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Complexities in the Ring-Opening Polymerization of Lactide by Chiral Salen Aluminum Initiators

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The preparation of (*R*,*R*)- and (*S*,*S*)-salen Al(OR) complexes, where R = Et, $CH_2{}^iPr$, $CH_2{}^tBu$, and $CH_2CH(S)MeCl$, are reported, along with their reactions with *rac*-lactide (salen = *N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamino). Rapid, reversible coordination of LA to the salen metal complex is observed, and it is shown that the relative rates of alcohol/alkoxide exchange are comparable to the NMR time scale while the rate of chain transfer involving (*R*,*R*)-salenAl(O-*R*-R) and (*S*,*S*)-salenAl(O-*S*-R) is much faster than the initial rate of ring opening of the LA monomer. For a primary [Al-OR] moiety, the ring opening of *rac*-LA is much faster than the ring-opening polymerization/enchainment of LA, and in the initial ring-opening event, the diastereoselectivity is dependent on the solvent, the chirality of the salen ligand, and the OR group. Irrespective of the initiator group OR or the solvent, the system moves to a pseudostatic equilibrium concentration of L- and D-LA which is dependent on the nature of the chirality of the salen ligand. Further studies show that the relative rate of trans-esterification is slower than the rate of LA enchainment and that the rate of epimerization is the slowest reaction in the system. Adventitious water leads to loss of catalytic activity and formation of the inert oxo-bridged compound $[(salen)Al]_2(\mu\text{-}O)$ which has been structurally characterized.

Introduction

One of the truly great successes in organometallic chemistry during the second half of the twentieth century was the elucidation of the mechanism of olefin polymerization by well-defined metal complexes.[1,2] From the time of the discoveries of Ziegler and Natta to the understanding of stereocontrol at single-site metallocene catalysts took some 50 years, but then, with this knowledge, the production of poly-α-olefins with a designed microstructure was possible.[3–5] In contrast, the control of microstructure in polyoxygenates is much less well-understood and has as of yet been relatively little studied. For example, in the polymerization of propylene oxide (PO) (*rac*) by base catalysis to give regioregular head-to-tail (HT) triads, stereocontrol is still lacking. KOH gives a statistical mixture of *ii*, *is*/*si*, and *ss* triads, whereas coordinate catalysts such as (TPP)AlOR, where TPP = tetraphenylporphyrin, give modest preferences for *ii* triads: *ii*:*ss* ∼ 3:1, comparable to the heterogeneous Union Carbide calcium amide/alkoxide or zinc glutarate catalysts.[6–9] The rationale for this type of stereopreference is not known beyond being able to be termed as "chain-end control". In the polymerization of lactide (LA) which comes in three stereoisomers, namely, L-(*S*,*S*), D-(*R*,*R*), and *meso*-(*R*,*S*)-lactides, and when present as a 50:50 mixture of L and D is called *rac*-LA, only three types of stereosequenced polymers are known: isotactic-PLA from either L-LA or D-LA, heterotactic-PLA (*isi*+*sis*) from *rac*- or *meso*-LA, and syndiotactic-PLA (*sss*) from *meso*-LA, together with stereoblock polymers from *rac*-LA.[10–13] The monomers of LA

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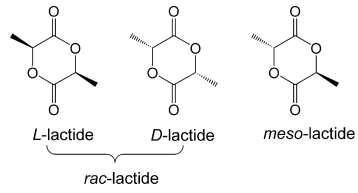
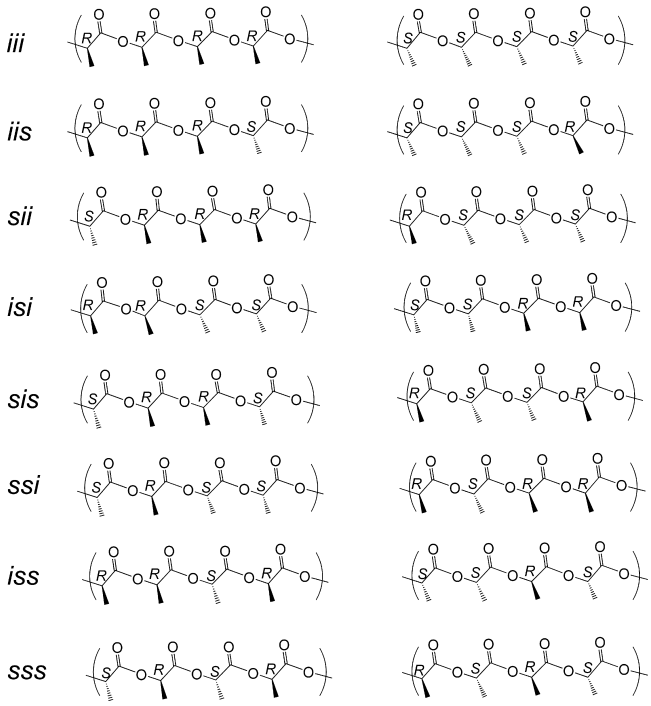
and the tetrads from these stereosequences are shown below.





The bulky achiral ligands employed by Coates in (BDI)ZnOR initiators, where BDI = 2-((2,6-diisopropylphenyl)amido)-4-((2,6-diisopropylphenyl)imino)-2-pentene, have achieved a significant degree of stereoselectivity as a result of chain-end control.[14] However, the origin of stereoselectivity is not well-understood, although it has recently been modeled by computational procedures.[15] Chiral Schiff base binaph and salen ligands have also been employed particularly with Al^{3+} alkoxides.[16–21] Once again, stereoselectivity has been observed, but the origin is unclear. Notably, Al^{3+} complexes with achiral salen and salan ligands have shown significant stereocontrol in the ring-opening polymerization of lactides.[22–25] The aluminum systems are among the slowest of all catalysts studied to date[12,14,26–36] and thus present the opportunity to interrogate the initiation step and the propagation with regard to stereoselectivity together with the competing side reactions of chain-end exchange, transesterificaion, and chain termination. We describe here our detailed studies of the reactions of (*S*,*S*)- and (*R*,*R*)-salen aluminum(III) OR complexes, where salen = *N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamino and R = Et, $CH_2{}^i$Pr, $CH_2{}^t$Bu, and CH_2CH(*S*)MeCl. This work provides insight into the complexities of this system and complements the earlier work of Feijen[20,21] and Coates.[19] It reveals how important the solvent can be in influencing the diastereoselectivity in the ring-opening event and furthermore establishes the relative rates of the various competing reactions within this dynamic system.

Results and Discussion

Syntheses of (Salen)AlOCH$_2$R Complexes. The chiral (salen) aluminum(III) alkoxides were prepared according to the. reactions shown in Scheme 1. The reactions between the (salen)AlMe complex and the alcohols take 5 h (R = CH_2CH_3) at room temperature or, for R = $CH_2{}^i$Pr, $CH_2{}^t$Bu, and CH_2CH(*S*)Me, 5 h at 40 °C in hexane. In all cases, the reaction proceeds to yield the (salen)AlOR complexes as off-white/pale yellow precipitates in hexane. These alkoxides are soluble in aromatic hydrocarbon solvents (benzene, toluene) and very soluble in THF, CH_2Cl_2, and $CHCl_3$, but only sparingly soluble in hexane. The solutions are pale yellow and moisture sensitive. The preparation via $AlMe_3$ noted in Scheme 1 is much faster and more convenient than the direct reaction between the $Al(OR)_3$ compounds and the salen-H_2 ligand, which requires extensive heating (80 °C,

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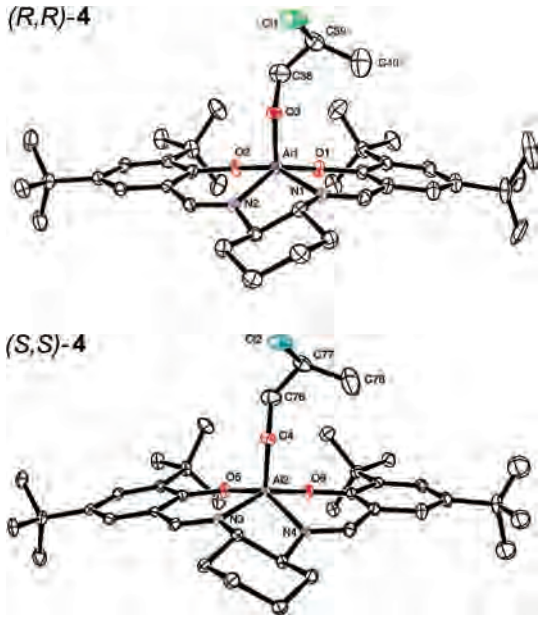
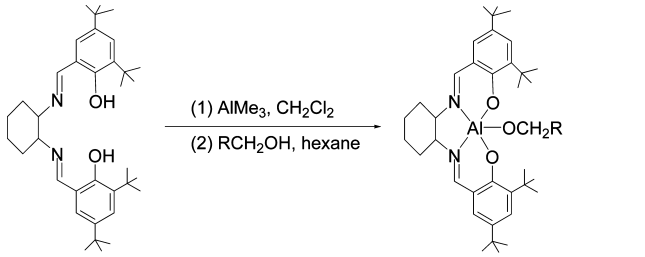


Figure 1. Molecular structures of (*R*,*R*)-**4** and (*S*,*S*)-**4**, deduced from single-crystal X-ray studies.[37]

Scheme 1. Preparation of the (salen)AlOR catalysts



toluene, 3 days) to drive the reaction to completion.[20]

The crystal and molecular structures of the compounds (*S*,*S*-salen)AlOCH$_2$CH(*S*)MeCl and (*R*,*R*-salen)AlOCH$_2$CH(*S*)MeCl have been determined and, as reported in an earlier preliminary communication, adopt a monomeric square pyramidal structure in the solid state.[37] For reference, these structures are shown in Figure 1 In contrast, the related (binaph)AlOMe is known to be dimeric in the solid state.[19]

The four complexes of this study are (salen)AlOEt, **1**; (salen)AlOCH$_2$^{i}Pr, **2**; (salen)AlOCH$_2$^{t}Bu, **3**; and (salen)-AlOCH$_2$CH(*S*)MeCl, **4**. For each complex, we have prepared both enantiomers based on (*S*,*S*)-salen or (*R*,*R*)-salen supporting ligands. The utilized complexes are thus eight in total.

