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Controlled Synthesis of High-Molecular-Weight and Isotactic Cyclic Polylactides from *rac*-Lactide Using Aminophenolate Zinc Chlorides

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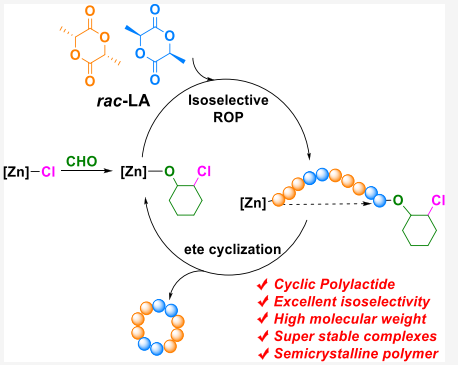
ABSTRACT: No-end topology provides cyclic polyesters with potential abstracting applications, but more efficient and selective routes still need to be explored to access cyclic polyesters with high molecular weights and tacticity control. We report here that a series of aminophenolate zinc chlorides display hyperstability and hyper productivity toward the ring-opening polymerization of technical grade *rac*-lactide (*rac*-LA) in cyclohexene oxide, capable of converting up to 20,000 equiv of *rac*-LA (TONs up to 18,600) to cyclic polymers with high molecular weights and narrow to moderate distributions (M_n up to 58.0 kg/mol, $Đ$ = 1.19−1.60). At ambient temperature, highly isotactic cyclic poly(*rac*-LA)s could be obtained (e.g., complex **6**, P_m = 0.87, M_n = 23.5 kg/mol, 25 °C; with P_m further improved to 0.93 at −45 °C), which show to possess stereoblocky microstructures. Selective end-to-end cyclization proved to be thoroughly involved in the polymerization, leading to cyclic polylactides with only even-numbered lactyl units.



INTRODUCTION

Polylactide (PLA) not only has physical/mechanical properties similar to those of polyolefins but also has good biodegradability and biocompatibility in addition to the advantage of its raw material being derived from biorenewable resources, which make this material a great focus of scientists nowadays.[1−8] In comparison to the commonly studied linear PLA, its simplest topological isomer, cyclic PLA normally exhibits several properties different from its linear counterpart of the same molecular weight, such as higher glass transition and melting temperatures, higher thermostability, lower hydrodynamic volume, and lower intrinsic and melt viscosities.[9−15] These interesting features provide cyclic PLA with important potential applications, for instance, as carriers of sustained-release medicines to achieve long-term stable release of drugs to maintain plasma drug concentration.[16] In addition, it is known that the stereochemistry of linear PLA is of great importance, which affects the mechanical and thermal properties of the polymer fundamentally. For example, isotactic stereoblock linear PLAs synthesized via the isoselective ring-opening polymerization (ROP) of *rac*-lactide (*rac*-LA) possess higher melting temperatures (170−220 °C) than the homochiral ones prepared from *L*-LA or *D*-LA by forming stereocomplexed structures, leading to a better fit for injection molding, blow molding, and spinning.[17−19] Thus, it would be quite attractive to obtain high-molecular-weight cyclic PLAs with stereoblock chain structures, which are expected to possess enhanced properties compared to linear ones. Currently, different approaches have been developed to chemically synthesize cyclic PLAs,[20−25] whereas routes combining both efficiency and controllability in obtaining cyclic poly(*rac*-LA)s with high molecular weights and high isotacticities still need to be explored, which would of course largely rely on the exploration of new catalysts.

So far, there are remarkably some catalysts capable of giving cyclic PLAs from *rac*-LA either with control on molar mass and distribution or high efficiency or isoselectivity[26−29] but not all of them, with major examples including *N*-heterocyclic carbenes (NHCs)[20,30−33] and metal-containing complexes.[21,34−40] For example, a tin complex bearing two iminophenolate ligands (Chart 1, **I**) reported by Phomphrai's group afforded the cyclic poly(*rac*-LA) with a high molecular weight (M_n = 132 kg/mol) via intramolecular esterification but showed no isoselectivity.[41] Getzler's group used an alumatrane complex, (^{t}Bu-SalAmEE)Al (Chart 1, **II**), to afford cyclic poly(*rac*-LA)s with M_n values of up to 24 kg/mol in a controlled manner via ring-expansion polymerization, but these still suffered from the drawback of low efficiencies of aluminum complexes.[21] By taking into account the cooperation of Lewis acid−base pairs in catalysis,[42] Bourissou and co-workers used a $Zn(C_6F_5)_2$/PMP dual system (Chart 1, **III**) via zwitterionic polymerization to produce cyclic PLAs from *rac*-LA with M_n up to 33.7 kg/mol at a feed ratio of $[LA]_0/[Zn]_0/[PMP]_0$ = 100:1:1 (PMP: 1,2,2,6,6-pentamethylpiperidine) but failed to

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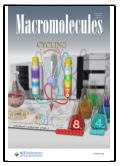

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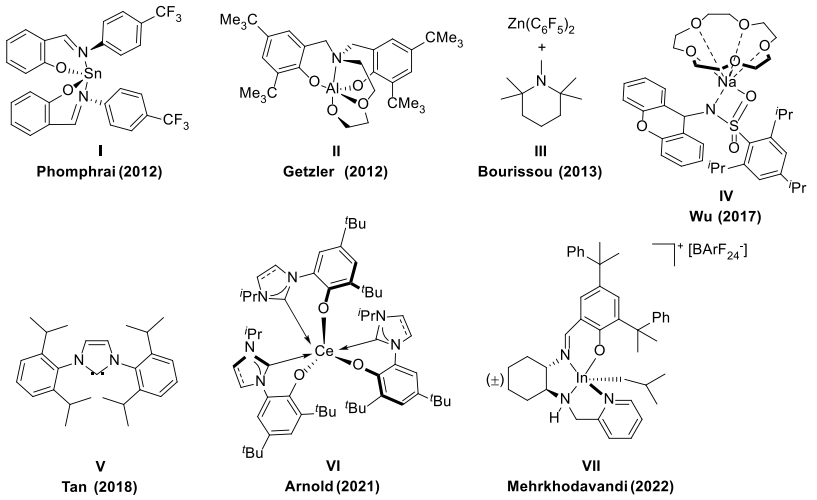
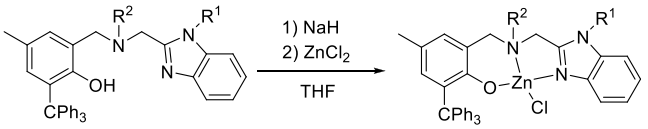
Chart 1. Catalysts reported previously for cyclic PLAs.



