

POLYMERIZATION OF LACTIC *O*-CARBOXYLIC ANHYDRIDE USING ORGANOMETALLIC CATALYSTS*

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Abstract The ring-opening polymerization of 5-methyl-1,3-dioxolane-2,4-dione (lactic *O*-carboxylic anhydride, LacOCA) using organometallic complexes, including Co(III) complexes with Schiff base ligands, Tin(II) alphasates and Al(III) complexes with Schiff base ligands, was explored. The polymerization was carried out by treatment of the organometallic complexes with LacOCA in toluene under mild conditions. The corresponding poly(lactic acid) was characterized by spectroscopy and thermal analyses, which revealed insight into the structure of the effective catalyst for the polymerization of LacOCA.

Keywords: Organometallic; Poly(lactic acid); Ring-opening polymerization.

INTRODUCTION

Poly(lactic acid) (PLA) has been receiving much attention as biodegradable materials in recent years^[1, 2]. It has found many applications in the field of biomedical purposes, such as suture, drug delivery and tissue engineering^[3–5]. Because the starting material of PLA is agricultural products such as corn, PLA is an environmentally sustainable alternative to petrochemically-derived products^[6]. It can be employed in the preparation of biodegradable plastics. PLA can be prepared by direct polycondensation of lactic acid^[7]. However, it is usually difficult to obtain high molecular weight PLA by polycondensation. Currently, ring-opening polymerization (ROP) of lactide is a preferred route to prepare PLA because of the higher controllability of the polymerization^[1]. Indeed, high molecular-weight PLA can be obtained by ROP. The driving force for the ROP of lactide is the ring strain of the monomer. As a polymerizable six-membered ring, the ring strain of lactides is modest. Therefore, high temperatures are usually required for the ROP of lactides^[8]. Undesirable transesterification and racemization often take place in these cases^[1], which significantly reduce the mechanical properties of the corresponding PLA. Consequently, a polymerizable activated monomer of the lactide equivalent is highly desirable.

5-Methyl-1,3-dioxolane-2,4-dione is a five-membered *O*-carboxyanhydride (LacOCA) derived from the lactic acid. It can be readily obtained by the reaction of lactate salt with diphosgene^[9]. Bourissou *et al.* reported that the ROP of LacOCA proceeded in the presence of an organocatalyst, dimethylaminopyridine (DMAP)^[10, 11]

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or lipase^[12]. The ROP of LacOCA catalyzed by DMAP is well controllable. PLA with high molecular weight and narrow polydispersity index has been obtained under mild polymerization conditions. This indicates that the ROP of LacOCA is an alternative route to prepare PLA^[10].

Organometallic complexes have been widely used as catalysts in a variety of polymerization. For instance, stannous octoate^[8], alkylaluminum, aluminum alkoxides^[13–18], zinc alkyl^[19], calcium alkoxides^[20, 21] and strontium alkoxide^[22] have been used as the catalyst/initiator for the ROP of lactides. However, to the best of our knowledge, there has been no report on the ROP of LacOCA using organometallic complexes as catalysts. Considering the high toxicity of DMAP, it is important to explore the organometallic complexes as the catalyst of the ROP of LacOCA. We have focused on Co(III) complexes with Schiff base ligands as the versatile and highly active catalysts, based on their potential activities to catalyze many kinds of reactions including Baeyer-Villiger oxidation^[23], hydrolysis of epoxides^[24], cyclizations of dianhydro sugar alcohols^[25] and copolymerization of epoxides and carbon dioxide^[26]. Tin(II) aliphates^[8] and Al(III) complexes with Schiff base ligands^[27, 28] have also been reported as the conventional catalysts for the ROP of lactides. Herein, we report for the first time the ROP of LacOCA using Co(III) complexes with Schiff base ligands, Tin(II) aliphates and Al(III) complexes with Schiff base ligands as catalysts.

EXPERIMENTAL

General Procedures

LacOCA (Fig. 1) and Co(III) complexes with Schiff base ligands (Fig. 2) were prepared according to the already published procedures^[29, 30]. Toluene was dried by distillation over sodium under the protection of nitrogen.