The Reversible Binding of LA to the Salen Al(OR) Complexes. Substrate binding to a metal alkoxide initiator can be anticipated as the first step in the ring-opening process. No structural characterization of a 1:1 LA:metal complex is currently known though it can reasonably be assumed that coordination to the metal occurs as indicated by the ring-opening reaction shown in Scheme 2.

While it is, of course, possible to envisage a direct attack of the alkoxide oxygen on the ketonic ester carbon, the coordination of Lewis bases to five-coordinate Al(III) centers has numerous precedents, and in the case of lactide coordination, this would polarize the C−O double bond of LA to enhance nucleophilic attack by the neighboring alkoxide group. This is akin to a migratory 1,2-addition of an alkyl group to a coordinated olefin. From ^{1}H NMR spectroscopy, we find evidence for the facile and reversible interaction of *rac*-LA with the chiral aluminum complex as evidenced by the methine proton signals shown in Figure 2. With a 1:1 mixture of *rac*-LA to [Al], complex **1**, we observe two sharp overlapping quartets. A further addition of less than 1 equiv of L-LA selectively enhances the downfield quartet thus allowing the discrimination of L- and D-LA in the presence of chiral **1**. Cooling the sample in toluene-d_8 does not allow for the freezing out of an LA:**1** adduct. The dynamic equilibrium is fast on the NMR time scale and does not indicate a specific binding preference for L-LA or D-LA. Upon increasing the relative concentration of *rac*-LA to 5:1 with respect to **1**, the methine signal becomes just one quartet, consistent with the presence of an equilibrium mixture that strongly favors the free (noncoordinated) LA.

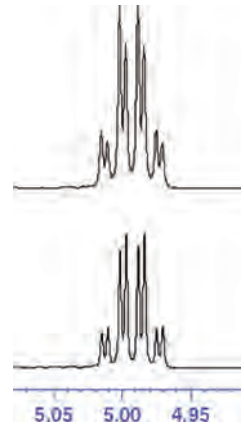


Figure 2. ^{1}H NMR methine resonance of *rac*-lactide in a $CDCl_3$ solution of (*R*,*R*-salen)AlOEt. Bottom spectrum shows 1:1 ratio of *rac*-LA:[Al], while the top spectra show the affect of addition of L-LA to the same sample.

Studies of the Ring-Opening Event. By employing a primary alkoxide, we have followed the reactions of complexes **1**−**4** with 20 equiv of *rac*-LA at room temperature and in various solvents. In all cases, the reaction proceeds according to Scheme 3, wherein the product of the single ring-opening event is formed. No subsequent ring opening of a second LA molecule occurs at room temperature, as was similarly seen for the insertion of LA into Sn−OMe in Ar$_3$SnOMe compounds.[38] The time of this reaction, however, is sensitive to the steric properties of the OR group: R = Et (<12 h) versus R = CH$_2$CH(*S*)MeCl (3 days).

The diastereoselectivity of the reaction was followed by ^{1}H NMR spectroscopy where the ratio of [Al]-(L-LA)OR to [Al]-(D-LA)OR can reasonably be established to within ±5%. The assignment of the signals arising from [Al]-(L-LA)OR was established by the independent reaction employing L-LA (Figure 3). A related assignment can be seen in the literature.[21] The results of these experiments are summarized in Table 1, where the diastereoselectivity (de%) is noted for the reaction of **1**−**4** in various solvents.

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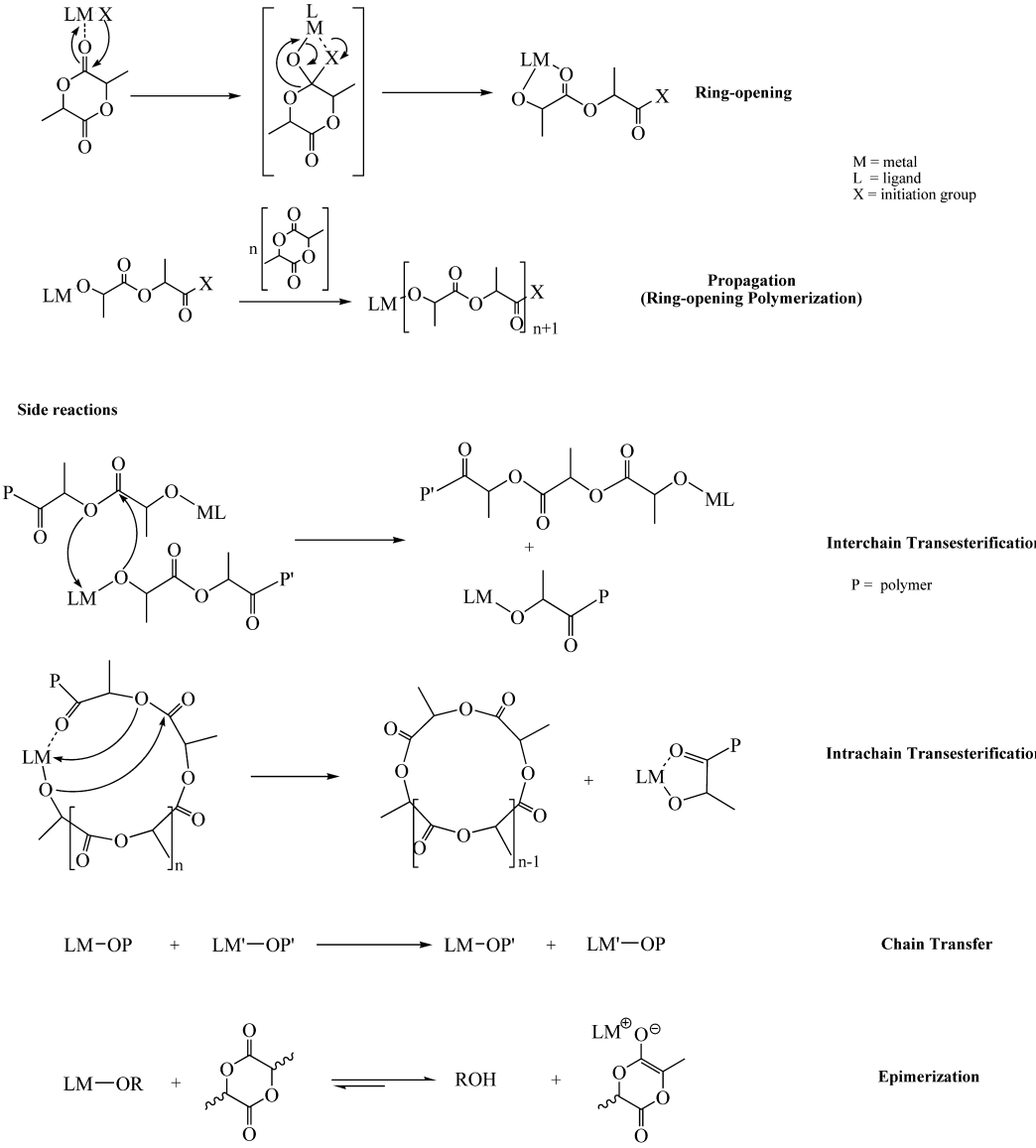
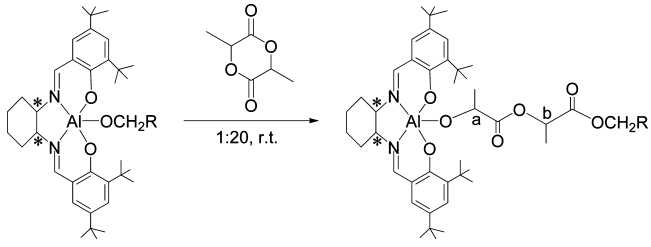
Scheme 2. Reactions Involved in Ring-Opening Polymerization of Lactide Using a Coordination Catalyst



Scheme 3. Single Ring-Opening Reaction of (Salen)AlOCH$_2$R and Lactide



For any achiral alkoxide complex (e.g., **1**, **2**, **3**), the diastereoselectivity resulting from the use of (*S*,*S*)-salen or (*R*,*R*)-salen complexes should be equal in magnitude but opposite in handedness. Within the limits afforded by this NMR assessment, this is seen to be true.

All of the de% values are relatively modest, <40%, which suggests that the chirality of the salen ligand is not very imposing. Furthermore, the influence of solvent is such as to change the order of diastereoselectivity in the reactions involving **1** in $CHCl_3$ versus other solvents. In general, the donor solvents such as THF and pyridine produce a somewhat higher de% than the nonpolar benzene or toluene which have similar effects. The influence of the chiral solvents (*S*)-PO, (*R*)-PO, or *rac*-PO had little effect.

