

Macromolecular Engineering of Polylactones and Polylactides. X. Selective End-Functionalization of Poly(D,L)-Lactide

I. BARAKAT, Ph. DUBOIS, R. JÉRÔME,* and Ph. TEYSSIE

Center for Education and Research on Macromolecules (CERM), University of Liège, Sart Tilman B6, B-4000-Liège, Belgium

SYNOPSIS

Functional aluminum alkoxides, such as $\text{Et}_{3-p}\text{Al}(\text{O}-\text{CH}_2-\text{X})_p$, where $p = 1,3$ and X = a functional group, are very effective initiators for the (D,L)-lactide polymerization in toluene at 70°C. The coordination-insertion type of polymerization is living. Linear polyesters of a predictable molecular weight and a narrow molecular weight distribution are obtained within the period of time required for the total monomer conversion. The functional group (X) associated with the active alkoxy group of the initiator is selectively and quantitatively attached to one chain end, whereas the second end group is systematically a hydroxyl function resulting from the hydrolysis of the living growing site. Asymmetric telechelic polylactides are thus obtained in a perfectly controlled way. A kinetic study has shown that the polymerization is first order in both the monomer and initiator. © 1993 John Wiley & Sons, Inc.

Keywords: polylactide • end-functionalization • living polymerization • kinetics • mechanism

INTRODUCTION

Due to a remarkable combination of biodegradability, biocompatibility, and high mechanical strength, polylactides (PLA) and their copolymers with glycolide are currently used in the biomedical field as biomaterials in surgery and sustained drug delivery.¹⁻⁴

In addition to polycondensation of lactic acids, polylactides can be synthesized by ring-opening polymerization of lactides, i.e., cyclic diesters of various isomeric forms: L, D, DL, and meso.⁵ Polymers derived from the L- and D-monomers are semicrystalline, whereas the D,L-monomer (a racemic mixture of L and D isomers) promotes the formation of an amorphous material.

Despite the abundant literature on the polymerization of lactides (see References 6-8 and references therein), the molecular parameters of the polylac-

tides are rarely controlled, i.e., the molecular weight distribution is broad, the number-average molecular weight cannot be predicted from the monomer/initiator molar ratio, and the nature of the end groups is out of control. During the last decade, it has been reported that the "aluminum alkoxide" functions of bimetallic (Al, Zn) μ -oxoalkoxides, tetraphenylporphinato-aluminum, and Al triisopropoxide, are very effective in the controlled polymerization of lactides⁹⁻¹¹ and unsubstituted lactones.¹²⁻¹⁴ Moreover, these initiators allow block copolymers of lactones (e.g., ϵ -caprolactone) and lactides to be synthesized in a controlled way, indicating that the chain propagation is living.^{15,16} Recently, some of us have reported on the living polymerization and selective end-functionalization of poly(ϵ -caprolactone) (PCL) initiated by aluminum alkoxides carrying functional alkoxy groups.^{17,18} Various functional end groups have thus been attached to PCL chains, such as an unsaturated group, a halogen, a tertiary amine, and best, a methacrylic double bond which has made PCL macromonomers available.¹⁹

This article deals with the possible extension of functional aluminum alkoxides to the polymeriza-

* To whom all correspondence should be addressed.

tion of lactides and the synthesis of α , ω -functional PLA chains. The discussion will mainly focus on the synthetic aspects, the control of the end groups, and the kinetics of polymerization.

EXPERIMENTAL

Materials

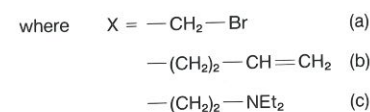
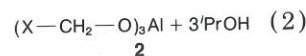
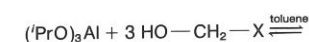
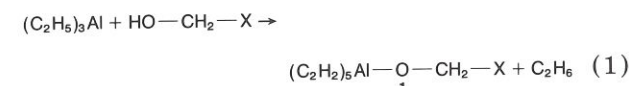
(D,L)-lactide was purchased from Boehringer and recrystallized three times from dried ethyl acetate at 60°C. The monomer was dried for 24 h at 25°C under reduced pressure (10^{-2} mm Hg) before polymerization. 4-Penten-1-ol (Aldrich) and 3-diethylamino-1-propanol (Aldrich) were dried over calcium hydride for 48 h at room temperature and distilled under reduced pressure just before use. 2-Bromomethanol (Aldrich) was repeatedly treated with a saturated aqueous solution of K_2CO_3 , dried over P_2O_5 , and freshly distilled under reduced pressure. Previously distilled aluminum isopropoxide (Aldrich) and triethylaluminum (Fluka) were dissolved in dry toluene. The solution concentration was determined by complexometric titration of Al by EDTA. Toluene and ethyl acetate were dried by refluxing over CaH_2 and $CaCl_2$, respectively, and distilled under nitrogen atmosphere.