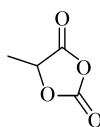


Fig. 1 Structure of LacOCA

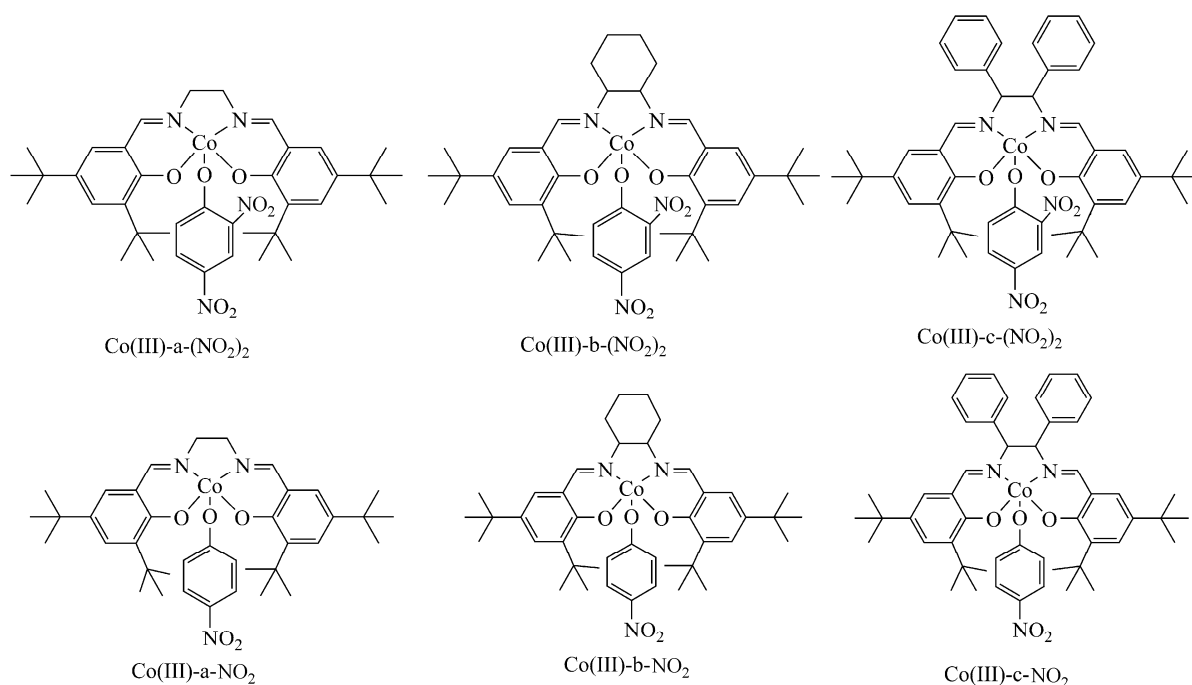


Fig. 2 Structures of Co(III) complexes with Schiff base ligands employed in this study

^1H -NMR spectra were recorded on Bruker AV 300 MHz, Bruker AV 400 MHz or Bruker AV 600 MHz spectrometer in CDCl_3 at 25°C . Chemical shifts were referenced to tetramethylsilane (TMS) for the ^1H -NMR measurement. Gel permeation chromatography (GPC) was performed in THF (flow rate 1.00 mL/min at 35°C) on a Waters 410 GPC. The columns were calibrated against polystyrene (PS) as the external standard. Differential scanning calorimetry (DSC) analyses were carried out at a heating rate of 10 K/min on a Perkin Elmer Instruments DSC-7.

Polymerization of LacOCA

All of the procedures were carried out under the protection of dry argon. In a typical procedure, LacOCA (2.92 mmol, 0.34 g), 2-propanol (0.029 mmol, in 0.34 mL of toluene), $\text{Co(III)-c-(NO}_2)_2$ (0.029 mmol, 0.0258 g), and toluene (5.5 mL) were added to a dried ampoule equipped with a magnetic stirrer bar. The initial concentration of LacOCA monomer in toluene was 0.5 mol/mL. The ampoule was placed in an oil bath at 70°C . After polymerization, the polymer was dissolved in chloroform and isolated by precipitation into cold ethanol, which was collected by filtration and dried under vacuum at room temperature for 24 h.

