Bulk Ring-Opening Polymerization of Lactides Initiated by Ferric Alkoxides

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ABSTRACT: Ferric alkoxides ($Fe(OR)_3$), where R = Et, ^{n}Pr, ^{i}Pr, and ^{n}Bu, were used as initiators for bulk ring-opening polymerization of lactides. It was showed that these ferric alkoxides were efficient initiators for the ring-opening polymerization of lactides with higher than 90% of monomer conversions polymerized at 130 °C for 36 h. Maximum molecular weights were achieved at 1/1000 of [I]/[M] mole ratio and then decreased gradually with increasing amount of initiator and prolonging polymerization time. Poly(DL-lactide) and poly(L-lactide) with the maximum viscosity-average molecular weights (M_v) of 7.28×10^4 and 19.00×10^4, respectively, were synthesized by using ferric ethoxide as initiator. The molecular weight decreased and the molecular weight distribution broadened as the polymerization temperature increased. With increasing the bulkiness of the ligands of the ferric alkoxides, the molecular weight decreased and the molecular weight distribution broadened. ^{1}H and ^{13}C NMR analyses indicated that no racemization occurred during the ring-opening polymerization of L-lactide, while isotactic stereoselectivity addition was found in the ring-opening polymerization of DL-lactide. Intermolecular transesterification took place during polymerization of DL-lactide as evidenced by the results of MALDI−TOF MS analysis, and the quantitative evaluation for each initiation system was made by ^{13}C NMR analysis. ICP-AES, ^{1}H NMR, and MALDI-TOF MS analyses indicated that the polymerization of lactides proceeded via a coordination−insertion mechanism involving cleavage of the acyl−oxygen bond of the lactides. All alkoxy groups in $Fe(OR)_3$ were converted into polylactide growing chains.

Introduction

Polylactides (PLAs), due to their good mechanical properties, biocompatibility, and biodegradability, have been widely used in medicine and pharmacy as resorbable implant and controlled drug delivery materials.[1−3] These polymers are mostly synthesized by ring-opening polymerization of lactides using organometallic compounds as initiators or catalysts. Many organometallic compounds have been tested and found to be active on the ring-opening polymerization of lactides, such as those of tin,[4,5] lead,[6] aluminum,[7−9] zinc,[4,10] yttrium,[11,12] and bismuth.[6] In practice, almost all PLAs commercially used are prepared by using tin compounds as initiators because of their high initiation activity and low racemization. The biomedical application of PLAs necessarily requires low levels of impurities. However, as a result of polymerization mechanisms, the complete elimination of highly toxic tin compounds from the products is practically impossible.[2] This may affect the degradation environment in a harmful way and possibly even results in accumulation. Therefore, it is necessary in practice to develop active catalysts or initiators that contain low-toxicity metals for the polymerization of lactides.

A number of iron compounds have been found in living organisms and in nature. They are regarded as less harmful than most other metal compounds. Attempts have been made to use ferric oxide,[6,13] ferric chloride,[13,14] iron porphyrins,[15] iron lactate,[16] and monocarboxylic iron derivatives[17] as initiators for the polymerization of lactones. However, experimental results show that these iron compounds are sluggish on the ring-opening polymerization of lactides and require high polymerization temperature. In addition, racemization also occurs during polymerization. It is worth notice that some simple metal alkoxides, such as $Al(^iOPr)_3$,[7,8] $Sn(OBu)_2$,[5] and $Ti(OBu)_3$,[8] can readily polymerize lactides. It is thus suggested that simple ferric alkoxides may be efficient catalysts for the polymerization of lactides. And this was supported recently by the results of Tolman et al.[18] and Dobrzynski et al.[19] Tolman et al. reported that two ferric alkoxides, i.e., $Fe_5(\mu_5\text{-}O)(OEt)_{13}$ and $Fe_2(OCMe_2Ph)_6$, showed good catalytic activity for the polymerization of lactides in toluene, and no racemization occurred. Dobrzynski et al. employed ferric ethoxide for the copolymerization of glycollide with L-lactide and found that the copolymers could replace successfully the ones obtained in the presence of tin compounds as far as their medical application is concerned. However, detailed studies about the influence of the ligands of ferric alkoxides on the polymerization of lactides are still lacking in the literature. Besides, the initiation mechanism of ferric alkoxides in the ring-opening polymerization of lactides still needs to be clarified.

In this paper, a series of ferric alkoxides were used as initiators for the ring-opening polymerization of lactides in bulk. The effects of initiator content and polymerization time at a given temperature were investigated. In addition, special attention has been paid to the initiation mechanism and the influence of particular initiators on the transesterification process as well as the microstructure of polymer chains.

