Defining Stereochemistry in the Polymerization of Lactide by Aluminum Catalysts: Insights into the Dual-Stereocontrol Mechanism

Appie Peterson,[‡] Rami Hador,[◊] Maren Pink,[†] Yanay Popowski,[‡] Moshe Kol,[◊,*] and William B. Tolman[‡,*]

[‡]Department of Chemistry, Washington University in St. Louis, Campus Box 1134, 1 Brookings Drive, St. Louis, MO 63130, USA. [◊]School of Chemistry, Tel Aviv University, Ramat Aviv, Tel Aviv 69997801, Israel. [†]Indiana University Molecular Structure Center, 800 East Kirkwood Ave, Bloomington, IN 47405, USA.

KEYWORDS. Polymerization, catalysis, lactide, stereochemistry, mechanisms

ABSTRACT: Aspects of the proposed pathway combining chain-end and enantiomorphic site control for the stereospecific polymerization of lactide (LA) were investigated through studies of aluminum complexes supported by enantiopure and racemic bipyrrolidine-based salan ligands, Lig[1]AlOBn and Lig[2]AlOBn. Spectroscopic analysis of stoichiometric initiation reactions and the definition of the stereochemistry of the selective formation of the "match" single-insertion products by X-ray crystallography led to key conclusions about the observed stereocontrol. Notably, it was determined to rely heavily on the preference for the trio of stereocenters around the metal to have a "match" formation (*RR*-ligand + *S*-polymer), which works synergistically with the enantiomorphic site preference of the catalyst to ring-open next to a stereocenter of a monomer of the same chirality as that of the ligand, resulting in highly heterotactic or syndiotactic PLA from *rac*- or *meso*-LA, respectively.

INTRODUCTION

Polylactide (PLA) is an attractive alternative to fossil-fuel based commodity plastics due to its renewable origins, degradability, and wide range of physical properties that are critically impacted by stereochemistry (tacticity).[1] Control of PLA tacticity may be achieved through stereoselective ring-opening polymerization (ROP) of *rac*- or *meso*-lactide (LA).[2] Among the common metal-alkoxide catalysts, stereocontrol in ROP of *rac*-LA afforded by aluminum catalysts ligated by chiral binapthyl Schiff base ligands[3-6] or sterically bulky achiral salen ligands[7] has drawn particular attention. Stereoselective ROP of *meso*-LA by metal-based catalysts also has been reported.[4,5,8-12]

Aluminum catalysts are ideal for mechanistic investigation as they often proceed with rates that are convenient to monitor by conventional spectroscopic methods, and operate via the well-established coordination-insertion mechanism whereby the LA monomer is coordinated to the metal center via σ-donation from an oxygen lone pair, followed by ring-opening by nucleophilic attack of the catalyst alkoxide (an initiating group or propagating polymer chain) on the electron deficient adjacent carbonyl. Stereoselective sequential monomer enchainment can be governed by chain-end control (CEC), whereby the stereochemistry of a given monomer inserted into the metal center determines the stereochemistry of the next monomer inserted, or enantiomorphic site control (ESC), whereby the chirality of the ligand framework surrounding the metal center selects the stereochemistry of all subsequent monomers selected. Both mechanisms of control are presumed to contribute to some degree to every stereoselective polymerization, with one mechanism generally dominating.[1,2]

Enantiopure binaphthyl[4,5] or bipyrrolidine[12] aluminum catalysts have been shown to stereoselectively polymerize *meso*-LA to yield highly crystalline syndiotactic PLA (Figure 1a). The results were rationalized by invoking the effects of the chirality afforded to the metal center from the ligands driving preference for the ring-opening of *meso*-LA at only one of its acyl-oxygen sites ("match" insertion). However, in the polymerization of *meso*-LA by *racemic* binaphthyl-aluminum catalysts, the resulting PLA is heterotactic (P_r = 0.8). This finding was rationalized by a proposed rapid exchange of lactidyl units between enantiomers of catalyst, which then ring open *meso*-LA at acyl-oxygen sites with proximal stereocenters identical to those inherent in the ligand (Figure 1b).

For the bipyrrolidine system, heterotactic PLA (P_r = 0.93-0.99) was obtained from the polymerization of *rac*-LA with *rac*-catalyst, and a similar mechanism of lactidyl exchange between enantiomers of catalyst was postulated to rationalize the results. A "match" combination of the trio of stereocenters proximal to the aluminum center (ex. (*R*,*R*)-LigAl-L(*S*,*S*)-LA) was proposed to be active towards ring-opening a monomer of the opposite chiral sense to that of the chain-end (in this case D(*R*,*R*)-LA), which would result in a "mismatch", which here is (*R*,*R*)-LigAl-D(*R*,*R*)-LA. In a polymerization with both enantiomers of catalyst present, lactidyl exchange between two "mismatch" complexes (ex. (*R*,*R*)-LigAl-D(*R*,*R*)-LA and (*S*,*S*)-LigAl-L(*S*,*S*)-LA) would generate "match" complexes, which were proposed to have higher activity towards ROP than the "mismatch" complexes (Figure 2). The observation that polymerizations of *rac*-LA by enantiopure bipyrrolidine catalysts were slower and less

stereocontrolled than with racemic catalysts was invoked as evidence that the "mismatch" (ex. (*R,R*)-LigAl-D(*R,R*)LA-OBn) is "inactive towards any lactide".[12] Gas-chromatographic (GC) analysis of the remaining monomer from the polymerizations of *rac*-LA with enantiopure Lig[1] or Lig[2]AlOBn revealed a preference for (*R,R*) catalyst to ring-open D(*R,R*)-LA, and vice versa for (*S,S*) catalyst, which suggested that these complexes operate by an enantiomorphic site control mechanism in the absence of another enantiomer of catalyst.

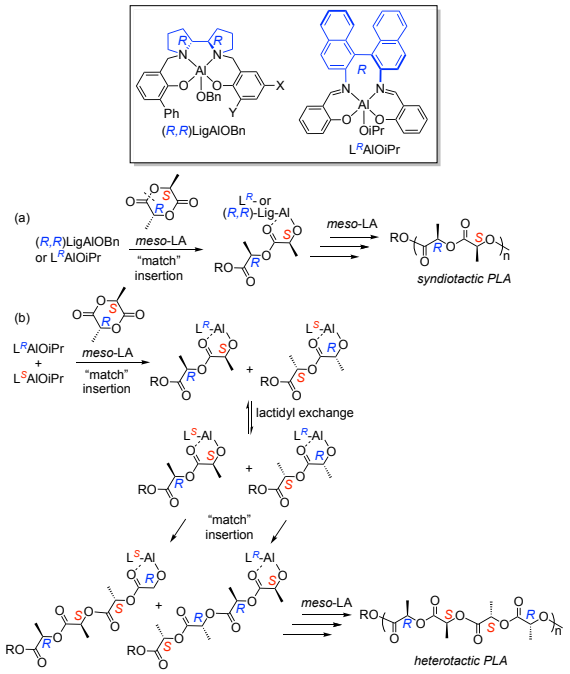

Figure 1. Proposed mechanisms of stereoselective polymerization of *meso*-LA using chiral aluminum-alkoxide catalysts (in box; "Lig" refers to Lig[1] = X = H, Y = Ph or Lig[2] = X = Y = Cl), showing (a) formation of syndiotactic PLA from enantiopure catalysts via stereoselective insertions, and (b) formation of heterotactic PLA from racemic catalyst via stereoselective insertions and lactidyl exchanges.