It is certainly difficult to interpret the solvent effects for reactions employing **1**, **2**, and **3**, but we do note that $CHCl_3$ and, to a lesser extent, CH_2Cl_2 may hydrogen bond to oxygen, either the ketonic oxygen of the LA molecule or to the Al−O bonds and as such may be significantly involved in the transition state of the ring-opening event. The donor solvents, THF or pyridine, may coordinate to the Al(III) center, and we have previously noted the influence of THF versus CH_2Cl_2 in controlling the microstructure of PLA produced by single-site magnesium and calcium catalysts.[31,39] The greater bulk of the alkoxide ligand in **3**, in comparison with that of **1** and **2**, does not lead to enhanced

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Table 1. Stereoselectivity in the Single Ring-Opening Reactions of (Salen)Al Complexes and *rac*-Lactide

	L−D (de%)[a]							
solvents	(*R,R*)-**1**	(*S,S*)-**1**	(*R,R*)-**2**	(*S,S*)-**2**	(*R,R*)-**3**	(*S,S*)-**3**	(*R,R*)-**4**	(*S,S*)-**4**
toluene	12	−17	−25	32	−16	11	−33	−37
C_6H_6	20	−18	−31	32	−15	11	−31	−40
$CHCl_3$	−16	14	−24	40	−9	10	−30	−3
CH_2Cl_2	6	−6	−23	31	−15	12	−22	−4
THF	22	−20	−32	32	−40	31	−33	−13
pyridine	20	−17	−30	36	−29	30	−39	−4
(*S*)-PO	17	−13	−23	22	−32	28	−32	−12
(*R*)-PO	14							
rac-PO	17							

[a] The de% is estimated from ^{1}H NMR spectra and is proposed to be ∼ ±5%.

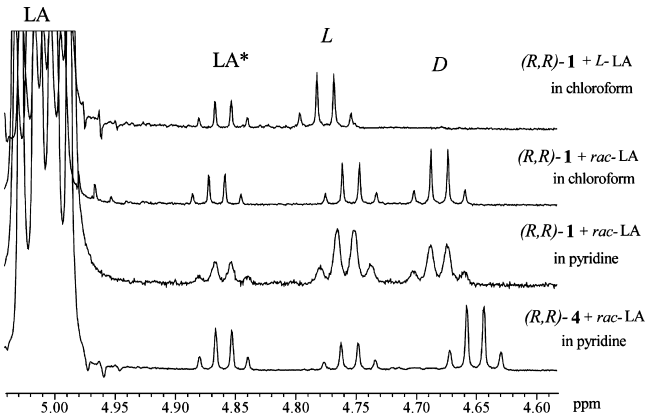

Figure 3. Selected ^{1}H (500 MHz, $CDCl_3$) NMR spectra showing the methine proton region (H_b in Scheme 3) of the products in single ring-opening reactions of lactide by (salen)AlOCH_2R. LA, unreacted lactide; LA*, LA satellite signals; L,L-LA ring-opened product; D,D-LA ring-opened product. Sample concentration can affect methine resonance position as seen in (*R,R*)-**1** + L-LA versus (*R,R*)-**1** + *rac*-LA in chloroform-*d*.

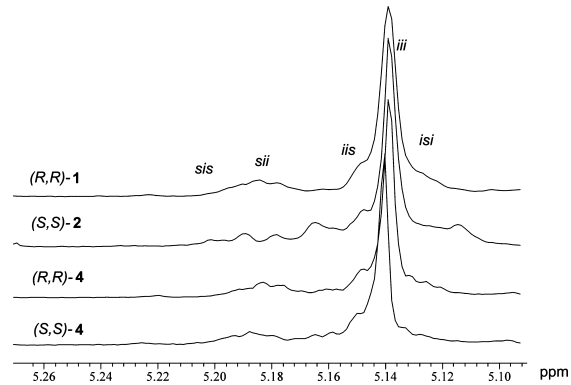

Figure 4. ^{1}H (500 MHz, $CDCl_3$) NMR spectra of the homodecoupled methine proton (C*H*) resonance of polylactide formed from *rac*-lactide in toluene by using (salen)AlOCH_2R initiators.

stereoselectivity in the ring-opening event as we had anticipated in comparison with **1** and **2**, and the handedness of **1** differs from **2** and **3**.

The reactions involving compounds **4** are even more puzzling. In just looking at the de% obtained in benzene or toluene, one might believe that chain-end control was dominant. However, in the donor solvents (THF and pyridine) and the chlorinated solvents ($CHCl_3$ and CH_2Cl_2), the selectivity is significantly different. Finally, the comparison of the data for compounds **2** and **4** is interesting inasmuch as one Me group is substituted by Cl. The entries for (*R,R*)-**2** and (*R,R*)-**4** are similar in both magnitude and handedness, but the corresponding entries for the (*S,S*)-salen complexes **2** and **4** are notably different from each other. This once again underscores the complicated and perplexing manner in which diastereoselectivity is realized.

Ring-Opening Polymerization of Lactide. We have followed the polymerization of *rac*-LA by various initiators (**1**−**4**), and irrespective of the initiator employed, the polymer microstructure appears the same as shown in Figure 4. This clearly indicates that irrespective of the initiation step, the enchainment process moves to a dynamic equilibrium position (vide infra). The polymer microstructure deduced from NMR spectroscopy reveals the marked preference for isotactic triads, *iii*.[40] Also noteworthy is that *sis* triads are significantly less than *iis*, *sii*, and *isi*, and that at 40% conversion, trans-esterification is negligible as deduced from mass spectroscopy, which principally shows polymeric chains of differing length in units of 144 Da.[41] Thus within the polymer chains, there are mostly sequences of the type (L-LA)$_n$−(D-LA)$_m$ which can readily arise from chain-end control (we address the matter of chain transfer later). In order to observe *sis* tetrads, there must be (L-LA)$_n$−(D-LA)−(L-LA)$_m$ or (D-LA)$_n$−(L-LA)−(D-LA)$_m$ sequences.

The above microstructure is the same as that reported by Feijen in his study of the polymerization of *rac*-LA with (*rac*-salen)AlO^iPr and (*R,R*-salen)AlO^iPr as initiators.[20,21] Feijen also noted that (*R,R*-salen)AlO^iPr preferentially enchained L-LA and that the relative rates of polymerization of L-LA to D-LA was 14:1 at 80 °C. This ratio of rates was determined from separate experiments involving L-LA or D-LA with (*R,R*-salen)AlO^iPr.

During the polymerization of *rac*-LA by a coordinate catalyst, there are four rate constants that contribute to the overall k_{obs} as shown in Scheme 4. In order to further interrogate this system, we have followed the reaction with time by monitoring the relative concentration of L-LA to D-LA, the unconsumed monomer residue. By employing (*S,S*)-**2**, which is known to preferentially ring open L-LA in the first step (i.e., the opposite of what is preferred during

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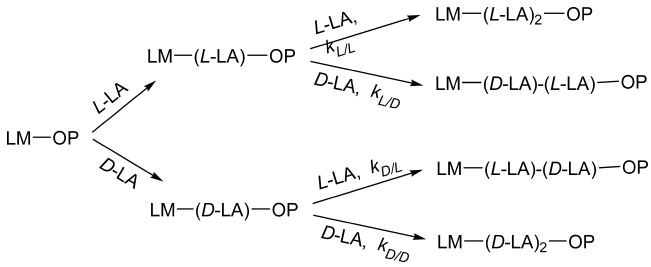
Scheme 4. Four Ring-Opening Events Involved in the Polymerization of *rac*-Lactide Employing a Single-Site Metal Catalyst (L = Ancillary Ligands and OP the Growing Chain)



the polymerization, based on Feijen's work), we have monitored the L-LA to D-LA ratio by gas chromatography equipped with a chiral β-cyclodextrin column as a function of % conversion at 80 °C in toluene.

As shown in Figure 5, we have followed this reaction to 80% conversion which was achieved in about 2 months. This effectively represents a t_∞ situation as there is a significant equilibrium concentration of LA with PLA at this temperature. With increasing % conversion, one sees the preferential enchainment of D-LA (as expected from Feijen's work) until there is a constant ratio of L-LA to D-LA of the order of 70:30. At this relative concentration of L-LA to D-LA, the (*S*,*S*-salen)Al catalyst is enchaining both to the same extent.

From the analysis of the residual L-LA to D-LA concentrations, we can also determine the relative ratio of each contained in the growing polymer chain, and these data are shown in Figure 6. The initial entry points represent the ring-opening event that occurs at room temperature, and one sees how this is "corrected" within 10% conversion, which represents just five monomer units in this study involving LA:**2** = 50:1. At 40% conversion, which corresponds to the microstructure of the PLA shown in Figure 4, the ratio D-LA to L-LA in the polymer is 2:1, and these units are present as stereoblocks.

Recognizing that the ratio of L-LA to D-LA of ~2:1 represents a pseudostatic condition wherein each is consumed at 80 °C in toluene at an equivalent rate, we examined the polymerization of the 70:30 L/D lactide mixture by (*S*,*S*)-**2** as a function of time in order to interrogate the polymer microstructure (Figure 7). As shown in Figure 8, the polymer that is formed is comparable in stereosequence to that noted

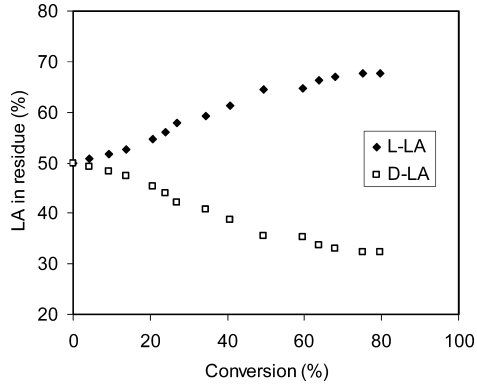


Figure 5. The relative concentrations of unreacted lactide monomers during the polymerization of *rac*-LA by using (*S*,*S*)-**2**. The ratio of LA to **2** was 50:1.

