31) were obtained by treatment of **100** with Ph_2MeCOH, no polymerization experiment initiated by them has been reported.

Complex **102** is the analogue of **50** (Fig. 32) [35,80]. Interestingly, **102** is much more active than **50** and its Sm analogue for the bulk copolymerization of *rac*-lactide and glycolide. At 140 °C, polymerization can be completed with up to 90% conversions after 20 min, and very high molecular weight copolymers are obtained (M_n = 85,150, PDI = 1.9).

Two bulky amidinate ligands have been used to synthesize related tin alkoxide complexes **103a** and **103b** (Fig. 33) [81]. The X-ray structures show that both complexes exist



103a R = $SiMe_3$
103b R = $SiMe_2Ph$

Fig. 33. Bulky amidinato tin alkoxide complexes **103a** and **103b**.

as three-coordinated monomeric structures with a distorted pyramidal geometry, which clearly indicate a stereochemically active lone pair. NMR data showed that monomeric structures observed in the solid state are retained in solution. **103a** can catalyze polymerization up to 93% conversion after 35 min with M_n = 63,500, and PDI = 1.48 in toluene at 80 °C, while for **103b**, polymerization completed up to 92% conversion after 165 min with M_n = 28,900 and PDI = 1.18. In the presence of 1.0 equiv. of an exogenous alcohol, the controlled polymerization of LA by **103b** can be observed with first order in [LA] and about one-third order in $[Sn]_0$. Polymerizations of LA using **103a** or **103b** alone or **103b** in combination with BnOH in toluene at 80 °C yield PLA with a slight heterotactic bias which may result from a consequence of the stereochemically active lone pair of electrons on Sn(II).

6. Summary and conclusions

Polylactides (PLA) and related polyesters are of great interest in the past three decades for their applications in the medical field due to the biodegradable, biocompatible, and permeable properties. Ring-opening polymerization (ROP) of cyclic esters is the major polymerization method employed to synthesize these polymers. In this article, the application of well defined main group metal complexes supported by a variety of ligands in ROP of lactide and related cyclic esters were reviewed. Many metal alkyls, amides, thiolates, aryloxides, and alkoxides as well as metal complexes in the presence of alcohol have been used as initiators for the ROP of lactides and related cyclic esters. Among them, metal alkoxides bear the highest activity together with good controlled manner.

When a diol is used as a supporting ligand, groups 1 and 2 metal complexes are more active than groups 13 and 14 metal complexes. This result is due to the different polarities of the M–OR bonds. Furthermore, there has been increasing interest in the development of efficient and low cytotoxic catalysts for the preparation of PCL and PLA. As a result, lithium, magnesium and calcium alkoxides will become more important and interested.

Many metal complexes have demonstrated highly selective activity toward ROP of *rac*- and *meso*-lactide, such as diketiminate zinc alkoxides, Salen-aluminum alkoxides and tris(pyrazolyl)borate calcium-amide or alkoxide complexes. Highly isotactic poly(*rac*-lactide) was produced only from Salen-aluminum alkoxides, however, its activity is low. To find active complexes for the stereoselection of *rac*-lactide with isotactic microstructure and large molecular weights has drawn our attention.

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