show any isoselectivity.[28] In 2017, Wu's group reported a sodium sulfonamidate complex coordinated with a crown ether (Chart 1, **IV**), which afforded low isotactic cyclic PLAs (P_m = 0.63, at 25 °C) from *rac*-LA by ring-expansion polymerization in the absence of alcohol.[23] In 2018, Tan's group used a NHC (Chart 1, **V**) to catalyze the isoselective ROP of *rac*-LA (P_m = 0.57 at r.t.; P_m = 0.91 at −70 °C) but only affording cyclic oligomers of low molecular weights (M_n = 2.6−5.0 kg/mol) due to the sensitivity of the catalyst.[43] Recently, the synthesis of atactic cyclic PLAs with very high molecular weights (M_n values of up to 253 kg/mol) was reported by Arnold's group by adopting a homogeneous Ce(III)−NHC catalyst (Chart 1, **VI**), where the lactide monomer was activated by the Ce center and ring opened by the labile NHC moiety.[40] In the following year, Mehrkhodavandi and co-workers further increased the molecular weight of the cyclic poly(*rac*-LA)s to 416 kg/mol by using a cationic indium catalyst (Chart 1, **VII**), which however showed no stereoselectivity.[44] In summary, so far, there is still no report on stable catalysts exhibiting excellent stereocontrol while producing cyclic PLAs with high molecular weights.

Recently, complexes of nontoxic, biocompatible metals, such as zinc, have been widely adopted in the catalytic ROP of lactides, exhibiting high catalytic activities and good controllability, as well as high isoselectivities in some cases, but all produced linear PLAs exclusively.[45−51] For instance, benzoimidazolyl-based aminophenolate zinc complexes reported previously by our group could efficiently catalyze the ROP of *rac*-LA to afford isotactic linear PLAs (TOFs up to 900 h^{-1}, P_m = 0.87 at 25 °C; P_m = 0.93 at −40 °C).[47] While Kricheldorf and co-workers' studies showed that polymer chains end-capped with strong acids tended to cyclization to form cyclic PLAs easily.[52−55] Capacchione's group also found that the ROP of *rac*-LA initiated by the [OSSO]-type iron chlorides in cyclohexene oxide (CHO) produced cyclic PLAs in low molecular weights.[24] Inspired by these results, we are interested in combining the isoselective structural features of zinc catalysts with an initiation group having a tendency to trigger cyclization. Therefore, we synthesized a series of benzoimidazolyl-based aminophenolate zinc chlorides **1**−**7** (Scheme 1), which proved to be capable of catalyzing the ROP of technical grade *rac*-LA up to 20,000 equiv to afford isotactic cyclic PLAs. As we know, this is the first report of discrete zinc complexes used alone to produce cyclic PLAs. By adjusting the polymerization conditions, high-molecular-weight cyclic poly(L-lactide)s with M_n values of up to 71.7 kg/mol could be obtained. Moreover, these zinc complexes showed outstanding isoselectivity (P_m = 0.93, at −45 °C) when *rac*-LA was used as a monomer and are the most isoselective catalysts adopted for the synthesis of cyclic PLAs so far.

Scheme 1. Synthesis of Aminophenolate Zinc Chlorides 1−7



L^1H, **1**: R^1 = Bn, R^2 = Bn
L^2H, **2**: R^1 = Bn, R^2 = Cy
L^3H, **3**: R^1 = Bn, R^2 = 3-Methylbutyl
L^4H, **4**: R^1 = Me, R^2 = Bn
L^5H, **5**: R^1 = Me, R^2 = 3-Methylbutyl
L^6H, **6**: R^1 = Me, R^2 = ^{n}Octyl
L^7H, **7**: R^1 = ^{i}Pr, R^2 = Cy

RESULTS AND DISCUSSION

Synthesis and Structures of Aminophenolate Zinc Chlorides. Benzoimidazolyl-based aminophenol proligands L^1H, L^2H, and L^4H were prepared according to the methods provided in the literature.[47] In addition, different primary amines and haloalkanes were involved in similar procedures to produce proligands L^3H and $L^{5-7}H$ in moderate yields (see Supporting Information, Scheme S1). At room temperature, the proligands $L^{1-7}H$ were treated with excess NaH in THF to form the corresponding sodium salts, which were then reacted with zinc dichloride in a 1:1 molar ratio, respectively, to afford complexes **1**−**7** after recrystallization in yields of 43−53%. All of these aminophenolate zinc chlorides were fully characterized by ^1H, $^{13}C\{^1H\}$ NMR spectroscopic methods and elemental analysis (see Figures S10−S21).

The molecular structure of **7** was further determined by X-ray diffraction study, which indicated the presence of a pair of racemic isomers (S_NS_{Zn} and R_NR_{Zn}) in the unit cell. In the solid state, **7** possesses a monomeric structure, where the zinc atom

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is coordinated by the tridentate aminophenolate ligand and the chloride ligand, forming a distorted tetrahedral geometry (Figure 1), as evidenced by the angles of O1−Zn1−N1 (97.24(9)°) and N2−Zn1−N1 (81.52(9)°) deviating obviously from 109.51° in a regular tetrahedron. Since the steric bulkiness of the chloride ligand is much smaller than that of the bis(trimethylsilyl)amido group, which allows the approach of the aminophenolate ligand, the related bond lengths in **7** such as Zn1−O1 (1.890(2) Å), Zn1−N1 (2.168(2) Å), and Zn1−N2 (2.014(2) Å) are all shorter than those in the analogous bis(trimethylsilyl)amido zinc complex bearing the same ligand (Zn1−O1 (1.928(19) Å), Zn1−N1 (2.267(2) Å), Zn1−N2 (2.051(3) Å)).[47] When compared with the corresponding bond lengths in the analogous bis(trimethylsilyl)amido zinc complex bearing a benzoxazolyl-based aminophenolate ligand (Zn1−O1 (1.910(2) Å), Zn1−N1 (2.293(2) Å), and Zn1−N2 (2.074(3) Å)),[48] reductions in these bond lengths in **7** are also witnessed. All of these facts indicate a stronger chelating effect between the Zn center and the aminophenolate ligand in **7**, which is thought to improve the stability of the complex.