RESULTS AND DISCUSSION

Polymerization of LacOCA using Co(III) Complexes with Schiff Base Ligands

Polymerization of LacOCA using Co(III) complexes with Schiff base ligands was performed at 70°C in toluene. The results of the polymerization are listed in Table 1.

Table 1. Polymerizations of LacOCA

Entry	Initiating system	[M]/[I]	Temp. ($^\circ\text{C}$)	Time (h)	$M_n \times 10^{-3}$	PDI
1	$\text{Co(III)-a-(NO}_2)_2/^i\text{PrOH}$	100/1	70	35	4.0	1.3
2	$\text{Co(III)-b-(NO}_2)_2/^i\text{PrOH}$	100/1	70	35	4.3	1.2
3	$\text{Co(III)-c-(NO}_2)_2/^i\text{PrOH}$	100/1	70	35	9.6	1.4
4	$\text{Co(III)-a-NO}_2/^i\text{PrOH}$	100/1	70	35	6.4	1.4
5	$\text{Co(III)-b-NO}_2/^i\text{PrOH}$	100/1	70	35	3.3	1.1
6	$\text{Co(III)-b-NO}_2/^i\text{PrOH}$	200/1	70	60	6.0	1.5
7	Co(III)-b-NO_2	200/1	70	60	7.6	1.4
8	$\text{Co(III)-c-NO}_2/^i\text{PrOH}$	100/1	70	35	3.6	1.2
9	Stannous benzoate/ $^i\text{PrOH}$	120/1	70	15	6.4	1.2
10	Stannous benzoate	120/1	70	15	7.0	1.3
11	Stannous octoate/ $^i\text{PrOH}$	150/1	60	15	7.9	1.4
12	(Cyclohexylsalen)AlEt/BnOH	150/1	70	11	—	—
13	(Dimethylsalen)AlEt/BnOH	150/1	70	11	—	—

$^i\text{PrOH}$: isopropyl alcohol; BnOH: benzyl alcohol

Poly(lactic acid) (PLA) was obtained in all experiments using the Co(III) complexes with Schiff base ligands as the catalyst. When the monomer/initiator ratio was 100/1 (Table 1), the number average molecular weight (M_n) of PLA was in the range of 3.3×10^3 – 9.6×10^3 , and the polydispersity index (PDI) of PLA was in the range of 1.1–1.5. The M_n of the obtained PLA was low in all experiments except the $\text{Co(III)-c-(NO}_2)_2$ initiating system, which gave PLA with a high M_n (9.6×10^3). The molecular weight distribution of the product obtained with the $\text{Co(III)-c-(NO}_2)_2$ catalyst was relatively broad (PDI = 1.4). When the $\text{Co(III)-b-NO}_2/^i\text{PrOH}$ initiating system (where $^i\text{PrOH}$ was isopropanol) was employed, the M_n of PLA increased from 3.3×10^3 to 6.0×10^3 and the PDI broadened from 1.1 to 1.5 as the monomer/initiator ratio increased from 100/1 to 200/1 (Table 1, Entries 5 and 6). The Co(III)-b-NO_2 initiating system without $^i\text{PrOH}$ also catalyzed the polymerization of LacOCA. Compared with the $\text{Co(III)-b-NO}_2/^i\text{PrOH}$ initiating system, the M_n of the resulting PLA using the Co(III)-b-NO_2 initiating system was slightly higher ($M_n = 7.6 \times 10^3$). The molecular weight distribution of PLA was also broad (PDI = 1.4), which was similar to that of the $\text{Co(III)-b-NO}_2/^i\text{PrOH}$ initiating system. These results demonstrated that the Co(III) complexes with Schiff base ligands acted as the catalysts for the ROP of

LacOCA. The present ROP method somehow allowed the control of the molecular weight of PLA, but the molecular weight distribution was broad in most cases of the polymerization examined in this study, especially when the polymerization time was increased. The large polydispersity implies that the ROP may have been accompanied by undesired intra- and/or inter-transesterification reactions.