Since experimental details were published elsewhere,^{9,12,13,15,17-19} only key points are reported hereafter.

Preparation of the Initiators

Diethylaluminum alkoxides **1** were prepared by slowly adding a toluene solution of a selected alcohol into a flask containing an equimolar amount of $AlEt_3$ [eq. (1)]. The glass reactor was equipped with a rubber septum connected to a gas buret through an oil valve. It was previously flamed and purged with nitrogen. The reaction proceeded under nitrogen with vigorous stirring at room temperature. When the emission of ethane stopped, the catalyst solution was kept stirred at room temperature for an extra hour.

Aluminum trialkoxides **2** were synthesized by the reaction of $Al(O^iPr)_3$ with 3 equiv of the appropriate alcohol [eq. (2)] in a carefully dried and nitrogen purged distillation apparatus. The toluene/isopropanol azeotrope was distilled off continuously.



Polymerization Procedure

Polymerization took place under stirring, in toluene, at 70°C, in a previously flamed and nitrogen-purged glass reactor. Below 70°C, (D,L)-lactide was insoluble in toluene. The addition of the monomer into the reactor was carried out in a glovebox under a nitrogen atmosphere. Solvent and initiator were then successively added through a rubber septum with a syringe or a stainless steel capillary. The reaction was stopped by adding an excess (relative to the initiator) of 2N HCl solution.

The initiator residues were extracted four times with a dilute acid-solution. The reaction mixture was then washed with water to a neutral pH and the polymer was precipitated into an excess of methanol, filtered, and dried under vacuum to a constant weight.

NMR and IR Measurements

$^1\text{H-NMR}$ spectra of PLA were recorded in $CDCl_3$ with a Bruker AM 400 apparatus at 25°C.

IR spectra were recorded with a Perkin-Elmer 1600 Series FTIR apparatus.

Molecular Weight Determination

Molecular weight and molecular weight distribution were determined by using a gel permeation chromatograph (GPC Hewlett-Packard 1090) operating in THF and calibrated with polystyrene standards. The universal calibration method was applied for poly-(D,L) LA on the basis of the following viscometric relationships, valid in THF at 30°C²⁰:

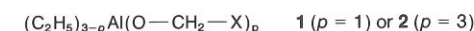
$$[\eta] = 1.25 \times 10^{-2} \bar{M}^{0.717}, \text{PSt and}$$

$$[\eta] = 5.49 \times 10^{-2} \bar{M}^{0.639}, \text{poly(D,L)LA.}$$

Low molecular weights ($\bar{M}_n < 15000$) were also measured by $^1\text{H-NMR}$ and by vapor pressure osmometry (VPO: Ateliance Instruments, France) in toluene at 47°C. \bar{M}_n ($^1\text{H-NMR}$) was calculated from the signal intensities of the functional ester end group and the methine ester groups of the polyester chain. A good agreement was usually observed between \bar{M}_n s obtained by VPO, GPC, and NMR.

RESULTS AND DISCUSSION

It has been shown previously that aluminum triisopropoxide is very effective in promoting the living polymerization of ϵ -caprolactone¹² and lactides⁹ in toluene at 0 and 70°C, respectively. It has been demonstrated that the polymerization proceeds through the coordinative insertion of the monomer into an aluminum alkoxide bond of the initiator.^{9,12} That insertion mechanism involves the selective cleavage of the acyl-oxygen bond of the monomer and accordingly controls the nature of the polyester end groups, i.e., an ester and a hydroxyl group, respectively. On that basis, end-reactive PCL chains have been synthesized by using functional Al alkoxides as initiators.^{17,18} These functional Al derivatives can actually contain p ($p = 1-3$) functional alkoxide groups, associated with 3- p inactive alkyl groups, respectively.



where X is the functionality, e.g., CH_2Br (a), $(CH_2)_2CH=CH_2$ (b), $(CH_2)_2NEt_2$ (c).

The results reported in this paper demonstrate that the **1** and **2** functional Al alkoxides are also able to initiate the ring-opening polymerization of (D,L) lactide and to lead to the end-functionalization of the related polyester chains.