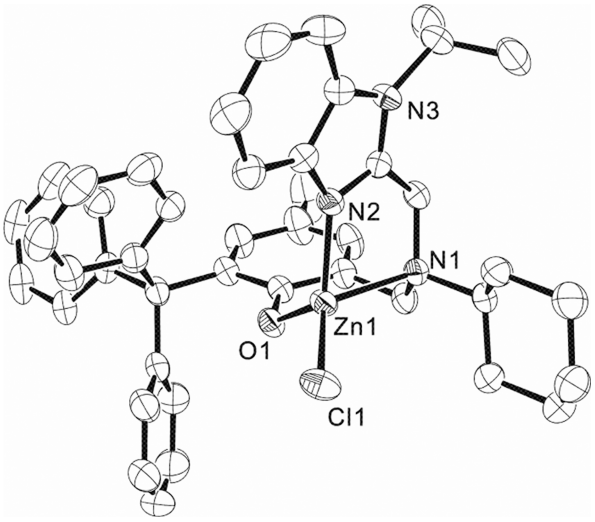

Figure 1. Molecular structure of complex **7**. Thermal ellipsoids represent 30% probability surfaces. Hydrogen atoms have been omitted for the sake of clarity. Selected bond lengths (Å) and angles (°): Zn1−O1 = 1.890(2), Zn1−N1 = 2.168(2), Zn1−N2 = 2.014(2), Zn1−Cl1 = 2.1968(8), O1−Zn1−N1 = 97.24(9), O1−Zn1−N2 = 120.44(10), O1−Zn1−Cl1 = 116.06(6), N1−Zn1−N2 = 81.52(9), N1−Zn1−Cl1 = 124.37(7), and N2−Zn1−Cl1 = 112.57(8).

Polymerization of Technical Grade *rac*-LA. All synthesized complexes **1**−**7** were evaluated in the ROP of *rac*-LA. First, the ROP process was investigated in different solvents. There was no polymer isolated when the polymerization runs were carried out in toluene (110 °C) or THF (65 °C) after 12 h (Table 1, entries 1−2), indicating the covalent bonding between the chlorine atom and the zinc center of the complexes is too inert to initiate the ROP of *rac*-LA. A small amount of polyether was detected when the complex was mixed with excess CHO for 24 h at 80 °C (Table 1, entry 3), implying that the Zn−Cl bond is capable of ring-opening CHO to generate metal alkoxide species, which are known active species for lactide polymerization. Thus, CHO was adopted as a solvent in the following studies.[24,37] As expected, complex **1** exhibited a high catalytic activity for the ROP of *rac*-LA in CHO, even when a technical grade monomer was adopted, that is, a conversion of 90% for 200 equiv of technical grade *rac*-LA was achieved within 30 min at 80 °C (Table 1, entry 4). The rest of the complexes also exhibited sufficient catalytic activities for the ROP of technical grade *rac*-LA in CHO, which were somewhat influenced by the various substituents on the ligand framework.

Keeping the substituent on the N atom of the benzoimidazolyl moiety unchanged, the substituent on the skeleton N atom of the ligand showed a significant effect on the activity of the corresponding complex. For instance, complex **2** with a rigid cyclohexyl on the skeleton N atom required 84 min to convert 200 equiv of technical grade *rac*-LA to 90%, showing a much lower activity compared with **1**, while

Table 1. ROP of Technical Grade *rac*-LA[a]

entry	cat	$[LA]_0/[Zn]_0$	solvent	temp. [°C]	time [min]	conv.[b] [%]	TON[c]	TOF[d] [h^{-1}]	$M_{n,calcd}$[e] [kg/mol]	M_n[f] [kg/mol]	$Đ$[f]	P_m[g]
1	**1**	200/1	Tol	110	12 h	0	0	0				
2	**1**	200/1	THF	65	12 h	0	0	0				
3[h]	**1**	0/1	CHO	80	24 h	5[i]	0	0				
4	**1**	200/1	CHO	80	30	90	180	360	25.9	20.6	1.22	0.65
5	**1**	200/1	*rac*-ECH[j]	80	22	96	192	523	26.8	10.4	1.29	
6	**1**	500/1	CHO	80	42	84	420	600	60.5	20.2	1.23	0.55
7	**1**	1000/1	CHO	80	100	87	870	522	125	20.8	1.22	
8[k]	**1**	1000/1	CHO	80	80	83	830	622	120	25.2	1.21	
9	**1**	4000/1	CHO	80	8 h	87	3480	435	501	21.3	1.21	
10	**1**	20,000/1	CHO	80	50 h	88	17,600	352	2534	20.9	1.25	
11	**2**	200/1	CHO	80	84	90	180	129	25.9	20.4	1.22	0.68
12	**3**	200/1	CHO	80	35	93	186	319	26.8	22.9	1.24	0.69
13	**4**	200/1	CHO	80	32	93	186	348	26.8	21.3	1.24	0.65
14	**5**	200/1	CHO	80	38	94	188	297	27.1	25.1	1.23	0.69
15	**6**	200/1	CHO	80	40	90	180	270	25.9	21.6	1.18	0.72
16	**7**	200/1	CHO	80	107	93	186	104	26.8	24.0	1.22	0.68

[a] $[rac\text{-}LA]_0$ = 2.0 mol/L, in 0.5 mL of CHO. [b]Determined by ^1H NMR spectroscopy. [c]Turnover number (TON) = mol of product (PLAs)/mol of catalyst. [d]Turnover frequency (TOF) = mol of product (PLAs)/mol of catalyst per hour. [e] $M_{n,calcd} = ([LA]_0/[Zn]_0) \times 144.13 \times$ conv. %. [f]Determined by GPC. [g] P_m is the probability of forming a new m-dyad, determined by homonuclear decoupled ^1H NMR spectroscopy. [h]No *rac*-LA was added. [i]Conversion of CHO. [j]*rac*-ECH: *rac*-epichlorohydrin. [k]Purified *rac*-LA was used.