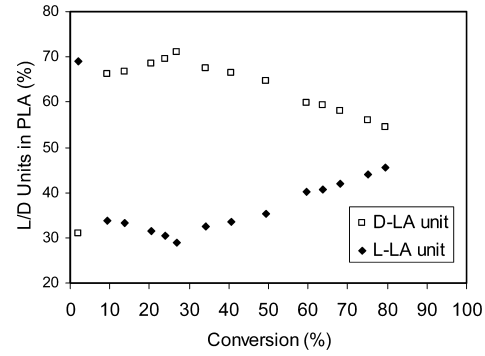


Figure 6. The enchained L/D-lactide units in PLA during the polymerization of *rac*-LA by using (*S*,*S*)-**2**.

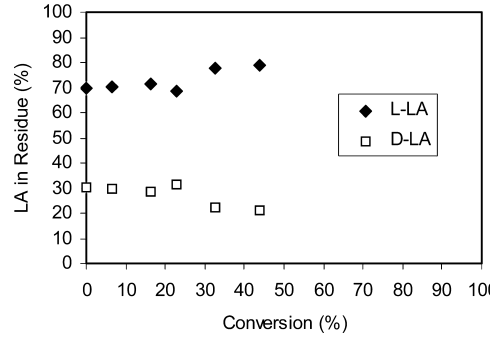


Figure 7. The relative concentrations of unreacted lactide monomers during the polymerization of 70:30 L/D-lactides by using (*S*,*S*)-**2**.

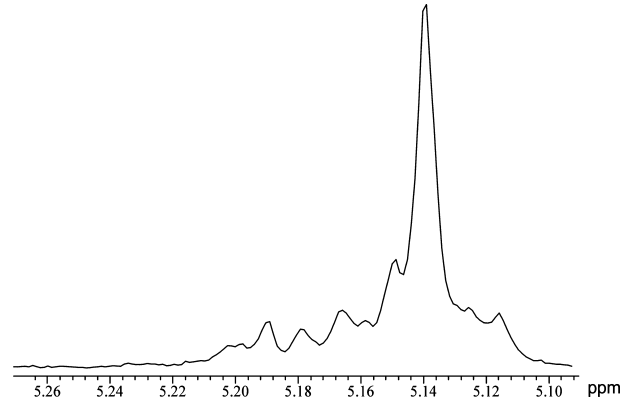
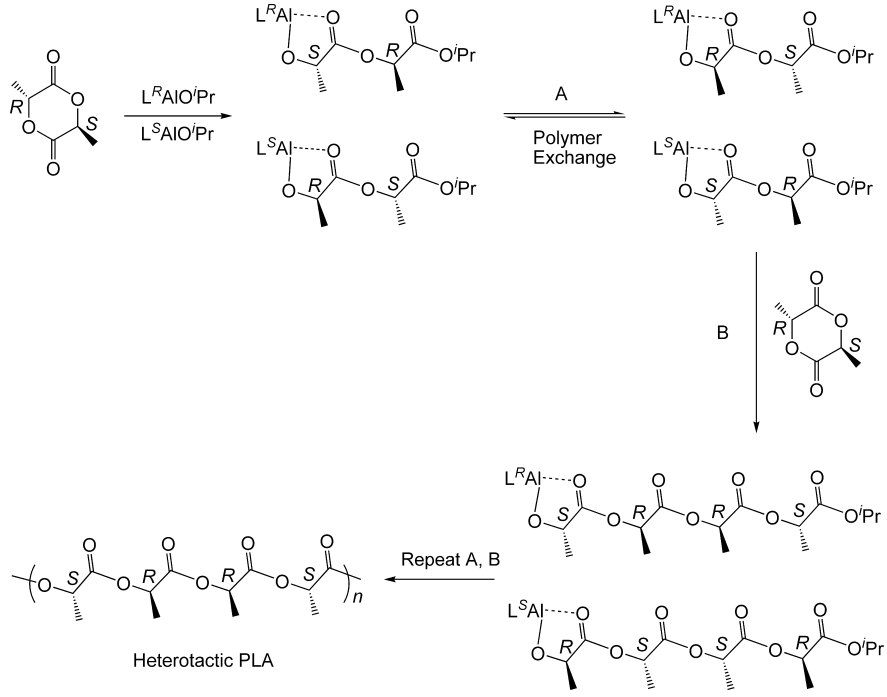


Figure 8. ^{1}H (500 MHz, $CDCl_3$) NMR spectra of the homodecoupled methine proton (C*H*) resonance of polylactide formed from 70:30 L/D-lactides in toluene by using (salen)AlOCH$_2$R initiators.

before in having ~80% *iii* tetrads. This is also seen by examination of the ^{13}C signal of the ketonic carbon (see Supporting Information). Thus stereoblocks are preferred, and thus under this pseudostatic concentration, rate $r_{D/D} > r_{D/L}$, $r_{L/L} > r_{L/D}$, and $r_{D/D} + r_{L/D} = r_{L/L} + r_{D/L}$ (Scheme 4).

Chain Exchange Reactions. In a study of the polymerization of *meso*-LA by the (*rac*-binaph)AlOR catalyst system, Coates and co-workers observed the formation of heterotactic PLA (*isi* + *sis*), and they invoked a polymer chain exchange mechanism. See Scheme 5.[19] This proposal was made because the same workers noted that the (*R*-binaph)AlOR catalyst system with *meso*-LA gave syndiotactic PLA (*sss*). In Scheme 5, in order to obtain heterotactic PLA, the polymer chain exchange reaction must be more rapid than the rate of enchainment. As noted earlier, the ground-state structures of the (*R*,*R*-salen)AlOR and the (binaph)AlOR complexes

Scheme 5. Coates' Proposed Mechanism of Heterotactic PLA Formation by (*rac*-binaph)Al Catalyst (Reproduced with Permission from Ref 19)



differ: the former are monomeric (Figure 1), while the latter are dimeric with two OR bridges. However, in order to test for the significance of an exchange process involving (salen)AlOR complexes, we studied the solutions of the mixture of compounds formed from the ring opening of L-LA and D-LA as shown in eq 1 below where Np = $CH_2{}^tBu$.

$$(R,R\text{-salen})\text{Al(L-LA)ONp}+(S,S\text{-salen})\text{Al(D-LA)ONp} \rightleftharpoons (R,R\text{-salen})\text{Al(D-LA)ONp}+(S,S\text{-salen})\text{Al(L-LA)ONp} \quad (1)$$

The chain-end exchange reaction was observed to be rapid at room temperature in chloroform-*d* as determined by ^{1}H NMR spectroscopy, and its approach to equilibrium has been monitored starting from both sides. We also note that the equilibrium favors the (*R*,*R*-salen)Al(D-LA)ONp and (*S*,*S*-salen)Al(L-LA)ONp mixture by 2:1, and that this is the preference for the initial enchainment of L-LA and D-LA during the ROP of *rac*-LA by the respective (*R*,*R*)- and (*S*,*S*)-salen complexes (Table 1). The facility of this exchange reaction, equilibrium 1 above, provides unequivocal evidence in support of Coates' proposal[19] for the chain-end exchange mechanism in the stereoselective polymerization of *meso*-LA to give syndiotactic PLA.

Alcohol for Alkoxide Exchange. In the above experiment, one can not rigorously distinguish between chain-end exchange and salen-ligand group exchange. The latter, however, is much less likely to be as rapid since the salen ligand is a dianionic tetradentate ligand. To establish salen group exchange would require a double labeling experiment and in any event would not obviate the suggestion by Coates[19] that ligand scrambling was occurring faster than ring enchainment despite the relative concentrations of the species present when [LA] >> [Al].

Chain-end exchange can occur by either a bimolecular path involving alkoxide bridges (as supposed above) or by the presence of an adventitious alcohol molecule. In living polymerizations of LA, the addition of alcohol merely increases the number of growing chains and can be used to control the molecular weight of the polymer if alcohol−alkoxide exchange is much faster than ring enchainment. In order to estimate the relative facility of alcohol−alkoxide exchange, a number of simple reactions were monitored. First, addition of EtOH to the aluminum neopentoxide complex readily displaced neopentanol with formation of the ethoxide ligand. Second, when (*R*,*R*-salen)AlOEt was allowed to react with EtOH in benzene-d_6, line broadening of the ethoxide resonance was observed when the [EtOH][Al] ratio was 6:1. No coalescence was observed, but this reaction was clearly very rapid in even approaching the NMR time scale of $\sim 10\ s^{-1}$.

Trans-Esterification Reactions. In polymerizations of *rac*- or *meso*-lactide that lead to heterotactic or syndiotactic polymers, there are always some detectible stereosequences corresponding to errors. Indeed, in the polymerization of *rac*-LA by a racemic salen Al catalyst that was originally claimed to be a stereoplex polymer, it was the errors that Coates[18] noted that led it to be correctly assigned as a blocky polymer with sequences $-(\text{L-LA})_n-(\text{D-LA})_m-$ where $n \sim m \sim 11$. Stereosequence errors can arise at the enchainment step and also by trans-esterification reactions involving the growing polymer chain. Unlike the polymerization of olefins which leads to a saturated hydrocarbon chain, the ring-opening polymerization of a cyclic ester leads to a linear chain

(42) Chisholm, M. H.; Gallucci, J. C.; Yin, H. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 15315.
(43) Culkin, D. A.; Jeong, W.; Csihony, S.; Gomez, E. D.; Balsara, N. P.; Hedrick, J. L.; Waymouth, R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 2627.

polyester that remains susceptible to esterification reactions. Intrachain trans-esterification leads to cyclic esters, and this has been a topic of recent interest in lactide chemistry,[42–44] while interchain trans-esterifications leads to the formation of longer and shorter growing chains with a loss of polydispersity and, in an otherwise stereoselective ring-opening polymerization, the scrambling of stereocenters along the chain. It has generally been assumed that, in ROP by salen AlOR and related Schiff base AlOR initiators, trans-esterification is inoperative. The evidence for this comes from the generally observed narrow PDIs and from the predominant appearance of ions separated by mass units of 144 corresponding to whole LA units in the mass spectrum with that of an oligomeric unit.

