Optimization of the Reaction Conditions and Characterization of ʟ-Lactic Acid Direct Polycondensation Products Catalyzed by a Non-Metal-Based Compound

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ABSTRACT: In this article, we deal with the investigation into a poly(lactic acid) (PLA) preparation process catalyzed by a non-metal-based compound. Low-molecular-weight PLA was synthesized by the direct melt polycondensation of ʟ-lactic acid catalyzed by methanesulfonic acid (MSA). This study was focused on the investigation into optimal MSA concentration determination and into the temperature (130, 145, 160, 175, and 190°C) and time (6, 12, 18, and 24 h) influence on the structure (Fourier transform infrared spectroscopy), molecular weight (viscometric measurements and gel permeation chromatography), and thermal properties (differential scanning calorimetry) of the samples. The results show an optimal MSA content of 0.5 wt %. The highest molecular weight of PLA prepared by this method was reached after 18 h of reaction at 175°C (weight-average molar mass = 17.2×10^3 g/mol). © 2010 Wiley Periodicals, Inc. J Appl Polym Sci 116: 1597–1602, 2010

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INTRODUCTION

Biodegradable polymers have attracted increasing interest over the past 2 decades, both in fundamental research and also for practical use. Poly(lactic acid) (PLA) is a synthetic biodegradable polyester, and it represents potential applicability in a growing number of technologies, such as orthopedics, drug delivery, sutures, and scaffolds, because of its excellent biocompatibility and bioresorbability.[1,2] The synthesis of PLA can be carried out through either the ring-opening polymerization of lactones or the direct polycondensation of the ʟ-lactic acid (LA) monomer. The former method can be characterized by high-purity requirements set on reactants and enables production of products with high and medium molecular weights. On the other hand, the latter does not provide high-molecular-weight products. Both of the mentioned methods require the presence of a catalyst.[3] There are many publications dealing with PLA synthesis with metal-based compounds as catalysts, frequently those based on tin.[4] However, the residual metal catalyst can pose a problem with regard to both the thermal stability and biocompatibility of PLA.[5]

In this article, we deal with PLA preparation by direct melt polycondensation using a nonmetal catalyst based on methanesulfonic acid (MSA). This simple organic acid was already reported as a catalyst for the polycondensation of glycolic/LAs by Moon et al.[6] Their results show that MSA could be more effective than conventional metal salts. In addition, MSA is expected to be particularly versatile for biomedical application of the resulting PLA because it can readily be removed from the product by washing or evaporation to reduce the risky effects produced by the residual catalyst.[6] On the other hand, there is no literature reporting MSA catalyst use for the polycondensation of LA itself.

With these observations in mind, a detailed examination of the catalytic effect of MSA on PLA synthesis was the aim of this study. Special attention was paid to the optimization of the catalyst concentration and the characterization of the resulting polymer in terms of structure, molecular weight, and thermal properties.

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EXPERIMENTAL

Materials

An 80% water solution of pure LA with an optical rotation of 10.6° (measured by an Optech P1000 polarimeter at 22°C, concentration = 10%; Krüss, Hamburg, Germany) was purchased from Lachner Neratovice, Czech Republic. MSA (CH_4O_3S; 99.5%) was supplied by Sigma Aldrich (Steinheim, Germany). The solvents chloroform ($CHCl_3$), acetone (C_3H_6O), and methanol (CH_4O; analytical grade) were bought from IPL Lukes (Uhersky Brod, Czech Republic). All chemicals were used as obtained without further purification.

Polycondensation

A typical procedure was as follows: LA (50 mL) was added to a double-necked flask (250 mL) equipped with a Teflon stirrer. The flask was then placed in an oil bath heated by a magnetic stirrer with heating and connected to a laboratory apparatus for distillation under reduced pressure. The dehydration step followed (in all cases; 160°C, 15 kPa, 4 h, continuous mixing at 250 rpm). After LA dehydration, the reactor was disconnected from the vacuum pump, and the relevant amount (see details later) of MSA was added dropwise under continuous stirring. The flask with dehydrated LA and the relevant amount of MSA was connected back to the source of the vacuum (15 kPa), and the reaction continued for a given period of time (6, 12, 18, or 24 h) at temperatures of 130, 145, 160, 175, and 190°C. The beginning of the reaction time (time = 0 h) was considered the time of catalyst addition in this study. The resulting product, in the form of colorless or light brown viscous melt, was allowed to cool to room temperature and dissolved in C_3H_6O then. The polymer solution was precipitated in a mixture of chilled CH_4O/distilled water 1 : 1. The obtained powder was filtered, washed with CH_4O, and dried at 45°C for 48 h.