Experimental Section

Materials. DL-Lactide was prepared in our laboratory by known procedures.[20] The obtained products were recrystallized from dry ethyl acetate for several times, dried in a vacuum at 40 °C, and stored over P_2O_5 in a vacuum prior to use. The pure

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DL-lactide remained as a white crystalline solid with melting point of 125.8−127.1 °C by differential scanning calorimetry-(DSC) at a heating rate of 10 °C/min. L-Lactide (Purac, 99.5%) was recrystallized from dry ethyl acetate twice and then dried in a vacuum over P_2O_5 at 40 °C for at least 24 h prior to polymerization. The pure L-lactide remained as white acerous crystals with melting point of 98.5−99.7 °C by DSC at a heating rate of 10 °C/min. Ferric alkoxides, $Fe(OR)_3$, where R = Et, ^{n}Pr, ^{i}Pr, and ^{n}Bu, were synthesized by reactions of ferric chloride with respective alcohols and ammonia according to ref 21. All ferric alkoxides were stored and used in toluene solution. Toluene was dried and distilled from sodium under dry nitrogen prior to use. All solvents used were of analytical grade.

Polymerization Procedures. Under nitrogen, 5 g of freshly recrystallized monomer was placed in a glass ampule with inner silanized glass walls, and the required amount of an $Fe(OR)_3$ solution in toluene was added. The amount of initiator varied corresponding to [I]/[M] mole ratios of 0.5×10^{-3}−2.0×10^{-3}, in some experiments the [I]/[M] mole ratio as high as 20 for the end-group analysis. The toluene was evaporated under mild vacuum (15 kPa, 1 h), followed by a high vacuum (12 Pa) for another hour, and the ampule was sealed under vacuum. The polymerizations were performed in a thermostatically controlled oil bath at temperatures ranging from 130 to 150 °C for the desired time (24−72 h).

The resulting PDLLA was dissolved in acetone and precipitated in water, and PLLA was dissolved in CH_2Cl_2 and precipitated into cold methanol; both were dried under vacuum to constant weight. For the iron content measurements and the end-group analysis some PDLLA samples were extracted with a hydrochloric acid solution and washed in distilled water before the analysis.

Characterizations. ^{1}H NMR (500 MHz) measurements, performed on a Varian INOVA 500NB spectrometer, were used to determine the monomer conversion and the end groups. Spectra were recorded using 1.5 wt % solutions in $CDCl_3$ at room temperature. Conversions of the crude products were determined from the relative intensities of the monomer and polymer methine quartet at δ 5.2 ppm.

^{13}C NMR (125 MHz) measurements, performed on the same spectrometer, were used to define the chain microstructure and the transesterification in polymerizations. Spectra were obtained in $CDCl_3$ at room temperature with 3000 scans, acquisition time 1.8 s, pulse width 2.2 μs (22.5°), and delay of 3 s between pulses.

Molecular weights and molecular weight distributions were determined by gel permeation chromatography (GPC). The instrument was equipped with a Waters 1515 pump, a Waters 2414 refractive index detector, and three Styragel columns (HR1, HR3, and HR4; 300 × 7.8 mm for each) packed with 5 μm particles, and the ranges of molecular weight were 100−5000 (HR1), 500−30 000 (HR3), and 5000−500 000 (HR4). Tetrahydrofuran (THF) was used as a mobile phase with a flow rate of 1.0 mL/min. The measurements were carried out at 40 °C with an injection volume of 20 μL, and the sample solution was filtered through a 0.2 μm filter before the injection. Narrow polystyrene standards from Shodex in the 1700−706 000 g/mol range were used for the calibration.

In addition, molecular weights were also determined using an Ubbelohde viscometer. From the inherent viscosities of the obtained polymer solutions in $CHCl_3$ at 25 °C, the viscosity-average molecular weight (M_v) of PDLLA and PLLA were calculated using the formula $[\eta] = 2.21 \times 10^{-4} M_v^{0.77}$ for PDLLA and $[\eta] = 5.45 \times 10^{-4} M_v^{0.73}$ for PLLA.[22]

Thermal characterizations were carried out using differential scanning calorimetry (DSC) (TA Instruments 2910) in a nitrogen atmosphere at a heating rate of 10 °C/min. The instrument was calibrated with gallium and indium for temperature and enthalpy changes. Values of glass transition temperature (T_g) were taken from the midpoints of the transition zones.

Iron content measurements were performed on an IRIS (HR) inductively coupled plasma−atomic emission spectrometer (ICP-AES, TJA Co.). The samples were treated with nitric acid, and the measurements were performed at 259.94 nm.

MALDI−TOF MS analyses were carried out on a commercial Reflex III MALDI−TOF mass spectrometer (Bruker Co., Germany) equipped with delayed extraction technology. Ions formed by a pulsed UV laser beam with 3 nm pulse (nitrogen laser, λ = 337 nm) were accelerated through 20 kV and detection voltage was set at 1.60 kV. The laser was adjusted by the experiments slightly above the threshold, and the mass spectra were obtained from the results of 35 laser shots in positive mode. The matrix, *trans*-3-indoleacrylic acid (IAA), was dissolved in purified THF (0.1 mol/L), and the solution was mixed with the polymer solution in THF (5 mg/mL) in a 1:1 v/v ratio.