In order to check on the relative inertness of this system toward trans-esterification, we examined (*R*,*R*-salen)Al-(L-LA)-OEt. In chloroform-*d* at room temperature, this compound appeared chemically persistent, but at +70 °C over a period of days, this compound reacted to yield (*R*,*R*-salen)AlOCHMeC(O)OEt and other species formulated as (*R*,*R*-salen)Al(OCHMeC(O))$_n$-OEt where $n > 2$. The presence of the ethyllactate complex was readily confirmed by a comparison of the ^{1}H NMR spectra with an authentic sample prepared from the reaction between (*R*,*R*-salen)AlMe and HOCHMeC(O)OEt, and evidence of the oligomers Al(OCHMeC(O))$_n$-OEt was seen in the spectra as additional methine quartet resonances from ring-opened lactide oligomers. Thus we can conclude that the aluminum system under study is capable of undergoing trans-esterification reactions. These are, however, somewhat slower than the ring-opening reactions, but with time, these will occur.

Epimerization. In our study, we have found no evidence of epimerization of LA or the poly-L-LA by these aluminum alkoxides. This is consistent with the view that only the polar M−OR bonds typically found for the electropositive metals such as Mg, Ca, the lanthanides, and alkali metals affect this. The more covalent bonds associated with Zn(II), Al(III), and Sn(II and IV) do not bring about epimerization.

Termination: Catalyst Death. A common problem encountered in metal coordinate ROP is the sensitivity of the metal complex to water. Typically, rigorously dried solvents and atmospheres must be employed, and even the lactide has to be doubly or triply sublimed. Also in studies of the kinetics of these ROP reactions, the data are flawed by the presence of trace amounts of water. Coates noted irreproducible data in studies of >100 equiv of LA, and we have even encountered problems with 50 equiv on occasion. In studying the order of the reaction based on the concentration of the metal complex, we[45] and others[46] have noted nonzero intercept plots for κ_{obv} versus [M] indicative of a consistent loss in activity due to removal of some of the active species. In this work, our attempts to recover the metal complex as an alkoxide or to obtain crystals of the single ring-opened product of LA have repeatedly led to crystals of the oxo-bridged compound [salen-Al]$_2$(μ-O). The molecular structure of this complex is shown in Figure 9, and full crystallographic details and metric parameters are given in the Supporting Information. One possible pathway leading to this compound is by hydrolysis: [Al]–OR + H_2O → [Al]–OH + ROH; [Al]–OH + [Al]–OR → [Al]–O–[Al] + ROH and is inactive toward ROP of LA. Its formation represents the death of the catalyst and is formed with chain release from the metal.

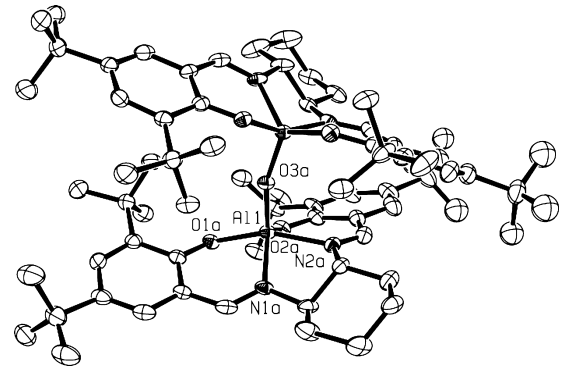


Figure 9. Molecular structure of oxo-bridged compound [*R*,*R*-salen-Al]$_2$(μ-O), deduced from single-crystal X-ray studies. Hydrogen atoms have been omitted for clarity, and 30% anisotropic displacement ellipsoids are drawn. A 2-fold rotation axis passes through O(3a).

Concluding Remarks

The study of the (salen)AlOR lactide system is particularly informative with regard to the fundamental reactions that are involved in and compete with lactide polymerization. We have seen evidence for the reversible coordination of LA with the metal complex, a reaction which may typically occur prior to the ring-opening event. By the use of primary alkoxide groups, we have observed the products formed by the ring opening of a single LA molecule. The chirality of the metal complex exerts a very modest diastereoselectivity in the initial ring-opening event, and this is quite significantly influenced by the nature of the solvent such that the preference is reversed in toluene from that in chloroform. The influence of the chiral center of the alkoxide which forms the polymer end group attached to the metal has a markedly greater influence. This is becoming increasingly apparent in studies of stereoselective polymerizations of LA by achiral metal complexes and is well exemplified by the work of Coates and Gibson.[15,47] In the [salen-Al] system under study, the polymerization of *rac*-LA moves to a static residual concentration of L to D of ca. 70:30 when the (*R*,*R*)-salen ligand is employed, and the polymer chain microstructure remains essentially constant having ~80% *iii* tetrads. The virtual absence of the *sis* tetrad is a clear indication that the polymer is a stereoblock polymer, and this once again emphasizes the importance of chain-end control in the enchainment process since, with an enantiomerically pure metal center, chain transfer can not be responsible. However, our work unequivocally demonstrates that the rate of chain-

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(47) Hormnum, P.; Marshall, E. L.; Gibson, V. C.; Pugh, R. I.; White, A. J. P. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 15343.

end exchange/transfer between the metal centers is much faster than the enchainment step and trans-esterification, though the latter is detectable at +70 °C in chloroform-*d* over a period of days and may well be responsible for some of the minor tetrad sequences that are apparent in the PLA after several days. Thus, in the overall system, we can note the kinetic order of reactions as: 1, reversible LA coordination >2, alcohol−alkoxide group exchange >3, chain-end exchange >4, ring opening of LA > 5, trans-esterification >6, epimerization which is effectively not detectable.

Experimental Section

All syntheses and solvent manipulations were carried out under a nitrogen atmosphere using standard Schlenk-line and dry box techniques. Solvents were dried using standard procedures. Trimethylaluminum (2.0 M solution in hexane, Aldrich), 4-dimethylaminopyridine (Aldrich), (*R*,*R*)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamine (Aldrich), (*S*,*S*)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamine (Aldrich), (*S*)-2-chloro-1-propanol (Aldrich), 2-methyl-1-propanol (Fisher), and neopentyl alcohol (Fisher) were used as received. Lactides (L and *rac*, Aldrich) were sublimed three times under reduced pressure prior to use. Deuterated solvents were stored over 4 Å molecular sieves for 24 h prior to use.

X-ray Crystallographic Studies [*R*,*R*-Salen)Al]2(μ-O). The data collection crystal was a yellow, blade-like fragment. Examination of the diffraction pattern on a Nonius Kappa CCD diffractometer indicated a monoclinic crystal system. All work was done at 150 K using an Oxford Cryosystems Cryostream Cooler. The data collection strategy was set up to measure a quadrant of reciprocal space with a redundancy factor of 3.4, which means that 90% of the reflections were measured at least 3.4 times. A combination of φ and ω scans with a frame width of 1.0° was used. Data integration was done with Denzo,[48] and scaling and merging of the data was done with Scalepack.[48] Merging the data and averaging the symmetry equivalent reflections resulted in an R_{int} value of 0.040.

The structure is expected to contain a single enantiomer. As no systematic absences were observed, the space group choice is limited to *P*2. The direct methods in SHELXS-97[49] were used to solve the structure. The Al complex is a μ-oxo-bridged dimer which contains a crystallographic 2-fold rotation axis. There are two half-dimer molecules in the asymmetric unit (labeled as A and B), along with two half-molecules of toluene. Each toluene molecule is also on a 2-fold axis. Full-matrix least-squares refinements based on F^2 were performed in SHELXL-97,[50] as incorporated in the WinGX package.[51]

Two *t*-butyl groups are disordered, and each is modeled with two sets of carbon atoms. The group containing atom C(33A) consists of C(34A), C(35A), and C(36A) in the major orientation with an occupancy factor of 0.595(9) and C(34D), C(35D), and C(36D) in the minor orientation with an occupancy factor of 0.405(9). The other group contains atom C(33B) and consists of C(34B), C(35B), and C(36B) as the major orientation with an occupancy factor of 0.51(1) and C(34C), C(35C), and C(36C) in the minor orientation with an occupancy factor of 0.49(1). DFIX and SADI restraints were used for modeling this disorder, and the carbon atoms were refined isotropically.

The FLAT restraint was used for one of the toluene solvent molecules containing atoms C(1C), C(2C), C(3C), C(4C), and C(5C). This molecule was refined anisotropically. The other toluene group containing atoms C(1D), C(2D), C(3D), C(4D), and C(5D) was refined only isotropically.

For the methyl groups, the hydrogen atoms were added at calculated positions using a riding model with $U(\mathrm{H}) = 1.5 \times U_{eq}$(bonded carbon atom). The torsion angle, which defines the orientation of the methyl group about the C−C bond, was refined for most of the methyl carbon atoms. (For the two disordered *t*-butyl groups and the methyl carbon atoms of the toluene molecules, these torsion angles were not refined.) The remaining hydrogen atoms were included in the model at calculated positions using a riding model with $U(\mathrm{H}) = 1.2 \times U_{eq}$(bonded carbon atom).

