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Ring-Opening Homo- and Co-polymerization of Lactides and ε-Caprolactone by Salalen Aluminum Complexes

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ABSTRACT: Aluminum complexes of non-chiral-salalen ligands were investigated in the catalysis of Ring-Opening Polymerization (ROP) of lactide and ε-caprolactone and in their copolymerization. The aluminum-salalen complexes were found to polymerize all varieties of lactide, namely: L-, D-, *rac*- and *meso*-lactide and showed moderate productivities. *Rac*-LA gave rise to isotactic polylactide (with P_m up to 72%), while *meso*-LA gave rise to heterotactic polylactide (with P_m of 79%). An experiment was designed for distinguishing between chain-end control and enantiomorphic-site control combined with polymeryl exchange for the isotactic stereoblock microstructure observed for the PLA produced from *rac*-LA; it gave a strong evidence for polymeryl exchange between propagating species. Finally, this class of catalysts promoted the copolymerization of ε-caprolactone and lactides. In particular, compound **2b** allowed controlled random copolymerization of ε-caprolactone and L-lactide.

INTRODUCTION

In the last decades, the plastics market has been dominated by petroleum-derived polymers such as polyethylene, polypropylene and polystyrene. However, the rising price of their non-renewable resources combined with their lack of biodegradability post-consumption have been a driving force in the search for environmentally benign alternatives. Polyesters, especially polycaprolactone (PCL) and polylactide (PLA), are among the most studied alternative polymers that are finding applications as packaging and medicinal products.[1]

The Ring-Opening Polymerization (ROP) of cyclic esters with metal-based initiators is the most efficient method for the production of polyesters with well-defined structures and properties, in terms of molecular weight, composition, microstructure and comonomer incorporation. In particular, the stereocontrolled ROP of cyclic esters that include stereogenic centers (like lactide or β-butyrolactone) has enabled the facile manipulation of the tacticity of the resultant polymers,

considerably affecting their physical and chemical properties. Lactide, the monomer leading to PLA, is a cyclic diester that includes two stereogenic centers, leading to three possible stereoisomers, namely L-LA, D-LA (and their racemic mixture *rac*-LA) as well as *meso*-LA. From this basic set of monomers many polymer microstructures can be constructed (i.e., atactic, isotactic, heterotactic and syndiotactic).[1a,b]

Polymerization of the homochiral monomers L-LA or D-LA leads to the isotactic polymers PLLA or PDLA, respectively. For *rac*-LA and *meso*-LA, stereoselection may be achieved by either the enantiomorphic-site control mechanism (SCM; where the choice of the inserting enantiomer of *rac*-LA or the stereocenter of *meso*-LA is determined by the configuration of the active site) or chain-end control mechanism (CEM; where these choices are made by the stereogenic center of the last repeating unit of the bound polymeryl chain). Each of these mechanisms has its typical stereoerror signature and kinetic behaviour. However, since they often act in concert, and since polymeryl exchange between propagating species is common, it is difficult to differentiate between their respective contributions to a given polymer microstructure.[2]

Notably, the highest stereocontrol in *rac*-LA polymerization in terms of isoselectivity has been obtained by aluminum complexes[3] bearing salen[4,2c] or salan[5] ligands. Salalens[6] are hybrid salan/salen ligands including an amine and an imine neutral donors and two phenolate arms. Salalen-based complexes have found use as asymmetric oxidation catalysts,[7] and as catalysts for polymerization of α-olefins.[8] Recently, aluminum complexes of salalen ligands[9] were also found able to catalyze the polymerization of lactide.[10] Very recently, we described the aluminum complexes of chiral salalen ligands assembled around the aminomethylpyrrolidine motif. These complexes, which formed as single diastereomers, catalyzed the ROP of *rac*-LA leading to a new polymeric microstructure, namely the gradient isotactic multiblock PLA.[2d] We demonstrated that both SCM and CEM stereocontrol mechanisms are active in the polymerization reactions catalyzed by this class of aluminum complexes.

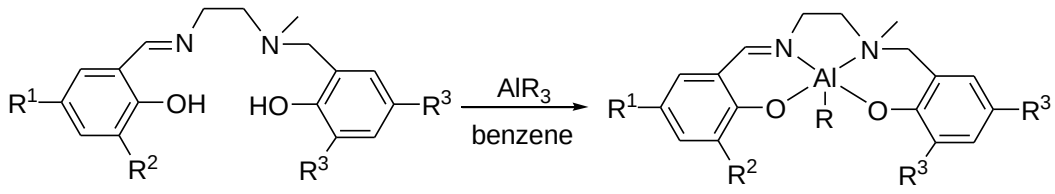
The composition of the polymeric material is another aspect of fundamental importance in the tuning of the properties of the final product. The physical properties of PCL and PLA are quite different and, to some extent, complementary. For this reason, the copolymerization of ε-CL and LA could enable the preparation of materials having improved features in comparison with the parent homopolymers. In spite of the growing interest in this field, only few examples of catalysts capable of producing truly random LA/CL copolymers have been reported,[11] while in most of the cases either diblock or gradient copolymers or random copolymers arising from transesterification events, have been obtained.[12] Thus far, while both salen[11a,11c] and salan[11d] aluminum complexes

were found to be active initiators in the copolymerization of ε-CL and LA, salalen based complexes have not been tested in this reaction.

In this paper we describe a class of aluminum complexes bearing non-chiral salalen ligands, and their behaviour as initiators in the ROP of lactides and ε-caprolactone. Polylactides with different microstructures were produced from *rac*-LA and *meso*-LA and the mechanism of stereocontrol was investigated. Moreover, we show that this class of catalysts is active in the random copolymerization of ε-caprolactone and lactide.

RESULTS AND DISCUSSION

The proligands were synthesized following a previously published synthetic procedure consisting of condensation of *N*-methyl-1,2-diaminoethane with a substituted salicylaldehyde followed by nucleophilic substitution on a substituted bromomethylphenol.[8] Complex **1a** was synthesized in toluene by methane elimination reaction between the corresponding proligand and 1 equiv of $AlMe_3$ according to a previously reported synthesis.[9a] Complexes **2b** and **3b** were synthesized by direct reaction of the ligand precursors with $Al(O^iPr)_3$ in toluene at 70°C. Complexes **1a**, **2b**, and **3b** were subsequently recovered by evaporation of the solvent in vacuo, as yellow powders in good yields. All compounds were characterized by multinuclear NMR spectroscopy and elemental analysis. Additional studies of complex **2b** in solution were carried out by COSY experiment.



