Ring-Opening Polymerization of D,L-Lactide Using Rare-Earth μ-Oxo Isopropoxides as Initiator Systems

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Introduction. Polylactides are important biodegradable materials having biomedical, pharmaceutical, and environmental applications.[1−5]

These polymers can be synthesized by ring-opening polymerization of lactides using anionic, cationic, or coordinated type initiators.[6−10] In order to obtain polymers with controlled characteristics (structure, molecular weight), initiators leading to a living type process are desirable. Ideally, they should also promote rapid polymerization.

Anionic initiators such as alkali-metal alkoxides lead to some side reactions.[6,11] Aluminum alkoxides can be used for controlled polymerization, but they exhibit a relatively low activity.[8,9] The livingness of the polymerization systems was discussed in terms of the selectivity of the involved elementary reactions.[12]

It was reported recently that rare-earth alkoxides show a very high reactivity for the polymerization of lactones and lactides.[13−18] A living type behavior was observed for some of them. Yttrium oxo isopropoxide is presently a commercially available compound. Stevels et al.[19,20] have recently studied the kinetics and mechanism of L-lactide polymerization with commercial yttrium oxo alkoxide and with other yttrium alkoxides prepared in situ from exchange reaction between the bulky tris(2,6-di-*tert*-butylphenoxy)yttrium and various alcohols. The rate of polymerization with the latter initiators was found to be several orders of magnitude higher than that observed with the commercial yttrium oxo isopropoxide.

Originally, the synthesis and the characteristics of yttrium oxo isopropoxide $Y_5(\mu\text{-O})(OiPr)_{13}$ was described by Poncelet et al.[21] It is a cluster compound in which five yttrium atoms are linked to a single central oxygen atom.

In this paper we describe the results of the polymerization of D,L-lactide using different rare-earth oxo alkoxide clusters of $Ln_5(\mu\text{-O})(OiPr)_{13}$ type where Ln is La, Sm, Y, and Yb. Previously, only the polymerization of L-lactide with commercial yttrium oxo isopropoxide was reported.[17,20]

Experimental Section. All μ-oxo isopropoxide initiators were prepared according to the procedure described by Poncelet et al.[21] for yttrium. Commercial yttrium oxo isopropoxide (Aldrich, France) was also used after washing with toluene, removal of insolubles by filtration, and drying in vacuo. D,L-Lactide (Purac Biochem b.v., Gorinchem, the Netherlands) was purified by sublimation under vacuum. Dichloromethane was distilled from calcium hydride and toluene from sodium benzophenone ketyl prior to use. The polymerizations were run in Schlenk tubes under argon. At the concentrations used [(2.2−2.8) × 10^{-3} M], Sm and Yb initiators are soluble in dichloromethane, while Y and La initiators are not completely soluble in dichloromethane, but are soluble in toluene. For this reason the latter initiators were dissolved in the minimum required volume of toluene and introduced as such in polymerization vessels. The solution of D,L-lactide in dichloromethane was added to a solution of the initiator in the corresponding solvent. The polymerization proceeds under homogeneous conditions with a monomer concentration close to 1 M and initiator concentration between 2.2×10^{-3} and 2.8×10^{-3} M in the reaction mixture. Periodically, samples were withdrawn from the reaction mixture for conversion and molecular weight analysis. ^{1}H NMR spectra were recorded using a Bruker 200 MHz spectrometer and $CDCl_3$ as solvent. Size-exclusion chromatography (SEC) determinations were carried out in tetrahydrofuran (THF) with a Waters apparatus equipped with μ-Styragel columns: 10^5, 10^4, 10^3, 500, 100 Å (detection, refractometric and UV (254 nm); flow rate, 1 mL/min; calibration referred to polystyrene standards).

Results and Discussion. The results of D,L-lactide homopolymerization in dichloromethane solution at room temperature using Y, La, Sm, and Yb oxo isopropoxide initiators are given in Table 1. The conversion was monitored by ^{1}H NMR. The conversion is established from integration of lactide monomer and polymer methyl signals located respectively at 1.56 and 1.63 ppm in $CDCl_3$.

The theoretical molecular weights $\bar{M}$n(th) for each conversion were calculated on the basis of the possible number of sites available for polymerization in the initiator, which is equal to 2.6 (13/5). Experimental molecular weights were determined from ^{1}H NMR analysis (isopropylate end-chain group methyl doublets around 1.24 ppm)[17] and size-exclusion chromatography (SEC) in THF referring to polystyrene standards. The experimental numbers of active sites per metal atom are deduced from $\bar{M}$n(^{1}H NMR) values.

The polymerization proceeds in all cases through acyl-oxygen cleavage of the lactide ring, as revealed from ^{1}H NMR analysis of end groups (methyl doublets of isopropoxycarbonyl groups around 1.24 ppm). A similar type of ring-opening was already observed for yttrium oxo isopropoxide initiator.[17,20]

With the yttrium initiator, the polymerization is relatively fast, with a half-reaction time ($t_{1/2}$) of 70 min. The results obtained with the commercial initiator and with the synthesized initiator are almost identical. A narrow molecular weight distribution ($\bar{M}$w/$\bar{M}$n) is observed up to very high conversions and long polymerization times.