The final refinement cycle was based on 11294 intensities, 27 restraints, and 811 variables and resulted in agreement factors of $R1(F) = 0.081$ and $wR2(F^2) = 0.159$. For the subset of data with $I > 2\sigma(\mathrm{I})$, the $R1(F)$ value is 0.061 for 9088 reflections. The final difference electron density map contains maximum and minimum peak heights of 0.39 and −0.29 e/Å^3. Neutral atom scattering factors were used and include terms for anomalous dispersion.[52] The correct enantiomer was chosen based on the known chiral centers. The Flack parameter[53] was refined during the final cycles, and its final value was 0.07(23).

NMR Experiments. ^{1}H and ^{13}C{^{1}H} NMR experiments were carried out with a Bruker DRX-500 (5 mm broadband probe) and a Bruker DRX-600 (5 mm broadband probe) spectrometers, operating at proton Larmor frequency of 500 MHz. Their peak frequencies were referenced against the solvent, chloroform-*d* at 7.24 ppm for ^{1}H and 77.0 ppm for ^{13}C{^{1}H} NMR .

Chromatographies. Gel permeation chromatographic (GPC) analysis was performed at 35 °C on a Waters Breeze system equipped with a Waters 410 refractive index detector and a set of two columns, Waters Styragel HR-2 and HR-4 (Milford, MA). THF (HPLC grade) was used as the mobile phase at 1.0 mL/min. The sample concentration was 0.1%, and the injection volume was 100 μL. The samples were centrifuged and filtered before analysis. The calibration curve was made with six polystyrene standards covering the molecular weight range from 580 to 460 000 Da. Gas chromatographic (GC) analysis was performed on a Hewlett-Packard 5890 equipped with a permethylated hydroxypropyl β-cyclodextrin (Chiraldex) capillary column (40 m × 0.25 mm i.d.) and an FID detector connected to an HP 3396 integrator. Helium was used as carrier gas with a flow rate of 1 mL/min. Dichloromethane was used as solvent, with an injection volume of 2 μL, an injection temperature of 275 °C, and a column temperature of 140 °C. In all cases, baseline separations of L/D-lactides were observed with retention time $t_L = 21.5$ min and $t_D = 22.3$ min.

Synthesis of (*R*,*R*)-Salen Aluminum Ethoxide. To a solution of (*R*,*R*-salen)H_2 (1.0 g, 1.8 mmol) in 20 mL of dichloromethane was added a solution of trimethylaluminum ($AlMe_3$, 2.0 M solution in hexane, 1.1 mL, 2.2 mmol), and the mixture was stirred for 3 h at room temperature. A yellow powder was obtained after the removal of volatile fractions under vacuum. The powder was redissolved in hexane, followed by the addition of 0.2 mL of ethanol (3.4 mmol), and stirred for 3 h. A yellow precipitate was obtained as the product in 75% yield. ^{1}H NMR ($CDCl_3$, δ, ppm): 0.85 (dd, CH_3−CH_2O), 3.45 (m, CH_3CH_2O), 1.29, 1.30, 1.52, 1.55 (s, C(CH_3)), 1.44, 2.06, 2.42, 2.58, 3.05, 3.83 (cyclohexyl), 6.99, 7.04,

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(53) (a) Flack, H. D. *Acta Crystallogr.* **1983**, *A39*, 876–881. (b) Bernardinelli, G.; Flack, H. D. *Acta Crystallogr.* **1985**, *A41*, 500–511.

7.47, 7.50 (aromatic), 8.15, 8.35 (*H*C═N). $^{13}C\{^1H\}$ NMR ($CDCl_3$, δ, ppm): 20.80 (*C*H_3CH$_2$), 23.76, 24.29, 27.28, 28.85 (*C*H_2 in cyclohexyl), 29.71, 29.93, 31.39, 31.45 ((*C*H_3)$_3$C), 33.95, 33.98, 35.58, 35.66 ((CH$_3$)$_3$*C*), 57.66 (H$_2$*C*−O), 62.63, 65.78 (H*C*−N), 118.15, 118.40, 127.29, 127.70, 129.66, 130.90, 137.53, 138.05, 140.66, 140.86, 162.42, 164.23 (phenyl), 162.86, 167.95 (H*C*═N). Anal. Calcd: C, 73.99; H, 9.31; N, 4.54. Found: C, 73.48; H, 9.33; N, 4.48.

Synthesis of (*S*,*S*)-Salen Aluminum Ethoxide. To a solution of (*S*,*S*-salen)H$_2$ (1.0 g, 1.8 mmol) in 20 mL of dichloromethane was added a solution of trimethylaluminum (AlMe$_3$, 2.0 M solution in hexane, 1.1 mL, 2.2 mmol), and the mixture was stirred for 3 h at room temperature. A yellow powder was obtained after the removal of volatile fractions under vacuum. The powder was redissolved in hexane, followed by the addition of 0.2 mL of ethanol (3.4 mmol), and stirred for 3 h. A yellow precipitate was obtained as the product in 73% yield. ^1H NMR ($CDCl_3$, δ, ppm): 0.85 (dd, C*H*$_3$−CH$_2$), 3.44 (m, CH$_3$C*H*$_2$), 1.29, 1.30, 1.52, 1.55 (s, C(C*H*$_3$)), 1.44, 2.06, 2.43, 2.58, 3.05, 3.83 (cyclohexyl), 6.99, 7.04, 7.48, 7.50 (aromatic), 8.15, 8.35 (*H*C═N). $^{13}C\{^1H\}$ NMR ($CDCl_3$, δ, ppm): 20.80 (*C*H_3CH$_2$), 23.76, 24.29, 27.28, 28.85 (*C*H_2 in cyclohexyl), 29.71, 29.93, 31.39, 31.45 ((*C*H_3)$_3$C), 33.95, 33.98, 35.58, 35.66 ((CH$_3$)$_3$*C*), 57.66 (H$_2$*C*−O), 62.63, 65.78 (H*C*−N), 118.15, 118.40, 127.29, 127.70, 129.66, 130.90, 137.53, 138.05, 140.65, 140.86, 162.42, 164.23 (phenyl), 162.86, 167.95 (H*C*═N). Anal. Calcd: C, 73.99; H, 9.31; N, 4.54. Found: C, 73.25; H, 9.24; N, 4.42.

Synthesis of (*R*,*R*-Salen)AlOCH$_2$CHMe$_2$. To a solution of (*R*,*R*-salen)H$_2$ (1.0 g, 1.8 mmol) in 20 mL of dichloromethane was added a solution of trimethylaluminum (AlMe$_3$, 2.0 M solution in hexane, 1.1 mL, 2.2 mmol), and the mixture was stirred for 3 h at room temperature. A yellow powder was obtained after the removal of volatile fractions under vacuum. The powder was redissolved in hexane, followed by the addition of 0.20 mL of 2-methyl-1-propanol (2.2 mmol), and stirred for 3 h at 50 °C. A yellow precipitate was obtained as the product in 64% yield. ^1H NMR ($CDCl_3$, δ, ppm): 0.52, 0.59 (d, d (C*H*$_3$)$_2$CH), 3.06, 3.15 (m, OC*H*$_2$), 1.32 (m, C*H*Me$_2$), 1.29 (d, C(C*H*$_3$)), 1.52 (d, C(C*H*$_3$)), 1.46, 2.06, 2.41, 2.58, 3.04, 3.82 (cyclohexyl), 6.98, 7.04, 7.47, 7.49 (aromatic), 8.15, 8.33 (*H*C═N). $^{13}C\{^1H\}$ NMR ($CDCl_3$, δ, ppm): 19.22, 19.24 ((*C*H$_3$)$_2$CH), 23.83, 24.30, 27.30, 28.84 (*C*H$_2$ in cyclohexyl), 29.73, 30.00, 31.39, 31.45 ((*C*H$_3$)$_3$C), 32.24 (H*C*−Me$_2$), 33.94, 33.98, 35.57, 35.65 ((CH$_3$)$_3$*C*), 62.72, 65.78 (H*C*−N), 70.14 (H$_2$*C*−O), 118.25, 118.42, 127.25, 127.63, 129.64, 130.81, 137.50, 138.01, 140.64, 140.83, 162.46, 164.21 (phenyl), 162.84, 167.92 (H*C*═N). Anal. Calcd: C, 74.50; H, 9.53; N, 4.34. Found: C, 73.75; H, 9.47; N, 4.33.

Synthesis of (*S*,*S*-Salen)AlOCH$_2$CHMe$_2$. To a solution of (*S*,*S*-salen)H$_2$ (1.0 g, 1.8 mmol) in 20 mL of dichloromethane was added a solution of trimethylaluminum (AlMe$_3$, 2.0 M solution in hexane, 1.1 mL, 2.2 mmol), and the mixture was stirred for 3 h at room temperature. A yellow powder was obtained after the removal of volatile fractions under vacuum. The powder was redissolved in hexane, followed by the addition of 0.20 mL of 2-methyl-1-propanol (2.2 mmol), and stirred for 3 h at 50 °C. A yellow precipitate was obtained as the product in 59% yield. ^1H NMR ($CDCl_3$, δ, ppm): 0.52, 0.59 (d, d (C*H*$_3$)$_2$CH), 3.06, 3.15 (m, OC*H*$_2$), 1.32 (m, C*H*Me$_2$), 1.29 (d, C(C*H*$_3$)), 1.53 (d, C(C*H*$_3$)), 1.46, 2.06, 2.42, 2.58, 3.05, 3.83 (cyclohexyl), 6.98, 7.04, 7.47, 7.49 (aromatic), 8.15, 8.33 (*H*C═N). $^{13}C\{^1H\}$ NMR ($CDCl_3$, δ, ppm): 19.22, 19.24 ((*C*H$_3$)$_2$CH), 23.81, 24.29, 27.29, 28.83 (*C*H$_2$ in cyclohexyl), 29.72, 30.00, 31.38, 31.45 ((*C*H$_3$)$_3$C), 32.23 (H*C*−Me$_2$), 33.94, 33.97, 35.57, 35.64 ((CH$_3$)$_3$*C*), 62.71, 65.77 (H*C*−N), 70.13 (H$_2$*C*−O), 118.24, 118.41, 127.24, 127.62, 129.63, 130.80, 137.50, 138.00, 140.63, 140.82, 162.46, 164.20 (phenyl), 162.83, 167.91 (H*C*═N). Anal. Calcd: C, 74.50; H, 9.53; N, 4.34. Found: C, 73.86; H, 9.37; N, 4.39.