1a, 2b, **3b**

1H$_2$: $R_1 = R_2 = Cl$; $R_3 = {}^tBu$
2H$_2$: $R_1 = R_2 = {}^tBu$; $R_3 = Cl$
3H$_2$: $R_1 = Me$ $R_2 = Ad$; $R_3 = Cl$

1a: R = Me
2b: R = O^iPr
3b: R = O^iPr

Scheme 1. Synthesis of the Aluminum Complexes.

^1H NMR revealed that in all cases mononuclear complexes had formed in which the pentacoordinate aluminum centre was bound to one salalen ligand and one labile group (methyl for complex **1a** and isopropoxide for complexes **2b** and **3b**). The ^1H and ^{13}C NMR spectra of all compounds contain a single set of resonances, indicative of the existence of a single species of C_1-symmetry on the NMR time scale. The hydrogen atoms of the backbone =NCH_2CH_2N- as well as

those of the methylene group on the amine side –NCH_2Ar are diastereotopic and each appears as a part of an A_nB_n system (n=2 for the hydrogen atoms of the backbone and n=1 for the hydrogen atoms of the methylene group on the amine side). ^{1}H-^{1}H COSY NMR spectrum of complex **2b** allowed the assignment of each signal to the different hydrogen atoms of the ligand skeleton (see Figures S1-S3).

Upon the chelation of the ligand to the metal both the tertiary amine and the metal center become stereogenic. As only a single pattern of signals is visible for each complex, we suggest that these two sources of stereogenity are dependent, viz., one inducing the formation of the other, such that eventually, only a single pair of enantiomeric complexes is formed from these achiral ligands.[9a]

Ring-Opening Polymerization of Lactides

We evaluated the catalytic abilities of the prepared aluminum complexes in the ROP of lactides. The methyl complex **1a** was converted in situ to the alkoxo derivative by reaction with one equivalent of benzyl alcohol, while complexes **2b** and **3b** were used directly as single-site initiators. All the systems were found to catalyze the polymerization of lactides in toluene at 80°C. Representative results are reported in Table 1.

Table 1. Ring-Opening Polymerization of lactides promoted by Salalen Aluminum Complexes. [a]

Run	Monomer	Cat	Time (days)	Conv (%)	$M_{n,calcd}$ [c] (Kg/mol)	$M_{n,exp}$ [b] (Kg/mol)	PDI	P_m [d]
1	*rac*-LA	**1a**	1	63	9.1	6.3	1.07	0.45
2	*rac*-LA	**2b**	5[e]	52	7.5	8.7	1.06	0.72
3	*rac*-LA	**3b**	7[e]	54	7.8	9.4	1.07	0.69
4	L-LA	**2b**	5	82	11.8	11.3	1.05	-
5	D-LA	**2b**	5	93	16.9	13.0	1.03	-
6	*meso*-LA	**2b**	3	98	14.1	7.9	1.17	0.79

[a] General conditions: initiator: 20 μmol; toluene: 2 mL; lactide: 2 mmol; temperature: 80 °C.

[b] Experimental M_n values were determined by GPC analysis in THF using polystyrene standards and corrected by the factor 0.58.

[c] 144.13 x $[LA]_0/[I]_0$ x conv LA.

[d] P_m is the probability of meso linkages as determined by NMR analysis (Bernoullian statistics).

[e] After a polymerization time of one day: run 2, conversion: 14%; run 3, conversion: 22%.

The activity of complex **1a** (mixed with 1 equiv of BnOH) in the polymerization of *rac*-lactide was slightly lower than that reported in a previous paper (in which a higher initiator amount was used).[9a] Complexes **2b** and **3b** were less active than system **1a**/BnOH. Moreover, a maximum conversion of about 50% was obtained with both the catalysts, even for prolonged reaction times, supporting the degradation of the active species at the polymerization temperature in less than a week. On the other hand, the polymerizations of both L-LA and D-LA by complex **2b** were found to be faster than the polymerization of *rac*-lactide and proceeded up to 93% of conversion in five days. As all the monomers were purified in the same manner, we rule out the possibility that technical sources were responsible for the observed different polymerization rates. On the other hand, the slower reactivity of complex **2b** towards *rac*-LA relative to its reactivity towards the homochiral monomers L-LA and D-LA may be due to its homochiral insertion preference, which should lead to isotactically-inclined PLA in polymerization of *rac*-LA (vide infra).

Kinetics studies of L- and *rac*-LA polymerization catalyzed by complex **2b** were carried out. Plots of $\ln([LA]_0/[LA])$ versus time show that both polymerizations proceed with a first order dependence on monomer concentration (Figure 1). In agreement with the polymerization results, the $k_{(app)}$ of the L-LA polymerization was about twice of that of the *rac*-LA polymerization.

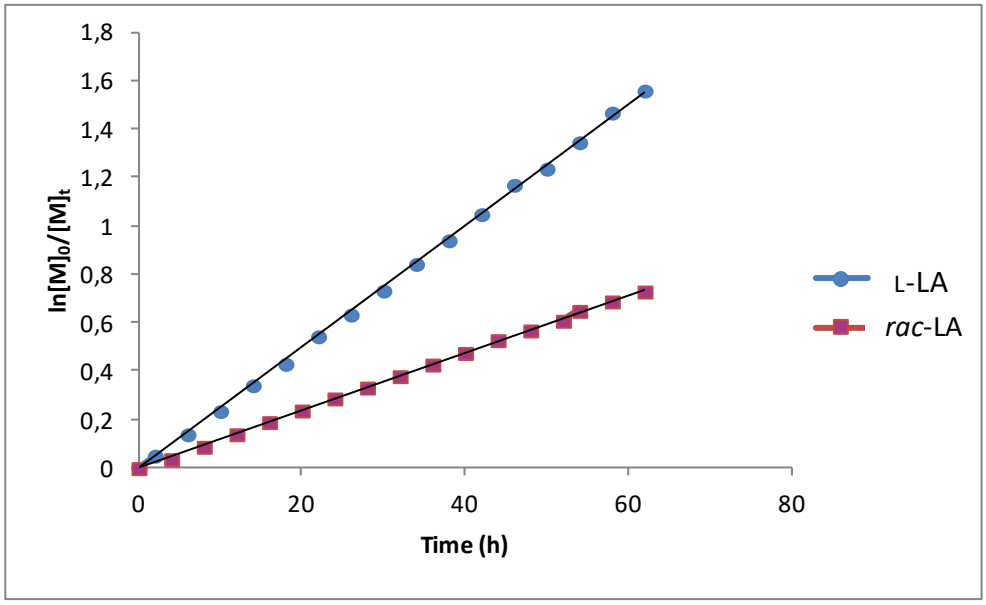


Figure 1. Pseudofirst-order kinetic plots for ROP of *rac*-lactide and L-LA promoted by **2b**. [Al]=1.0 x 10^{-2} M; [LA]/[Al]=100; T= 80 °C; toluene-d_8 as solvent. k_{app} (*rac*-LA) = 0.012 h^{-1}; k_{app} (L-LA) = 0.025 h^{-1}.