Table 1. Results of Polymerization of DL-Lactide in Bulk at 130 °C for 48 h with Ferric Alkoxides as Initiators at Different [I]/[M] Ratios

initiators	[I]/[M]	conv/%[a]	$M_n \times 10^{-4}$ [b]	MWD[c]	$M_v \times 10^{-4}$ [d]	T_g/°C[e]
$Fe(OEt)_3$	0.5×10^{-3}	86.2	4.36	1.62	5.73	52.9
	1.0×10^{-3}	94.4	6.14	1.61	7.28	54.9
	1.5×10^{-3}	95.4	5.87	1.60	6.62	54.1
	2.0×10^{-3}	96.8	5.26	1.63	6.44	53.2
$Fe(OPr)_3$	0.5×10^{-3}	85.3	3.94	1.65	4.86	53.7
	1.0×10^{-3}	93.9	5.08	1.68	6.24	53.2
	1.5×10^{-3}	95.3	4.20	1.68	5.51	52.9
	2.0×10^{-3}	96.5	3.61	1.69	4.72	52.6
$Fe(O^iPr)_3$	0.5×10^{-3}	83.4	2.10	1.72	3.05	51.3
	1.0×10^{-3}	91.6	2.96	1.73	4.51	53.3
	1.5×10^{-3}	92.1	2.87	1.74	4.28	52.5
	2.0×10^{-3}	92.6	2.77	1.76	3.86	53.0
$Fe(OBu)_3$	0.5×10^{-3}	86.0	1.90	1.98	3.17	50.7
	1.0×10^{-3}	96.2	1.86	1.92	3.14	50.2
	1.5×10^{-3}	96.8	1.84	1.92	2.99	49.3
	2.0×10^{-3}	96.9	1.78	1.88	2.78	48.6

[a] Determined by ^{1}H NMR. [b] Number-average molecular weight determined by GPC. [c] Polydispersity index (M_w/M_n) determined by GPC. [d] Viscosity-average molecular weight. [e] Glass transition temperature determined by DSC.

Results and Discussion

Effects of Polymerization Condition on the Polymerization. Effect of Initiator Content. The ring-opening polymerizations of DL-lactide using ferric alkoxides as initiators in different molar ratios of [I]/[M] were carried out at 130 °C for 48 h. As shown in Table 1, the monomer conversion increased with the increase of [I]/[M] ratio; when the [I]/[M] ratio was higher than 1.0×10^{-3}, the monomer conversion of over 90% was obtained, and little difference was found for all the ferric alkoxides. The molecular weights of the polymerization products were also affected by the [I]/[M] ratio; the maximum was achieved at a [I]/[M] ratio of 1.0×10^{-3}. It is possible that a higher initiator concentration will result in more growing chains, thus giving a lower molecular weight product, while a lower initiator concentration will produce less initiation sites, thus leading to lower monomer conversion. The molecular weight and molecular weight distribution of the products are very related to the ligands of ferric alkoxides. It can be seen from Table 1 that the bulkier the ligand size of the ferric alkoxide, the lower the molecular weight and the broader the molecular weight distribution of the polymerization product. For instance, at [I]/[M] = 1.0×10^{-3}, the viscosity-average molecular weight (M_v) of the product was 7.28×10^4 with molecular weight distribution of 1.63 by using $Fe(OEt)_3$ as the initiator, while the corresponding figures were 3.14×10^4 and 1.92, respectively, by using $Fe(OBu)_3$. These results may be caused by the difference of the ferric alkoxides in transesterification process during polymerization.

Table 2. Results of Polymerization of DL-Lactide in Bulk for 48 h at Different Temperatures with Ferric Alkoxides as Initiators ([I]/[M] = 1.0 × 10^{-3})

initiators	T/°C	conv/%[a]	$M_n \times 10^{-4}$ [b]	$M_w \times 10^{-4}$ [c]	MWD[d]	$M_v \times 10^{-4}$ [e]
$Fe(OEt)_3$	130	94.4	6.14	9.88	1.61	7.28
	140	94.9	5.82	9.66	1.66	6.82
	150	96.0	4.98	9.16	1.84	5.17
$Fe(OPr)_3$	130	93.9	5.08	8.53	1.68	6.24
	140	94.3	4.77	8.20	1.72	5.93
	150	95.2	4.60	8.19	1.78	5.69
$Fe(O^iPr)_3$	130	91.6	3.34	5.78	1.73	4.51
	140	92.4	3.01	5.47	1.82	4.30
	150	93.0	2.76	5.13	1.86	4.17
$Fe(OBu)_3$	130	90.5	2.07	3.97	1.92	3.14
	140	91.7	1.82	3.57	1.96	3.04
	150	92.1	1.74	3.45	1.98	2.96

[a] Determined by ^{1}H NMR. [b] Number-average molecular weight determined by GPC. [c] Weight-average molecular weight determined by GPC. [d] Polydispersity index(M_w/M_n) determined by GPC. [e] Viscosity-average molecular weight.