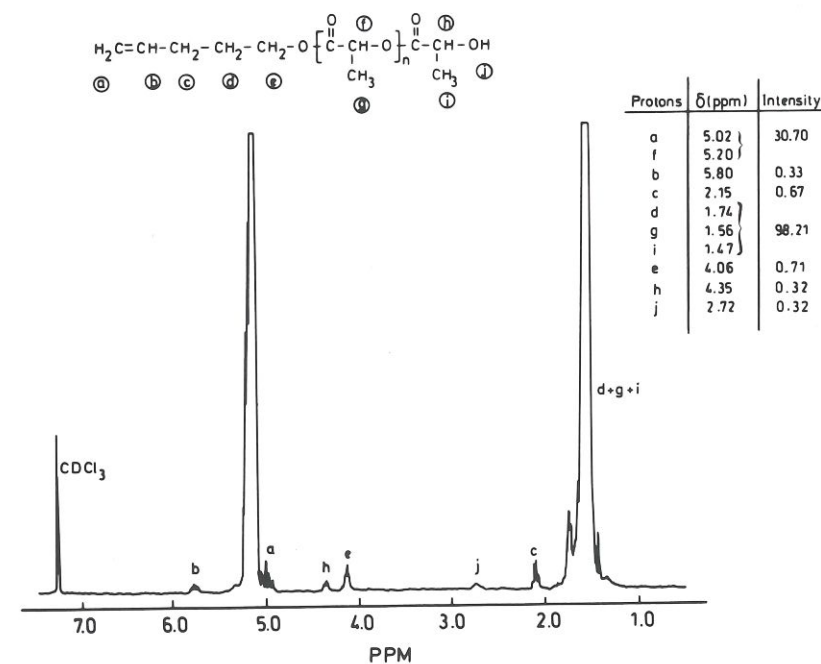


Figure 1. $^1\text{H-NMR}$ spectrum of a typical α -1-pentene, ω -hydroxyl poly(D,L) lactide in $CDCl_3$.

Table I. $^1\text{H-NMR}$ Chemical Shifts (δ , ppm, with Respect to TMS) of Hydrolyzed PLA Chains Initiated with the **2a** Diethylaluminum Alkoxide and the **1b** and **1c** Al Trialkoxides (Toluene, 70°C):

$$\text{X}-\text{CH}_2-\text{O}-\left[\overset{\text{O}}{\parallel} \text{C}-\underset{\text{f}}{\text{CH}}(-\underset{\text{g}}{\text{CH}_3})-\text{O}- \right]_n \underset{\text{h}}{\text{C}}-\underset{\text{i}}{\text{CH}}(-\text{CH}_3)-\text{OH}$$

(ppm) : $\text{H}_f = 5.20$; $\text{H}_g = 1.56$; $\text{H}_h = 4.35$, and $\text{H}_i = 1.47$

Code	Initiator	Chemical Shifts, δ (ppm) (Intensity)							Theoretical ^e \bar{M}_n	$^1\text{H-NMR}$ \bar{M}_n	GPC	VPO	\bar{M}_w/\bar{M}_n
		H_a	H_b	H_c	H_d	H_e	H_h	H_i					
2a	$\text{X}-\text{CH}_2-\text{O}$	H_a	H_b	H_c	H_d	H_e	H_h	H_i	5500	5600	5900	—	1.15
	$\text{Br}-\text{CH}_2-\text{CH}_2-\text{O}$	3.50 (0.48)	4.46 (0.78) ^b	—	—	—	4.35 (0.78) ^b	—	—	—	—	—	—
	$\text{H}_2\text{C}=\text{CH}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{O}$	5.02 (—) ^c	5.80 (0.33)	2.15 (0.67)	1.74 (—) ^d	4.06 (0.71)	4.35 (0.32)	—	6600	6700	6500	—	1.25
	$[\text{CH}_3-\text{CH}_2]_2\text{N}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{O}$	1.02 (1.20)	2.54 (1.09)	—	1.78 (—) ^d	4.29 (0.56) ^e	4.35 (0.56) ^e	—	4600	4400	—	4500	— ^f

^a Theoretical molecular weight as calculated by eq. (3).

^b Total intensity of overlapping signals at 4.46 ppm (H_b) and 4.35 ppm (H_h).

^c Superimposed to signal at 5.20 ppm of the ester methine group in the polymer chain.

^d Superimposed to signal at 1.56 ppm of the methyl group in the polymer chain.

^e Total intensity of overlapping signals at 4.29 ppm (H_e) and 4.35 ppm (H_i).

^f Undetermined due to the adsorption of the amino-terminated chains on the chromatographic support.

For instance, the telechelic polyester as initiated by the **1b** initiator presents as many unsaturated H_b protons at $\delta = 5.80$ ppm (intensity = 0.33) as α -hydroxyl methine ones at $\delta = 4.35$ ppm (intensity = 0.32). A very close agreement is observed between the number-average molecular weight as determined by GPC, VPO, and $^1\text{H-NMR}$, which confirms the quantitative end-capping of the chains. In the latter case, \bar{M}_n has been calculated from the integration of the signals corresponding to the ester methine group in the polyester chain $[-\text{C}(\text{O})\text{O}-\text{CH}(\text{Me})-]$ at $\delta = 5.20$ ppm, and the integration of either the α -hydroxymethine end group $[-\text{CH}(\text{Me})-\text{OH}]$ at $\delta = 4.35$ ppm, or protons $\text{H}_{(a-e)}$ of the functional ester end group.