Herein, we present the results of an investigation of the "dual-stereocontrol" mechanism (Figures 1 and 2) proposed for the chiral bipyrrolidine catalysts. According to this mechanism, a combination of chain-end and enantiomorphic site control defines the stereochemistry of the growing chain, whereby the combination of the catalyst's chirality *and* the proximal stereogenic center of the last inserted monomer preferentially ring-open an incoming monomer with a proximal stereogenic center of the *opposite* chirality. We sought to isolate and assign the exact stereochemistry of the "match" and "mismatch" complexes and examine their reactivities through studies of initiation (stoichiometric ring-opening of LA stereoisomers). This approach was used previously to understand ROP by complexes of indolide ligands related to salen.[13] A key finding from this previous study is that ring-opening stereochemistry is derived from differences in thermodynamic stability of rapidly interconverting diastereomeric complexes. Here, we evaluate the involvement of stereoisomer interconversion between catalytic aluminum centers via lactidyl exchange in the ring opening of *rac*- and *meso*-LA by the bipyrrolidine catalysts. Ultimately, we aimed to obtain fundamental chemical insights into the nature of stereocontrolled ROP of lactide by highly selective catalysts.

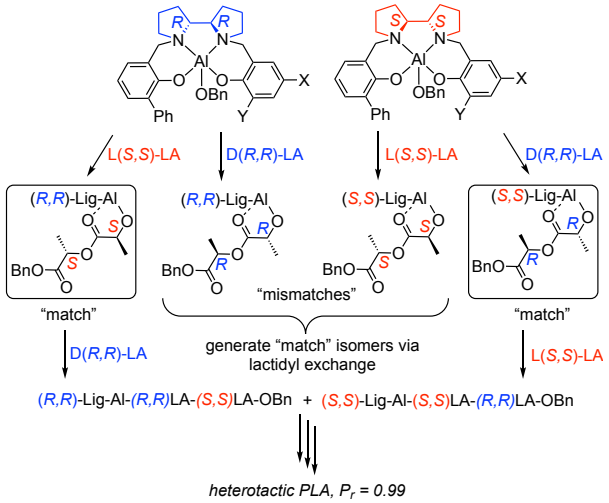

Figure 2. Proposed mechanism for stereoselective ROP of *rac*-LA to yield heterotactic PLA using *rac*-LigAlOBn.

RESULTS AND DISSCUSSION

Initiation Studies with Enantiopure LigAlOBn Complexes and D, L, or rac-Lactide. As in the previous study,[13] stereoselectivity in initiation was explored as a model for stereocontrol in LA polymerization, here by the complexes supported by Lig[1] (X = H, Y = Ph) and Lig[2] (X = Y = Cl). Enantiopure (*R,R*)- and (*S,S*)-Lig[1]AlOBn and Lig[2]AlOBn (Figure 2) were prepared according to reported methods.[12] In a first round of experiments, focusing only on ligands with *R,R* stereocenters, (*R,R*)-Lig[1]AlOBn and (*R,R*)-Lig[2]AlOBn were separately mixed with 1 equivalent of D(*R,R*)-, L(*S,S*)-, or *rac*-LA at room temperature in CD_2Cl_2.

Monitoring of the reactions of (*R,R*)-Lig[1]AlOBn with enantiopure D(*R,R*)-LA (Table 1, entry 1) or L(*S,S*)-LA (Table 1, entry 2) by ^{1}H NMR spectroscopy (using 2D NMR analysis to make assignments, Figures S1-S8) showed conversion of the starting complex to a single new species in each case, and the data showed differences consistent with these species being diastereomers. For example, the peaks associated with the AlOC$\underline{H}_2$Ph protons in (*R,R*)-Lig[1]AlOBn sharpen and migrate from their original position at 5.14 ppm to 5.08 ppm in the reaction with L(*S,S*)-LA (Figures S1 and S9, bottom spectrum), and to 4.95 ppm and 4.63 ppm in the reaction with D(*R,R*)-LA (Figures S5 and S9, middle spectrum). Doublets arising from methyl C$\underline{H}_3$ protons on the ring-opened lactide units arise at 1.22 ppm and 1.13 ppm in the reaction with L(*S,S*)-LA and at 1.37 ppm and 1.14 ppm in the reaction with D(*R,R*)-LA. Also, there are significant qualitative differences

Table 1. Results of 1:1 Monomer:LAlOBn Experiments

Entry	Catalyst	Monomer	Conversion (%)[a]	Time (h)	"Match": "Mismatch"	% d.e.[b]	k_{rel}[c]
1	*R,R*-Lig[1]AlOBn	D(*R,R*)-LA	81	22	--	--	--
2	*R,R*-Lig[1]AlOBn	L(*S,S*)-LA	70	22	--	--	--
3	*R,R*-Lig[1]AlOBn	*rac*-LA	42; 83	2; 21	1:2.6; 1:1.4	44; 17	3.5; 2.9
4	*rac*-Lig[1]AlOBn	*rac*-LA	36; 78	0.17; 5	5:1; 5:1	67; 67	7.3; [d]
5	*R,R*-Lig[1]AlOBn	*meso*-LA	44; 82	0.08; 1	5:1; 5:1	67; 67	8.5; [d]
6	*R,R*-Lig[2]AlOBn	D(*R,R*)-LA	75	22	--	--	--
7	*R,R*-Lig[2]AlOBn	L(*S,S*)-LA	57	22	--	--	--
8	*R,R*-Lig[2]AlOBn	*rac*-LA	54; 77	1; 20	1:1.1; 1:2.1	5; 35	1.2; [d]
9	*rac*-Lig[2]AlOBn	*rac*-LA	56; 79	0.17; 5	3:1; 3:1	50; 50	5.6; [d]
10	*R,R*-Lig[2]AlOBn	*meso*-LA	75; 84	0.08; 1	[e]	[e]	[e]

Conditions: $[LigAlOBn]_i = [LA]_i = 0.017$ M in CD_2Cl_2, $T = 21$ °C [a]calculated from ^{1}H NMR integrations [b]$d.e. = \frac{(a-b)}{(a+b)}$ where a = major diastereomer, b = minor diastereomer [c] $k_{rel} = \frac{\ln[1-c(1+de)}{\ln[1-c(1-de)}$ where c = conversion,[1] [d]imaginary number, equation is not applicable to high conversions and high d.e.'s [e]not able to quantify due to significant peak overlap between diastereomers

in the aromatic (8.0-6.5 ppm) regions of the ^{1}H NMR spectra of the reaction products (Figure 3 and S9). On the basis of the NMR data, we assign the products of the reactions as diastereomeric ring-opened products (*R,R*)-Lig[1]Al-D(*R,R*)LA-OBn and (*R,R*)-Lig[1]Al-L(*S,S*)LA-OBn (Figure 3). Note that the apparent sensitivity of the aromatic protons of the bipyrrolidine-based ligand to the proximal stereocenter of the ring-opened lactide unit provides a distinct "thumbprint" region (8.0-6.5 ppm) in the ^{1}H NMR spectra that enables clear identification of diastereomeric initiation products (*vide infra*).

