Polym. Bull. (2010) 64:435–443
DOI 10.1007/s00289-009-0148-6

ORIGINAL PAPER

Effect of metal triflates on direct polycondensation of lactic acid

Sachiyo Konishi · Teruhiko Yokoi · Bungo Ochiai ·
Takeshi Endo

Received: 2 September 2008 / Revised: 23 July 2009 / Accepted: 12 August 2009 /

Abstract Various metal triflates were employed for direct polycondensation of lactic acid to afford poly(lactic acid). Screening of the metal triflates was conducted with the polycondensation of lactic acid at 160–180 °C for 16 h under reduced pressure (1.4 kPa) after a pre-dehydration process under an air atmosphere. Examined metal triflates are scandium, yttrium, ytterbium, lanthanum, hafnium, copper, and silver triflates. Polycondensation using scandium triflate afforded poly(lactic acid) with high molecular weights ($M_n = 4.3 \times 10^4$) in a good yields (62%) under the following conditions; catalyst amount = 0.05 mol%, pre-dehydration at 180 °C for 2 h, and polycondensation at 180 °C for 16 h. Active metal triflates coordinated with lactic acid strongly, confirmed by ^{1}H NMR and FT-IR spectroscopy.

Keywords Polycondensation · Lactic acid · Poly(lactic acid) · Lewis acid · Catalyst

Introduction

Poly(lactic acid) (PLA) is one of the most important biodegradable and biocompatible polymers synthesized from naturally occurring substances [1–5]. The raw

---

S. Konishi · T. Yokoi
Aozora Daichi, Tsuchizaki-aza-ueno 230-1, Misato-cho, Senboku, Akita 019-1541, Japan

B. Ochiai
Department of Polymer Science and Engineering, Faculty of Engineering,
Yamagata University, 4-3-16 Jonan, Yonezawa, Yamagata 992-8510, Japan

T. Endo (✉)
Molecular Engineering Institute, Kinki University, 11-6 Kayanomori, Iizuka,
Fukuoka 820-8555, Japan
e-mail: tendo@mol-eng.fuk.kindai.ac.jp

material, lactic acid, is an important product in glycolysis in bacteria and animal cells. Lactic acid is industrially produced by fermentation of plants with high contents of starch, such as corn, potato, rice, and cane. Direct polycondensation of lactic acid typically affords oligomers due to the formation of cyclic oligomers and the equilibrium between the ester, the free acid, and water. As a result, PLA is typically prepared by ring-opening polymerization of lactide [6–11], synthesized by de-polymerization of oligo(lactic acid) prepared by direct condensation of lactic acid. However, this multi-stage synthetic procedure is responsible for the high production cost of PLA. More facile methods, that is, direct polycondensation of lactic acid affording satisfactorily high molecular weight PLA, are demanded to produce PLA economically. In this point of view, many researchers have developed direct polycondensation of lactic acid [12–24]. Stannous complexes are the most popular catalysts to obtain high-molecular weight PLA (e.g., $M_w = 3 \times 10^5$) in spite of their toxicity [12–22]. For application to medical and biocompatible materials, low toxicity catalysts and avoidance of organic solvents are advantageous. Rare earth metal complexes are typically less toxic [25–27], in spite of their utility in various catalyses [24, 28–34]. For example, typical 50% lethal dose (LD_{50}) values for rats and mice are tens to thousands mg/kg, originating from the fast evacuation of rare earth metal ions due to the slow penetration into cell membranes, and in some cases, growths are enhanced [27]. Recently, Takasu et al. reported that scandium trifluoromethanesulfonate [$Sc(OTf)_3$] and scandium trifluoromethanesulfonimide effectively catalyze the direct polycondensation of lactic acid [24]. The Sc catalysts catalyze polycondensation of various diols and dicarboxylic acids as well [31–34]. They prepared high molecular weight PLA ($M_n = 5.1 \times 10^4$–7.3×10^4) in good yields by tuning the polymerization conditions. The catalysts can be recycled owing to the stability in water and lactic acid. We also have investigated the direct polycondensation of lactic acid using various metal trifluoromethanesulfonates (triflates) including rare earth metal triflates, and explored effective metal triflates. Herein, we wish to report the effect of metal triflates on direct polycondensation of lactic acid. The methods to understand the differing catalyst activities by investigation of the interaction between lactic acid and metal triflates are also discussed.