Synthesis of (*R*,*R*-Salen)AlOCH$_2$CMe$_3$. To a solution of (*R*,*R*-salen)H$_2$ (1.0 g, 1.8 mmol) in 20 mL of dichloromethane was added a solution of trimethylaluminum (AlMe$_3$, 2.0 M solution in hexane, 1.1 mL, 2.2 mmol), and the mixture was stirred for 3 h at room temperature. A yellow powder was obtained after the removal of volatile fractions under vacuum. The powder was redissolved in hexane, followed by the addition of 0.20 g of neopentyl alcohol (2.2 mmol), and stirred for 12 h at 50 °C. A yellow precipitate was obtained as the product in 67% yield. ^1H NMR ($CDCl_3$, δ, ppm): 0.57 (s, (C*H*$_3$)$_3$CCH$_2$), 3.04 (m, OC*H*$_2$), 1.28, 1.30, 1.49, 1.55 (s, C(C*H*$_3$)), 1.44, 2.06, 2.41, 2.57, 3.04, 3.82 (cyclohexyl), 6.96, 7.04, 7.46, 7.49 (aromatic), 8.15, 8.32 (*H*C═N). $^{13}C\{^1H\}$ NMR ($CDCl_3$, δ, ppm): 26.52 ((*C*H$_3$)$_3$CCH$_2$O), 23.89, 24.35, 27.28, 28.97 (*C*H$_2$ in cyclohexyl), 29.70, 30.05, 31.40, 31.46 ((*C*H$_3$)$_3$CPh), 33.38 (OCH$_2$*C*Me$_3$), 33.93, 33.98, 35.55, 35.64 ((CH$_3$)$_3$*C*Ph), 62.69, 65.96 (H*C*−N), 73.50 (H$_2$*C*−O), 118.23, 118.47, 127.16, 127.59, 129.58, 130.75, 137.29, 137.90, 140.65, 140.83, 162.37, 164.33 (phenyl), 162.51, 168.14 (H*C*═N). Anal. Calcd: C, 74.73; H, 9.64; N, 4.25. Found: C, 73.85; H, 9.56; N, 4.26.

Synthesis of (*S*,*S*-Salen)AlOCH$_2$CMe$_3$. To a solution of (*S*,*S*-salen)H$_2$ (1.0 g, 1.8 mmol) in 20 mL of dichloromethane was added a solution of trimethylaluminum (AlMe$_3$, 2.0 M solution in hexane, 1.1 mL, 2.2 mmol), and the mixture was stirred for 3 h at room temperature. A yellow powder was obtained after the removal of volatile fractions under vacuum. The powder was redissolved in hexane, followed by the addition of 0.20 g of neopentyl alcohol (2.2 mmol), and stirred for 12 h at 50 °C. A yellow precipitate was obtained as the product in 71% yield. ^1H NMR ($CDCl_3$, δ, ppm): 0.57 (s, (C*H*$_3$)$_3$CCH$_2$), 2.99 (m, OC*H*$_2$), 1.28, 1.30, 1.49, 1.55 (s, C(C*H*$_3$)), 1.44, 2.06, 2.41, 2.57, 3.04, 3.82 (cyclohexyl), 6.96, 7.04, 7.46, 7.48 (aromatic), 8.15, 8.32 (*H*C═N). $^{13}C\{^1H\}$ NMR ($CDCl_3$, δ, ppm): 26.52 ((*C*H$_3$)$_3$CCH$_2$O), 23.89, 24.35, 27.29, 28.97 (*C*H$_2$ in cyclohexyl), 29.71, 30.05, 31.40, 31.46 ((*C*H$_3$)$_3$CPh), 33.38 (OCH$_2$*C*Me$_3$), 33.93, 33.98, 35.55, 35.64 ((CH$_3$)$_3$*C*Ph), 62.69, 65.96 (H*C*−N), 73.51(H$_2$*C*−O), 118.23, 118.48, 127.17, 127.60, 129.58, 130.75, 137.29, 137.90, 140.66, 140.83, 162.37, 164.33 (phenyl), 162.52, 168.14 (H*C*═N). Anal. Calcd: C, 74.73; H, 9.64; N, 4.25. Found: C, 73.77; H, 9.53; N, 4.24.

Synthesis of (*R*,*R*-Salen)AlOCH$_2$C(S)HMeCl. To a solution of (*R*,*R*-salen)H$_2$ (1.0 g, 1.8 mmol) in 20 mL of dichloromethane was added a solution of trimethylaluminum (AlMe$_3$, 2.0 M solution in hexane, 1.1 mL, 2.2 mmol), and the mixture was stirred for 3 h at room temperature. A yellow powder was obtained after the removal of volatile fractions under vacuum. The powder was redissolved in hexane, followed by the addition of 0.19 mL of (*S*)-2-chloro-1-propanol (2.2 mmol), and stirred for 3 h. A yellow precipitate was obtained as the product in 75% yield. Crystals of this complex were obtained by slow evaporation of the solvent from a concentrated benzene solution of the complex. ^1H NMR ($CDCl_3$, δ, ppm): 1.17 (d, C*H*$_3$−CHCl), 3.40, 3.50 (m, OC*H*$_2$), 3.68 (m, C*H*Cl), 1.29 (d, C(C*H*$_3$)), 1.51 (d, C(C*H*$_3$)), 1.44, 2.07, 2.43, 2.58, 3.06, 3.90 (cyclohexyl), 7.00, 7.05, 7.48, 7.51 (aromatic), 8.17, 8.35 (*H*C═N). $^{13}C\{^1H\}$ NMR ($CDCl_3$, δ, ppm): 21.43 (*C*H$_3$CH), 23.75, 24.27, 27.27, 28.80 (*C*H$_2$ in cyclohexyl), 29.67, 29.94, 31.36, 31.43 ((*C*H$_3$)$_3$C), 33.96, 33.99, 35.56, 35.64 ((CH$_3$)$_3$*C*), 61.10, 62.64 (H*C*−N), 65.86 (H*C*−Cl), 69.25 (H$_2$*C*−O), 118.12, 118.35, 127.37, 127.75, 129.84, 131.11, 137.82, 138.29, 140.59, 140.79, 162.27, 163.92 (phenyl), 163.02, 168.19 (H*C*═N). Anal. Calcd: C, 70.41; H, 8.79; N, 4.21. Found: C, 69.16; H, 8.44; N, 4.03.

Synthesis of (*S*,*S*-Salen)AlOCH$_2$C(S)HMeCl. To a solution of (*S*,*S*-salen)H$_2$ (1.0 g, 1.8 mmol) in 20 mL of dichloromethane was added a solution of trimethylaluminum (AlMe$_3$, 2.0 M solution in hexane, 2.2 mL, 2.2 mmol), and the mixture was stirred for 3 h at room temperature. A yellow powder was obtained after the removal of volatile fractions under vacuum. The powder was redissolved in hexane, followed by the addition of 0.19 mL of (*S*)-2-chloro-1-propanol (2.2 mmol), and stirred for 3 h. A yellow precipitate was obtained as the product in 70% yield. Crystals of this complex were obtained by slow evaporation of the solvent from a concentrated benzene solution of the complex. ^{1}H NMR (CDCl$_3$, δ, ppm): 1.22 (d, C*H*$_3$−CHCl), 3.46 (m, OC*H*$_2$), 3.69 (m, C*H*Cl), 1.29 (d, C(C*H*$_3$)), 1.52 (d, C(C*H*$_3$)), 1.44, 2.06, 2.43, 2.58, 3.06, 3.93 (cyclohexyl), 7.00, 7.05, 7.48, 7.51 (aromatic), 8.17, 8.36 (*H*C═N). ^{13}C{^{1}H} NMR (CDCl$_3$, δ, ppm): 21.40 (*C*H$_3$CH), 23.78, 24.30, 27.28, 28.74 (*C*H$_2$ in cyclohexyl), 29.67, 29.97, 31.38, 31.43 ((*C*H$_3$)$_3$C), 33.97, 34.00, 35.57, 35.65 ((CH$_3$)$_3$*C*), 61.52 (H*C*−Cl), 62.55, 65.87(H*C*−N), 69.56 (H$_2$*C*−O), 118.18, 118.33, 127.41, 127.79, 129.84, 131.05, 137.75, 138.33, 140.54, 140.83, 162.19, 164.00 (phenyl), 163.00, 168.28 (H*C*═N). Anal. Calcd: C, 70.41; H, 8.79; N, 4.21. Found: C, 69.64; H, 8.73; N, 4.02.

Ring-Opening Reactions of 1 Equiv of Lactides. Twenty milligrams of lactide (L or *rac*, 0.14 mmol) and 5 mg of (salen)AlOCH$_2$R (∼0.008 mmol) were dissolved in 1 mL of solvent in a J-Young NMR tube and allowed to react at room temperature for 12 h to 3 days for completion. The solvent was removed under vacuum, and the resulting mixture was redissolved in 1 mL of CDCl$_3$ for ^{1}H NMR measurement. The products in the reaction of L-lactide and each (salen)AlOCH$_2$R complex were analyzed by ^{1}H NMR as references for identifying products in the reactions involving *rac*-lactide.