Next, we determined the stereochemistry of the PLA samples, obtained from *rac*-LA (runs 1-3), by recording the homonuclear decoupled ^{1}H NMR spectra. The peaks were assigned to the appropriate tetrads in accordance with the shifts reported in the literature, and P_m values were evaluated by integrating the suitable peaks. P_m values of 0.45, 0.72 (see Figure 2) and 0.69 were recorded for

polymerization of *rac*-LA by **1a**, **2b** and **3b**, respectively (these values are consistent with previous phenolate substitution pattern effects on tacticity reported by Jones).[9a] As noted earlier, each complex exists as a single pair of enantiomers in solution, which we propose to remain intact during the propagation process. Significantly, in all cases, the reactions proceeded in a controlled fashion, leading to polymers with monomodal and narrow molecular weight distributions (M_w/M_n = 1.05 – 1.07 for runs 1-5 in Table 1).

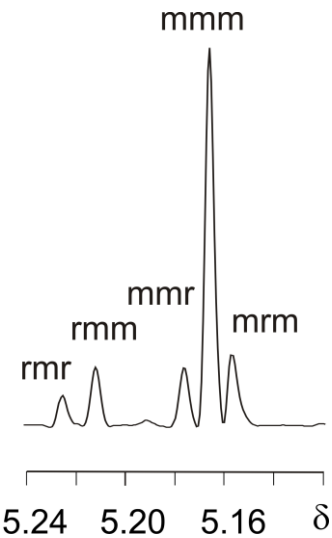
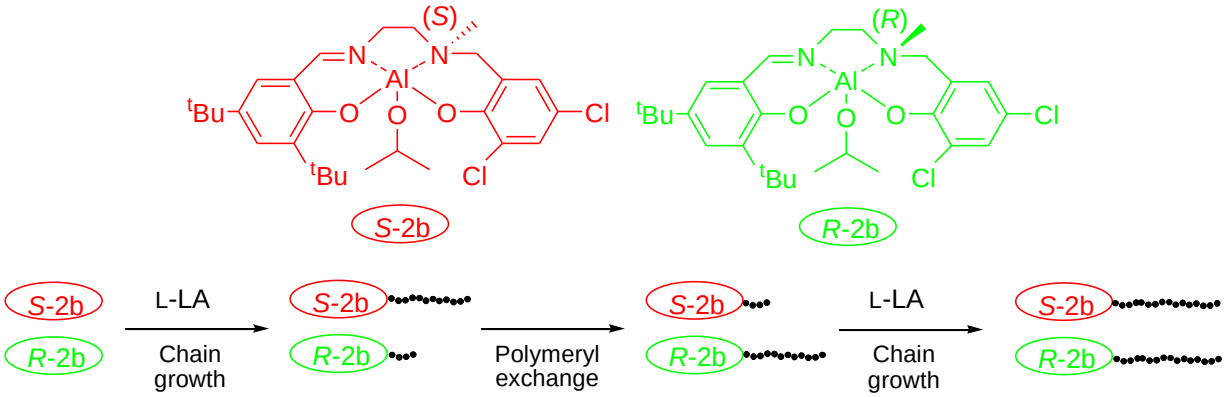
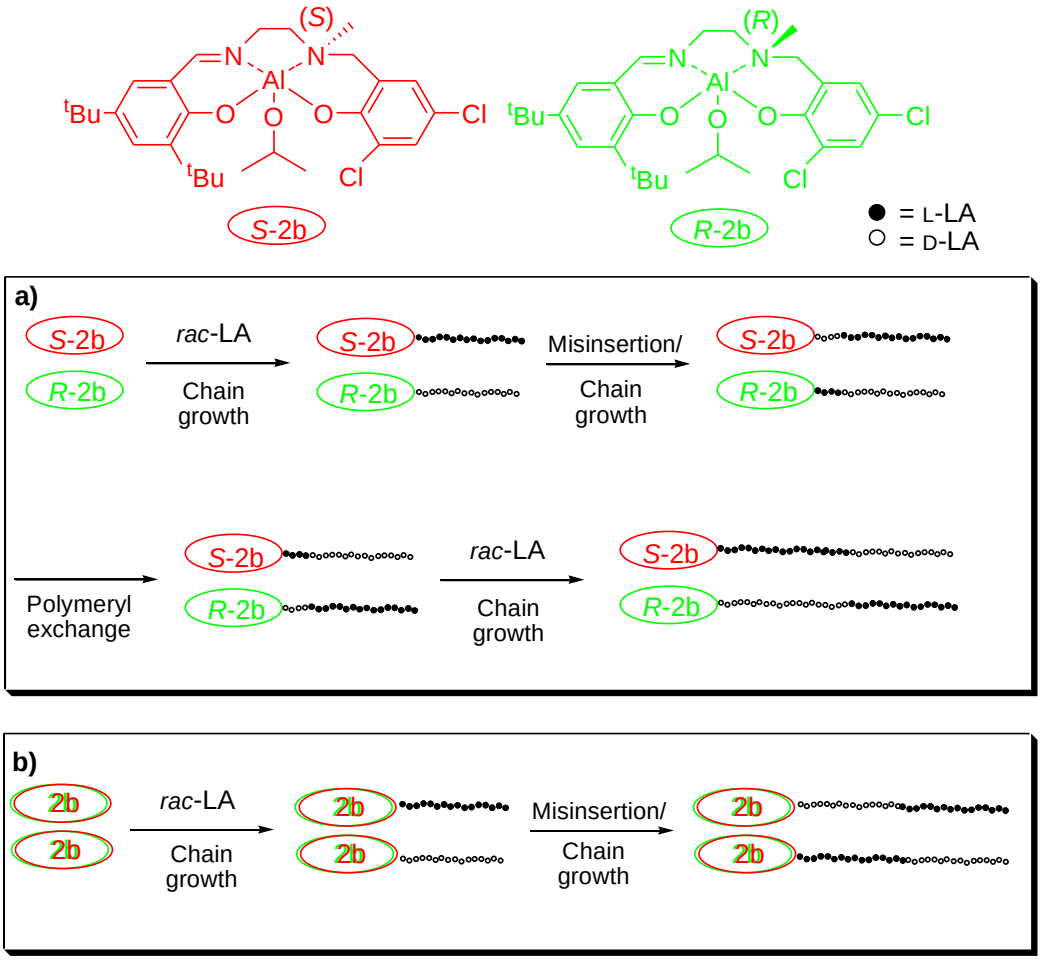


Figure 2. Methine region of the homonuclear decoupled ^{1}H NMR of the PLA sample obtained by complex **2b** and *rac*-LA in toluene at 80 °C.