Experimental

Measurements

^{1}H (400 MHz) nuclear magnetic resonance (NMR) spectra were measured on a JEOL ECX-400 instrument using tetramethylsilane as an internal standard at ambient temperature. Size exclusion chromatography (SEC) measurements were performed on a system consisting of a Tosoh DP-8020 pump, a Viscotek TDA model 300 detector (RI), and polystyrene-gel tandem columns (Tosoh TSK gels GMH_{XL}, $G4000_{XL}$, $G3000_{XL}$, and $G2500_{XL}$) using THF (1.0 mL/min) as an eluent at 40 °C. Polystyrene standards were used for calibration. Fourier transfer infrared (FT-IR) spectra were recorded with a Horiba FT-IR 210 instrument equipped with a

SensIR Technologies DuraScope attenuated total reflectance accessory. The mixtures of equimolar amounts of lactic acid and Lewis acids for IR spectrometry were prepared by drying the tetrahydrofuran solutions of the mixtures under reduced pressure at ambient temperature overnight. Melting temperatures (T_m) of polymers were measured by differential scanning calorimetry using a Seiko Instruments DSC-6200 instrument under a nitrogen atmosphere (flow rate: 40 °C/min, scanning rate: 10 °C/min, second heating scan).

Materials

Lactic acid (85% aqueous solution) (Tokyo Kasei Kogyo), $Sc(OTf)_3$ (Tokyo Kasei Kogyo), yttrium triflate [$Y(OTf)_3$] (Tokyo Kasei Kogyo), ytterbium triflate *n* hydrate [$Yb(OTf)_3$, $n = 3.5$ (determined by TGA)] (Tokyo Kasei Kogyo), lanthanum triflate [$La(OTf)_3$] (Tokyo Kasei Kogyo), hafnium triflate [$Hf(OTf)_4$] (Tokyo Kasei Kogyo), copper triflate [$Cu(OTf)_2$] (Tokyo Kasei Kogyo), and silver triflate (AgOTf) (Tokyo Kasei Kogyo) were used as received. Other materials were also used as received.

Polycondensation of lactic acid (typical procedure)

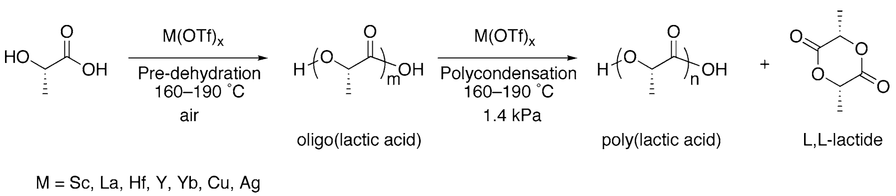
Lactic acid (85% aqueous solution) (3.0 g, 28 mmol) and metal triflate (0.01–0.1 mol%) were added into a test tube containing a magnetic stir bar. The mixture was stirred at 160–180 °C for 2 h under an air atmosphere. Then, a three-way stopcock was attached to the test tube, and the mixture was stirred at that temperature for 16 h under reduced pressure (1.4 kPa). A trace amount of the resulting solid was used for estimation of the molecular weight. After sublimed L,L-lactide was removed, poly(lactic acid) was isolated by reprecipitation with methanol from chloroform solutions.

Results and discussion

Direct polycondensation of lactic acid catalyzed by metal triflates

A typical procedure for our direct polycondensation of lactic acid follows (Scheme 1). A mixture of lactic acid and metal triflate (0.01–0.1 mol%) was stirred for 1–4 h under an air atmosphere at 160–190 °C. In this pre-dehydration process, condensation of lactic acid proceeded (Fig. 1a). For example, a 78% amount of lactic acid was consumed in run 12. Then, the successive polycondensation was conducted for 16 h under reduced pressure (1.4 kPa) at that temperature. The viscosity of the mixture increased as the polycondensation proceeded, and the mixture finally became so viscous that the magnetic stir bar stopped. In some polymerizations, trace amounts of L,L-lactide sublimed were found inside the test tube and in the resulting reaction mixture (Fig. 1b).