The conversion in the reaction of (*R,R*)-Lig[1]AlOBn with D(*R,R*)-LA was slightly higher than in the reaction with

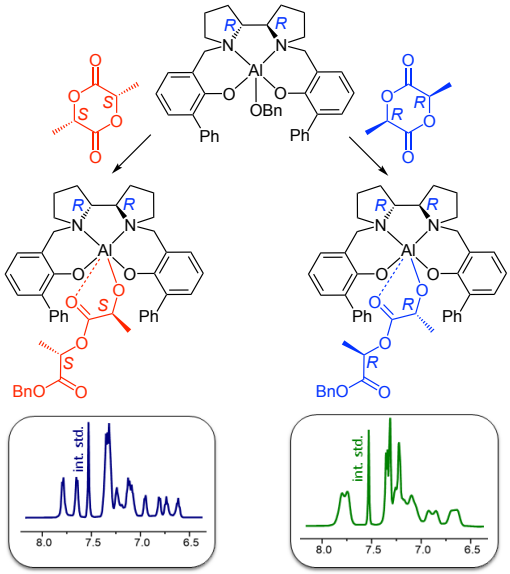

Figure 3. Products of the reaction of (*R,R*)-Lig[1]AlOBn with D(*R,R*)-LA (right), and L(*S,S*)-LA (left) in CD_2Cl_2 after 22 h, showing aromatic "thumbprint" region of ^{1}H NMR spectra.

L(*S,S*)-LA (81% vs. 70%, ratio of 1.16:1, after 22 h). A mixture of the two products was observed in the reaction of (*R,R*)-Lig[1]AlOBn with equimolar *rac*-LA (Table 1, entry 3), with a similar preference: after 2 h, 42% of the free *rac*-LA was consumed and the ratio of (*R,R*)-Lig[1]Al-D(*R,R*)LA-OBn ("mismatch"):(*R,R*)-Lig[1]Al-L(*S,S*)LA-OBn ("match") was 2.6:1, which diminished after 21 h at which point 83% of the free *rac*-LA was consumed to a 1.4:1 ratio (Figure S9, top spectrum).[xiv] Exchange spectroscopy (EXSY) experiments on the product solution from the reaction of *rac*-Lig[1]AlOBn with L(*S,S*)-LA showed cross-peaks indicative of rapid equilibration between the two diastereomeric initiation products (Figures S10-S11). These data are consistent with lactidyl exchange, a key element of the dual stereocontrol hypothesis.

Analogous results were observed in the reactions of (*R,R*)-Lig[2]AlOBn with D(*R,R*)-, L(*S,S*)-LA, and *rac*-LA (Table 1, entries 6-8, Figures S12-S17), with the level of stereoselectivity in ring-opening being slightly greater for this system. Thus, after 22 h, 75% of D(*R,R*)-LA and 57% of L(*S,S*)-LA reacted, a 1.3:1 conversion ratio, while the product ratio in the reaction with *rac*-LA was 2.1:1 after 77% conversion. While we hesitate to overinterpret the difference between these two ratios that are based on conversion values and relative integrations that have significant inherent errors associated with them, the preference for (*R,R*) ligated complexes to ring-open D(*R,R*)-LA ("mismatch") aligns with the hypothesis that (*R,R*)-LigAl-OR preferentially inserts at the acyl-carbon proximal to an *R* stereocenter, in accordance with enantiomorphic site control, a result with ramifications for the polymerization of *meso*-LA (*vide infra*).

We were able to confirm the structural hypotheses based on NMR spectroscopy through determination of the X-ray crystal structure of the product derived from the reaction of (*R,R*)-Lig^{2}AlOBn with L(*S,S*)-LA (Figure 4). Crystals suitable for X-ray diffraction were grown by layer diffusion of a concentrated toluene solution with pentane at room temperature. The complex crystallizes in a chiral space group ($P2_12_12_1$) and the asymmetric unit comprises the entire complex with two molecules of toluene (solvent of crystallization). The structure features a distorted octahedral geometry for the aluminum center, with a weak interaction with the proximal carbonyl oxygen (O4) of the lactidyl ligand to yield what is effectively bidentate coordination. The Al-O4 distance (3.20 Å) is longer than all other metal-ligand bonds (Table S1) and is 1.0-1.4 Å longer than other aluminum-carbonyl oxygen bonds reported for comparable ring-opened lactide or methyl-lactate structures.[7,13,xv-xxii] The remaining metal-ligand bond distances and angles are all very similar to those of (*R,R*)-Lig^{2}AlOBn,[12] save for N1-Al-O3, which is increased from 12(9)° to 13(9)° to accommodate the backbiting carbonyl (O4). Overall, the X-ray structure confirms the connectivity and stereochemistry of one of the ring-opened products of initiation by an enantiopure starting complex and validates the applicability of the NMR characterization protocol.

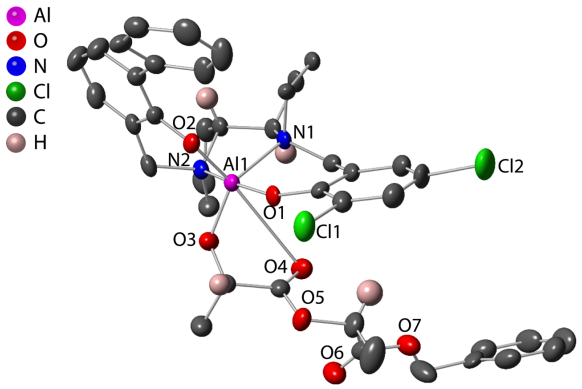

Figure 4. Representation of the X-ray crystal structure of the ring-opened product (*R,R*)-Lig^{2}Al-L(*S,S*)LA-OBn resulting from the reaction of (*R,R*)-Lig^{2}AlOBn with 1 equivalent of L(*S,S*)-LA. All nonhydrogen atoms are presented as 50% thermal ellipsoids; pink spheres are H atoms on stereogenic centers. The asymmetric unit consists of the entire ring-opened complex with two molecules of toluene, omitted here along with non-stereocenter associated hydrogen atoms for clarity. Selected bond distances (Å) and angles (deg): Al-O1, 1.808(1); Al-N1, 2.081(6); Al-N2, 2.066(2); Al-O2, 1.775(6); Al-O3, 1.757(3); Al-O4, 3.19(8); N2-Al-O1, 166.(4); N1-Al-O3, 139.(5); O2-Al-O3, 112.(4); O3-Al-O4,

Initiation Studies with Racemic LigAlOBn Complexes and Racemic Lactide. A key finding from the original report was that reaction of *rac*-Lig^{1}AlOBn with *rac*-LA (100 equiv.) at 50 °C in toluene resulted in highly stereoregular heterotactic PLA (P_r = 0.99).[12] To explain this result, it was hypothesized that rapid polymeryl exchange between (*R,R*)- and (*S,S*)-catalysts occurs, allowing for regeneration of the "match" (*R,R*-catalyst with proximal stereocenter *S*-polymer, or vice versa) before error propagation (sequential insertions of monomers bearing the same chiral sense, i.e. *meso* rather than *racemic* enchainments). We aimed to test this hypothesis by examining the stoichiometric reaction of *rac*-Lig^{1}AlOBn with *rac*-LA in CD_2Cl_2 at room temperature (Table 1, entry 4).