Methods

Viscometric measurements

Viscosity measurements were performed in $CHCl_3$ at 30°C in an Ubbelohde viscometer with capillary 0a (Technosklo, Drzkov, Czech Republic). The intrinsic viscosity ($[\eta]$) was calculated with eq. (1):

$$[\eta] = \lim_{c \to 0} \frac{\eta_{rel} - 1}{c} \qquad (1)$$

where η_{rel} is the relative viscosity, which is equal to the ratio of the polymer solution and pure solvent viscosities, and c is the concentration of the polymer solution (0.4, 0.8, and 1.2 wt/vol %).

Determination of the molecular weight by gel permeation chromatography (GPC)

GPC analyses were performed with a Breeze chromatographic system (Waters, Milford, MA) equipped with a PLgel Mixed-D column (300×7.8 mm^2, 5 µm; Polymer Laboratories, Ltd.). For detection, a Waters 2487 dual-absorbance detector at 239 nm was used. Analyses were carried out at room temperature with a flow rate of 1.0 mL/min in $CHCl_3$. The column was calibrated with narrow-molecular-weight polystyrene standards with molar masses ranging from 580 to 480,000 g/mol (Polymer Laboratories, Ltd.). A 100-µL injection loop was used for all measurements. The sample concentration ranged from 1.6 to 2.2 mg/mL. Data processing was carried out with Waters Breeze GPC software (Waters). The weight-average molar mass (M_w), number-average molar mass (M_n), and polydispersity of the tested samples were determined.

Infrared spectroscopy

To identify the physicochemical structure of the LA polycondensation products, Fourier transform infrared (FTIR) analysis was carried out. The investigation was conducted on a NICOLET 320 FTIR spectrometer (Nicolet Instruments Co., Madison, WI) equipped with an attenuated total reflectance (ATR) accessory with a Zn–Se crystal and the software package OMNIC (Nicolet Instruments Co.) over the range 4000–650 cm^{-1} at room temperature. A uniform resolution of 2 cm^{-1} was maintained in all cases.

Differential scanning calorimetry (DSC)

For the determination of the glass-transition temperature (T_g), melting point, and crystallinity (χ_c) of the polycondensates, DSC was used. Approximately 4 mg of sample was placed in an aluminum pan, sealed, and analyzed on a PerkinElmer (Waltham, MA) Pyris 1 differential scanning calorimeter calibrated with indium in terms of temperature and heat flow. The experiments were performed under a nitrogen atmosphere (20 mL/min) in two scans in the temperature range 0–170°C and at a heating rate of 10°C/min. χ_c (%) was estimated by the following equation:

$$\chi_c = \frac{\Delta H_m}{\Delta H_m^0} \times 100 \qquad (2)$$

where ΔH_m^0 is the enthalpy of mixing for 100% crystalline PLA (93.7 J/g) adopted from Fischer et al.[7] and ΔH_m represents the measured melting enthalpy of the sample taken from the first heating scan.

RESULTS AND DISCUSSION

Optimal catalyst concentration determination

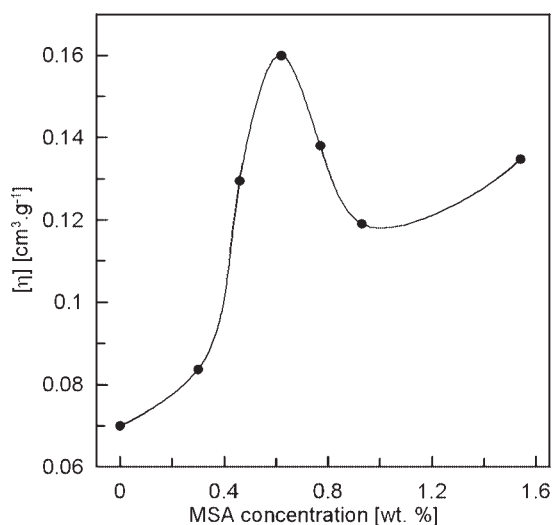The syntheses of PLA were performed with the method of the direct polycondensation of LA in the