The yields and the molecular weights of resulting poly(lactic acid) are indicated in Table 1. First, the polycondensation was conducted for 16 h using 0.05 mol% of metal triflates with respect to lactic acid at 170 °C after the pre-hydration process for 2 h at 170 °C (runs 1–7). All the polymerizations afforded poly(lactic acid) in higher yields



Scheme 1 Direct polycondensation of lactic acid

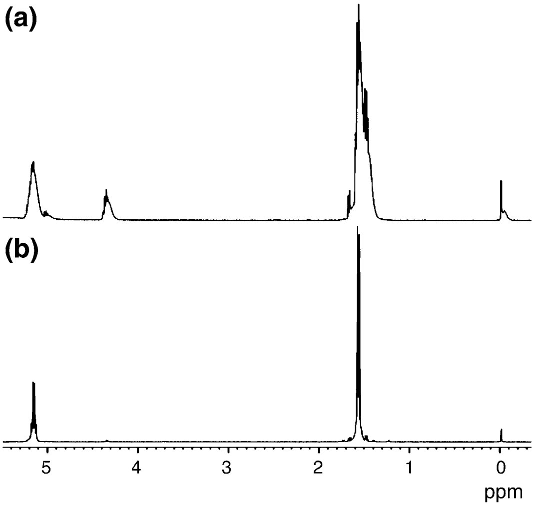


Fig. 1 ^{1}H NMR spectra of the mixtures **a** after pre-dehydration and **b** after polycondensation in run 12 in Table 1

than the case of the polymerization without metal triflate (run 8). Rare earth metal and copper triflates afforded poly(lactic acid) with relatively high molecular weights in high yields, whereas AgOTf afforded an oligomer owing to the low Lewis acidity of AgOTf discussed later. Then, the polycondensation was conducted at 160 (runs 14–16), 180 (runs 9–13), and 190 °C (runs 17 and 18). The polycondensation at 160 °C resulted in significantly lower molecular weights probably due to the inefficient stirring originating from high viscosity of PLA (melting point = 150–175 °C) [13, 15, 24] whereas scandium Lewis acids are effective even at 130 °C [24]. Sublimation of L,L-lactide is also a reason for the low yields. The best results were obtained in the polycondensation at 180 °C except the polymerization using La(OTf)$_3$ (run 12). Sc(OTf)$_3$ afforded PLA with the highest molecular weights among those examined (run 11). The low molecular weight of PLA obtained using La(OTf)$_3$ may be ascribed to de-polymerization due to the high Lewis acidity of La(OTf)$_3$ (discussed later). The lower molecular weights in the polycondensation at 190 °C are ascribable to the transesterification and de-polymerization. The effect of the amount of catalysts was examined using Yb(OTf)$_3$ (runs 19 and 20). The lower amount (0.01 mol%) resulted in very slow condensation, and both the yield and the molecular weight are low. The higher amount (0.10 mol%) of the catalyst increased the yield, probably by the polymerization of L,L-lactide or oligomers. However, the molecular weight is lower, and it suggests that transesterification concomitantly occurred.

Table 1 Direct polycondensation of lactic acid catalyzed by metal triflates

Run	Catalyst	Catalyst amount (mol%)	Temp. (°C)	M_n (M_w/M_n)[a]	Yield of PLA (%)[b]	Yield of lactide (%)[c]
1	$Sc(OTf)_3$	0.05	170	13500 (1.54)	65	20
2	$La(OTf)_3$	0.05	170	11100 (1.34)	75	8
3	$Hf(OTf)_4$	0.05	170	7100 (1.39)	70	2[d]
4	$Y(OTf)_3$	0.05	170	6700 (1.32)	80	1.1
5	$Yb(OTf)_3$	0.05	170	9900 (1.27)	70	1[d]
6	$Cu(OTf)_2$	0.05	170	6300 (1.20)	75	1>
7	AgOTf	0.05	170	3200 (1.26)	89	1.2
8	None	0	170	3700 (1.96)	49	18
9	$Sc(OTf)_3$	0.05	180	43400 (1.41)	61	21
10	$La(OTf)_3$	0.05	180	5500 (1.66)	62	18
11	$Hf(OTf)_4$	0.05	180	14000 (1.34)	63	1>[d]
12	$Y(OTf)_3$	0.05	180	24000 (1.29)	63	1[d]
13	$Yb(OTf)_3$	0.05	180	24000 (1.30)	65	2[d]
14	$La(OTf)_3$	0.05	160	6900 (1.69)	66	26
15	$Y(OTf)_3$	0.05	160	2800 (2.30)	79	7
16	$Yb(OTf)_3$	0.05	160	3400 (2.00)	80	6
17	$Y(OTf)_3$	0.05	190	6300 (1.31)	87	1>
18	$Yb(OTf)_3$	0.05	190	6000 (1.44)	90	1
19	$Yb(OTf)_3$	0.01	180	9400 (1.34)	46	n.d.[e]
20	$Yb(OTf)_3$	0.10	180	16000 (1.31)	71	1