As hypothesized, complex **2b** polymerized *rac*-LA to isotactic PLA, justifying the observed slower rate relative to its rate in polymerization of the homochiral monomers L-LA and D-LA. Homochiral preference in *rac*-LA polymerization can result from either a chain-end control mechanism, or from a site-control mechanism. Possibly, these two control mechanisms may act in concert. For the site control mechanism, since each catalyst enantiomer reacts at a different rate with a given lactide monomer, a broad (or bimodal) molecular weight distribution is expected for the polymerizations of L-LA and D-LA by **2b**. This reservation could be lifted if polymeryl chain exchange between propagating species takes place, as shown in Scheme 2. Such polymeryl exchange events may also occur in the polymerization of *rac*-lactide, in particular after the insertion of the "wrong" lactide monomer which slows down the polymerization (if a SCM mechanism is active, see Scheme 3a). Thus, the distinction between chain-end control mechanism and enantiomorphic-site control combined with polymeryl exchange mechanism is not obvious.



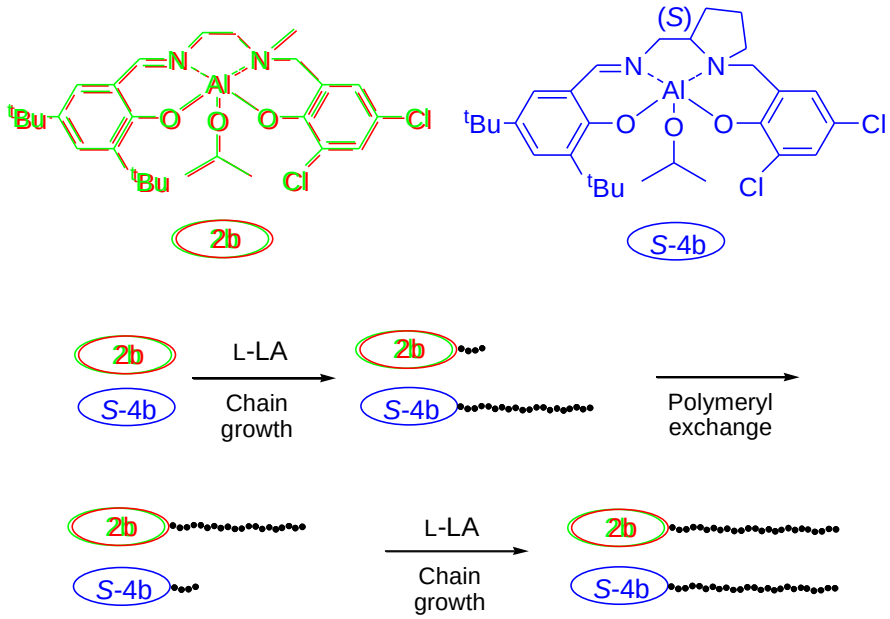
Scheme 2. Effect of the polymeryl exchange events on the narrowing of molecular weight distribution in the polymerization of L-LA by complex **2b**. *S*-**2b** is formally assigned as the catalyst enantiomer which reacts faster than *R*-**2b** with L-LA.



Scheme 3. Polymerization of *rac*-LA by complex **2b**: a) According to the SCM mechanism + polymeryl exchange; b) According to the CEM mechanism (in this case: **2b** represents the two enantiomers (*S*-**2b** and *R*-**2b**) which do not have a preference for a specific lactide enantiomer; the polymeryl exchange step is omitted as it is degenerate)

For the polymeric samples obtained in runs 2 and 3 we calculated the tetrad probabilities based on both Bernoullian (CEM) and SCM statistics, and these values were compared with the experimental values obtained by the NMR analysis (see Tables S1-S3 in the ESI). In both cases the experimental values deviated from the theoretical values calculated by the SCM statistical treatment (excluding polymeryl exchange), while a good agreement was observed with the tetrad probabilities based on the Bernoullian statistics. However, we have previously demonstrated that polymeryl exchange does occur in polymerization of lactide by the related aluminum complexes of chiral Salalen ligands.[2d] Hence, we propose that SCM cannot be ruled out, because polymeryl exchange events could make the statistical error distributions in these two scenarios very similar.

To reveal the possible involvement of polymeryl exchange between propagating species (and consequently the possible involvement of site-control in PLA stereoregularity) we designed the following polymerization experiment: A 1:1 mixture of the racemic catalyst **2b** and an enantiomerically-pure catalyst of a very similar structure (*S*-**4b**; see Scheme 4) was used in the polymerization of L-LA. The experimentally measured $k_{(app)}$ values for the polymerization of L-LA are 0.025 h^{-1} for **2b** (see Figure 1) and 0.241 h^{-1} for *S*-**4b**.[2d] In the absence of polymeryl exchange events polymeric chains of different lengths would be expected, resulting in a bimodal distribution of molecular weights. If, on the other hand, polymeryl exchange between **2b**- and **4b**-based propagating species takes place, narrow molecular weight distributions should result. We observed a PDI value close to 1 (M_w/M_n = 1.05) for the obtained polymeric sample, with an experimental molecular weight in excellent agreement with the theoretical molecular weight, assuming the growth of a single chain per averaged aluminum site (taking into account the metal centers of both the catalysts, see table S4 for experimental details). This strong evidence for polymeryl exchange between **2b**- and **4b**-based propagating species also supports the polymeryl exchange between **2b**-based enantiomers, as proposed above. Altogether, we propose that enantiomorphic site-control combined with polymeryl exchange between propagating species is responsible, at least in part, for the stereochemical consequences of *rac*-LA polymerization by these racemic aluminum catalysts derived from non-chiral salalen ligands. This control is probably combined with chain-end control, as was previously found for the aluminum catalysts derived from chiral salalen ligands.