Consumption of starting materials proceeded, and a new set of new peaks appeared (78% conversion after 5h; Figures S19-S20). The data suggest that of the four stereoisomers that are possible ring-opened products, one diastereomer (pair of enantiomers) is favored (ratio of 5:1, 67% d.e.) over the other. This favored diastereomer was identified by comparison of the ^{1}H NMR spectrum with those of the previously characterized products of the reactions of (*R,R*)-Lig^{1}AlOBn with enantiopure D(*R,R*)-LA or L(*S,S*)-LA (Figure S20). Differences between the three spectra are subtle in the aliphatic region (5.0-2.5 ppm) due to the broad peaks arising from protons associated with the bipyrrolidine backbone. However, inspection of the "thumbprint" aromatic region (8.0-6.5 ppm) reveals that this spectral region for the reaction of *rac*-Lig^{1}AlOBn with *rac*-LA (Figure 5, bottom) and that from the reaction of (*R,R*)-Lig^{1}AlOBn with L(*S,S*)-LA ("match" complex, Figure 3, left) are nearly identical. Thus, we assign the predominant species in the reaction of *rac*-Lig^{1}AlOBn with *rac*-LA as (*R,R*)-Lig^{1}Al-L(*S,S*)LA-OBn and its enantiomer (*S,S*)-Lig^{1}Al-D(*R,R*)LA-OBn (both "match" complexes, in boxes in Figure 5).

The reaction of *rac*-Lig^{2}AlOBn and a stoichiometric amount of *rac*-LA in CD_2Cl_2 proceeded similarly (Table 1, entry 9, Figures S21-S22), with appearance of a set of peaks in the NMR spectrum interpreted analogously to indicate formation of a major ring-opened diastereomer that we attribute to the "match" enantiomers (*R,R*)-Lig^{2}Al-L(*S,S*)LA-OBn and (*S,S*)-Lig^{2}Al-D(*R,R*)LA-OBn. This reaction of *rac*-Lig^{2}AlOBn proceeded at a comparable rate to that of *rac*-Lig^{1}AlOBn, reaching 79% conversion after 5 h, but with less selectivity in the formation of the major diastereomer (ratio of 3:1, 50% d.e.). This reaction was faster than the reaction of enantiopure (*R,R*)-Lig^{2}AlOBn with *rac*-LA (77% conversion in 20h, Table 1, entry 8), in line with the previously reported[12] polymerization rates (*rac*-Lig^{2}AlOBn more active than enantiopure (*R,R*)-Lig^{2}AlOBn).

We confirmed the product assignment for the reaction of *rac*-Lig^{2}AlOBn with *rac*-LA through X-ray crystallographic analysis of crystals isolated from the product solution (grown by layering pentane on a toluene solution at room temperature). The structure was solved in the monoclinic crystal system and centrosymmetric space group $P2_1/c$. The asymmetric unit consists of one ring-opened complex (Z' = 1), and the unit cell has Z = 4, comprising two units each of the "match" initiation products (*R,R*)-Lig^{2}Al-L(*S,S*)LA-OBn and (*S,S*)-Lig^{2}Al-D(*R,R*)LA-OBn (Figure

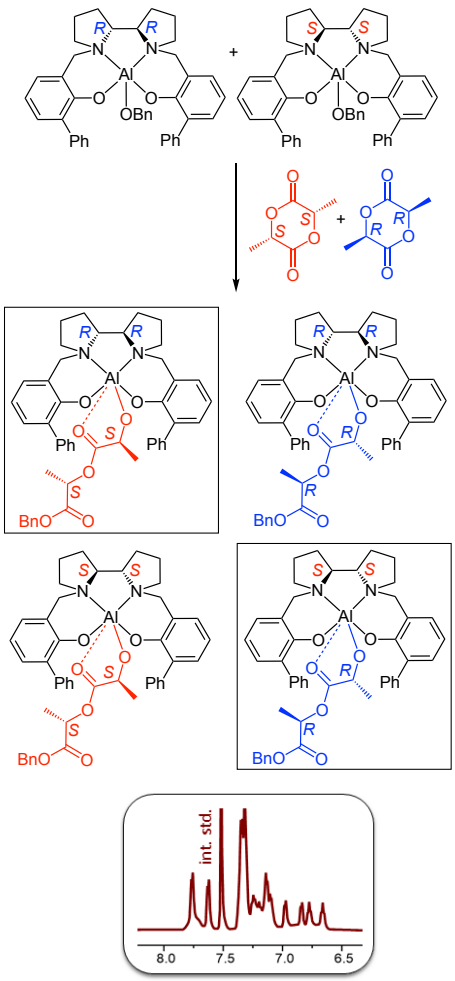

Figure 5. Reaction of *rac*-Lig^{1}AlOBn with *rac*-LA showing the four possible ring-opened products. Those in boxes are those concluded to form in the reaction (the "match" complexes (*R,R*)-Lig^{1}Al-L(*S,S*)LA-OBn and its enantiomer (*S,S*)-Lig^{1}Al-D(*R,R*)LA-OBn). The "thumbprint" region of the ^{1}H NMR spectrum is shown below, which matches closely with the spectrum on the left in Figure 3.

S40). The bond lengths and angles (Table S2) are very similar to those obtained from the separately determined X-ray structure of (*R,R*)-Lig^{2}Al-L(*S,S*)-LA-OBn (Figure 4), including the weak interaction of the lactidyl carbonyl (Al-O4 = 3.17 Å). Importantly, the ^{1}H NMR spectrum of redissolved crystals in CD_2Cl_2 was identical to that of the crude reaction mixture (with the exception of the presence of unreacted *rac*-LA; Figures S21-S22). This result supports the conclusion that the isolated crystals are the predominant species in solution, indicative of selective formation of the "match" stereoisomers in the reaction of *rac*-Lig^{2}AlOBn (and, by extension, *rac*-Lig^{1}AlOBn) with *rac*-LA.

To rationalize the results of the reactions of *rac*-LigAlOBn complexes with *rac*-LA, we propose that the major products are the most stable species that result from rapid lactidyl exchange. Several observations support this hypothesis, which is in alignment with what was proposed in the original report of the "dual-stereocontrol" mechanism,[12] but for which the stereochemical aspects are now fully determined. The finding that reactions of enantiopure (*R,R*)-LigAlOBn complexes with *rac*-LA yields both "match" and "mismatched" ring-opened products (Figures 3, S9, and S17) indicates that both stereoisomers are accessible. The higher conversion in reactions to yield the "mismatched" products ((*R,R*)-LigAl-D(*R,R*)LA-OBn) suggests that these are favored, which can be rationalized by enantiomorphic site control. Yet the fact that these products are observed as the minor diastereomers in the reaction of *rac*-LigAlOBn with *rac*-LA argues against pure enantiomorphic site control in this case. We hypothesize that all four possible stereoisomers may form initially (perhaps slightly favoring formation of the "mismatched" ones), but through rapid lactidyl exchange they equilibrate to the more stable "matched" pair.

We tested this hypothesis by separately preparing the "mismatched" complexes – (*R,R*)-Lig^{1}Al-D(*R,R*)LA-OBn and (*S,S*)-Lig^{1}Al-L(*S,S*)LA-OBn – and then mixing them together (maintaining a consistent concentration of [Al] = [LA] = 0.017 M). Conversion from the "mismatched" complexes to the "matched" complexes as major products – (*R,R*)-Lig^{1}Al-L(*S,S*LA-OBn and (*S,S*)-Lig^{1}Al-D(*R,R*)LA-OBn – was observed within 1 h of mixing, as evident from comparison of the new spectrum (Figure S23) to that of the previously characterized species (Figure S24). This result confirms the occurrence of lactidyl exchange. In addition, identification of cross peaks in the NOESY/EXSY NMR spectrum (Figure S25) corresponding to exchange between major and minor diastereomers confirms selective formation of the "match" diastereomer (product ratio of 6:1) via rapid polymeryl exchange.