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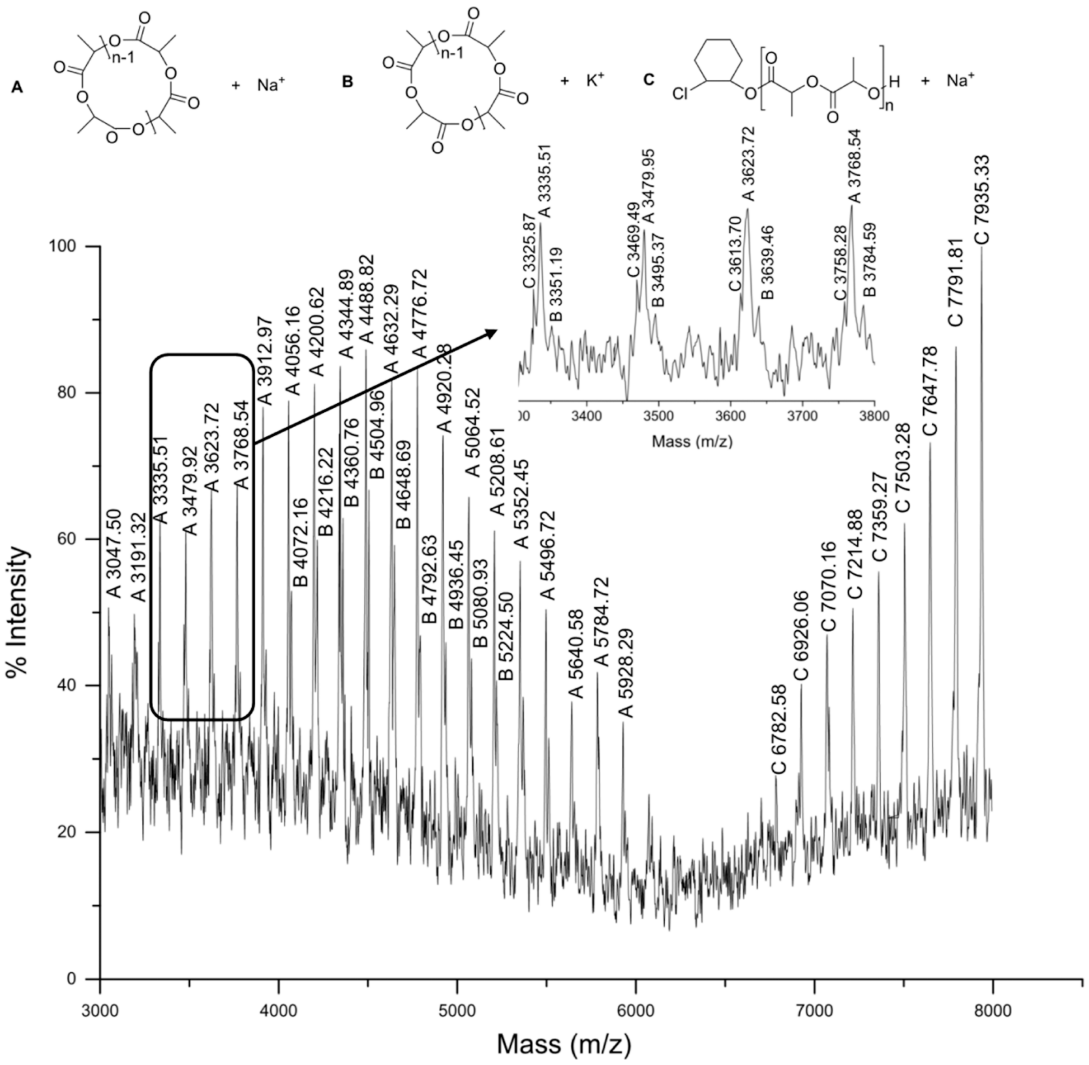

Figure 2. MALDI-TOF mass spectrum of the oligomer of technical grade *rac*-LA obtained by complex **1** ([*rac*-LA]/[**1**] = 200:1, 80 °C, conv. 33%).

the introduction of flexible *N*-isoamyl in complex **3** also resulted in a decreased catalytic activity (**1**: TOF = 360 h^{-1}; **2**: TOF = 129 h^{-1}; **3**: TOF = 319 h^{-1}; Table 1, entries 4, 11, and 12). A similar trend was observed for complexes **4**−**6**. It seems that the introduction of a rigid or steric bulky group on the skeleton N atom is not favored for the catalytic activity,[46,56,57] while a substituent with an electron-withdrawing character, such as benzyl, does show a positive effect on the activity by increasing the Lewis acidity of the metal center, which favors the coordination/insertion of a monomer.[47]

The substituent on the N atom of benzoimidazolyl also affected the activities of these complexes. For example, complex **4** with a methyl group on the N atom of benzoimidazolyl showed a decreased reactivity (TOF = 348 h^{-1}, Table 1, entry 13) when compared to complex **1** with a benzyl group (TOF = 360 h^{-1}, Table 1, entry 4). Again, the electron-withdrawing nature of the substituent seems to be favorable for the polymerization.[47,48] In complex **7**, steric bulky groups, cyclohexyl and isopropyl, were introduced to both N atoms of the ligand, leading to complex **7** displaying the lowest catalytic activity in this series (**7**: TOF = 104 h^{-1}; Table 1, entry 16).

We happily found that these complexes were not deactivated under the conditions of gradually increased feed ratios and exhibited ultrahigh tolerance to impurities; that is, as high as 20,000 equiv of technical grade *rac*-LA could be polymerized with a TON value of 17,600 by complex **1** (Table 1, entries 6−7, 9−10). To our surprise, the molecular weights of the resultant polymers seemed to be limited to ca. 25 kg/mol, which was much smaller than the theoretical values. When purified *rac*-LA was adopted for the ROP, the molecular weight of the resultant polymer was only 4.4 kg/mol higher than that obtained from technical grade *rac*-LA (Table 1, entry 7 vs entry 8), indicating that the significant deviation of the molecular weights from theoretical values in these cases was not caused by the impurities in the technical grade monomer.

According to the literature,[58,59] when cyclization reactions were thoroughly involved during the polymerization process, the molecular weights of polymers were always significantly lower than the theoretical values. We thus speculated that the polymeric active chains initiated by these zinc complexes might have a great tendency to trigger cyclization and produce cyclic PLAs in the end.[25,39,54] To verify our conjecture, MALDI-TOF mass spectroscopic analysis of polymer samples obtained under different conditions was carried out.