Figure 1 [η] of the polycondensates (160°C, 24 h, and 15 kPa) versus the amount of the catalyst (MSA).

presence of MSA as non-metal-based catalyst. The use of this simple alkylsulfonic acid for the catalysis of LA and glycolic acid polycondensation was already reported by Moon et al.[6] The authors used a fixed amount of MSA (0.3 wt %). However, the catalyst content plays an important role in relation to the resulting product. The determination of the optimal MSA concentration for LA polycondensation was made through a series of experiments with different MSA contents (from 0 to 1.6 wt % related to the initial mass of LA) according to the method described previously. The temperature of reaction was 160°C, the pressure was 15 kPa, and the time was 24 h. The products were investigated by viscometric measurements. The dependence of [η] on the MSA catalyst content is shown in Figure 1. As shown, [η] of the polymer solutions representing the molecular weight of the products rose significantly with increasing content of MSA up to 0.5 wt %. Further additions of the catalyst led to [η] reduction. A color change, observed as a darkening of the product, was noticed also; it probably occurred because of the side and degradation reactions that may have taken place at higher MSA concentrations. Interestingly, a slight [η] enhancement was observed at the highest investigated MSA content, that is, 1.6 wt %. On the basis of these results, 0.5 wt % of MSA was selected as the optimal catalyst content for further experiments.

Viscometric characterization of the products

The results obtained from the viscosity measurements of the diluted polymer solutions (CHCl₃, 30°C) are summarized in Table I. The table shows values of [η] depending on the reaction time and

temperature. Generally, a higher reaction time produced a higher molecular weight (represented by [η]) of the products. The only exceptions was found for the sample series prepared at 175°C, where the PLA obtained after 18 h of reaction showed a higher [η] than the product synthesized for 24 h. This unexpected result was verified several times with the same outcome. The data shown in Table I reveal the optimal polycondensation temperature and time of 175°C and 18 h, respectively. The lower reaction temperatures did not provide the product with comparable properties nor did the highest tested temperature of 190°C, which was more favorable for degradation reactions.

GPC analysis

The molecular weight of the polycondensation products prepared under various conditions was determined by the GPC method. The results of the analysis are presented in Table II. As shown, in accordance with viscosity, the highest molecular weight was detected in the sample with a polycondensation temperature of 175°C and a time of 18 h. The polydispersity of the sample was below 2 in all cases, which corresponded to the generally accepted polydispersity of polycondensation polymers.

The comparison of [η] (Table I) and M_w (Table II) showed a reasonably good correlation between these two parameters. Differential distribution curves recorded for the reactions conducted at the optimum temperature of 175°C for various reaction times are depicted in Figure 2. It was obvious that at a given temperature, the molecular weights of PLA increased with prolonged reaction time up to 18 h. This was evidenced by the gradual shift in the distribution curves to high-molecular-weight regions [Fig. 2(a,b,d)]. However, the reaction time of 24 h provided PLA with an M_w value that was lower than that observed in the sample synthesized for 18 h [Fig. 2(c)]. Here, a decrease in the molecular weight occurred because of decomposition.

TABLE I
Temperature and Reaction Time Effects on the [η] Values of the Prepared PLA

| Temperature (°C) | [η] in CHCl₃ at 30°C (cm³/g) | | | |
	6 h	12 h	18 h	24 h
130	0.07	0.10	0.10	0.17
145	0.05	0.08	0.13	0.16
160	0.09	0.08	0.10	0.16
175	0.10	0.17	0.21	0.19
190	0.15	0.09	0.11	0.14

The catalyst was 0.5 wt % MSA, and the pressure was 15 kPa.

TABLE II
GPC Characterization of the LA Polycondensation Products Prepared Under Various Conditions

Temperature (°C)	Reaction time (h)	M_n (10^3 g/mol)	M_w (10^3 g/mol)	M_w/M_n
130	6	3.0	4.1	1.3
	12	4.8	6.1	1.3
	18	3.3	4.9	1.5
	24	5.5	7.3	1.3
145	6	3.3	4.0	1.2
	12	4.0	4.7	1.2
	18	7.1	10.3	1.4
	24	9.4	14.3	1.5
160	6	3.9	4.7	1.2
	12	4.5	5.3	1.2
	18	6.0	8.6	1.4
	24	5.5	6.9	1.3
175	6	5.0	7.7	1.6
	12	8.2	14.1	1.7
	18	10.6	17.2	1.6
	24	7.9	11.6	1.5
190	6	7.6	11.6	1.5
	12	5.1	6.8	1.3
	18	8.6	12.8	1.5
	24	8.9	13.5	1.6

Reaction time 0 was considered to be the time of catalyst addition.