Table 3. Results of Polymerization of L-lactide in Bulk at 130 °C for Different Times with Ferric Alkoxides as Initiators ([I]/[M] = 1.0 × 10^{-3})

initiators	t/h	conv/%[a]	$M_w \times 10^{-4}$ [b]	$M_n \times 10^{-4}$ [c]	MWD[d]	$M_v \times 10^{-4}$ [e]
$Fe(OEt)_3$	24	92.6	19.98	12.98	1.54	18.19
	36	97.5	21.71	13.97	1.55	19.00
	48	98.0	16.36	10.63	1.54	14.87
	72	100.0	12.83	8.42	1.52	11.85
$Fe(OPr)_3$	24	90.8	15.92	9.83	1.62	14.60
	36	95.3	16.39	10.07	1.63	15.01
	48	96.7	14.76	9.03	1.63	13.36
	72	100.0	14.13	8.60	1.64	12.67
$Fe(O^iPr)_3$	24	86.2	10.73	6.24	1.72	9.84
	36	92.1	10.95	6.31	1.74	9.99
	48	96.5	9.45	5.43	1.74	8.67
	72	100.0	9.35	5.32	1.76	8.31
$Fe(OBu)_3$	24	90.5	4.42	2.37	1.87	5.14
	36	95.5	7.64	4.08	1.87	8.52
	48	96.5	5.71	3.03	1.89	7.01
	72	100.0	5.11	2.67	1.91	4.11

[a] Determined by ^{1}H NMR. [b] Weight-average molecular weight determined by GPC. [c] Number-average molecular weight determined by GPC. [d] Polydispersity index(M_w/M_n) determined by GPC. [e] Viscosity-average molecular weight.

Effect of Polymerization Temperature. For polymerization in bulk, the polymerization temperature was chosen higher than the melting point of the lactide monomers (127 °C). Table 2 shows the results of the ring-opening polymerizations of DL-lactide performed at temperatures ranging from 130 to 150 °C for 48 h. It can be seen that with increasing temperature the monomer conversion increased for each polymerization system; however, the molecular weight decreased, and the molecular weight distribution broadened for all ferric alkoxides. The highest molecular weight was achieved by polymerization at 130 °C for each ferric alkoxide. This may be ascribed to the thermal depolymerization[24] and the acceleration of transesterification as the polymerization temperature increases. Similar to the polymerization of DL-lactide at different initiator contents, the ferric alkoxide with larger ligand gave a product with lower molecular weight and broader molecular weight distribution.

Effect of Polymerization Time. The results of the ring-opening polymerizations of L-lactide by ferric alkoxides at 130 °C for different times are shown in Table 3. It can be seen that a high monomer conversion of more than 90% was also obtained for all ferric alkoxides. The highest M_v of the products was achieved by polymerization for 36 h and then decreased with prolonging polymerization time. This may also be attributed to the thermal depolymerization[24] as the polymerization time increases. There are several factors that influence the molecular weight of the polylactides, such as the vacuum degree of the polymerization system, the purity of the monomers, etc.[2] Compared with the polymerization of DL-lactide, the polymerization of L-lactide gave an higher molecular weight product for each ferric alkoxide probably due to higher purity of L-lactide monomer. Similar to the polymerization of DL-lactide, the ferric alkoxide with larger ligand gave a product with lower molecular weight and broader molecular weight distribution.

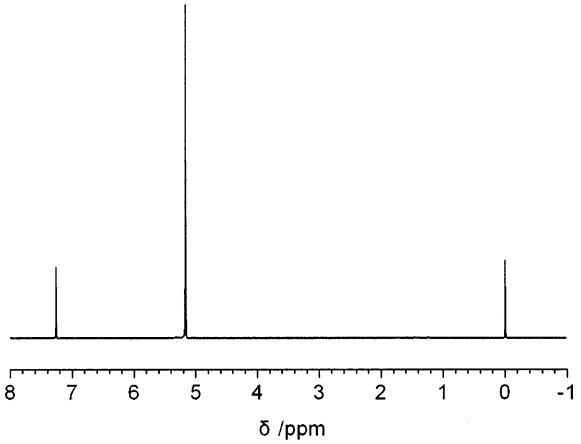


Figure 1. Homonuclear-decoupled methine ^{1}H NMR spectrum (500 MHz, 28 °C, $CDCl_3$ solvent) of poly(L-lactide) synthesized at 130 °C for 72 h in bulk using $Fe(OEt)_3$ as initiator at [I]/[M] = 1.0 × 10^{-3}.