Conditions: pre-dehydration for 2 h under an air atmosphere, polycondensation for 16 h under reduced pressure (1.4 kPa)

[a] Molecular weights of the products before isolation estimated by SEC (THF, polystyrene standard)

[b] Isolated yield after precipitation with methanol

[c] Isolated yield of L,L-lactide adhered inside the test tubes

[d] Oligo(lactic acid) (M_n = 2300–3600) was also adhered inside the test tubes, and the yields were 6–18%

[e] A mixture of oligo(lactic acid) and L,L-lactide was adhered inside the test tubes (Yield = 36%)

The racemization degree of PLA obtained in run 12 (Table 1) was evaluated by ^{1}H NMR spectroscopy (Fig. 2). The homodecoupled ^{1}H NMR spectrum shows a sharp signal at 5.16 ppm and a very small signal at 5.19 ppm. These peaks were assigned to the methine protons in the *mmm* and *rmm* (or *mmr*) triads by Kricheldorf et al. [31]. The average length of *meso* sequence is at least 18.5 (i.e., the degree of racemization is <5%). The racemization degrees of some PLA samples was also evaluated by DSC measurement of T_m. Typical T_m values of PLLA are 162–167 °C, depending on molecular weight and degree of crystallization [35, 36] (e.g., 164 °C for PLA with M_n = 12400 [37]). The T_ms of PLA obtained from runs 1 (Sc), 2 (La), 4 (Y), and 5 (Yb) were 162, 169, 160, and 158 °C respectively. Although the T_m of the polymer obtained using $Yb(OTf)_3$ was lower possibly due to the low molecular weight, others are in an agreeable range for PLA. The NMR and DSC results indicated that the racemization degrees of the examined samples are lower than 5%.

Interactions between lactic acid and metal triflates

The differing catalytic activity was evaluated by FT-IR and ^{1}H NMR spectroscopic measurements of mixtures containing lactic acid and metal triflates (1.1 equivalents with respect to lactic acid). The FT-IR absorptions of the carbonyl group were summarized in Table 2. The active catalysts Sc(OTf)$_3$, Y(OTf)$_3$, and Yb(OTf)$_3$ shifted the absorption more than 100 cm^{-1}, demonstrating that the strong coordination of these Lewis acid decreased the double bond characters of the carbonyl groups. AgOTf, which is the most inactive catalyst, did not shift the IR absorption to the lower wavenumber region. We attributed the weak activity of AgOTf to the neglibible coordination from this result and the fact that AgOTf can be an effective catalyst in aqueous media [38].

The ^{1}H NMR spectrometry measurements were conducted in CD$_3$OD at 30 °C (Table 3). The commercial lactic acid contains some oligomers due to the self-condensation, as confirmed by the presence of signals at the low magnetic field regions (Fig. 3a). The addition of Y(OTf)$_3$, which is one of the most active catalysts, shifted the signals of the methine protons toward the low magnetic field, and increased the relative intensity of the signals of the oligomers (Fig. 3b). The low magnetic field shift originates from the strong electron-donation of the carbonyl group to the Lewis acid, and the signal at 4.6 ppm indicates that the activation resulted in the formation of the oligomers or d_3-methyl lactate even at room temperature. A similar decrease of lactic acid was observed in the case of La(OTf)$_3$. Contrary to this, the addition of AgOTf, which is the least active catalyst, resulted in negligible change (Fig. 3c).