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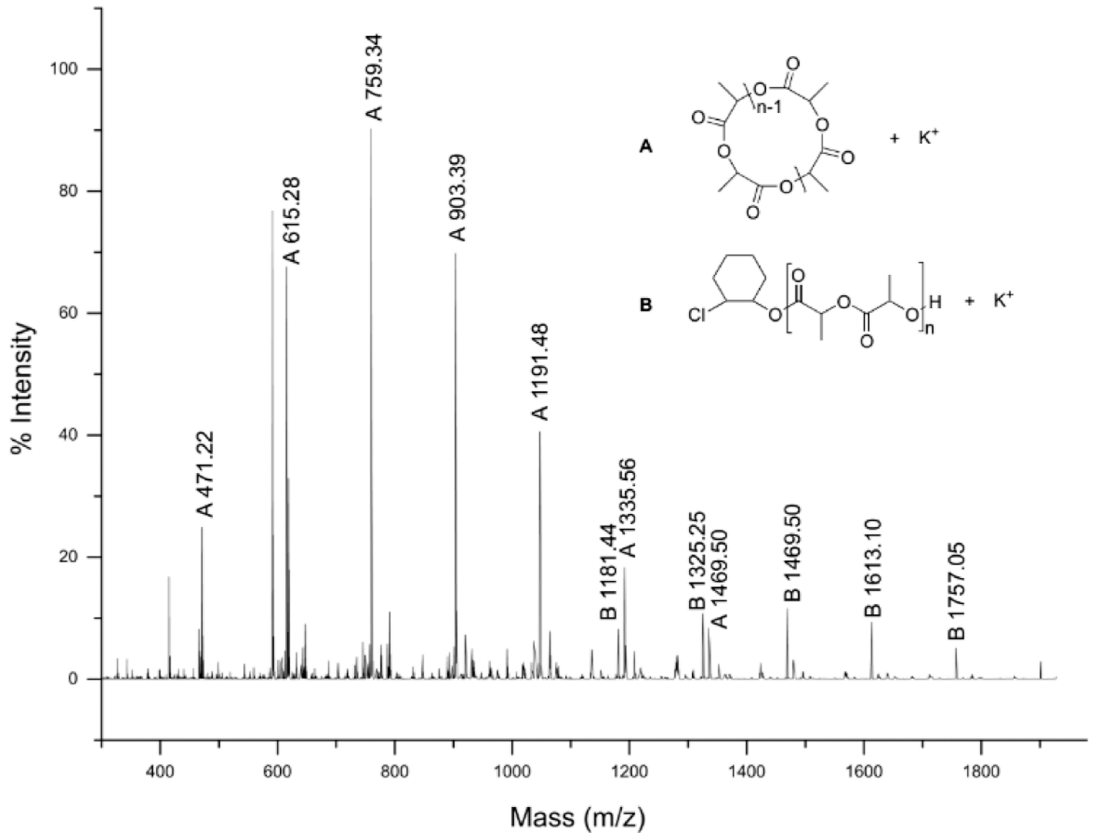

Figure 3. MALDI-TOF mass spectrum of oligomer of technical grade *rac*-LA obtained by complex **1** (80 °C, CHO, $[rac\text{-LA}]_0/[\mathbf{1}]_0$ = 20:1, conv. 89%).

In the MALDI-TOF mass spectrum of a typical polymer sample produced by the ROP of 200 equiv of technical grade *rac*-LA at a low conversion of 33% (Figure 2), the presence of a series of peaks, 3768.54, 3912.97, 4056.16... (**A**: $m/z = 144.04n + Na^+$) and 4072.16, 4216.23, 4360.76... (**B**: $m/z = 144.04n + K^+$), indicates undoubtedly the formation of cyclic PLAs. At the same time, a series of peaks at 6926.06, 7070.16, 7214.88... (**C**: $m/z = 133.04 + 144.04n + 1 + 22.99$) obviously correspond to m ($ClC_6H_{10}O$) + m ($C_6H_8O_4$) + m (H) + m (Na^+), which is consistent with the ^{1}H NMR spectrum of the polymer sample (see Figure S22), where the signals of linear PLAs end-capped by $ClC_6H_{10}O-$ and −OH termini could be assigned properly. Moreover, the linear series is located at a higher mass region when compared with the two cyclic series. These results suggest that the catalyst initiated the ring-opening of CHO initially to form zinc alkoxide active species "LZn−$OC_6H_{10}Cl$", which then quickly catalyzed the ROP of *rac*-LA via a coordination−insertion pathway to produce linear PLAs; meanwhile, cyclic PLAs were formed even at low monomer conversions due to intramolecular cyclization. In the MALDI-TOF mass spectrum of a polymer sample obtained at a high monomer conversion of 89% (20 equiv of *rac*-LA), both the cyclic series and the linear series end-capped with $ClC_6H_{10}O-$ and −OH termini are also observed (see Figure 3), which are further supported by the bimodal distribution of the GPC trace of this sample (see Figure S23). It is noticed that, being different from the MALDI-TOF mass spectrum of the polymer sample obtained at a relatively low conversion, in Figure 3 the abundances of the linear series are considerably lower than those of the cyclic series, which implies that by the end of the polymerization almost all linear chains would be converted to cyclic ones. To verify this point, a polymerization run of 40 equiv of technical grade *rac*-LA catalyzed by complex **1** was brought to completion; from the ^{1}H NMR spectrum of the resultant polymer ($[rac\text{-LA}]_0/[\mathbf{1}]_0$ = 40:1, 98%, see Table S2, Figure S24), there are no terminal methine hydrogen (ca. 4.30 ppm) and hydroxyl hydrogen resonances (ca. 2.65 ppm) assignable to linear PLAs, indicating that the polymers are exclusively cyclic ones at the end of the polymerization.

In comparison with zinc silylamido analogues bearing the same types of ligands, these zinc chlorides exhibited a great tendency to lead to the formation of cyclic polymers; we thus suppose that during the polymerization the $ClC_6H_{10}O-$ end group might have some weak interaction with the metal center, which then favors the occurrence of intramolecular cyclization.

It is further noticed that the mass peaks of cyclic series in both MALDI-TOF mass spectra have an interval of 144.04 exclusively, which means cyclic PLAs were formed through end-to-end (ete) cyclization in a very controlled manner (Scheme 2),[55,60] and nonselective intramolecular transesterifications generally observed in most metal-catalyzed ROPs of *rac*-LA are absent in our case. We thus speculate that the inclusion of a Cl atom in the end group of the active polymer chain makes the carbon atom of the adjacent carbonyl more positive, which becomes the sole target spot of a nucleophilic attack, leading to ete cyclization specifically.[54] To verify this conjecture, *rac*-epichlorohydrin instead of CHO was used as the solvent for the polymerization of *rac*-LA catalyzed by complex **1**, with the aim of introducing a more acidic terminal on the active polymer chain. An enhanced TOF value of 523 h^{-1} was obtained when compared with that in CHO (360 h^{-1}, Table 1, entries 4 and 5), and as expected, the number-average

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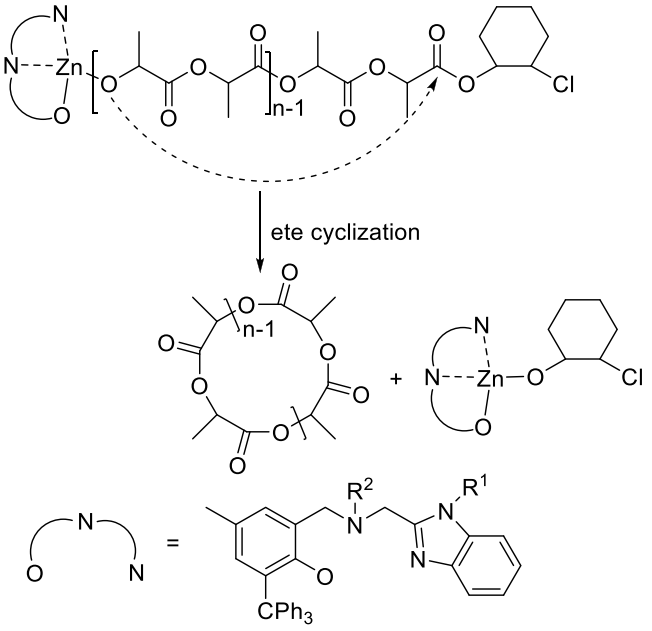
Scheme 2. Simplified Mechanism of ete Cyclization During Polymerization



molecular weight of the resultant PLAs was only 10.4 kg/mol, far less than that obtained in CHO (20.6 kg/mol), indicating that enhancement of the electron-withdrawing nature of the end group leads to cyclization reaction occurring more easily. It further proves that the carbon positivity of the terminal carbonyl group is enhanced by the Cl atom in the end group and leads to the cyclic PLAs through ete cyclization solely, in our case.