From the nature of the end groups, it must be concluded that the lactide is inserted into the $\text{Al}-\text{O}$ bond of the initiator through the selective cleavage of the acyl-oxygen bond of the monomer. This mechanism, which is also operative when the initiator is a nonfunctional aluminum alkoxide (e.g., aluminum isopropoxide), has been reported in detail elsewhere⁹ and it requires the coordination of the monomer to the initiator in agreement with observations reported by Feijen et al.²¹

It is worth pointing out that the experimental molecular weights are close to the theoretical values as calculated by eq. (3) (see next section) suggesting a "living" mechanism for the polymerization.

Living Character of the Polymerization

As it might be anticipated from the analysis of the PLA end groups, propagation of the (D,L) lactide

polymerization is perfectly "living" when it is initiated by the functional aluminum alkoxides of the **1** and **2** series. Figures 2 and 3 show that the molecular weight of poly(D,L)LA linearly increases with the monomer conversion when **1a** and **2b** aluminum monoalkoxides, and **2a** or **b** Al trialkoxides are used as initiators, respectively. A living propagation is also proved by the accurate agreement between the mean degree of polymerization (\bar{DP}) at total conversion and the monomer/initiator molar ratio (Fig. 4). It is worth pointing out that all the poly(D,L)LA chains prepared in this study display a rather narrow molecular weight distribution ($\bar{M}_w/\bar{M}_n = 1.05-1.30$).

These observations complete a previous study of the (D,L)LA polymerization initiated by aluminum isopropoxide in toluene at 70°C .⁹ It is clear that the polymerization is "living" whatever the structure of the aluminum alkoxide, i.e., functional or not, mono- or trialkoxide. It is worth recalling that, in the particular case of aluminum isopropoxide, the "living" character has also been demonstrated by resumption experiments and that the experimental \bar{DP} vs. theoretical \bar{DP} relationship is linear until a molecular weight of 90,000. Beyond that molecular weight, transesterification reactions occur and the polydispersity exceeds 1.4.

Since the slope of the linear dependence of the \bar{DP} vs. the $[\text{monomer}]/[\text{initiator}]$ molar ratio (Fig. 4) is 1 and 1/3 for the **1a**, **b** and **3a**, **b** initiators, respectively, it is obvious that each alkoxide group initiates the lactide polymerization in toluene at 70°C . Since the polymerization is "living," the mo-

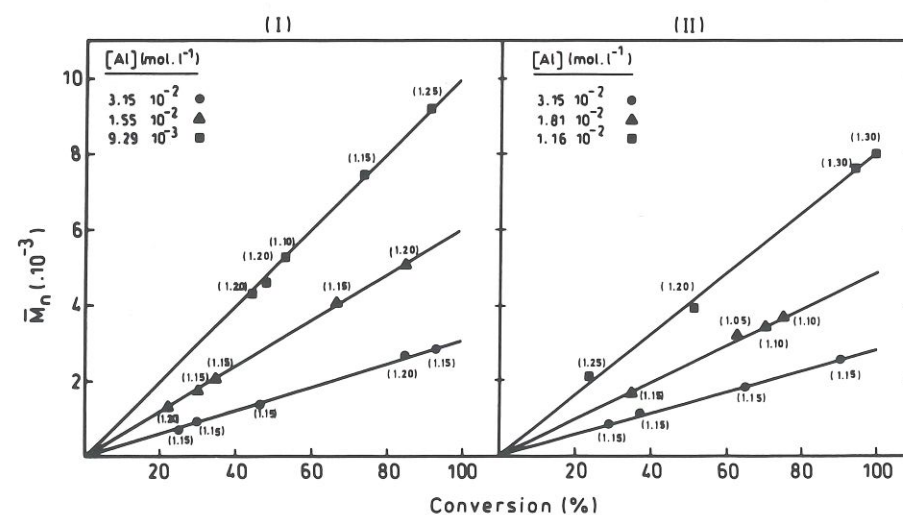


Figure 2. Relationship between \bar{M}_n (GPC) and monomer conversion (%) for the polymerization of (D,L) LA ($[\text{M}]_0 = 0.65 \text{ mol L}^{-1}$) in toluene at 70°C . The initiators are diethylaluminum alkoxides: (I) $\text{Et}_2\text{Al}-\text{O}-(\text{CH}_2)_3-\text{CH}=\text{CH}_2$ (**1b**); (II) $\text{Et}_2\text{Al}-\text{O}-(\text{CH}_2)_2-\text{Br}$ (**1a**). Polydispersity is reported in brackets.