Polymerization of LacOCA using Tin(II) or Al(III) Based Complexes

Tin(II) and Al(III) complexes are also widely used as the catalysts for the ROP of lactides. Based on the activity of the Co(III) complexes (*vide supra*), we turned to examine the ROP of LacOCA using these metal complexes with the similar (or identical) ligand as the catalyst. Stannous benzoate, stannous octate, (cyclohexylsalen)AlEt and (dimethylpropylsalen)AlEt (Fig. 3) were employed in this study. Both stannous benzoate and stannous octate were efficient catalysts for the ROP of LacOCA. When the stannous benzoate/*i*PrOH initiating system was used as the catalyst and the monomer/initiator ratio was 120/1, the M_n and PDI of the obtained PLA were 6.4×10^3 and 1.2, respectively (Table 1, Entry 9). When the stannous benzoate initiating system was applied, the resulting M_n of 7.0×10^3 was slightly higher than that obtained with the benzoate/*i*PrOH initiating system (Table 1, Entry 10). This result suggested that the addition of *i*PrOH was not effective to control the M_n of the product of the LacOCA polymerization when stannous benzoate was used as the catalyst, which was in contrast to the DMAP/alcohol mediated ROP of LacOCA where the alcohol was able to control the M_n of PLA^[10, 11].

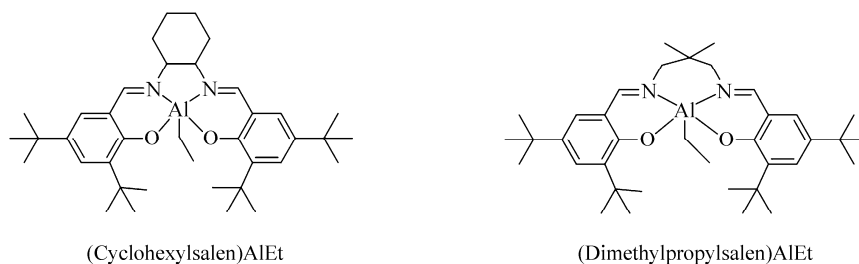


Fig. 3 Structures of aluminum based complexes employed in this study

(Cyclohexylsalen)AlEt^[31, 32] and (dimethylpropylsalen)AlEt^[28] (Fig. 3) are efficient Al based catalysts for the ROP of lactides. However, no polymer was isolated from the ROP of LacOCA using those catalysts (Table 1, Entries 12 and 13), which indicated that the aluminum based complexes were totally inactive for the ROP of LacOCA.

Characterization of the Obtained PLA

The ¹H-NMR spectrum of the obtained PLA is shown in Fig. 4. The doublet peaks at $\delta = 1.73$ were assigned to $\underline{\text{CH}}_3$ resonance of the polymer chain. The quartet peaks at $\delta = 5.15$ were attributed to that of the $\text{CH}\underline{\text{C}}\text{H}_3$ of PLA. ¹³C-NMR spectrum of the PLA is displayed in Fig. 5. The signals at $\delta = 169.5$, 69.0, and 16.6 corresponded to the carbon resonances of carbonyl, methine and methyl groups of the PLA chain, respectively.