The shifts in the signals of the methine proton in lactic acid are summarized in Table 3. Lanthanide triflates shifted the signals of the methine protons more than

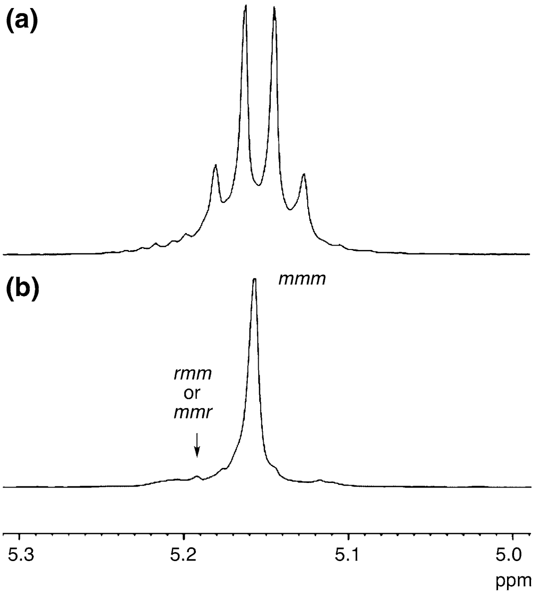


Fig. 2 **a** Non-decoupled and **b** homodecoupled ^{1}H NMR spectrum of PLA obtained in run 12 in Table 1

Table 2 IR absorptions of carbonyl groups in lactic acid in the presence of Lewis acids ($[M(OTf)_x]/[\text{lactic acid}] = 1.1$)

Catalyst	Wavenumber (cm^{-1})	Difference (cm^{-1})
None	1716	–
$Sc(OTf)_3$	1597	−119
$La(OTf)_3$	1689	−27
$Hf(OTf)_4$	1643	−73
$Y(OTf)_3$	1604	−112
$Yb(OTf)_3$	1612	−104
$Cu(OTf)_2$	1666	−50
AgOTf	1720	+4

Table 3 Shifts in ^1H NMR signals of methine proton in lactic acid in the presence of Lewis acids (CD_3OD, 30 °C, $[M(OTf)_x]/[\text{lactic acid}] = 1.1$)

Catalyst	Shift of methine proton in lactic acid[a]
$Sc(OTf)_3$	0.101
$La(OTf)_3$	0.251
$Hf(OTf)_4$	0.046
$Y(OTf)_3$	0.191
$Yb(OTf)_3$	n.d.[b]
$Cu(OTf)_2$	n.d.[b]
AgOTf	0.008

[a] Positive values indicate shifts toward lower magnetic field regions

[b] Not determined, because of the very broad signals

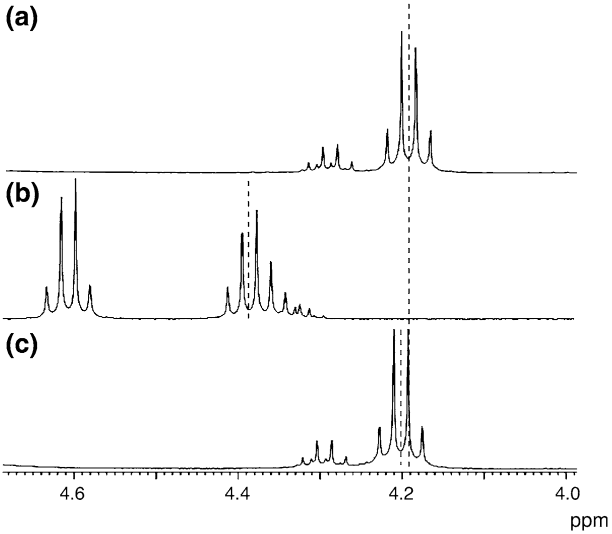


Fig. 3 ^1H NMR spectra of lactic acid **a** without additives, **b** in the presence of $Y(OTf)_3$, and **c** AgOTf (CD_3OD, 30 °C, $[M(OTf)_x]/[\text{lactic acid}] = 1.1$)

less active AgOTf. This result indicates that the high affinity between lactic acid and Lewis acid rules the polycondensation behavior. $La(OTf)_3$ shifted the signal most, although $La(OTf)_3$ did not lead to the best result. A plausible reason is the too high activity resulting in de-polymerization. This assumption is supported by the facts that; the polycondensation at 180 °C afforded PLA with a lower molecular weight than at 170 °C, and lactide presumably produced by depolymerization. Although both the FT-IR and ^1H NMR spectrometry analyses involved exceptions, these methods were informative to evaluate the activity. The analysis based on FT-IR spectrometry was better, considering the fact that the active three catalysts shifted the absorption significantly larger than the others.