Initiation Studies with LAlOBn Complexes and meso-Lactide. For both reports of highly syndiotactic PLA from the reaction of *meso*-LA with a chiral aluminum catalyst,[4,5,12] the mechanisms proposed to rationalize the results require stereoselective ring-opening of *meso*-LA. It was proposed for the case of the bipyrrolidine catalysts studied in this work that every ring-opening of *meso*-LA by enantiopure catalyst results in a "match" complex (Figure 1).[12] We sought to verify this proposal through studies of the initiation reaction.

Mixing (*R,R*)-Lig^{1}AlOBn with 1 equiv. *meso*-LA in CD_2Cl_2 at room temperature led to conversion of starting material (76% in 1 h, Table 1, entry 5) to a species with new peaks in the ^{1}H NMR spectrum assigned (^{1}H, ^{13}C, HSQC, COSY NMR, Figures S27-S30) to two diastereomeric ring-opened products in a 5:1 ratio (67% d.e., Figure 6). The ^{1}H NMR spectrum of the dominant diastereomer is nearly identical to the ^{1}H NMR spectrum of the solution resulting from reaction of (*R,R*)-Lig^{1}AlOBn with L(*S,S*)-LA (Figures S31-34) in the "thumbprint" aromatic region, with minor differences in the upfield portion of the spectra evident in the chemical shifts of the doublets arising from the methyl C*H*$_3$ protons in the lactidyl units. Both spectra are dramatically different from the ^{1}H NMR spectrum of the reaction of (*R,R*)-Lig^{1}AlOBn with D(*R,R*)-LA (Figure S33), especially in the aromatic region (8.0-6.5 ppm) when comparing line

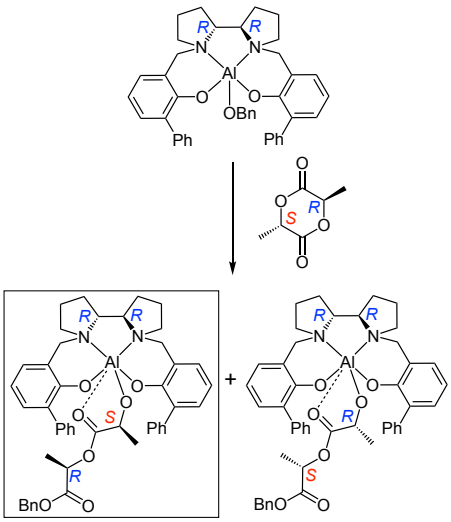

Figure 6. Reaction of (*R,R*)-Lig[1]AlOBn with *meso*-LA showing the two products, the "match" complex (*R,R*)-Lig[1]Al-(*S,R*)LA-OBn (major, in box on left) and the "mismatch" complex (*R,R*)-Lig[1]Al- (*R,S*)LA-OBn (minor, on right).

shape and peak separation. These results are consistent with the dominant product of the reaction of (*R,R*)-Lig[1]AlOBn with *meso*-LA having a proximal stereocenter with *S* configuration, the "match" complex (*R,R*)-Lig[1]Al-(*S,R*)LA-OBn. As expected, reaction of the enantiomer of the starting material (*S,S*)-Lig[1]AlOBn with *meso*-LA yielded the identical product NMR spectrum (5:1 ratio of diastereomers, Figure S34), consistent with the main product being the enantiomer having proximal *R* configuration, (*S,S*)-Lig[1]Al-(*R,S*)LA-OBn. While the minor diastereomer in both cases is more challenging to assign, the data are consistent with it being the opposite "mismatch" stereoisomer (Figures S31 and S33). Finally, through a series of NOESY/EXSY NMR experiments (Figures S35-S37) rapid exchange between the major and minor isomers was identified. It should be noted that lactidyl exchange in this experiment would not change the ratio of diastereomers (it is degenerate).

Similar results were found in studies of the reaction of (*R,R*)-Lig[2]AlOBn with stoichiometric *meso*-LA. The reaction reached 84% conversion in 1 h (Table 1, entry 10) and the resulting ^{1}H NMR spectrum featured peaks similar to those of the "match" complex (*R,R*)-Lig[2]Al-L(*S,S*)LA-OBn resulting from reaction of (*R,R*)-Lig[2]AlOBn with L(*S,S*)-LA. Thus, we hypothesized that the major product has a proximal *S* stereocenter (Figure S38). The NMR data were less conclusive than in previous examples, so we turned to structural characterization by X-ray crystallography. Success was achieved by layering pentane on a concentrated solution resulting from reaction of (*R,R*)-Lig[2]AlOBn with *meso*-LA in toluene at room temperature (Figure 7). The X-ray crystal structure confirmed the formation of a complex featuring ring-opened *meso*-LA with an *S* stereocenter proximal to the metal center. Notably, to the best of our knowledge this is the first published structure of ring-opened *meso*-LA bound to a catalytically active center. Given the importance of

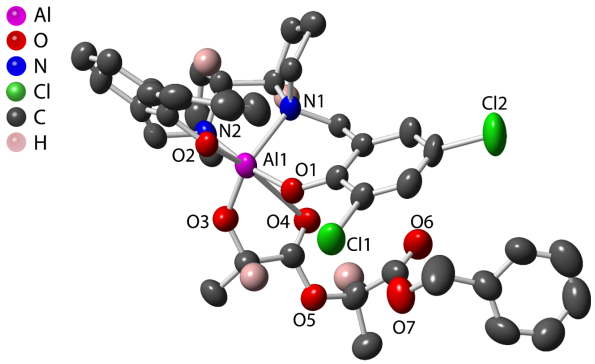

Figure 7. Representation of the X-ray structure of (*R,R*)-Lig[2]Al-(*S,R*)LA-OBn, resulting from the reaction of (*R,R*)-Lig[2]AlOBn with stoichiometric *meso*-LA. All nonhydrogen atoms are presented as 30% thermal ellipsoids; pink spheres are H atoms on stereogenic centers. All non-stereocenter associated hydrogen atoms and an additional ring-opened initiation product present in the asymmetric unit omitted for clarity. Selected bond distances (Å) and angles (deg): Al-O1, 1.796(7); Al-N1, 2.086(3); Al-N2, 2.112(3); Al-O2, 1.763(8); Al-O3, 1.749(9); Al-O4, 3.14(2); N2-Al-O1, 167.(3); N1-Al-O3, 141.(8); O2-Al-O3, 111.(5); O3-Al-O4, 59.(6).

meso-LA as a feedstock in biodegradable polymers, this structure is a milestone for understanding the initiation process.

We were not able to definitively confirm that this solid state structure is the major one adopted in solution due to the complexity of the ^{1}H NMR spectrum. However, when considered together with (1) the definitive NMR assignment of the reaction of (*R,R*)-Lig[1]AlOBn with *meso*-LA, and (2) the selectivity previously observed for (*R,R*)-LigAlOBn complexes in their reactions with D(*R,R*)-, L(*S,S*)-, and *rac*-LA, we propose that the diastereomer observed in the crystal structure is representative of that formed in solution.