Coordination of *rac*-Lactide to (*R*,*R*-Salen)AlONp. (*R*,*R*-Salen)AlONp (25 mg, 0.038 mmol) and *rac*-lactide (5.1 mg, 0.035 mmol) were dissolved in 0.6 mL of CDCl$_3$ and monitored using ^{1}H NMR spectroscopy. A small amount of L-lactide was added to the solution, and a ^{1}H NMR spectrum was obtained to differentiate L,D-lactide resonances. L,D-Lactide. ^{1}H NMR (500 MHz, CDCl$_3$, δ, ppm): 1.62 (d, C*H*$_3$ of D-LA), 1.63 (d, C*H*$_3$ of L-LA), 4.98 (q, C*H* of D-LA), 4.99 (q, C*H* of L-LA).

Alcoholysis. To a 0.029 M solution of (*R*,*R*-salen)AlOEt (11 mg, 0.018 mmol) in CDCl$_3$ (0.6 mL) were added aliquots of a 0.17 M ethanol solution in CDCl$_3$ via microsyringe, and the reaction was monitored using ^{1}H NMR spectroscopy. Selected ^{1}H NMR resonances are listed. **(*R*,*R*-Salen)AlOEt**. ^{1}H NMR (500 MHz, CDCl$_3$, δ, ppm): 0.85 (dd, C*H*$_3$CH$_2$O), 3.45 (m, CH$_3$C*H*$_2$O). **Ethanol**. ^{1}H NMR (500 MHz, CDCl$_3$, δ, ppm): 1.20 (t, C*H*$_3$CH$_2$OH), 3.68 (m, CH$_3$C*H*$_2$OH).

To a 0.025 M solution of (*R*,*R*-salen)AlONp (10 mg, 0.015 mmol) in CDCl$_3$ (0.6 mL) were added aliquots of a 0.17 M ethanol solution in CDCl$_3$ via microsyringe, and the reaction was monitored using ^{1}H NMR spectroscopy. Selected ^{1}H NMR resonances are listed. **(*R*,*R*-Salen)AlONp**. ^{1}H NMR (500 MHz, CDCl$_3$, δ, ppm): 0.57 (s, (C*H*$_3$)$_3$CCH$_2$O), 3.04 (m, (CH$_3$)$_3$CC*H*$_2$O). **Neopentanol**. ^{1}H NMR (500 MHz, CDCl$_3$, δ, ppm): 0.88 (s, (C*H*$_3$)$_3$CCH$_2$OH), 3.26 (d, (C*H*$_3$)$_3$CCH$_2$OH).

Chain-End Exchange Reaction. A 0.07 M CDCl$_3$ solution (0.5 mL) of (*R*,*R*-salen)Al(L-LA)ONp (0.035 mmol) was added to a 0.07 M CDCl$_3$ solution (0.5 mL) of (*S*,*S*-salen)Al(D-LA)ONp (0.035 mmol) at room temperature, and the reaction was monitored using ^{1}H NMR spectroscopy. The reaction of (*R*,*R*-salen)Al(D-LA)ONp and (*S*,*S*-salen)Al(L-LA)ONp was similarly run. **(*R*,*R*-Salen)Al(L-LA)ONp/(*S*,*S*-salen)Al(D-LA)ONp**. ^{1}H NMR (500 MHz, CDCl$_3$, δ, ppm): 0.57 (s, (C*H*$_3$)$_3$CCH$_2$), 1.19 (d, AlOCH(C*H*$_3$)C(O)−), 1.21 (d, −OCH(C*H*$_3$)C(O)ONp), 1.29, 1.30, 1.52, 1.54 (s, C(C*H*$_3$)), 2.05, 2.45, 2.58, 3.05, 4.05 (cyclohexyl), 3.74 (m, (C*H*$_3$)$_3$CC*H*$_2$), 4.24 (q, AlOC*H*(CH$_3$)C(O)−), 4.85 (q, −OC*H*(CH$_3$)C(O)ONp), 7.00, 7.05, 7.48, 7.49 (aromatic), 8.17, 8.37 (*H*C═N). **(*R*,*R*-Salen)Al(D-LA)ONp/(*S*,*S*-salen)Al(L-LA)ONp**. ^{1}H NMR (500 MHz, CDCl$_3$, δ, ppm): 0.61 (s, (C*H*$_3$)$_3$CCH$_2$), 1.18 (d, AlOCH(C*H*$_3$)C(O)−), 1.21 (d, −OCH(C*H*$_3$)C(O)ONp), 1.29, 1.30, 1.52, 1.56 (s, C(C*H*$_3$)), 2.04, 2.43, 2.52, 3.02, 4.30 (cyclohexyl), 3.74 (m, (C*H*$_3$)$_3$CC*H*$_2$), 4.26 (q, AlOC*H*(CH$_3$)C(O)−), 4.73 (q, −OC*H*(CH$_3$)C(O)ONp), 6.98, 7.06, 7.47, 7.51 (aromatic), 8.15, 8.30 (*H*C═N).

Trans-esterification Study. (*R*,*R*-Salen)AlOEt (22 mg, 0.035 mmol) and L-lactide (2.4 mg, 0.017 mmol) were added to a J-Young NMR tube and dissolved in 0.6 mL of CDCl$_3$. The reaction was monitored using ^{1}H NMR spectroscopy over a period of days at room temperature. The reaction temperature was then increased to 75 °C, and the reaction was monitored using ^{1}H NMR spectroscopy over a period of weeks. **(*R*,*R*-Salen)Al(L-LA)OEt**. ^{1}H NMR (500 MHz, CDCl$_3$, δ, ppm): 1.15 (d, AlOCH(C*H*$_3$)C(O)−), 1.17 (dd, C*H*$_3$CH$_2$O−), 1.27 (d, −OCH(C*H*$_3$)C(O)OEt), 1.29, 1.30, 1.54, 1.55 (s, C(C*H*$_3$)), 2.05, 2.45, 2.59, 3.05, 4.04 (cyclohexyl), 4.07 (q, CH$_3$C*H*$_2$-O−), 4.24 (q, AlOC*H*(CH$_3$)C(O)−), 4.78 (q, −OC*H*(CH$_3$)C-(O)OEt), 7.00, 7.05, 7.48, 7.49 (aromatic), 8.16, 8.37 (*H*C═N). **(*R*,*R*-Salen)AlOCHMeC(O)OEt**. ^{1}H NMR (500 MHz, CDCl$_3$, δ, ppm): 1.04 (dd, C*H*$_3$CH$_2$O−), 1.11 (d, −OCH(C*H*$_3$)C(O)OEt), 1.28, 1.29 (s, C(C*H*$_3$)), 1.51, 1.52 (s, C(C*H*$_3$)), 2.05, 2.39, 2.59, 3.05, 3.99 (cyclohexyl), 3.89 (mult, CH$_3$C*H*$_2$O−), 4.12 (q, −OC*H*(CH$_3$)C(O)OEt), 6.99, 7.04, 7.47, 7.48 (aromatic), 8.14, 8.37 (*H*C═N).

Ring-Opening Polymerization Reactions of *rac*-Lactide by the (Salen) Aluminum Catalysts. Typically (salen)AlOCH$_2$R (20 mg, 0.03 mmol) and *rac*-lactide (0.45 g, 3.1 mmol) were allowed to react in 15 mL of toluene at 80 °C for 10 days, yielding polylactide with 40% conversion. The obtained polymers were analyzed by NMR and GPC (M_n = 9000−11 000 Da, PDI = 1.13−1.16).

Competing Reaction between (*R*,*R*)-2 and (*S*,*S*)-2 with L-Lactide. (*R*,*R*)-**2** (10.2 mg, 0.016 mmol), (*S*,*S*)-**2** (10.2 mg, 0.016 mmol), and L-lactide (2 mg, 0.014 mmol) were dissolved in 1 mL of toluene in a J-Young NMR tube. The lactide was completely consumed after 20 h at room temperature. The reaction mixture was dried under vacuum and analyzed by ^{1}H NMR (CDCl$_3$). After that, CDCl$_3$ was removed under vacuum, and the mixture was then redissolved in toluene and placed in an oil bath at 80 °C. The reaction mixture was monitored by ^{1}H NMR with time.

Monitoring the Polymerization Reactions by Gas Chromatography. (*S*,*S*-Salen)AlOCH$_2$CHMe$_2$ (0.13 g, 0.2 mmol) and *rac*-lactide (1.44 g, 10.0 mmol) were allowed to react in 70 mL of toluene at room temperature for 12 h for initiation, and afterward, the temperature was increased to 80 °C for chain propagation. During the reaction, 2 mL aliquots were taken for analysis. The conversions were determined by ^{1}H NMR. After the removal of solvent from the aliquot, the monomer residue was separated and collected from the reaction mixture by sublimation under reduced pressure and was analyzed by chiral capillary gas chromatography.

(*S*,*S*-Salen)AlOCH$_2$CHMe$_2$ (0.046 g, 0.07 mmol) and *rac*-lactide (0.31 g, 2.2 mmol) were allowed to react in 25 mL of toluene at room temperature for 12 h for initiation. Afterward, 0.21 g of L-lactide (1.5 mmol) was added into the reaction system to make

L/D = 70/30, and the temperature was increased to 80 °C for chain propagation. The reaction was monitored as above.

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Supporting Information Available: Experimental section. ^{13}C NMR of PLA formed in the polymerization reaction of 70:30 L:D-lactide by employing (*S*,*S*)-**2**. ^{1}H NMR spectra of the exchange reactions. Crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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