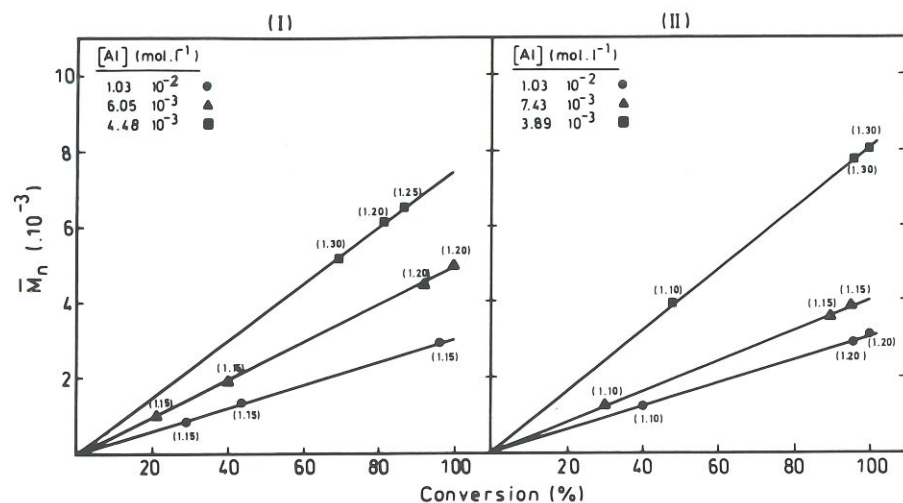


Figure 3. Relationship between \bar{M}_n (GPC) and monomer conversion (%) for the polymerization of (D,L)LA ($[M]_0 = 0.65 \text{ mol L}^{-1}$) in toluene at 70°C . The initiators are aluminum trialkoxides: (I) $\text{Al}[\text{O}-(\text{CH}_2)_3-\text{CH}=\text{CH}_2]_3$ (**2b**); (II) $\text{Al}[\text{O}-\text{CH}_2-\text{CH}_2-\text{Br}]_3$ (**2a**). Polydispersity is reported in brackets.

molecular weight of PLA can be predicted from the molar amount of the Al compound with respect to the monomer ($[\text{LA}]_0/[\text{Al}]$), the number of alkoxide group per Al (p) and the monomer conversion (x):

$$\bar{M}_n(\text{theoretical}) = \frac{[\text{LA}]_0 \text{MM}_{\text{LA}} x}{[\text{Al}]p} \quad (3)$$

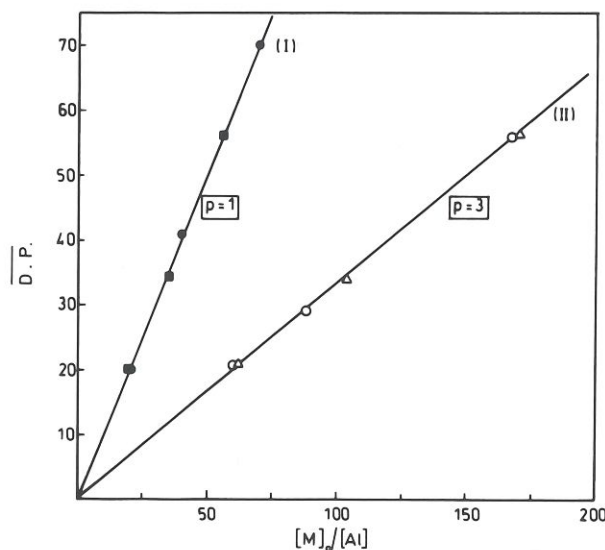


Figure 4. Dependence of $\overline{\text{DP}}$ at 100% conversion of monomer on the $[\text{monomer}]/[\text{initiator}]$ molar ratio for the polymerization of (D,L)LA ($[M]_0 = 0.65 \text{ mol L}^{-1}$) in toluene at 70°C . The initiators are: (I) $\text{Et}_2\text{Al}-\text{O}-(\text{CH}_2)_2-\text{X}$ with $\text{X} = -\text{Br}$ [**1a** (●)] and $\text{X} = -\text{CH}_2-\text{CH}=\text{CH}_2$ [**1b** (■)], (II) $\text{Al}[\text{O}-(\text{CH}_2)_2-\text{X}]_3$ with $\text{X} = -\text{Br}$ [**2a** (○)] and $\text{X} = -\text{CH}_2-\text{CH}=\text{CH}_2$ [**2b** (Δ)].

where MM_{LA} is the molecular mass of LA (144 g mol^{-1}). These results are in agreement with the polymerization of (D,L and L)LA by Al triisopropoxide where each of the three alkoxide groups of the initiator contributes to the lactide polymerization ($\bar{n} = 3$).⁹

Nevertheless, when the polymerization of ϵ -CL is initiated by the **1** and **2** functional Al alkoxides, all the alkoxide groups do not systematically participate in the monomer conversion.^{17,18} For instance, when the initiator is a diethylaluminum alkoxide of the **1a, b, c** series, the mean number of active alkoxide groups per Al (\bar{n}) is equal to 1 ($\bar{n} = p = 1$) at 25°C in toluene. In contrast to the monoalkoxides, \bar{n} depends on the nature of the X functional group when aluminum trialkoxides of the **2a, b, c** series are concerned ($\bar{n} < p$). Furthermore, only 75% of the alkoxide groups of a mono Al alkoxide of the **1a, b, c** series participate in the ϵ -CL polymerization in toluene at 0°C , whereas each of them is active at 25°C .