Scheme 4. Effect of the polymeryl exchange events on molecular weight and molecular weight distribution of PLLA in the polymerization of L-LA by complex **2b** + complex ***S*-4b**. (complex **2b** is a 1:1 mixture of *R*-**2b** and *S*-**2b**, both of which being involved in the polymeryl exchange events with ***S*-4b** as well as with each other (see Scheme 2)).

To shed light on the sources of stereocontrol in these salalen-aluminum complexes, we tested complex **2b** in the polymerization of *meso*-lactide in toluene at 80°C (run 6 in Table 1). After 3 days, 98% of conversion was reached. The PLA obtained was heterotactic (P_m = 0.79) with narrow polydispersity of 1.17.

The polymerization of *meso*-lactide may give rise to two ordered microstructures: Syndiotactic PLA featuring the ···RS-RS-RS··· structural motif and heterotactic PLA featuring the ···RS-SR-RS··· structural motif. Syndiotactic PLA may be produced either by a homochiral preference of SCM-stereocontrol of a chiral catalyst without polymeryl-transfer between enantiomorphous catalyst molecules which can be achieved by employing an enantiomerically-pure catalyst[13] or by a CEM-stereocontrol with heterochiral preference employing a non-chiral catalyst or a fluxional catalyst.[14] Hetereotactic PLA may be produced either by a CEM-stereocontrol with homochiral preference,[15] or by a combination of SCM-stereocontrol by a chiral-racemic catalyst and polymeryl exchange between the two enantiomorphous catalyst molecules.[2a,2d]

Tetrad distribution obtained by ^{13}C NMR analysis (Figure 2) of the PLA sample obtained from *meso*-LA, was found to be in agreement with the theoretical values calculated by Bernoullian statistics (Tables S5-S6 in the ESI). Again, the latter data, which is consistent with CEM stereocontrol, does not rule out the possibility of alternating SCM / polymeryl exchange control, since polymeryl-exchange was demonstrated in the polymerization of *rac*-LA by these catalysts as

well as in polymerization of *meso*-LA for the (aminomethyl-pyrrolidine based) homochiral-Salalen aluminum complexes.[2d]

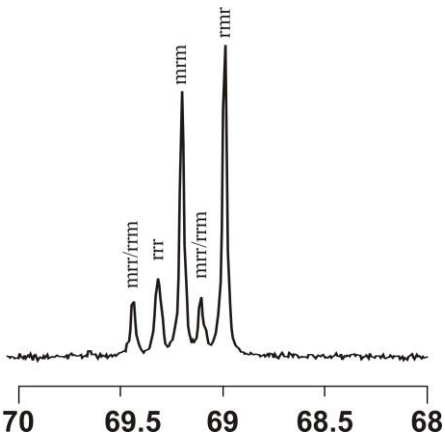


Figure 2. Methine region of the ^{13}C NMR spectrum of the PLA sample obtained by complex **2b** and *meso*-LA in toluene at 80 °C.

Ring-Opening Copolymerization of ε-Caprolactone and L-Lactide

Copolymerizations of ε-CL and L-lactide, in the presence of compounds **2b** and **3b**, were performed in toluene solution at 80 °C, by varying the ε-CL/L-LA molar ratio. The obtained polymer samples were characterized by ^{1}H and ^{13}C NMR spectroscopy, GPC, and DSC analyses. The main results are summarized in Table 2.

Table 2. Copolymerization of ε-Caprolactone and L-Lactide[a]

run	CL:L-LA (mol:mol)	CL in the cop (mol%)	L_{CL}[b]	L_{LA}[b]	Conv%		$M_{n,exp}$[c] (Kg/mol)	PDI	T_g (°C)	T_g[d] (°C)
					CL	LA				
7[e]	100:0	100	-	-	100	-	9.2	1.19	-	-
8	80:20	84	6.5	1.4	100	91	8.5	1.22	-47	-44
9	70:30	77	3.8	1.5	100	88	8.5	1.17	-38	-37
10	50:50	57	2.5	1.9	96	81	8.0	1.09	-17	-15
11	30:70	42	1.7	2.7	86	66	7.4	1.07	10	3
12	20:80	24	1.4	4.5	83	62	7.2	1.06	24	22
4[f]	0:100	-	-	-	-	82	11.3	1.05	-	-
13[g]	50:50	61	2.2	1.8	87	67	7.9	1.08	-20	-20
14[h]	50:50	59	2.2	1.9	93	65	8.4	1.09	-21	-18

[a] General conditions: initiator, **2b**: 20 μmol; toluene: 2 mL; monomers: 2 mmol; temperature: 80 °C, polymerization time: 48h.

[b] Average sequences length of the caproyl unit and of the lactidyl unit as determined by ^{13}C NMR analysis.

[c] Experimental M_n values were determined by GPC analysis in THF using polystyrene standards. M_{nGPC} x (conv CL x 0.56 + conv LA x 0.58).

[d] Theoretical values calculated by Fox equation, by using for the Tg of the homopolymers the following literature values: PCL: - 60 °C; PLLA: 57 °C.

[e] polymerization time: 6 minutes

[f] polymerization time: 72 hours

[g] polymerization time: 24 hours

[h] initiator, **3b**

Homopolymerization experiments of both ε-CL and L-LA, carried out in the same conditions, are also reported (runs 7 and 4 in Table 2) for comparison. The conversion of 100 equiv of monomers (ε-CL and L-LA) was almost complete in 2 days (runs 8-12) for compound **2b**. The composition in the copolymers was determined by ^1H NMR, from the ratio of the integrated values of the methylene signals of the ε-CL units (4.0 ppm) and the methine signals of LA (5.2 ppm). The amount of ε-CL present in the copolymer was found slightly higher than its initial concentration in the feed, suggesting a higher reactivity of ε-CL versus L-LA in the copolymerization (vide infra) as observed in the homopolymerization.

Analogous results were obtained in the presence of compound **3b**, having the bulkier adamantyl substituent in the ortho position of the phenolate ring (Table 2, run 14). A detailed characterization of the microstructure of the copolymer chains was performed by ^1H NMR and ^{13}C NMR analysis at the diads and triads level. The percentage of CL−LA heterodiads evaluated on the ^1H NMR spectrum, increased by increasing the amount of lactide in the feed.