Altogether, these data support the initial proposal of the selective formation of sequential "match" complexes in the

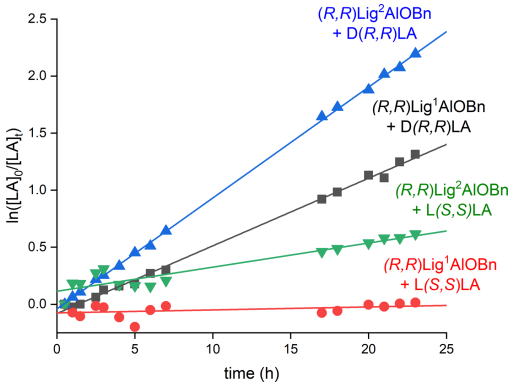

Figure 8. Plots of kinetic data for the polymerizations of L(*S,S*)- and D(*R,R*)-LA by (*R,R*)-LigAlOBn complexes, with linear fits. Fit parameters: blue triangles, (*R,R*)-Lig[2]AlOBn + D(*R,R*)LA, slope = k = 0.097 h^{-1}, R = 0.9996; green triangles, (*R,R*)-Lig[2]AlOBn + L(*S,S*)LA, slope = k = 0.021 h^{-1}, R = 0.8849; black squares, (*R,R*)-Lig[1]AlOBn + D(*R,R*)LA, slope = k = 0.059 h^{-1}, R = 0.9969; red circles, (*R,R*)-Lig[1]AlOBn + L(*S,S*)LA, slope = k = 0.0026 h^{-1}, R = 0.9658.

polymerization of *meso*-LA by enantiopure catalyst.[12] The stereoselectivity observed in initiation for (*R,R*)-Lig[1]AlOBn (formation of "match" stereoisomer with 67% d.e.) is within range of the stereoselectivity exerted by this catalyst in the polymerization of 50 equiv. *meso*-LA (P_s = 0.80-0.93, depending on conditions),[12] suggesting that enantiomorphic site control dominates in the latter. That said, the selectivities deviate enough to suggest that other forces (cf. chain-end effects) may play an important role in propagation compared to initiation.

Polymerizations with Enantiopure LigAlOBn Complexes. Critical to the dual-stereocontrol mechanism is different rates of ring opening of particular LA stereoisomers by particular enantiomers of catalyst. To quantify these differences, we measured the rates of polymerization of enantiopure L(*S,S*)- or D(*R,R*)-LA by (*R,R*)-LigAlOBn complexes by monitoring monomer consumption as a function of time via NMR spectroscopy. First-order plots were linear (Figure 8), and comparison of the rate constants showed faster reactions for polymerizations of D(*R,R*)-LA. For catalyst precursor (*R,R*)-Lig[1]AlOBn, polymerization of D(*R,R*)-LA was ~22x faster than L(*S,S*)-LA. That factor for the more reactive catalyst precursor (*R,R*)-Lig[2]AlOBn was ~4.5. Thus, after initiation, the "mismatched" catalyst (*R,R*)-LigAl-D(*R,R*)LA-OR reacts faster with the same monomer (D(*R,R*)-LA) than the "matched" catalyst (*R,R*)-LigAl-L(*S,S*)LA-OR with L(*S,S*)-LA. These findings corroborate and provide quantitative information for the previously reported observation via GC analysis of the remaining monomer from the polymerizations of *rac*-LA with enantiopure LigAlOBn complexes that revealed a preference for (*R,R*) catalyst to ring-open D(*R,R*)-LA, and vice versa for (*S,S*) catalyst. The previous report also hypothesized that the "mismatch" (ex. *RR*-LigAl-D(*R,R*)LA-OBn) is "inactive towards any lactide"[12]; in fact, our new findings suggest the "mismatch" is more active with the same stereoisomer of LA as the chain end than the "match". The poor reactivity of the "match" with the same stereoisomer of LA as the chain end potentially contributes to avoidance of isotactic sequences and enhances the preference for heterotacticity in polymerizations of *rac*-LA by *rac*-LigAlOBn catalysts.

SUMMARY AND CONCLUSIONS

We have investigated the stereoselectivity in initiation for a pair of highly selective bipyrrolidine complexes Lig[1]AlOBn and Lig[2]AlOBn with *rac*-, D(*R,R*)-, L(*S,S*)-, and *meso*-LA, with the goal of elucidating aspects of the novel dual-stereocontrol mechanism. In the absence of a chiral lactidyl initiating ligand, the complexes operate purely by enantiomorphic site-control, showing a preference to ring-open the enantiomer of lactide with the same chiral sense as the bipyrrolidine ligand and favoring formation of the "mismatch" complex. However, investigation of the polymeryl exchange between aluminum centers in the stoichiometric reaction of *rac*-catalyst with *rac*-LA reveals a preference for catalyst-lactide pairing of opposite chirality, the "match" complex, as indicated by ^{1}H NMR and X-ray crystallography. This key finding corroborates the postulated mechanism for the heteroselective polymerization of *rac*-LA by *rac*-catalyst, confirming synergistic enantiomorphic site-control and polymeryl exchange.

The stereoselective polymerization of *meso*-LA to produce highly crystalline syndiotactic PLA is rare,[4,5,8-12] and investigation of the mechanism by which a catalyst produces such a material is important for future catalyst design and the efforts to supplant our global dependence on fossil-fuel based plastics. Through stoichiometric initiation reactions, we have determined the ring-opening of *meso*-LA to be stereoselectively favored at the acyl carbon proximal to the *R* stereocenter when the bipyrrolidine ligand is of (*R,R*) chirality for both Lig[1] and Lig[2] systems. Thus, the ring-opened products were characterized by NMR (^{1}H, ^{13}C, HSQC, COSY) and identified as bearing a proximal stereocenter *S* to the aluminum on the lactidyl unit. This result was confirmed on the basis of comparison to analogous diastereomeric structures via the sensitivity of the aromatic protons of the bipyrrolidine ligand to the chirality of the proximal stereocenter of the ring-opened lactide unit (so-called "thumbprint" region). Unambiguous identification of the chirality of the initiation product of (*R,R*)-Lig[2]AlOBn and *meso*-LA was possible through characterization by X-ray crystallography and determined to be the "match" complex, validating the previous identification of this product on the basis of NMR and providing a rare example of crystallographic characterization of a ring-opened *meso*-LA unit bound to an active catalytic center.

The stereoselectivity in polymerization of enantiopure D(*R,R*)- or L(*S,S*)-LA by (*R,R*) ligated Lig[1] and Lig[2] also was investigated. Sequential isotactic enchainments were more facile with D(*R,R*)-LA than L(*S,S*)-LA, suggesting that: (1) enantiomorphic site control favors ring-opening of monomers bearing the same chiral sense as those inherent to the ligand and, (2) chain-end control effects contribute to ring-opening monomers bearing the opposite chiral sense to that of the chain-end. Enhanced stereoselectivity is observed when these two effects agree, as in the case of the "match" complex and the ROP of *meso*-LA. This polymerization stereocontrol may be explained by lower ground state energies of the "match" complexes over the "mismatch" complexes, followed by irreversible stereoselectivity-determining insertion of D(*R,R*)-LA by (*R,R*)-ligated complexes (enantiomorphic-site effects). Both phenomena were originally proposed,[12] but have been defined in the initiation studies described herein.