The main features of the polymerization of ϵ -CL and (D,L)LA in toluene at 25 and 70°C , respectively, have to be related to the well-known coordinative association of metal alkoxides in solution.²² The mean degree of association (\bar{N}) of the initiator in the absence of monomer depends on several factors, i.e., nature of the alkoxide group, nature of the solvent, addition of a ligand, and temperature. It has been shown that when \bar{N} changes, so does \bar{n} in the ϵ -CL polymerization.^{22,23} For instance, any dissociative factor, e.g. addition of an alcohol and rise in temperature, increases the number of alkoxide

groups available for chain initiation. Accordingly, it may be assumed that the unassociated alkoxide groups essentially contribute to the monomer conversion. It is the reason why a rise in temperature and the electron-donating capability of the X functional group on the initiator can shift the equilibrium of the Al-alkoxide coordinative association towards the formation of free alkoxide groups accounting for the experimental observations.

In conclusion, α -functional ($-\text{O}-\text{CH}_2-\text{X}$), ω -hydroxyl PLA chains can be prepared with a predictable molecular weight and a narrow molecular weight distribution. However, when the polymerization medium is kept at 70°C beyond the time required for the complete monomer conversion, the molecular weight distribution is observed to broaden. This effect is more likely due to intra- and intermolecular transesterification reactions, the occurrence of which has been unambiguously reported for the (D,L)LA polymerization initiated by $\text{Al}(\text{O}^i\text{Pr})_3$ under the same experimental conditions.⁹ Any increase in the polymerization time and temperature enhances the deleterious effect of the transesterification reactions. Accordingly, the experimental conditions must be optimized to reach a complete monomer conversion and the best control of the molecular characteristics of the PLA chains.

Kinetics

Kinetics of the (D,L) lactide polymerization initiated by the alkoxides of the **1a, b** and **2a, b** series has been investigated in toluene at 70°C . Kinetics were followed by gravimetric method. Samples of a precise volume were taken out of the reaction medium after different periods of time, hydrolyzed, and precipitated in cold *n*-heptane. After filtration and drying under vacuum up to a constant weight, P(D,L)LA samples were weighed allowing time dependence of monomer conversion to be known.

After an induction period, the polymerization is first order in monomer as shown by the linear relationship between the monomer conversion $[\ln([M]/[M]_0)]$ and the polymerization time (Figs. 5 and 6). An induction period is systematically observed when the polymerization of ϵ -CL and LA is promoted by Al triisopropoxide.^{9,12} This feature has been attributed to a rearrangement of the coordinative aggregates of the initiator in toluene upon addition of the monomer.

Polymerization of (D,L)LA is also first order in initiator as shown by the linear dependence of $\ln([LA]_0/[LA])/t$ on the initiator concentration (Fig. 7).

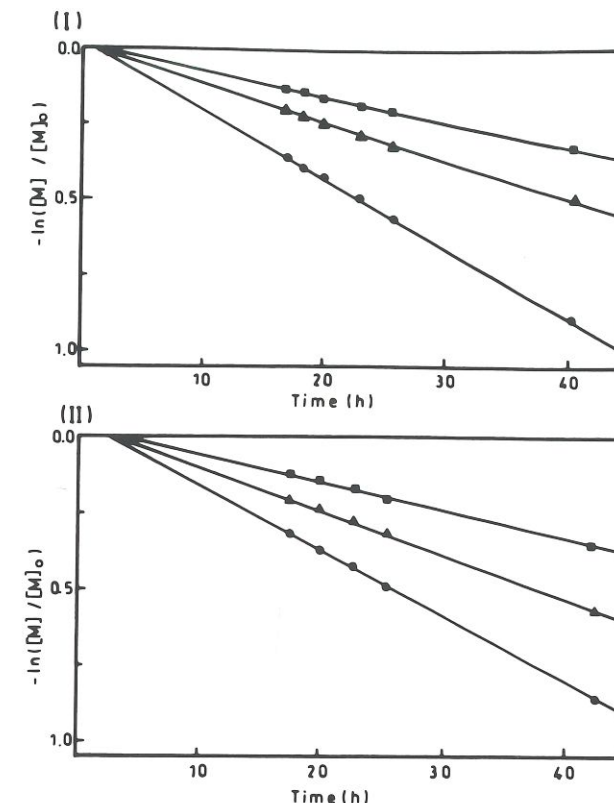


Figure 5. Order in monomer for the polymerization of (D,L)LA in toluene at 70°C . The initiators are: (I) $\text{Et}_2\text{Al}-\text{O}-\text{CH}_2-\text{CH}_2-\text{Br}$ (**1a**); (II) $\text{Et}_2\text{Al}-\text{O}-(\text{CH}_2)_3-\text{CH}=\text{CH}_2$ (**1b**). $[M]_0 = 0.65 \text{ mol L}^{-1}$. $[M]_0/[\text{Al}] =$ (●) 21, (Δ) 36, and (■) 56.