Conclusions

Various metal triflates were employed for bulk direct polycondensation of lactic acid. $Sc(OTf)_3$ [24], $Y(OTf)_3$ and $Yb(OTf)_3$ are effective catalysts that afford poly(lactic acid) with high molecular weights in good yields (>60%). Moderate interactions between lactic acid and metal triflates resulted in good catalytic activity, as confirmed by FT-IR and ^1H NMR spectroscopic measurements of mixtures of lactic acid and metal triflates. The FT-IR spectrometry evaluation on the interactions especially will help the optimization of polycondensation conditions for polymerization of lactide.

References

1. Anderson JM, Shive MS (1997) Biodegradation and biocompatibility of PLA and PLGA microspheres. Adv Drug Deliv Rev 28:5–24
2. Sodergard A, Stolt M (2002) Properties of lactic acid based polymers and their correlation with composition. Prog Polym Sci 27:1123–1163
3. Okada M (2002) Chemical syntheses of biodegradable polymers. Prog Polym Sci 27:87–133
4. Wee YJ, Kim JN, Ryu HW (2006) Biotechnological production of lactic acid and its recent applications. Food Technol Biotech 44:163–172
5. Tokiwa Y, Calabia BP (2006) Biodegradability and biodegradation of poly(lactide). Appl Microbiol Biotech 72:244–251
6. Leemslag JW, Pennings AJ (1987) Synthesis of high-molecuar-weight poly(L-lactide) initiated with tin 2-ethylhexanoate. Makromol Chem 188:1809–1814
7. Kricheldorf HR, Lee SR (1995) Polylactones. 32. High-molecular-weight polylactides by ring-opening polymerization with dibutylmagnesium or butylmagnesium chloride. Polymer 36:2995–3003
8. Nyce GW, Glauser T, Connor EF, Möck A, Waymouth RM, Hedrick JL (2003) In situ generation of carbenes: a general and versatile platform for organocatalytic living polymerization. J Am Chem Soc 125:3046–3056
9. Dechy-Cabaret O, Martin-Vaca B, Bourissou D (2004) Controlled ring-opening polymerization of lactide and glycolide. Chem Rev 104:6147–6176
10. Kunioka M, Wang Y, Onozawa S (2005) Poly(lactic acid) polymerized by aluminum triflate. Macromol Symp 224:167–179
11. Wu JC, Yu TL, Chen CT, Lin CC (2006) Recent developments in main group metal complexes catalyzed/initiated polymerization of lactides and related cyclic esters. Coord Chem Rev 250:602–606
12. Carothers WH, Dorough GL (1930) Studies on polymerization and ring formation. IV. Ethylene succinates. J Am Chem Soc 52:711–721