But how significant are the chain-end stereocontrol effects? To address this question, it is helpful to compare again the stereoselectivity of the binaphthyl-based Schiff base aluminum catalyst and the bipyrrolidine-based salan aluminum catalyst (Figure 1, top). The first catalyst, in its enantiomerically-pure form, is isoselective towards *rac*-LA and syndioselective towards *meso*-LA, while in its racemic form it is still isoselective towards *rac*-LA but heteroselective towards

meso-LA. These findings are in line with an enantiomorphic site control mechanism combined with the tendency of the aluminum center to bind to the same stereocenter it prefers to react with. When this catalyst is employed in its racemic form, the polymerization of *rac*-LA retains its stereoregularity, while the polymerization of *meso*-LA reverses stereoregularity from syndiotactic to heterotactic, through lactidyl exchange. In stark contrast, the bipyrrolidine-based salan aluminum catalyst, in its enantiomerically-pure form, is essentially non-selective towards *rac*-LA and syndioselective towards *meso*-LA, while in its racemic form it is highly heteroselective towards *rac*-LA and still syndioselective towards *meso*-LA. Notwithstanding the different stereochemical consequences, these two catalysts share common characteristics: (1) polymeryl exchange events are faster than chain propagation and may dictate the resulting stereoregularity of the formed PLA, and (2) enantiomorphic-site effects play a dominant role, otherwise the enantiomerically-pure and the racemic catalysts would have exhibited similar stereoselectivity in all cases. An important finding of the current work is the quantitative identification of the enantiomorphic-site control influence by measurement of the relative insertion tendencies of the two lactide enantiomers with an Al-benzyloxy group (initiation step) wherein chain-end effects do not play a role. A preference for an (*R,R*)-based catalyst towards D(*R,R*)-lactide to form the "mismatch" diastereomer over the L(*S,S*)-lactide was found. The "mismatch" stereoisomers were also found to be considerably more reactive than the "match" stereoisomers in homochiral lactide polymerizations. For example, (*R,R*)-Lig^{1}Al-D(*R,R*)-LA was 22 times more active towards D(*R,R*)-LA than (*R,R*)-Lig^{1}Al-L(*S,S*)-LA was towards L(*S,S*)-LA. Can this preference be assumed to persist in polymerization of *rac*-LA? A rate ratio of 20:1 for the polymerization of the two lactide enantiomers was reported for the enantiomerically-pure binaphthyl based aluminum catalyst, which resulted in a strong isotactic bias.[4,5] If the enantiomerically-pure bipyrrolidine-based catalysts operated solely by enantiomorphic-site control, we would anticipate that polymers with an isotactic bias would form, but the tacticity observed with the bipyrrolidine-based salan aluminum catalysts differs. We therefore conclude that, on top of the enantiomorphic-site control effects clearly demonstrated herein, chain-end stereocontrol effects must be involved in catalytic polymerizations as well. For example, in polymerization of *rac*-LA, a (*R,R*)-LigAl-D(*R,R*)-LA "mismatch" stereoisomer would be fast to form either from (*R,R*)-LigAlOBn as shown here or from a (*R,R*)-LigAl-L(*S,S*)-LA "match" stereoisomer, but once it forms it would not exhibit a preference to react with any of the lactide enantiomers over the other.

Thus, we conclude that in the polymerization of *rac*-LA by *rac*-catalyst, the "mismatch" stereoisomer is rapidly converted to the "match" stereoisomer via lactidyl exchange, followed by stereoselectivity-determining insertions which favor racemic monomer enchainments. In other words, our results support the notion that the "dual" in "dual-stereocontrol" is a synergistic combination of enantiomorphic site control which favors formation of the "mismatch" stereoisomer, followed by rapid interconversion (via polymeryl exchange) to the stereoisomer with the lower ground state energy, the "match", which accesses a lower energy reaction pathway through which the stereoselectivity-determining transformations (heteroselective insertions) proceed. These findings have implications for the conventional understanding of stereospecific lactide polymerizations and demonstrate the utility of trapping reactive intermediates as a technique to elucidate novel mechanisms of stereocontrol.

ASSOCIATED CONTENT

Supporting Information. This material is available free of charge via the Internet at http://pubs.acs.org.
CCDC Deposition Numbers: 2160320, 2160321, 2160322.

AUTHOR INFORMATION

Corresponding Authors

Moshe Kol – School of Chemistry, Tel Aviv University, Ramat Aviv, Tel Aviv 69997801, Israel; orcid.org/0000-0002-0098-1529; email: moshekol@tauex.tau.ac.il

William B. Tolman – Department of Chemistry and NSF Center for Sustainable Polymers, Washington University in St. Louis, St. Louis, Missouri 63130, United States; orcid.org/0000-0002-2243-6409; email: wbtolman@wustl.edu

Authors

Appie Peterson – Department of Chemistry and NSF Center for Sustainable Polymers, Washington University in St. Louis, St. Louis, Missouri 63130, United States; orcid.org/0000-0002-2824-7545

Rami Hador – School of Chemistry, Tel Aviv University, Ramat Aviv, Tel Aviv 69997801, Israel; orcid.org/0000-0003-2192-5259

Maren Pink – Indiana University Molecular Structure Center, 800 East Kirkwood Ave, Bloomington, Indiana 47405, United States; orcid.org/0000-0001-9049-4574

Yanay Popowski – Department of Chemistry and NSF Center for Sustainable Polymers, Washington University in St. Louis, St. Louis, Missouri 63130, United States; https://orcid.org/0000-0003-1569-0035

ACKNOWLEDGMENT

This work was supported by the NSF Center for Sustainable Polymers, CHE-1901635, and by grant No. 553/18 of the Israel Science Foundation. X-Ray diffraction data were collected using diffractometers acquired through NSF-MRI Award No. 1827756 (University of Missouri – Saint Louis), and support for the acquisition of the Bruker Venture D8 diffractometer through the Major Scientific Research Equipment Fund from the President of Indiana University and the Office of the Vice

President for Research is gratefully acknowledged. Analytical data were obtained from the CENTC Elemental Analysis Facility at the University of Rochester, funded by NSF CHE-0650456.

REFERENCES

[1] Becker, J. M.; Dove, A. P. Poly(Lactide)s as Robust Renewable Materials. In *Green Polymerization Methods: Renewable Starting Materials, Catalysis and Waste Reduction*; Mathers, R. T., R., M. M. A., Eds.; 2011; pp 201–220.

[2] (a) Thomas, C. M., "Stereocontrolled ring-opening polymerization of cyclic esters: synthesis of new polyester microstructures," *Chem. Soc. Rev.* **2010**, *39*, 165-173. (b) Stanford, M. J.; Dove, A. P., "Stereocontrolled ring-opening polymerisation of lactide," *Chem. Soc. Rev.* **2010**, *39*, 486-494. (c) Dijkstra, P. J.; Du, H.; Feijen, J., "Single site catalysts for stereoselective ring-opening polymerization of lactides," *Polymer Chemistry* **2011**, *2*, 520-527. (d) Tschan, M. J. L.; Gauvin, R. M.; Thomas, C. M., "Controlling polymer stereochemistry in ring-opening polymerization: a decade of advances shaping the future of biodegradable polyesters," *Chem. Soc. Rev.* **2021**, *50*, 13587-13608.