The evolution of GPC traces of polymers obtained at different conversions provides a clear view of the progress of ete cyclization through the polymerization process (Figure 4). When the monomer conversion was relatively low, such as below 45%, the right peak of the bimodal-distributed GPC trace assignable to cyclic PLAs is a minor one, which becomes dominant with the increase of monomer conversion to 80%. When a high conversion of 97% was reached, the GPC trace became monomodal and broader. All these suggest that at the beginning of the polymerization, chain propagation dominated to afford linear PLAs mainly; with the consumption of the monomer, the chain growth rate gradually decreased but the ete cyclization rate was unaffected, converting more linear polymers to cyclic ones, which became dominant or even the only topology structures by the end of the polymerization.

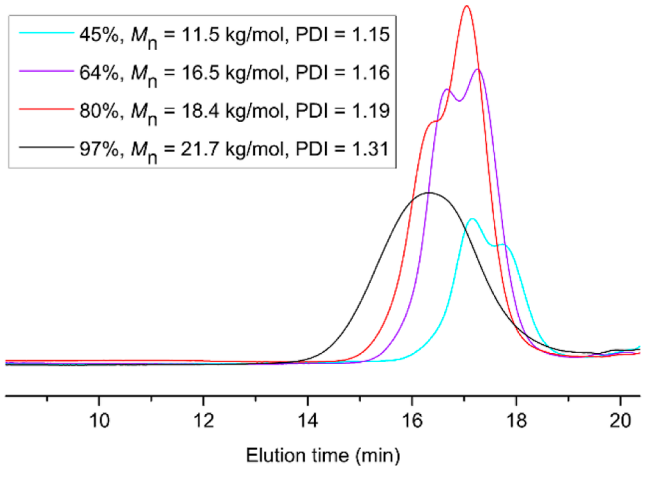


Figure 4. GPC traces of polymers of technical grade *rac*-LA obtained by complex **1** (80 °C, CHO, $[rac\text{-LA}]_0/[\mathbf{1}]_0$ = 1000:1, $[rac\text{-LA}]_0$ = 2.0 mol/L).

Since the formation of cyclic PLAs is governed by the competition between chain propagation and cyclization, it is considered that by increasing the chain growth rate, cyclic PLAs with higher molecular weights would be formed. Thus, polymerization runs by adopting different monomer concentrations were carried out. As shown in Table 2, the number average molecular weight of the resultant polymer increased from M_n = 10.1 to 20.8 to 30.6 kg/mol when the monomer concentration increased from 0.7 to 2.0 to 3.3 mol/L (Table 2, entries 1−3), respectively, which proved our conjecture. According to this regularity, we further increased the monomer concentration to 14.0 mol/L stepwise in order to obtain high-molecular-weight cyclic PLAs. As expected, the molecular weights of resultant polymers increased to 58.0 kg/mol (Table 2, entries 4−7), and their cyclic topology was further proved via TGA analysis since higher thermal stability was observed when compared with a linear PLA sample (M_n = 79.3 kg/mol) (Figure S25).[20,29,61,62] In considering the corresponding zinc silylamido complex bearing the same ligand exhibiting a much higher catalytic activity for the ROP of *L*-LA than for *rac*-LA,[47] complex **1** was used to catalyze the ROP of *L*-LA at a monomer concentration of 14.0 mol/L, and we happily found that it took complex **1** only 14 min to convert 1000 equiv of *L*-LA to 92% conversion and cyclic PLAs with a high molecular weight of M_n = 71.7 kg/mol were produced (Table 2, entry 8). Moreover, by reducing the concentration of complex **1**, 20,000 equiv of *rac*-LA (14.0 mol/L) could be polymerized with a conversion of 93% within just 9 h, affording cyclic PLAs with a high molecular weight of M_n = 55.3 kg/mol, indicating the great tolerance and stability of this series of zinc chloride complexes. It is worth noting that with a fixed monomer concentration such as $[rac\text{-LA}]_0$ = 2.0 mol/L, the increase of the monomer-to-catalyst ratio from 200 to 20,000 has negligible impact on the molecular weights of the polymers, which are all around 20 kg/mol (Table 1, entries 4, 6, 7, 9, 10), suggesting that the molecular weights of the resultant cyclic

Table 2. ROP of *rac*-LA with Different Monomer Concentrations Catalyzed by Complex 1[a]

entry	$[LA]_0$ [mol/L]	time [min]	conv.[b] [%]	$M_{n,calcd}$[c] [kg/mol]	M_n[d] [kg/mol]	$Đ$[d]
1[e]	0.7	235	87	125.3	10.1	1.23
2	2.0	100	87	125.3	20.8	1.22
3[f]	3.3	35	92	132.5	30.6	1.23
4	5.0	50	97	139.7	37.4	1.52
5	7.5	37	95	136.8	41.9	1.42
6	10.0	23	87	125.3	47.1	1.38
7[g]	14.0	50	97	135.4	58.0	1.60
8[g,h]	14.0	14	92	132.5	71.7	1.58
9[g,i]	14.0	9 h	93	2687	55.3	1.56

[a] $[LA]_0/[\mathbf{1}]_0$ = 1000:1, technical grade *rac*-LA was used, in 0.5 mL of CHO, at 80 °C. [b]Determined by ^{1}H NMR spectroscopy. [c] $M_{n,calcd}$ = $([LA]_0/[Zn]_0) \times 144.13 \times$ conv. %. [d]Determined by GPC. [e]In 0.3 mL of CHO. [f]In 0.5 mL of CHO and 1.0 mL of toluene. [g]At 100 °C. [h]Technical grade *L*-LA was used. [i] $[LA]_0/[\mathbf{1}]_0$ = 20,000:1.

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PLAs are solely determined by the relative ratio of propagation and cyclization rates.