Beyond the induction period, the polymerization kinetics of (D,L)LA obeys a simple kinetic law:

$$-\frac{d[M]}{dt} = k [M] \cdot [\text{Al}] \quad (4)$$

The same kinetic behavior has been observed for the polymerization of lactide initiated by $\text{Al}(\text{O}^i\text{Pr})_3$ under the same experimental conditions.⁹ A comparative study of the polymerization rate constants (k) for the (D,L) lactide polymerization initiated by $\text{Al}(\text{O}^i\text{Pr})_3$ and the functional Al alkoxides of the **1a, b** and **2a, b** series, respectively, has been conducted and the data are reported in Table II. It is clear that the rate constants are affected by the structure of the Al alkoxide (mono- or trialkoxide) and the nature of the alkoxide group (functional or inert). The rate of the (D,L)LA polymerization decreases when an Al trialkoxide (**2**) is replaced by the diethylaluminum monoalkoxide counterpart (**1**) ($k_{\text{Al}[\text{O}-\text{CH}_2-\text{X}]_3} > k_{\text{Et}_2\text{Al}-\text{O}-\text{CH}_2-\text{X}}$). Similar effects

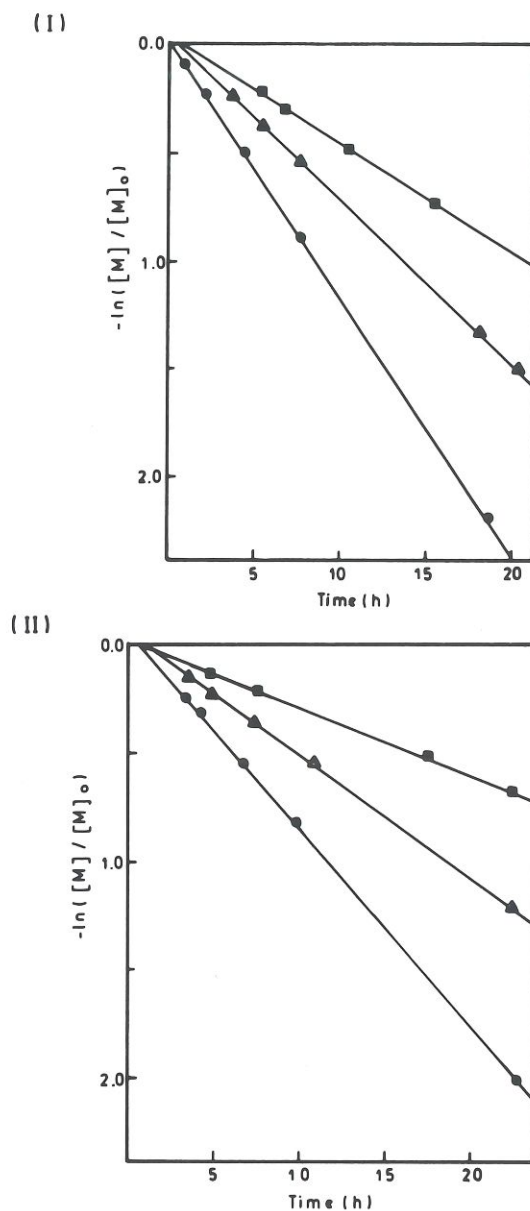


Figure 6. Order in monomer for the polymerization of (D,L)LA, in toluene at 70°C, initiated with: (I) Al(O—CH₂—CH₂—Br)₃ (**2a**); (II) Al[O—(CH₂)₃—CH=CH₂]₃ (**2b**). [M]₀ = 0.65 mol L⁻¹. [M]₀/[Al] = (●) 63, (▲) 107, (■) 167.

have been reported for the polymerization of ε-CL in toluene in the presence of the **1** and **2** initiators.^{18,24} The highest polymerization rate constants reported for the trialkoxides (**2**) could reflect a decrease in the electrophilicity of the Al atom when it is surrounded by three electron-donating alkoxide groups. This kinetic behavior will be discussed in more details in a forthcoming study.²⁴

CONCLUSIONS

When the (D,L)LA polymerization is initiated by Al mono- and trialkoxides in toluene at 70°C, the chemical structure of the end groups, the molecular weight, and the molecular weight distribution of the polyester chains allow a series of conclusions to be drawn:

1. Whatever the structure of the “—O—CH₂—X” alkoxide groups and their number per Al (1 or 3), each of them initiates one macromolecule in toluene at 70°C. In contrast, the alkyl aluminum bonds of the Al monoalkoxides (**1**) are completely inactive.
2. The ring-opening polymerization of the lactide must proceed through the acyl-oxygen bond scission of the monomer followed by its insertion into the “Al—O” bond of the active site. That is the only way to account for the nature of the end-groups, i.e. an ester carrying the “O—CH₂—X” radical of the initiator and a hydroxyl group, which results from the hydrolysis of the growing site [eq. (5)]:

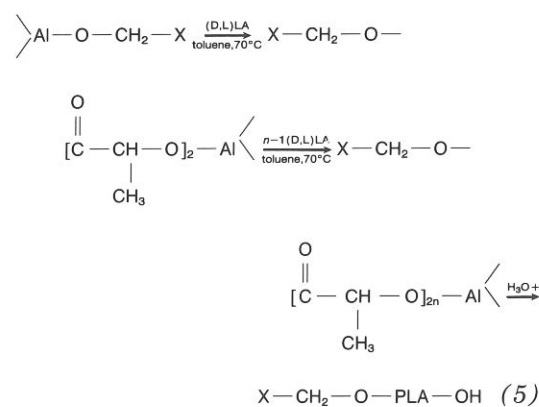


Table II. Rate Constants for the (D, L)LA Polymerization in Toluene at 70°C, Initiated by Al(OⁱPr)₃ and Functional Al Alkoxides of the **1a, b** and **2a, b** Series ([M]₀ = 0.65 mol L⁻¹)

Code	Initiator	<i>k</i> (L mol ⁻¹ min ⁻¹)
	Al(O ⁱ Pr) ₃	6.0 × 10 ⁻¹
2a	Al(O—CH ₂ —CH ₂ —Br) ₃	1.9 × 10 ⁻¹
2b	Al[O—(CH ₂) ₃ —CH=CH ₂] ₃	1.3 × 10 ⁻¹
1a	Et ₂ Al—O—CH ₂ —CH ₂ —Br	1.1 × 10 ⁻²
1b	Et ₂ Al—O—(CH ₂) ₃ —CH=CH ₂	1.0 × 10 ⁻²

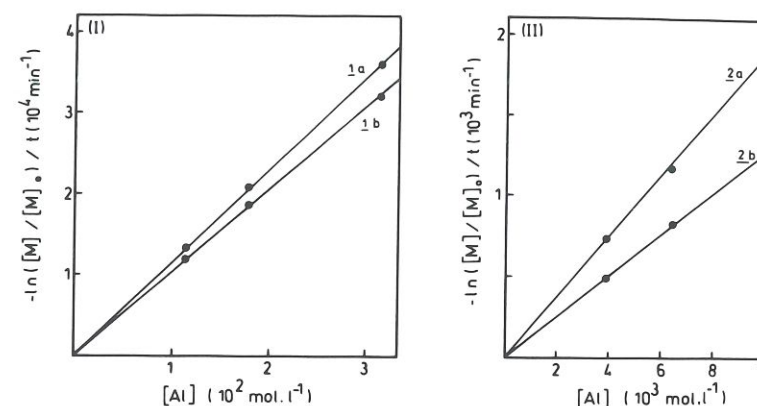


Figure 7. Order in initiator for the polymerization of (D,L)LA ([M]₀ = 0.65 mol L⁻¹), in toluene at 70°C, initiated with: (I) Et₂Al—O—(CH₂)₂—X with X = —Br (**1a**) and X = —CH₂—CH=CH₂ (**1b**); (II) Al[O—(CH₂)₂—X]₃ with X = —Br (**2a**) and X = —CH₂—CH=CH₂ (**2b**).

3. Side reactions of intra- and intermolecular transesterification do not appear to be effective during the time required for the monomer conversion to be complete. The “living” character of the chain propagation allows the molecular weight of the polyester to be predicted from the initial [monomer]/[initiator] molar ratio, the number of alkoxides per Al, and the degree of monomer conversion [see eq. (3)].
4. The rate of the (D,L)LA polymerization is enhanced when an aluminum trialkoxide (**2**) is used instead of the monoalkoxide counterpart (**1**).

Functional aluminum alkoxides are thus effective initiators for the ring-opening polymerization of (D,L) lactide and the synthesis of asymmetric α-hydroxy, ω-X functional poly(D,L)LA. The great versatility of their structure opens the way to the macromolecular engineering of the polylactides and to novel opportunities in the biomedical field. As an example, diethylaluminum 2-hydroxyethyl methacrylate has been synthesized and successfully used in the synthesis of ω-methacryloyl poly(ε-caprolactone). Similarly, well-defined polylactide macromonomers could be made available and used as promoters of original graft copolymers. These opportunities are under current investigation.

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