Additionally, there was only one methine peak in the decoupled ^{1}H NMR spectrum of the products, as shown in Figure 1, indicating that no racemization occurred during the polymerization of L-lactide initiated by ferric alkoxides.[23]

Earlier studies[13−17] showed that only at high temperatures the iron compounds exhibited efficient initiation activity in the ring-opening polymerization of lactide. However, as mentioned above, the four ferric alkoxides studied here exhibited high initiation activity for the ring-opening polymerization of lactides under relatively mild conditions.

Polymerization Mechanism. To understand the polymerization mechanism of lactides initiated by ferric alkoxides, the iron content of a PDLLA product was measured by inductively coupled plasma−atomic emission spectrometry (ICP-AES). Similarly to the method used by Stolt et al.,[17] the sample was purified three times by dissolution−precipitation by using acetone and water alternatively. The iron content of the purified sample was 69 ppm. However, after treating the sample with a 1 mol/L hydrochloric acid solution, no iron was detected in the treated sample. The results reveal that the iron atoms are chemically bound to the PDLLA chains, and this is an indication of coordination−insertion mechanism.[17]

The coordination−insertion mechanism was further confirmed by the end-group analysis in PDLLA chains using ^{1}H NMR spectroscopy. Figure 2a is the ^{1}H NMR spectrum of a PDLLA product (using $Fe(OEt)_3$ as initiator) after treatment with 1 mol/L HCl. Protons and the corresponding signals are assigned in the spectrum. Besides the strong signals of $d + d'$ at 1.68−1.73 ppm

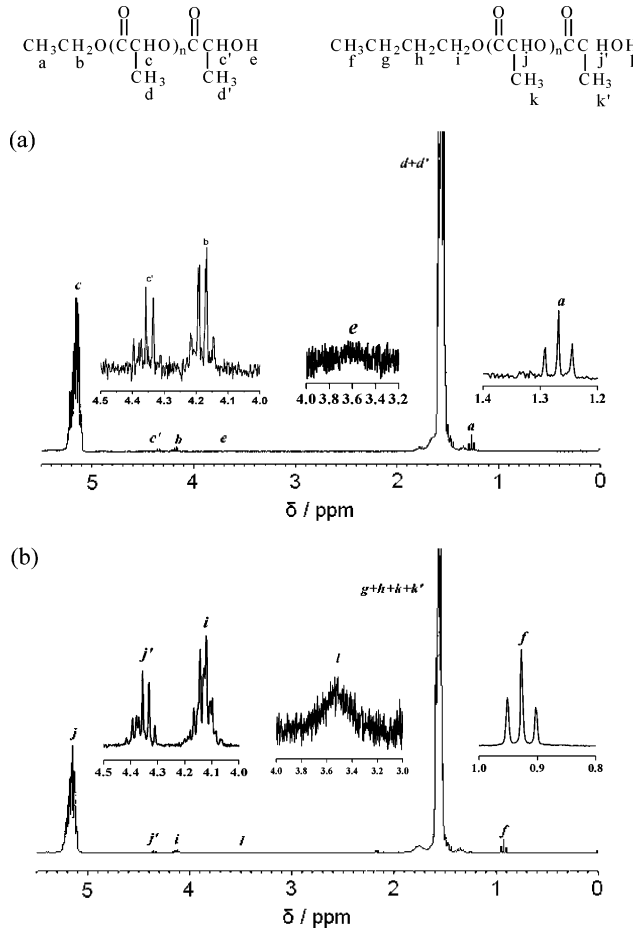


Figure 2. ^{1}H NMR spectra of [I]/[M] (1:20) poly(DL-lactide) samples treated with 1 mol/L HCl synthesized in bulk at 130 °C for 24 h (a) using $Fe(OEt)_3$ as initiator and (b) using $Fe(OBu)_3$ as initiator.

and *c* at 5.03 ppm from the methyl protons and methine protons of the PDLLA chain, respectively, two weak well-resolved signals *a* and *b* were also observed at 1.22−1.30 and 4.10−4.25 ppm. They should be respectively the resonance signals of the methyl and methylene protons of the ethoxy ester groups locating at the ends of PDLLA chains. Using $CDCl_3$ as the solvent, the hydroxyl end group only gave a very weak signal at 3.2−4.0 ppm, and the signal *c′* at 4.30−4.40 ppm should be from the proton of methine bound to the hydroxyl end group. Similar results were also obtained by the ^{1}H NMR analyses of the PDLLA products using $Fe(OBu)_3$ as the initiator, as shown in Figure 2b. The signals at 0.89−0.98 and 4.05−4.20 ppm should be from the protons *f* and protons *i* of the butoxy ester end group, respectively. However, signals from protons *g* and *h* in this group were not well-resolved because they were overlapped with the signals from protons *k* and *k′* of PDLLA chains. The existence of alkoxy ester end group in the PDLLA chains by using ferric alkoxides as initiators indicates that the initiation proceeds via a coordination−insertion mechanism, as described in Scheme 1. This process involves the insertion of lactide unit into the Fe−O bond of a ferric alkoxide molecule and the selective cleavage of the acyl−oxygen bond in lactide, which resulted in the formation of alkyl ester end group.