Thermal properties

A series of PLA samples synthesized at 175°C was selected for detailed DSC analysis; DSC heating thermograms (first heating scan) of the dehydrated LA (4 h of dehydration without catalyst at 160°C and 15 kPa) and PLA obtained after 6, 12, 18, and 24 h of polycondensation are shown in Figure 3. Generall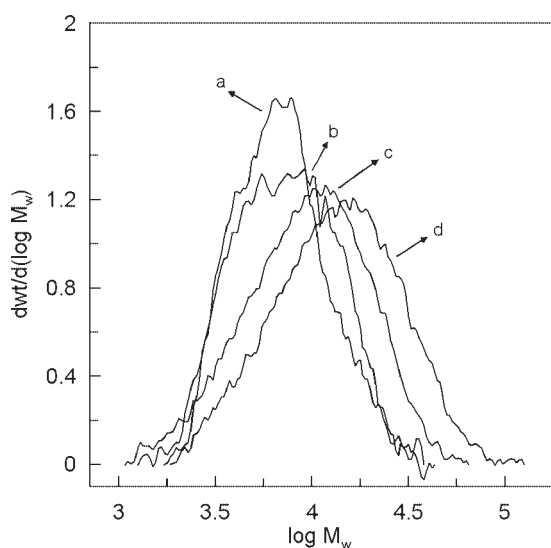y, the melting temperature is expected to increase with increasing M_w.[8] As shown, the product of LA dehydration [Fig. 3(a)] showed two exothermic peaks located at 98 and 115°C. The addition of catalyst and the subsequent course of the reaction led to a shift in the transition peaks to higher temperatures, as was to be expected with rising molecular weight of the polycondensates [Fig. 3(b–d)]. The sample with the highest M_w [Fig. 3(d)] also showed the highest melting temperature. Its endothermic peaks occurred at 132 and 147°C. The occurrence of two melting peaks and their shift with increasing M_w revealed the presence of two types of crystalline structures. On the other hand, the PLA sample that was prepared for 24 h [Fig. 3(e)] had only one peak, found at 145°C. This fact could mean that the increase in the reaction temperature caused the formation of a more uniform crystalline structure. The occurrence of two crystalline structures might also have been caused by the precipitation procedure used for crude product purification, where a mixture of CH_4O and water was used. It would be interesting to follow the thermal transition of PLA purified by a different solvent or by the same solvent mixture with various CH_4O/water ratios. The second heating scans of the samples (not presented here) showed a clear presence of T_g, which increased with rising M_w of the samples. This typical trend is depicted in Figure 4 as a result of detected T_g on [η]. As shown, the measured T_g varied from 34°C (for the sample [η] = 0.07 cm^3/g) to 57°C (for the sample [η] = 0.21 cm^3/g). The literature data presented by Jamshidi et al.[9] demonstrated that a typical PLA T_g varies with its molecular weight (PLA with M_n = 430 g/

Figure 2 Differential distribution curves of selected polycondensation products with various [η] values: (a) 0.1, (b) 0.17, (c) 0.19, and (d) 0.21 cm^3/g.
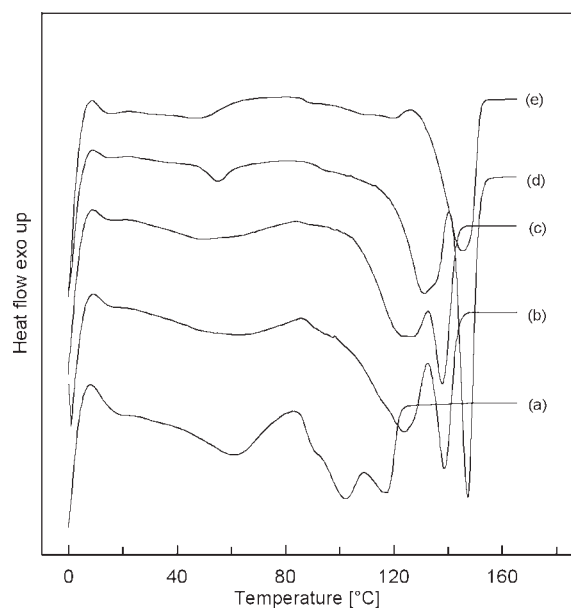