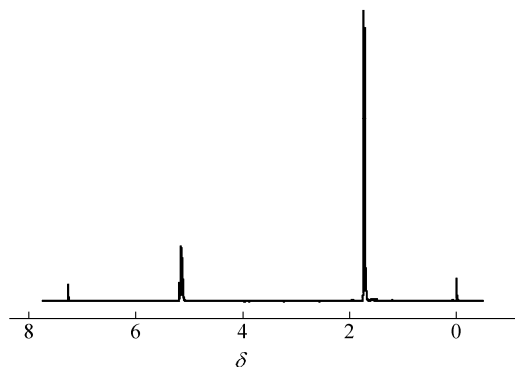


Fig. 4 ¹H-NMR spectrum of poly(lactic acid) from LacOCA

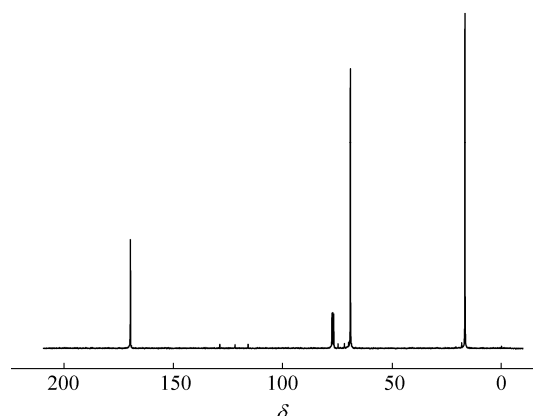


Fig. 5 ^{13}C -NMR spectrum of poly(lactic acid) from LacOCA

These results are consistent with the reported NMR spectra of PLA^[28], which demonstrated that PLA was formed by the polymerization of LacOCA. The carbonyldioxy group was eliminated from the polymerization system by the liberation of carbon dioxide.

The DSC thermogram of the obtained PLA is shown in Fig. 6. The glass transition temperature (T_g) of the corresponding PLA was 55°C. This is in consistent with the reported data in a literature (T_g ca. 55°C)^[33]. The melting point T_m of the PLA was 154°C, which was slightly lower than that for the poly(L-lactide) reported in the literature (T_m ca. 175°C)^[33]. TGA revealed that $T_{5\%}$, the temperature corresponding to 5% weight loss, was 231°C for the PLA produced by the LacOCA polymerization (Fig. 7). This was lower than that of the previously reported poly(L-lactide) ($T_{5\%}$ ca. 320°C)^[34].

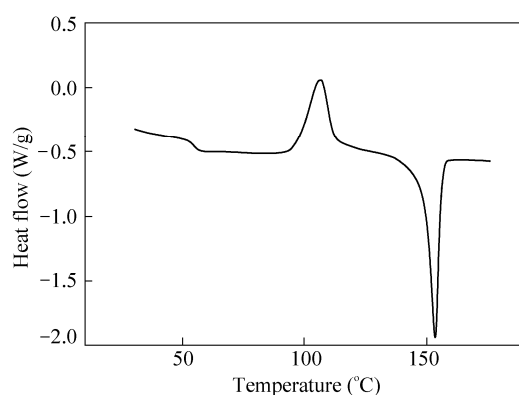


Fig. 6 DSC thermogram of poly(lactic acid) (Table 1, Entry 9)

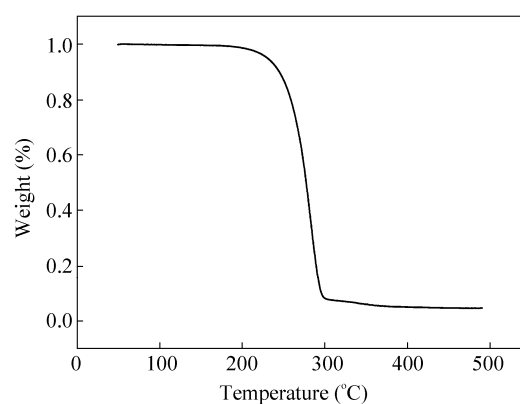


Fig. 7 TGA thermogram of poly(lactic acid) (Table 1, Entry 9)

These lower characteristic thermal transition temperatures were ascribed to the relatively low molecular weights of the PLA produced by the LacOCA polymerization. Increasing the molecular weights by suppressing the proposed side reactions such as the transesterification by tuning the catalytic activity with a suitably designed ligand around the cobalt center is the topics of our continuous research.

CONCLUSIONS

Co(III) complexes with Schiff base ligands and Tin(II) alphasates, were found to be the catalysts for the ROP of LacOCA to produce poly(lactic acid). Intra- and/or inter-transesterification were suggested to coincide with the polymerization, which resulted in a relatively large polydispersity in molecular weights. The carbonyldioxy

group was eliminated from the polymerization system. The corresponding PLA showed similar T_g but lower $T_{5\%}$ compared with PLA obtained from lactides, as a result of the lower molecular weights. Al(III) complexes with Schiff base ligands were not catalytically active for the polymerization of LacOCA.

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