Perusal of the ^{13}C NMR spectra in the carbonyl region (from 165 to 175 ppm) showed the eight triads expected for the case of a binary copolymerization, previously reported in the literature.[12a] Notably the signal at 171 ppm, related to the triad having one single “lactic” ester unit between two CL units, was not observed. That triad cannot result from the insertion of the lactide monomer into the chain, and it is indicative of the occurrence of transesterification reactions. The absence of transesterification reactions is further confirmed by the narrow molecular weight distributions of the polymers with dispersities values ranging between 1.05 and 1.22, as determined by GPC measurements. From the integrals of the triads sequences signals, the average length of the caproyl (L_{CL}) and lactidyl (L_{LA}) sequences was calculated, following previously reported methods.[12a] Both the L_{CL} and L_{LA} increased as a function of their relative ratio in the feed. Interestingly, for an equimolar ratio of the monomers in the feed, the L_{CL} and L_{LA} values were around 2, not only for the

almost full conversion run (see run 10 in Table 2), but also for a lower conversion run (67% for *rac*-LA and 87% for ε-CL) (see run 13, Table 2). These experimental features support a random copolymerization behaviour.

^{1}H NMR spectroscopic kinetic experiments were conducted to monitor the formation of the copolymer in reactions mediated by **2b** in toluene-d_8 at 80 °C (Figure 3). The kinetics of ε-CL and L-LA homopolymerization have been reported for comparison in the same plot. These data show that the ε-CL polymerization rate is lower in the copolymerization with respect to the rate in the homopolymerization, while no significant difference has been observed by comparing the behaviour of L-LA in the homo- and co-polymerization. These results indicate that the copolymerization of ε-caprolactone and L-lactide, mediated by this Al-salalen complex, displays a slight preference for the incorporation of ε-caprolactone over *rac*-lactide, in contrast with what is usually observed in such copolymerizations. More importantly, the k_{app} values of the two monomers in the copolymerization reactions turned out to be similar, as required for a random copolymerization.

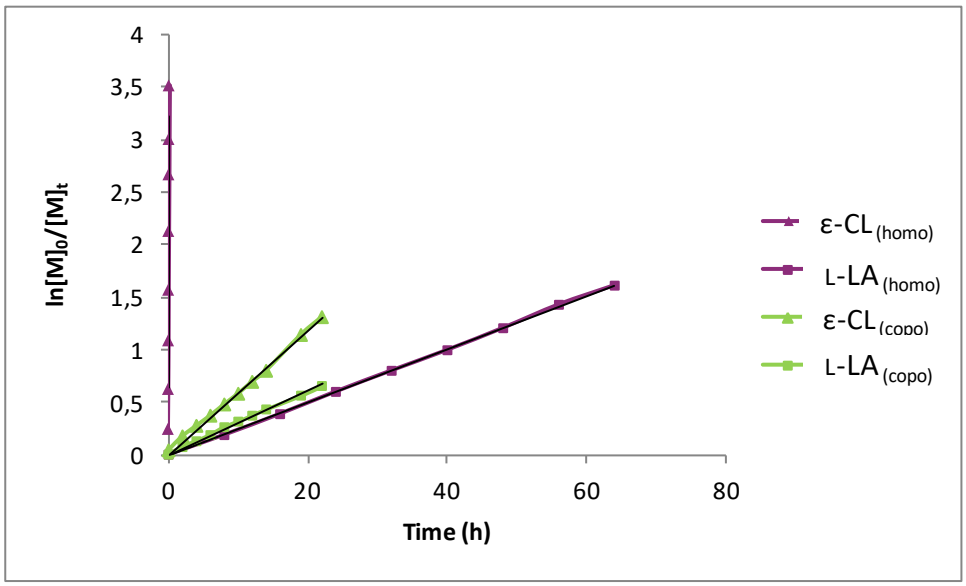


Figure 3. Pseudofirst-order kinetic plots for ROP of e-CL and L-LA in the homo- and in the co-polymerization reactions promoted by **2b**. [Al]=1.0 x 10^{-2} M; [M]/[Al]=100; [CL]:[LA]=1:1 in the copolymerization. T= 80°C; toluene-d_8 as solvent. k_{app} (homo ε-CL) = 21.46 h^{-1}; k_{app} (copo ε-CL) = 0.059 h^{-1}; k_{app} (copo L-LA) = 0.031 h^{-1}; k_{app} (homo L-LA) = 0.025 h^{-1}.

The determination of the reactivity ratios r_{LA} and r_{CL} was performed by using the nonlinear least-squares (NLLS) method carrying out the copolymerizations of the monomer with different compositions (LA:CL = 10:90, 30:70, 50:50, 70:30, and 90:10) at a low conversion (see Supporting Information). The values r_{LA} = 0.85 and r_{CL} = 2.95 indicate the propensity of this aluminum catalyst

to promote the random copolymerization of CL and LA, although with a slight preference for the insertion of the ε-caprolactone, as already envisaged from the previously discussed data.

Thermal analysis of the copolymers was carried out by differential scanning calorimetry (DSC) in the range from −100 to 200 °C. The obtained copolymers displayed unique glass transition temperature (T_g) with values intermediate between −60 °C of poly(caprolactone) and 57 °C of poly(L-LA). The T_g decreased as the percentage compositions of ε-CL in the copolymer increased, (see Figure S5 in the ESI) with a perfect agreement with the theoretical values calculated by the Fox equation (Figure 3) and with experimental data reported by several studies on LA-CL random copolymers.[12a,g,i] These data further support the random structure of copolymers.

It is worth noting that while the copolymers obtained in runs 12-15 are amorphous, the copolymer with CL:LA = 80:20 (run 8) has a T_m (c.a. 40 °C) compatible with the crystallization of CL units. Similar results have been reported by some authors who observed that random L-LA/ε-CL copolymers crystallize in PCL crystalline structure when the CL unit content is higher than 70% and the sequence length of CL units is higher than 4.75. [12e,g,h]

Conversely, copolymers having LA unit content less than c.a. 80%[12g,i] and length sequences of LA units less than 6.5,[11] remain amorphous and the typical crystallinity of PLLA is not observed.