Figure 3 DSC curves of (a) dehydrated LA (4 h, 160°C, and 15 kPa) and (b–e) PLA prepared at 175°C and 15 kPa for 6, 12, 18, and 24 h, respectively.
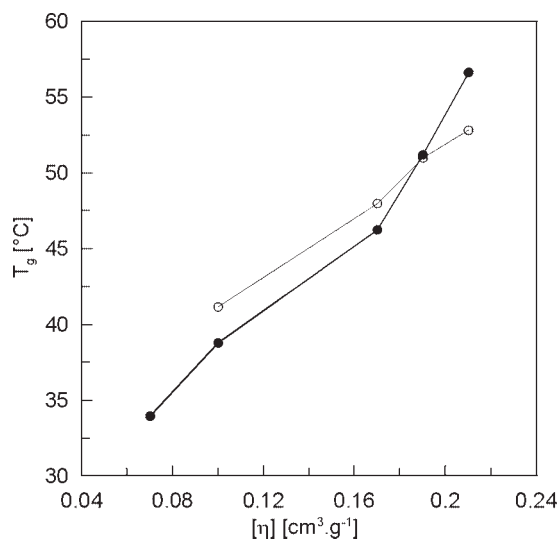
Figure 4 T_g versus [η] for the prepared PLA [full symbols represent experimental results, and empty symbols represent values calculated according to eq. (3)].

Figure 5 Development of χ_c with increasing polycondensation time (175°C, 0.5 wt % MSA, and 15 kPa).

mol shows $T_g = -8°C$ and PLA of $M_n = 23 \times 10^3$ g/mol shows $T_g = 55.5°C$).

The obtained results were in agreement with the T_g calculations (Fig. 4) performed according to the Fox–Flory equation:

$$T_g = T_g^\infty - \frac{K}{M_n} \quad (3)$$

where T_g^∞ is the glass-transition temperature at an infinite molecular weight of the polymer and K is a constant representing the excess free volume of the polymer chains end groups. The calculation of theoretical T_g was done with the M_n determined by GPC (Table II) and the values reported by Jamshidi et al.,[9] who reported $T_g^\infty = 58°C$ and $K = 5.5 \times 10^4$ for low-χ_c PLLA.[9] However, eq. (3) failed in the low-M_n product of LA dehydration ([η] = 0.07 cm³/g). A negative deviation of the theoretical value from the measured T_g values was noticed because of a rising χ_c (taken from the first heating scan), which occurred with the prolonged time of polycondensation (Fig. 5). However, T_g and χ_c depended on the thermal history of the sample, as reported in many articles.[3]