[3] Spassky, N.; Wisniewski, M.; Pluta, C.; Borgne, A. L., "Highly Stereoelective Polymerization of *Rac*-(D,L)-Lactide with a Chiral Schiff's base/Aluminium Alkoxide Initator," *Macromol. Chem. Phys.* **1996**, *197*, 2627-2637.

[4] Ovitt, T. M.; Coates, G. W., "Stereochemistry of Lactide Polymerization with Chiral Catalysts: New Opportunities for Stereocontrol Using Polymer Exchange Mechanisms," *J. Am. Chem. Soc.* **2002**, *124*, 1316-1326.

[5] Ovitt, T. M.; Coates, G. W., "Stereoselective Ring-Opening Polymerization of *meso*-Lactide: Synthesis of Syndiotactic Poly(lactic acid)," *J. Am. Chem. Soc.* **1999**, *121*, 4072-4073.

[6] Ovitt, T. M.; Coates, G. W., "Stereoselective Ring-Opening Polymerization of *rac*-Lactide with a Single-Site, Racemic Aluminum Alkoxide Catalyst: Synthesis of Stereoblock Poly(lactic acid)," *J. Polym. Sci., Part A: Polym. Chem.* **2000**, 4686-4692.

[7] Nomura, N.; Ishii, R.; Yamamoto, Y.; Kondo, T., "Stereoselective Ring-Opening Polymerization of a Racemic Lactide by Using Achiral Salen- and Homosalen-Aluminum Complexes," *Chem. - Eur. J.* **2007**, *13*, 4433-4451.

[8] Chamberlain, B. M.; Cheng, M.; Moore, D. R.; Ovitt, T. M.; Lobkovsky, E. B.; Coates, G. W., "Polymerization of Lactide with Zinc and Magnesium b-Diiminate Complexes: Stereocontrol and Mechanism," *J. Am. Chem. Soc.* **2001**, *123*, 3229-3238.

[9] Amgoune, A.; Thomas, C. M.; Roisnel, T.; Carpentier, J.-F., "Ring-Opening Polymerization of Lactide with Group 3 Metal Complexes Supported by Dianionic Alkoxy-Amino-Bisphenolate Ligands: Combining High Activity, Productivity, and Selectivity," *Chem. Eur. J.* **2006**, *12*, 169-179.

[10] Buffet, J. C.; Kapelski, A.; Okuda, J. "Stereoselective Polymerization of *meso*-Lactide: Syndiotactic Polylactide by Heteroselective Initiators Based on Trivalent Metals," *Macromolecules* **2010**, *43*, 10201–10203.

[11] Buffet, J.-C.; Okuda, J. "Initiators for the Stereoselective Ring-Opening Polymerization of *meso*-Lactide," *Polym. Chem.* **2011**, *2*, 2758–2763.

[12] Hador, R.; Botta, A.; Venditto, V.; Lipstman, S.; Goldberg, I.; Kol, M., "The Dual-Stereocontrol Mechanism: Heteroselective Polymerization of rac-Lactide and Syndioselective Polymerization of meso-Lactide by Chiral Aluminum Salan Catalysts," *Angew. Chem. Int. Ed.* **2019**, *58*, 14679-14685.

[13] Luke, A. M.; Peterson, A.; Chiniforoush, S.; Mandal, M.; Popowski, Y.; Sajjad, H.; Bouchey, C. J.; Shopov, D. Y.; Graziano, B. J.; Yao, L. J.; Cramer, C. J.; Reineke, T. M.; Tolman, W. B., "Mechanism of Initiation Stereocontrol in Polymerization of rac-Lactide by Aluminum Complexes Supported by Indolide–Imine Ligands," *Macromolecules* **2020**, *53*, 1809-1818.

[xiv] In a complementary experiment, the same product NMR spectrum, albeit with different ratio of products (0.8:1), was observed upon reaction of L(*S,S*)-LA with a racemic mixture of (*R,R*)- and (*S,S*)-Lig[1]AlOBn. To explain this result, we postulate formation of (*R,R*)-Lig[1]Al-L(*S,S*)LA-OBn and (*S,S*)-Lig[1]Al-L(*S,S*)LA-OBn, the enantiomer of (*R,R*)-Lig[1]Al-D(*R,R*)LA-OBn (Figure Sx).

[xv] Lewiński, J.; Zachara, J.; Justyniak, I. Structure Investigation of a Dimethylaluminium Derivative of Ethyl Rac-Lactate in the Solid State and Solution. First Evidence for Stereoselective Association of a Dialkylaluminium O,O′-Chelate Complex. *Chem. Commun.* **1997**, *20*, 1519–1520.

[xvi] Lewin, J.; Zachara, J.; Justyniak, I. Electronic Factors Determining the Rearrangement of Dialkylaluminum O , O ′ -Chelate Compounds from Dimeric Five- to Monomeric Four-Coordinated Complexes on Dissolution . Structure Investigations of Dialkylaluminum Chelate Derivatives of r- and -Hydroxy C. *Organometallics* **1997**, *16*, 4597–4605.

[xvii] Ko, B.-T.; Wang, F.-C.; Sun, Y.-L.; Lin, C.-H.; Lin, C.-C.; Kuo, C.-Y. Synthesis and Characterization of Aluminum Ethyl-(S)-Lactate Complexes and VT NMR Studies of [Bu2iAl((S)-(−)-M2-OC(H)(Me)C(O))Et))]2. *Polyhedron* **1998**, *17*, 4257–4264.

[xviii] Chumsaeng, P.; Haesuwannakij, S.; Bureekaew, S.; Ervithayasuporn, V.; Namuangruk, S.; Phomphrai, K. Polymerization of ϵ-Caprolactone Using Bis(Phenoxy)-Amine Aluminum Complex: Deactivation by Lactide. *Inorg. Chem.* **2018**, *57*, 10170–10179.

[xix] Oishi, M.; Ichinose, Y.; Iwata, N.; Nomura, N. Ring-Opening Polymerization of ϵ-Caprolactone Initiated by Multinuclear Aluminum Methanetris(Aryloxido) Complexes. *Organometallics* **2019**, *38*, 4233–4243.

[xx] Klitzke, J. S.; Roisnel, T.; Kirillov, E.; Casagrande, O. D. L.; Carpentier, J. F. Discrete O-Lactate and β-Alkoxybutyrate Aluminum Pyridine-Bis(Naphtholate) Complexes: Models for Mechanistic Investigations in the Ring-Opening Polymerization of Lactides and β-Lactones. *Organometallics* **2014**, *33*, 5693–5707.

[xxi] Dagorne, S.; Le Bideau, F.; Welter, R.; Bellemin-Laponnaz, S.; Maisse-François, A. Well-Defined Cationic Alkyl- And Alkoxide-Aluminum Complexes and Their Reactivity with ε-Caprolactone and Lactides. *Chem. - A Eur. J.* **2007**, *13*, 3202–3217.

[xxii] Lewiński, J.; Horeglad, P.; Wójcik, K.; Justyniak, I. Chelation Effect in Polymerization of Cyclic Esters by Metal

Alkoxides: Structure Characterization of the Intermediate Formed by Primary Insertion of Lactide into the Al-OR Bond of an Organometallic Initiator. *Organometallics* **2005**, *24*, 4588–4593.

Table of Contents Graphic