As shown in Table 1, these zinc chloride complexes exhibited certain isoselectivity in the ROP of *rac*-LA at 80 °C but only to a low to moderate extent, so we decreased the polymerization temperature in order to increase the isoselectivity of the complexes.[45,63−66] As shown in Table 3, complexes **1**−**7** did show higher isoselectivities at low temperatures (−45 and 25 °C). For example, complex **1** afforded moderately isotactic cyclic PLAs at 25 °C (P_m = 0.79, Table 3, entry 1), while it only gave low isotactic polymers at 80 °C (P_m = 0.65, Table 1, entry 4). In addition, the substituents of the complex also affected its isoselectivity.

Table 3. Isoselective ROP of Technical Grade *rac*-LA[a]

entry	cat	time [day]	conv.[b] [%]	$M_{n,calcd}$[c] [kg/mol]	M_n[d] [kg/mol]	$Đ$[d]	P_m[e]
1	**1**	3	93	26.8	22.9	1.15	0.79
2	**2**	4	92	26.5	21.9	1.10	0.83
3	**3**	3	84	24.2	19.8	1.12	0.84
4	**4**	3	91	26.2	19.6	1.14	0.79
5	**5**	3	90	25.9	20.9	1.13	0.83
6	**6**	3	93	26.8	23.5	1.10	0.87
7[f]	**6**	8	87	25.1	22.4	1.18	0.91
8[g,h]	**6**	14	96	8.3	7.6	1.15	0.93
9	**7**	4	91	26.2	23.6	1.14	0.82

[a] $[rac\text{-LA}]_0$ = 2.0 mol/L, $[LA]_0/[Zn]_0$ = 200:1, in 0.5 mL of CHO, at 25 °C. [b]Determined by ^{1}H NMR spectroscopy. [c]$M_{n,calcd}$ = $([LA]_0/[Zn]_0) \times 144.13 \times$ conv. %. [d]Determined by GPC. [e]P_m is the probability of forming a new *m*-dyad, determined by homonuclear decoupled ^{1}H NMR spectroscopy. [f]At −20 °C. [g]At −45 °C. [h]$[LA]_0/[Zn]_0$ = 60:1.

Keeping the substituents on the N atom of benzoimidazolyl unchanged, the substituents on the skeleton N atom exerted a significant effect on the isoselectivity of complexes. Complexes **1** and **4** with a benzyl group on the skeleton N atom showed relatively lower isoselectivities in comparison with those of the rest of the complexes bearing an alkyl group (**1**, **4**: P_m = 0.79; **2**, **3**, **5**−**7**: P_m = 0.82−0.87, Table 3). Among them, complex **6** with a linear octyl group on the skeleton N atom exhibited the highest isoselectivity of P_m = 0.87 at 25 °C. These trends however are consistent with those previously observed for the zinc silylamido analogues.[47] The electron-withdrawing nature of the benzyl substituent not only affects the catalytic activity of the complex but also exerts influence on the isoselectivity by changing the coordination parameters around the metal center as we previously suggested.[46−48] The preference of linear alkyl groups such as the *n*-octyl group in complex **6** than the rigid cycloalkyl for improving isoselectivity is likely due to their flexibility, which enables them to create steric hindrance dynamically, which is beneficial for the recognition of *D*-LA or *L*-LA.

The substituent on the N atom of the benzoimidazolyl moiety has little influence on the isoselectivity of complexes **1**−**7**. For example, keeping the benzyl group on the skeleton N atom unchanged, the replacement of benzyl on the N atom of the benzoimidazolyl ring with methyl results in complex **4** showing the same isoselectivity as complex **1** (**1**: P_m = 0.79; **4**: P_m = 0.79, Table 3, entries 1 and 4); the same applies for complexes **2** and **7** (**2**: P_m = 0.83; **7**: P_m = 0.82, Table 3, entries 2 and 9). As illustrated in the molecular structure (Figure 1), the substituent on the N atom of benzoimidazolyl is located far from the metal center, which hardly has any steric influence on the coordination sphere of the central metal.

The isoselectivity of complex **6** toward the ROP of *rac*-LA was further evaluated at low temperatures of −20 °C and −45 °C, and an enhancement of P_m to 0.91 and 0.93 was witnessed, respectively (Table 3, entries 7 and 8). In these cases, cyclic PLAs with high isotacticities were obtained from *rac*-LA for the first time. DSC analysis showed that the polymers produced by complex **6** form stereocomplexed structures to have melting points as high as 189 °C (see Figures S26−S28).

In the ROP of *rac*-LA, complexes afforded highly isotactic PLAs mainly through two pathways: a chain-end control mechanism (CEM) or a site control mechanism (SCM), sometimes involving both of them.[65,67,68] In order to have some insights on the mechanism of these complexes exerting isoselective control, a typical polymer sample obtain by complex **6** ($[rac\text{-LA}]_0/[\mathbf{6}]_0$ = 60:1, −45 °C, P_m = 0.93) was analyzed by the homonuclear decoupled ^{1}H NMR spectrum (see Figure S33), where the signal ratio of [*rmm*]/[*mmr*]/[*mrm*] was quite close to 1:1:1, indicating that the dominant stereoerrors were blocky-type, such as −*RRRRSSSS*−. With a lack of chain exchange processes as we usually observed for the ROP of *rac*-LA initiated by tridentate aminophenolate zinc complexes,[48] the stereoblocky polymer chain can only be formed via CEM.[48,49] Further kinetic studies of the ROP of *rac*-, *L*-, and *D*-LA catalyzed by complex **1** (80 °C, $[LA]_0/[Zn]_0$ = 200:1) afforded basically the same apparent rate constants for *L*-LA and *D*-LA polymerization ($k_{app(D)}$ = (2.04 ± 0.04) × 10^{-1} min^{-1}, $k_{app(L)}$ = (1.98 ± 0.16) × 10^{-1} min^{-1}) and a lower one for *rac*-LA polymerization ($k_{app(rac)}$ = (1.26 ± 0.04) × 10^{-1} min^{-1}) (Figure S34),[49] supporting the involvement of CEM in the polymerization in the case of without polymer chain exchanges. However, in each case, an obvious induction period could be observed, which should be due to the slow ring-opening of CHO by the Zn−Cl bonding of the complex to generate the active alkoxide species.

It is further noticed that, for all complexes, the decrease of polymerization temperature to 25 °C hardly influenced the molecular weights of resultant polymers, which were still more or less around 20 kg/mol (Table 3, [*rac*-LA] = 2.0 mol/L), implying nearly the same extent of decrease of both the chain growth rate and the ete cyclization rate.