13. Ajioka M, Enomoto K, Suzuki K, Yamaguchi A (1995) Basic properties of polylactic acid produced by the direct condensation polymerization of lactic acid. Bull Chem Soc Jpn 68:2125–2135
14. Otera J, Kawada K, Yano T (1996) Direct condensation polymerization of L-lactic acid catalyzed by distannoxane. Chem Lett 225–226
15. Hiltunen K, Seppälä JV, Härkönen M (1997) Effect of catalyst and polymerization conditions on the preparation of low molecular weight lactic acid polymers. Macromolecules 30:373–379
16. Moon SI, Lee CW, Miyamoto M, Kimura Y (2000) Melt polycondensation of L-lactic acid with Sn(II) catalysts activated by various proton acids: a direct manufacturing route to high molecular weight poly(L-lactic acid). J Polym Sci A 38:1673–1679
17. Moon SI, Taniguchi I, Miyamoto M, Kimura Y, Lee CW (2001) Synthesis and properties of high-molecular-weight poly(L-lactic acid) by melt/solid polycondensation under different reaction conditions. High Perform Polym 13:189–196
18. Kim KW, Woo SI (2002) Synthesis of high-molecular-weight poly(L-lactic acid) by direct polycondensation. Macromol Chem Phys 203:2245–2250
19. Kajiyama T, Taguchi T, Kobayashi H, Kataoka K, Tanaka J (2003) Physicochemical properties of high-molecular-weight poly(alpha,beta-malic acid) synthesized by direct polycondensation. Polym Bull 50:69–75
20. Zhao YM, Wang ZY, Wang J, Mai HZ, Yan B, Yang F (2004) Direct synthesis of poly(D,L-lactic acid) by melt polycondensation and its application in drug delivery. J Appl Polym Sci 91:2143–2150
21. Shyamroy S, Garnaik B, Sivaram S (2005) Structure of poly(L-lactic acid)s prepared by the dehydropolycondensation of L-lactic acid with organotin catalysts. J Polym Sci A 43:2164–2177
22. Nagahata R, Sano D, Suzuki H, Takeuchi K (2007) Microwave-assisted single-step synthesis of poly(lactic acid) by direct polycondensation of lactic acid. Macromol Rapid Commun 28:437–442
23. Chen GX, Kim HS, Kim ES, Yoon JS (2006) Synthesis of high-molecular-weight poly(L-lactic acid) through the direct condensation polymerization of L-lactic acid in bulk state. Eur Polym J 42:468–472
24. Takasu A, Narukawa Y, Hirabayashi T (2006) Direct dehydration polycondensation of lactic acid catalyzed by water-stable Lewis acids. J Polym Sci A 44:5247–5253
25. Lachine EE, Noujaim AA, Ediss C (1976) Toxicity, tissue distribution and excretion of $^{46}ScCl_3$ and ^{46}Sc-EDTA in mice. Int J Appl Radiat Isot 27:373–377
26. Hirano S, Suzuki KT (1996) Exposure, metabolism, and toxicity of rare earths and related compounds. Environ Health Perspect 104(Suppl I):85–95
27. He ML, Wang YZ, Zu ZR, Chen ML, Rambeck WA (2003) Effect of dietary rare earth elements on growth performance and blood parameters of rats. J Anim Physiol Anim Nutr 87:229–235
28. Yasuda H (2000) Organo transition metal initiated living polymerizations. Prog Polym Sci 25:573–626
29. Hou ZM, Wakatsuki Y (2002) Recent developments in organolanthanide polymerization catalysts. Coord Chem Rev 231:1–22
30. Kobayashi S, Sugiura M, Kitagawa H, Lam WWL (2002) Rare-earth metal triflates in organic synthesis. Chem Rev 102:2227–2302
31. Kricheldorf HR, Boettcher C, Tönnes KU (1992) Polylactones. 23. Polymerization of racemic and meso D,L-lactide with various organotin catalysts stereochemical aspects. Polymer 33:2817–2824
32. Takasu A, Oishi Y, Iio Y, Inai Y, Hirabayashi T (2003) Synthesis of aliphatic polyesters by direct polyesterification of dicarboxylic acids with diols under mild conditions catalyzed by reusable rare-earth triflate. Macromolecules 36:1772–1774
33. Takasu A, Iio Y, Oishi Y, Narukawa Y, Hirabayashi T (2005) Environmentally benign polyester synthesis by room temperature direct polycondensation of dicarboxylic acid and diol. Macromolecules 38:1048–1050
34. Takasu A, Iio Y, Mimura T, Hirabayashi T (2005) Room-temperature polycondensation of dicarboxylic acids and diols catalyzed by water-stable lewis acids. Polym J 37:946–953
35. Yui N (1996) Stereo-block-copolymers (of L- and D-lactides). In: Salamore JC (ed.) Polymeric materials encyclopedia, vol 10. CRC Press, Boca Raton, pp 7944–7950
36. Ninomiya N, Kato K, Fujimori A, Masuko T (2007) Transcrystalline structures of poly(L-lactide). Polymer 48:4874–4882
37. Nomura N, Ishii R, Akakura M, Aoi K (2002) Stereoselective ring-opening polymerization of racemic lactide using aluminum-achiral ligand complexes: Exploration of a chain-end control mechanism. J Am Chem Soc 124:5938–5939
38. Loncaric C, Manabe K, Kobayashi S (2003) AgOTf-catalyzed aza-Diels-Alder reactions of Danishefsky's diene with imines in water. Adv Synth Catal 345:475–477