Table 4. Viscosity-Average Molecular Weights (M_v) of Polymerization Products of DL-Lactide Using $Fe(OR)_3$ as Initiators before and after 1 mol/L HCl Treatment

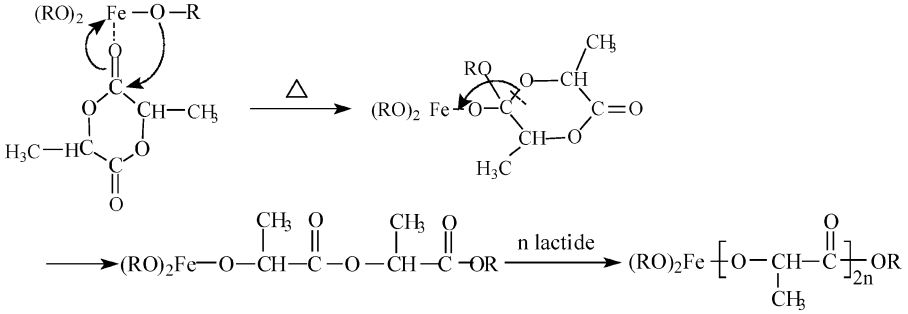
initiators	[I]/[M]	*T*/°C	*t*/h	$M_v \times 10^{-4}$ [a]	$M_v \times 10^{-4}$ [b]	$M_v{}^a/M_v{}^b$
$Fe(OEt)_3$	1.0×10^{-3}	130	36	2.568	0.845	3.0
	1.5×10^{-3}	130	48	3.240	1.278	2.5
	1.0×10^{-3}	130	48	1.985	0.823	2.4
$Fe(OBu)_3$	1.0×10^{-3}	130	36	1.070	0.470	2.3
	1.5×10^{-3}	130	48	2.481	1.115	2.2
	1.0×10^{-3}	130	48	4.562	1.712	2.7

[a] Before treatment with 1 mol/L HCl solution. [b] After treatment with 1 mol/L HCl solution.

According to the polymerization mechanism mentioned above, the number of alkoxy groups in a ferric alkoxide molecule participating in the initiation process may be quantitatively analyzed by the change in molecular weight of PDLLA product before and after treatment with a 1 mol/L of hydrochloric acid solution at room temperature. To inspect the influence of HCl treatment on the degradation of PDLLA, two times of tests were done on a PDLLA product, and the results are presented in the last line of Table 4. After the first HCl treatment, the M_v of the PDLLA product decreased from 4.56×10^4 to 1.71×10^4. No change in molecular weight was observed after the second HCl treatment. These results indicated that the HCl treatments did not degrade the PDLLA chains. As listed in Table 3, the ratio of molecular weights before and after treatments lied between 2.0 and 3.0. Taking into account the loss of the low molecular weight portion in the purification process of PDLLA, it could be considered that all the alkoxy groups in each of the ferric alkoxides were converted into the growing chains of PDLLA. This result was in agreement with those of other metal alkoxides, such as those of Sn[5] and Al.[7,8]

Microstructure and Transesterification Analysis by ^{13}C NMR. It has been reported that carbonyl and methine are the stereo-sensitive groups leading to hexad and tetrad sequences, respectively.[24−27] Figure 3 shows the ^{13}C NMR spectra of carbonyl and methine groups in PDLLA prepared using ferric alkoxides as initiators. The corresponding hexad and tetrad stereo-