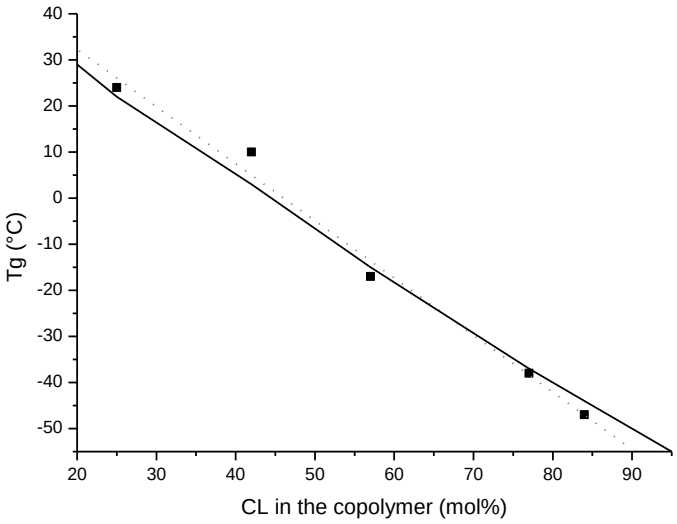


Figure 3. Experimental (—) and theoretical (···) T_g of the CL/LA copolymers as a function of the mole fraction of ε-CL unit.

CONCLUSION

Salalen-based aluminum complexes showed a good activity and a good control in the homopolymerization of lactides. As expected, PLLA and PDLA were obtained by polymerizing L-LA and D-LA respectively, while isotactic polylactide with P_m up to 72% was produced from *rac*-

LA and heterotactic polylactide with a P_m of 79% was obtained by polymerizing *meso*-LA. In all cases a good control of the polymerization process was observed.

Trying to shed light on the mechanism of stereocontrol active in the polymerization reactions promoted by this class of catalysts, some experimental results let us to hypothesize the occurrence of polymeryl exchange events between active enantiomorphous metal species. Chiral metal complexes derived from achiral ligands form as racemic mixtures. The distinction between chain-end stereocontrol and enantiomorphic-site combined with polymeryl exchange stereocontrol of the resulting polymer tacticity is difficult since both the NMR signature and the kinetic behaviour of these two scenarios should be identical. In this paper we introduced a new tool for supporting the occurrence of polymeryl exchange events: Performing a polymerization of a homochiral lactide (e.g., L-LA) by a catalyst mixture which contains an enantiomerically-pure complex derived from a chiral ligand and the racemic complex derived from the achiral ligand, (that should feature very similar ligand substitution patterns and different polymerization rates). Narrow molecular weight distributions and a good agreement between the experimental and the theoretical molecular weights support the polymeryl exchange between the two enantiomers of the racemic catalyst and the single enantiomer of the enantiomerically-pure catalyst. This suggests that a polymeryl exchange also takes place between the two enantiomers of the racemic catalyst derived from the achiral ligand. We propose that this tool may be applied for supporting polymeryl exchange events in other catalyst systems as well.

Finally, the versatility of this class of catalysts was demonstrated employing them in the copolymerization of ε-CL and L-LA. The obtained samples were fully characterized by DSC, GPC and NMR analyses. All the collected data demonstrated that tendentially random copolymers were obtained, e.g. the values of the reactivity ratios of the two monomers (r_{LA} = 0.85; r_{CL} = 2.95), the average lengths of the caproyl and lactidyl sequences for the copolymerization carried out with an equimolar ratio of the two monomers (L_{CL} = 2.5; L_{LA} = 1.9). Hence, the explored class of catalysts resulted able to prepare ε-CL and L-LA random copolymers with various compositions, i.e. polymeric samples with the thermal properties required for specific application.

EXPERIMENTAL SECTION

Materials and Methods

All manipulations of air- and/or water-sensitive compounds were carried out using standard Schlenk or glovebox techniques under an N_2 atmosphere. Glassware and vials used in the polymerizations were dried in an oven at 120 °C overnight and exposed to vacuum-nitrogen cycles thrice. Toluene and benzene (Sigma Aldrich) were distilled under nitrogen over sodium and sodium benzophenone respectively.

The aluminum precursors, $AlMe_3$ and $Al(O^iPr)_3$, were purchased from Aldrich and used as received. *Rac*-LA and L-LA were purchased from Aldrich. D-LA and *meso*-LA were given as gift from Purac. All lactides were purified by crystallization from dry toluene (twice).

ε-CL (Aldrich) was dried with CaH_2 for 24 h at room temperature and then distilled under reduced pressure.

Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc., degassed, and dried over activated 3-Å molecular sieves prior to use.

Instruments and Measurements

The NMR spectra were recorded on a Bruker Avance 400 spectrometer (^1H, 400.13 MHz; ^{13}C, 100.62 MHz) at 25 °C, unless otherwise stated. Chemical shifts (δ) are listed as parts per million and coupling constants (*J*) in hertz.

^1H NMR spectra are referenced using the residual solvent peak at δ = 7.16 for C_6D_6 and δ = 7.27 for $CDCl_3$. ^{13}C NMR spectra are referenced using the residual solvent peak at δ = 128.06 for C_6D_6 and δ = 77.23 for $CDCl_3$.

The molecular weights (M_n and M_w) and the molecular mass distribution (M_w /M_n) of polymer samples were measured by gel permeation chromatography (GPC) at 30 °C, using THF as solvent, flow rate of eluent 1 mL/min, and narrow polystyrene standards as reference. The measurements were performed on a Waters 1525 binary system equipped with a Waters 2414 RI detector using four Styragel columns (range 1000–1,000,000 Å). Every value was the average of two independent measurements. It was corrected using the factor of 0.58 for polylactide and 0.56 for ε-caprolactone according to the literature.

Elemental analyses of the aluminum complexes were measured on a Thermo Finningan Flash EA 1112 series C, H, N, analyzer in the microanalytical laboratory of the Chemistry and Biology Department of the University of Salerno.

Synthesis of Aluminum Complexes

Synthesis of 1a A benzene solution (2 mL) of the proligand (0.100 g, 0.215 mmol) was added dropwise into a stirred solution of $AlMe_3$ (0,016 g, 0.215 mmol) in benzene (2 mL).

The resulting mixture was stirred at room temperature for 2 hours. The solvent was removed *in vacuo* and the solid residue was washed using cold pentane twice (yield 80%). ^{1}H NMR spectrum was in agreement with the spectrum reported in the literature.[9a]

Synthesis of 2b Into a stirred solution of $Al(OiPr)_3$ (0.069 g, 0.340 mmol) in benzene (2 mL), a solution of the proligand (0.158 g, 0.340 mmol) in benzene (2 mL) was added dropwise.

The resulting mixture was stirred at 70°C for 24 hours. The solvent was removed *in vacuo* and the solid residue was washed using cold pentane twice (yield 80%).