Infrared spectroscopy

The typical FTIR–ATR spectra of the polycondensation products synthesized at various temperatures over 24 h are shown in Figure 6. The qualitative analysis of the obtained FTIR–ATR records showed the typical spectra of PLA, which were in agreement with the results reported elsewhere.[10,11] All presented spectra were characterized by peaks located at 2997 and 2945 cm⁻¹. These represented asymmet-
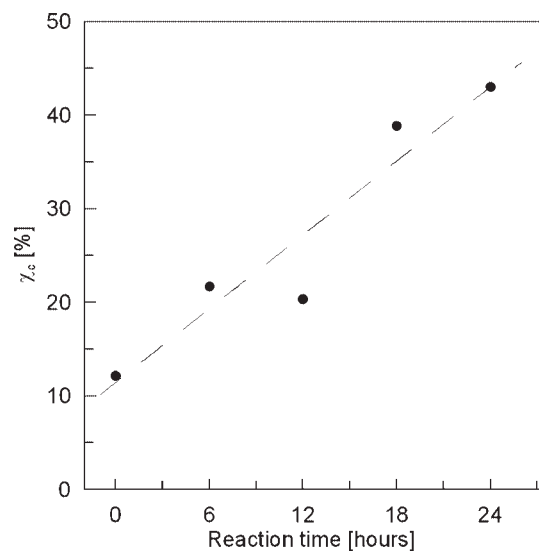
ric and symmetric —CH— stretching, respectively. The C=O absorbance region was found at 1753 cm⁻¹. The peak occurring at 1450 cm⁻¹ was typical for CH₃— banding. —CH— deformation and asymmetric banding appeared at 1381 and 1360 cm⁻¹, respectively. The peak at 1265 cm⁻¹, which was clear, especially in the case of the PLA prepared at 190°C, was assigned to the C—O stretching of the ester groups and carboxylic acid's oligomers.[12] The region between 1300 and 1050 cm⁻¹ showed four intensive absorption peaks at 1183, 1131, 1090
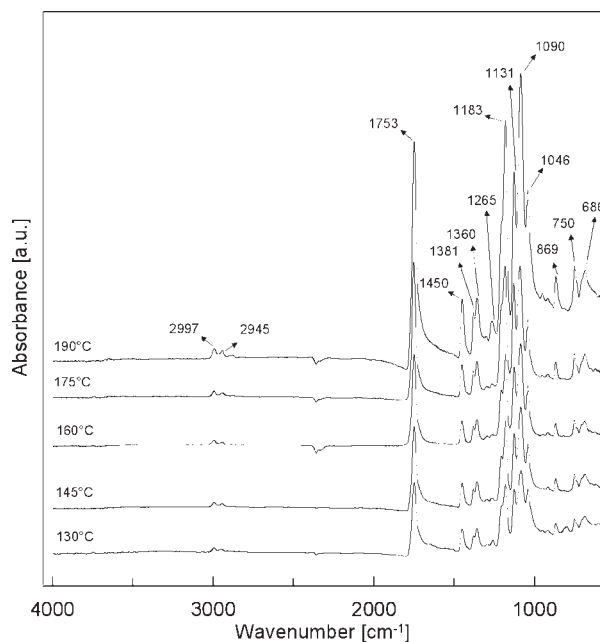

Figure 6 FTIR–ATR spectra of PLA prepared at various temperatures (24-h reaction time, 0.5 wt % MSA, and 15 kPa).

(C—O—C stretching), and 1046 cm^{-1} (—OH bending). According to Auras et al.,[3] the peaks located at 869 and 750 cm^{-1} corresponded to —C—C— stretching. In addition, the peak at 869 cm^{-1} was assigned to the amorphous phase, and the peak at 750 cm^{-1} was assigned to the crystalline phase.[3]

Qualitative analysis of FTIR–ATR spectra, that is, the estimation of the molecular weight based on recorded FTIR–ATR spectra is generally possible. The peak at 1450 cm^{-1} was reported to be a suitable internal standard for spectra normalization.[11] However, M_w differences among the samples prepared were not significant enough to reach reliable correlation between the normalized area of the selected peak and M_w in our case.

CONCLUSIONS

PLA was prepared by method of the direct melt polycondensation of LA with the nonmetal catalyst MSA as a potential substitute for heavy-metal-based catalysts commonly used for PLA preparation. The influence of reaction time and temperature at a given catalyst content and pressure on the molecular weight was investigated through the characterization of the resulting product. The optimal catalyst concentration, molecular weight (viscometric measurements and GPC), thermal properties (DSC), and structure (FTIR spectroscopy) of the obtained PLA were investigated subsequently.

The results reveal that the optimal concentration of MSA was 0.5 wt % related to the mass of LA. This MSA concentration was kept for all LA polycondensates prepared at various temperatures and reaction times.

Generally, a temperature of 175°C was observed to be the most favorable for the direct melt polycondensation of LA. The highest [η] was obtained after 18 h of reaction at 175°C and at a pressure of 15 kPa ([η] = 0.21 cm^3/g). This was in agreement with the molecular weight values measured by GPC analysis. The mentioned conditions provided PLA with $M_w = 17.2 \times 10^3$ g/mol and a polydispersity index below 2 in all cases. The thermal analysis of the prepared PLAs showed the possible occurrence of two crystalline phases. The melting temperature and T_g shifted toward higher values with rising M_w. The sample with the highest M_w showed melting peaks at 132 and 147°C, T_g at 57°C, and χ_c of 40%.

The qualitative analysis of the obtained infrared spectra confirmed the agreement with the data reported in already published literature sources dealing with structural characterization of PLA.

The use of non-metal-based catalysts for the synthesis of PLA through the direct melt polycondensation of LA provides an alternative to metal catalysts and is suitable for the production of low-molecular-weight biodegradable and biocompatible polymers designed for various biomedical applications.

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