Scheme 1. Polymerization Mechanism of Lactides Initiated by Ferric Alkoxides



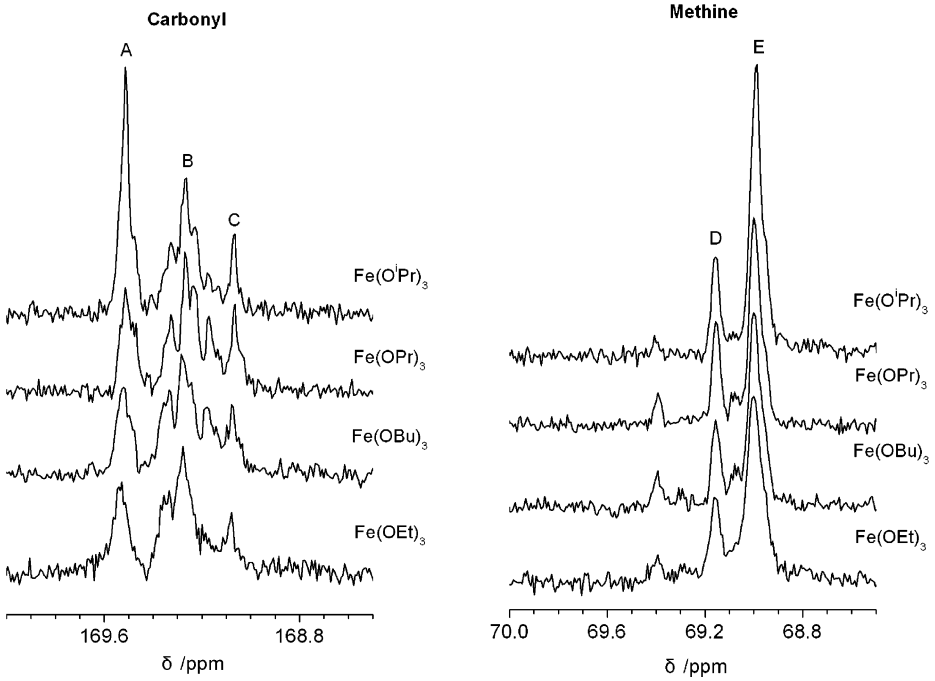


Figure 3. Expanded regions of carbonyl and methine carbon atoms in ^{13}C NMR (125 MHz) spectra of different poly(DL-lactide) samples reported in Table 5 where A (δ 169.45−169.6): iiiii + iiiis + siiii + siiis; B (δ 169.2−169.4): iiisi + iisii + sisii+ sisis + isiii; C (δ 169.05−169.15): isisi; D: isi; E: iii + iis + sii + sis.

Table 5. Intensities of Different Tetrad and Hexad Stereosequences Measured in ^{13}C NMR Spectra (Figure 3) of Various Poly(DL-latide) Prepared by Using Ferric Alkoxide as Initiators[a] and Calculated Transesterification Coefficients (*T*)

		tetrads[c]			hexads[d]				
initiators	MWD[b]	isi	iii, iis sii, sis	iss	A	B	C	P_i[e]	*T*/%
$Fe(OEt)_3$	1.61	22.2	69.3	8.5	26.2	61.3	13.7	0.56	68
$Fe(OPr)_3$	1.68	19.4	76.6	3.2	40.3	48.5	12.1	0.72	32
$Fe(O^iPr)_3$	1.73	22.9	66.5	10.0	23.5	58.1	14.1	0.54	80
$Fe(OBu)_3$	1.91	14.2	57.3	6.1	20.1	51.2	8.3	0.64	64

[a] Polymerization conditions: in bulk at 130 °C for 48 h at [I]/[M] = 1.0×10^{-3}. [b] Polydispersity index (M_w/M_n) determined by GPC. [c] Experimental values of tetrads (methine region) intensities in ^{13}C NMR spectra as shown in Figure 3. [d] Experimental values of hexads (carbonyl region) intensities in ^{13}C NMR spectra as shown in Figure 3. [e] The probability of isotatic addition.

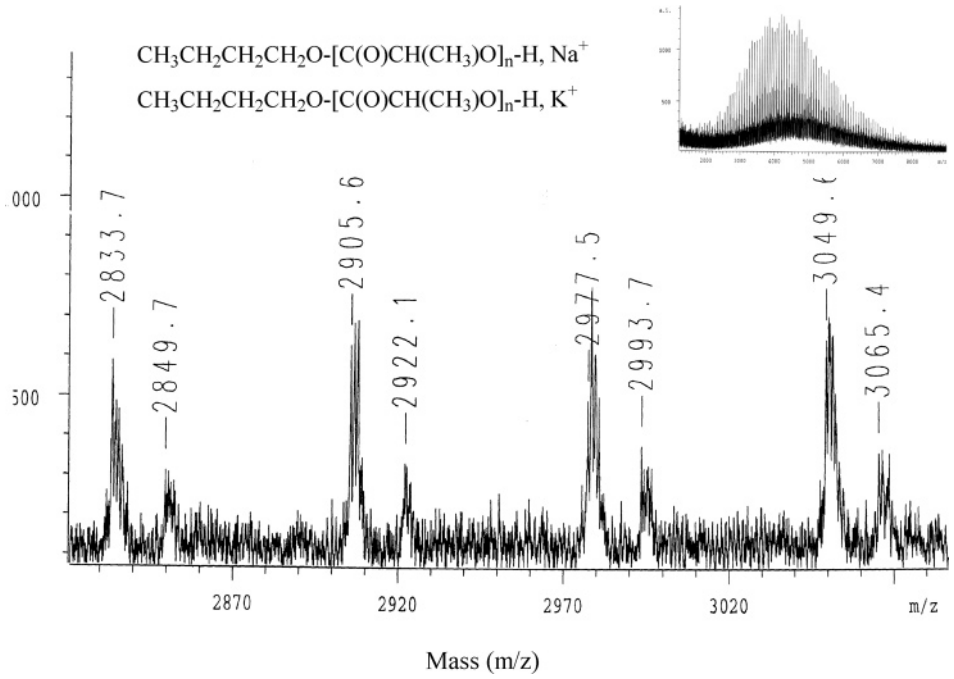


Figure 4. MALDI−TOF spectrum of a [I]/[M] (1:20) poly(DL-lactide) sample treated with 1 mol/L HCl synthesized at 130 °C for 24 h in bulk using $Fe(OBu)_3$ as initiator. Mass (m/z) = $M_{BuOH} + nM_{la} + M_{Na^+}$ or mass (m/z) = $M_{BuOH} + nM_{la} + nM_{K^+}$ (where $M_{BuOH} = 74$, $M_{la} = 72$, $M_{Na^+} = 23$, $M_{K^+} = 39$).