^{1}H NMR (400 MHz, C_6D_6, 298 K): δ 7.79 (d, $^4J_{H-H}$: 2.5, 1H, Ar-*H*), 7.40 (d, $^4J_{H-H}$: 2.6, 1H, Ar-*H*), 7.26 (s, 1H, *H*C=N), 6.78 (d, $^4J_{H-H}$: 2.5, 1H, Ar-*H*), 6.69 (d, $^4J_{H-H}$: 2.6, 1H, Ar-*H*), 4.62 (br s, 1H, O-C*H*), 3.18 (ABq, $^2J_{H-H}$: 12.9, 1H, N-CH_2-Ar), 2.42 (ABq, $^2J_{H-H}$: 12.9, 1H, N-CH_2-Ar), 2.59 (m, 2H, CH_2CH_2), 2.46 (m, 1H, CH_2), 2.03 (s, 3H, NCH_3), 1.85 (s, 9H, C(CH_3)$_3$), 1.65 (m, 1H, CH_2), 1.35 (9H, C(CH_3)$_3$ + 6H, O-CH(CH_3)$_2$) (see the ESI for more details).

^{13}C {^{1}H} NMR (100.62 MHz, C_6D_6, 298 K): δ 173.74 (*C*=N), 166.10 (*C*q), 155.37 (*C*q), 141.85 (*C*q), 137.65 (*C*q), 132.28 (*C*H), 129.90 (*C*H), 127.60 (*C*H), 127.14 (*C*H), 125.78 (*C*q), 124.72 (*C*q), 120.69 (*C*q), 117.90 (*C*q), 62.92 (O*C*H), 57.31 (*C*H_2), 53.82 (*C*H_2), 49.77 (*C*H_2), 44.74 (N*C*H_3), 35.81 (*C*(CH$_3$)$_3$), 34.16 (*C*(CH$_3$)$_3$), 31.59 (C(*C*H$_3$)$_3$), 30.10 (C(*C*H$_3$)$_3$), 28.21 (2C, CH*C*H$_3$).

Elemental analysis calcd (%) for $C_{28}H_{39}AlCl_2N_2O_3$: C, 61.20; H, 7.15; N, 5.10; found: C, 61.27; H, 7.19; N, 5.15.

Synthesis of 3b Into a stirred solution of $Al(OiPr)_3$ (0.061 g, 0.298 mmol) in benzene (2 mL) , a solution of the proligand (0.150 g, 0.298 mmol) in benzene (2 mL) was added dropwise. The resulting mixture was stirred at 70°C for 24 hours. The solvent was removed *in vacuo* and the solid residue was washed using cold pentane twice (yield 70%).

^{1}H NMR (300 MHz, C_6D_6, 298 K): δ 7.42 (d, $^4J_{H-H}$ = 2.6 Hz, 1H, Ar-*H*), 7.33 (d, $^4J_{H-H}$ = 2.3 Hz, 1H, Ar-*H*), 7.32 (s, 1H, *H*C=N), 6.66 (d, $^4J_{H-H}$ = 2.6 Hz, 1H, Ar-*H*), 6.52 (d, $^4J_{H-H}$ = 2.3 Hz, 1H, Ar-*H*), 4.56 (br s, 1H, Al-O-C*H*), 3.20 (d, $^2J_{H-H}$ = 12.8 Hz, 1H, CH_2), 2.65 (3H, Ad), 2.51 (3H, Ad + 1H CH_2), 2.29 (3H, Ad), 2.25 (s, 3H, Ar-CH_3), 2.20 (1H, CH_2), 2.11 (3H, Ad + 2H CH_2), 2.01 (s, 3H, N-CH_3), 1.90 (3H, Ad), 1.57 (m, 1H, CH_2), 1.41 (3H, O-CH(CH_3)$_2$), 1.22 (3H, O-CH(CH_3)$_2$).

^{13}C{^{1}H}NMR (75.84 MHz, C_6D_6, 298 K): δ 173.33 (*C*=N), 166.18 (*C*q), 155.34 (*C*q), 142.16 (*C*q), 136.30 (*C*H), 131.08 (*C*H), 129.81 (*C*H), 127.19 (*C*H), 125.50 (*C*q), 124.84 (*C*q), 124.30 (*C*q), 120.68 (*C*q), 118.32 (*C*q), 62.95 (O*C*H), 56.91 (*C*H_2), 54.24 (*C*H_2), 49.92 (*C*H_2), 44.81 (N*C*H_3),

40.72 (3C, *C*H_2 adamantyl), 40.15 (*C*q-adamantyl), 37.71 (3C, *C*H_2 adamantyl), 29.91 (3C, *C*H adamantyl), 28.20 (2C, CH*C*H_3), 20.81 (Ar-*C*H_3).

Elemental analysis calcd (%) for $C_{31}H_{39}AlCl_2N_2O_3$: C, 63.59; H, 6.71; N, 4.78; found: C, 63.56; H, 6.73; N, 4.76.

Polymerization studies

A typical experiment: in a Braun Labmaster glovebox, a 10 mL Schlenk tube was charged sequentially with monomer (2 mmol), 1.5 mL of dry solvent and a solution of the metal initiator (20 μmol in 0.5 mL of dry solvent), to which 2-propanol (20 μmol) was eventually added. The mixture was immediately stirred with a magnetic stir bar at the prescribed temperature. After a specified time, an aliquot of the reaction mixture was sampled with a pipette for determining the monomer conversion by ^{1}H NMR spectroscopy ($CDCl_3$, 400 MHz). The reaction mixture was quenched by adding wet *n*-hexane. The polymer was precipitated with an excess of *n*-hexane, filtered and dried in a vacuum oven at 40 °C for 16 h.

Kinetic Studies

In a typical experiment carried out in a Braun Labmaster glovebox, a screw-cap NMR tube containing 0.5 mmol of monomer was added a solution of 0.1 mL of the initiator (5 μmol) in deuterated toluene. Next, 0.4 mL of deuterated toluene were added to adjust the total volume to 0.5 mL. The NMR tube was then placed to the preheated NMR spectrometer at 70°C and the % conversion was evaluated from the integration of polymer and monomer signals.

ASSOCIATED CONTENT

Supporting Information. COSY NMR spectrum of complex **2b**; tables with tetrad distributions analysis; table with details of some polymerization experiments; copolymerization data for the determination of the reactivity ratios. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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Nanostructured polymeric materials with tailored molecular and crystalline structures, for advanced technologies and for the environment).

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Ring-Opening Homo- and Co-polymerization of Lactides and ε-Caprolactone by Salalen Aluminum Complexes

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