Among lanthanide oxo isopropoxide initiators, the La initiator is the most reactive with $t_{1/2}$ = 45 s and the Yb initiator is the least reactive with $t_{1/2}$ = 770 min. The range of reactivity La ≫ Sm ≫ Yb agrees with a decrease of reactivity as the size of the lanthanide atom increases. Similar trends were observed by McLain et al.[15] in the case of L-lactide polymerization with tris(2,2,6,6-tetramethylheptane-3,5-dionato)lanthanide initiator. For the La initiator, the polydispersity ($\bar{M}$w/$\bar{M}$n) increases with conversion and oligomeric products are observed in SEC traces even after a very short time of polymerization (1.25 min, 65% of conversion), indicating the occurrence of transesterification reactions. Inter-

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Table 1. Polymerization of D,L-Lactide Initiated with Ln_5 (μ-O) $(OiPr)_{13}$ Systems

Ln	$[M]_0/[Ln]_0$[a]	t_{polym} (min)	conv[b] (%)	$\bar{M}_n$(th)[c]	$\bar{M}_n$(NMR)[d]	$\bar{M}_n$(SEC)[e]	$\bar{M}_w/\bar{M}_n$[e]	N sites/Ln[b]	$t_{1/2}$[f] (min)
Y	68	1	4	150					
		30	31	1170	1550			2.0	
		90	62	2350	2100	3450	1.20	2.8	70
		180	73	2750	2600			2.75	
		6900	93	3500	3000	5000	1.20	3.0	
	170	120	41	3860	3700	4400	1.17	2.7	
Y[g]	77	990	85	3600	4100			2.3	
		3960	96	4100	4400	8700	1.22	2.4	
		0.5	44	1660	1500			2.9	
La	68	1.25	65	2450	2400	6700[h]	1.23	2.65	
		2.25	81	3050	3100			2.6	0.75
		5.75	95	3580	3500	8700[h]	1.57	2.65	
		60	97	3650	5000	7400[h]	2.14	1.9	
Sm	61	2	20	675	1000			1.7	
		30	57	1900	2600	3250	1.30	1.9	17
		60	77	2600	3400	4500	1.30	2.0	
		270	93	3150	3700			2.2	
		1350	96	3250	4470	5000	1.30	1.9	
Yb	61	30	12	400					
		60	19	650	900	800	1.40	1.85	770
		350	34	1150	1440	1750	1.28	2.1	
		1340	65	2200	2500	3300	1.18	2.3	
		1800	82	2800	2350	3250	1.20	3.0	

[a] Polymerization carried out in dichloromethane solution at room temperature (for other conditions see Experimental Section). [b] Determined from ^1H NMR. [c] On the basis of 2.6 sites/Ln. [d] From end-group by ^1H NMR. [e] SEC in THF versus polystyrene standard. [f] Time of half-reaction, calculated from conversion versus time curve. [g] Commercial initiator. [h] High molecular weight fraction (oligomers excluded).

or intramolecular transesterification reactions may be expected. They can be detected by SEC, NMR, and MALDI-TOF techniques.[9,22,23] The nature of these transesterification reactions is presently under study. With other initiators (Y, Sm, Yb) a narrow polydispersity is observed till high conversions and long times of polymerization. This indicates that these polymerizations are highly selective as concerning chain propagation relative to chain transfer.[12]

The number of active sites (alkoxide initiating groups) per metal derived from ^1H NMR results seems to change with the nature of the metal of the initiator and is not yet completely explained. It appears from Table 1 that for Y and La initiators almost every alkoxide group initiated a polymer chain (average values close to 2.6). For Sm and Yb initiators the ^1H NMR molecular weight determinations do not fit with the expected number of sites (2.6) but appear to be close to 2.0 reactive sites. These findings are not explained at the present time.

During the course of polymerization, a linear relation between ln $[M]_0/[M]$ and time is observed for all initiator systems till at least 60% conversion. From this linear part, rate constants can be evaluated on the basis of first-order kinetics in monomer and in initiator. The following range of values was found (K in L mol^{-1} min^{-1}): La (2.9×10^2), Sm (6.4), Y (5.0), Yb (0.2).

These values are only indicative and allow us to give a range of reactivity for this series of initiators in the conditions used. The reactivity of the La initiator is 3 orders higher than that of the Yb initiator. The former is, however, less reactive than the yttrium isopropoxide initiator prepared in situ by Stevels et al.[20] In the latter case, a monomeric $Y(OiPr)_3$ formulation is unlikely (3-coordinate yttrium can only be stabilized by bulky ligands such as aryl oxides or (trimethylsilyl)amides). The initiator generated by an alcohol exchange reaction from an aryl oxide is probably an isopropoxide solvate $[Y(OiPr)_3{\cdot}x\mathrm{iPrOH}]_m$ in which the metal is also 6-coordinate, as observed for $Y_5(\mu\text{-}O)(OiPr)_{13}$. However, the high lability of the Y−OHiPr bond gives a facile access to the metal. The formation of solvates is known; for example, $[Nd(OiPr)_3(iPrOH)]$ has been characterized as an intermediate on the route to $Nd_5(\mu\text{-}O)(OiPr)_{13}$.[24]

In conclusion, lanthanide oxo isopropoxy compounds are active initiators for the polymerization of D,L-lactide in dichloromethane solution at room temperature. Lanthanum oxo isopropoxide, the most reactive initiator, generates significant transesterification reactions. In the case of Y, Sm, and Yb initiators, a narrow molecular weight distibution is observed till high conversions. Block copolymers can be prepared by sequential addition of D,L-lactide to poly(ϵ-caprolactone). Such findings seem to be in favor of living type behavior. Other lactones, e.g., β-butyrolactone or δ-valerolactone, are also polymerized with these initiators. These results will be reported in a further publication.

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