sequences were assigned in the spectra. Their intensities were calculated according to the literature,[25−27] as shown in Table 5. In a random polymerization of DL-lactide, the probability(P_i) of either isotatic addition or syndiotactic addition is 0.5. According to Bernoullian statistics, the statistical values of various stereosequences in PDLLA are as follows: A = 0.375, B = 0.5, C = 0.125, D = 0.25, and E = 0.75. However, these statistical values were different from the calculated values in this study (see Table 5). It indicates the addition polymerizations of DL-lactide initiated by ferric alkoxides are not in random but show a stereoselectivity. According to the calculation method of P_i proposed by Coudane[28] and Kasperczyk,[29] on the basis of the relative intensity of isi tetrad stereosequence, the P_i values for the PDLLA samples prepared by using the four ferric alkoxides as initiators were all larger than 0.5. This suggests that the ring-opening polymerization of DL-lactide in the presence of ferric alkoxides show a preference of isotactic addition, which is in contrast with the result for $Sn(Oct)_2$ initiator.[28]

The extent of transesterification can be also evaluated on the basis of the intensity of the stereosequence for the methine signal in the ^{13}C NMR spectra.[23−25] According to Bero et al.,[26] the existence of iss tetrad with chemical shift at 69.4 ppm is the result of transesterification because iss tetrad is normally forbidden for a pair-addition mechanism in the polymerization of D- and L-lactides. Thus, the transesterification coefficient (T) expressed by the ratio I_{iss}/I_{max} allows a quantitative evaluation on the degree of transesterification, where I_{iss} is the intensity of an experimental iss tetrad and I_{max} is the maximal intensity of a iss tetrad in a completely transesterified PDLLA, which can be calculated from the single-addition mechanism of Bernoullian statistics ($I_{max} = 0.125$). The calculated values of T are given in Table 5. The data exhibit that the four ferric alkoxides show high activity for transesterification in the polymerization of DL-lactide.

Analysis of PDLLA by MALDI−TOF MS. The MALDI−TOF MS analysis of a PDLLA product by using $Fe(OBu)_3$ initiator further validated the coordination−insertion mechanism and transesterification. As shown in Figure 4, two series of signals from different homologues were observed. For the first series of peaks at the *m/z* of 2833.7, 2905.6, 2977.5, and 3049.6, there was a difference of 72 in *m/z* between every two neighboring peaks, which was also seen in the second series at the *m/z* of 2849.7, 2922.1, 2933.7, and 3065.4. Moreover, in the second series peaks in *m/z* were correspondingly 16 larger than those in the first series. Additionally, the weight number of lactyl group is 72. So it could be known by calculation that the first series peaks resulted from the open-chain oligomers terminated with *n*-butoxy groups and Na^+ ions, and K^+ ions instead of Na^+ ions for the second series. The existence of *n*-butoxy end group in the PDLLA chains implies that the initiation proceeded via a coordination−insertion mechanism. In addition, the calculation indicates that both even-membered and odd-membered oligomers are present in the spectrum. The presence of odd-membered oligomers cannot be explained by the pair-addition ring-opening polymerization process of DL-lactide, which only yields even-membered oligomers. It thus suggests that transesterification had taken place during the polymerization. Furthermore, the formation of the repeating lactyl unit in the oligomer chains shows that the transesterification is not intramolecular but intermolecular. The result was different from other metal alkoxides that induced backbiting in the polymerizaiton.[30−32]

Conclusions

Under relatively mild conditions, ferric ethoxide, ferric *n*-propoxide, ferric isopropoxide, and ferric *n*-butoxide all showed high initiation activity in the bulk polymerization of lactides. The ligand of ferric alkoxide played an important role in the molecular weight and the molecular weight distribution of polylactides. Ferric alkoxide with larger ligand gave a lower molecular weight and a broader molecular weight distribution. No racemization occurred in the polymerization of L-lactide. The ring-opening polymerization of lactide proceeded via a coordination−insertion mechanism involving the cleavage of the acyl−oxygen bond of lactide and the formation of alkyl ester end group. Moreover, all the alkoxy groups in each of ferric alkoxides were converted into PDLLA growing chains. During the ring-opening polymerization of DL-lactide initiated by ferric alkoxides, there was a preference of isotactic addition and the intermolecular transesterification also took place.

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