Mechanistic Discussion. Based on the above studies, we presume that the mechanism of ROP of *rac*-LA catalyzed by these complexes is a process of chain growth integrated with ete cyclization and meanwhile involving CEM to produce isotactic stereoblocky chain structures. With complex **6** as the example (Scheme 3), initially CHO coordinates to the zinc center of the complex, then is attacked by the Cl ligand to form zinc alkoxide species "($\mathbf{L^6}$)Zn−$OC_6H_{10}Cl$", which sequentially initiates the coordination−insertion ROP of *rac*-LA via CEM to produce an isotactic stereoblocky polymer chain. The end group $ClC_6H_{10}OCO$− of the active polymer chain makes the adjacent carbonyl more easily attacked by the metal-alkoxy bond on the other end of the same polymer chain, leading to the formation of isotactic stereoblocky cyclic PLAs via ete cyclization (**Path A**) and regenerating the initial active species "($\mathbf{L^6}$)Zn−$OC_6H_{10}Cl$" that could initiate a new round of ROP. When the polymerization mixture is terminated by a trace amount of water in petroleum ether, the active polymer chains are deactivated to give linear polymers end-capped with $ClC_6H_{10}O$− and −OH (**Path B**), with the already formed cyclic polymers uninfluenced.

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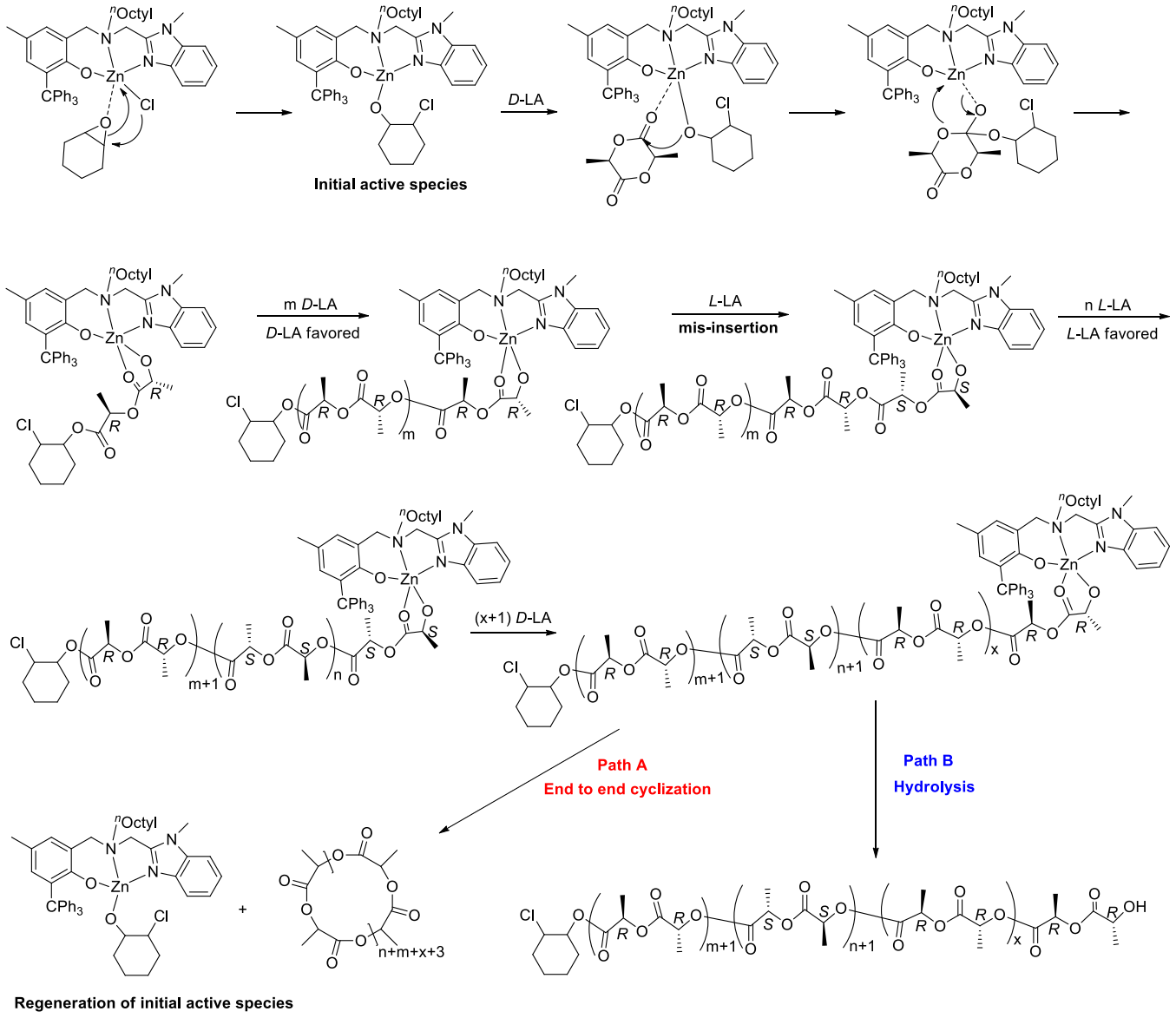
Scheme 3. Proposed Mechanism of the ROP of *rac*-LA Initiated by Complex 6 in CHO



CONCLUSIONS

We reported a series of benzoimidazolyl-substituted aminophenolate zinc chlorides that realized the ROP of large equivalents of technical grade *rac*-LA in CHO and showed extremely high tolerance to impurities. In addition, most of the new complexes exhibited good isoselectivities at ambient or low temperatures (P_m values of up to 0.93). Although the molecular weights of the resultant polymers are generally lower than the theoretical values due to cyclization reactions, cyclic poly(*L*-LA)s with a high molecular weight of 71.7 kg/mol were produced by carrying the polymerization at a high monomer concentration of 14 mol/L. Detailed mechanism studies and microstructure analysis of typical PLAs revealed that these complexes afforded cyclic PLAs through an ete cyclization reaction, and a CEM was involved to produce PLAs with isotactic stereoblocks. This paper provides a new idea for the synthesis of highly isotactic cyclic PLAs from *rac*-LA, and it also realizes the synthesis of cyclic PLAs with high molecular weights up to 58.0 kg/mol from *rac*-LA and 71.7 kg/mol from *L*-LA. In addition, the excellent stability of complexes permits them to have potential industrial applications.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.macromol.4c00937.

Experimental procedure and characterization data for new compounds; ^{1}H and ^{13}C NMR spectra of new proligands and zinc complexes **1**−**7**; ^{1}H NMR spectra of typical polymers, and polymerization data and figures (PDF)

X-ray data of complex **7** (CIF)

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Notes

The authors declare no competing financial interest.

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