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Poly(lactic acid) Synthesis and Characterization

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Abstract: Poly(lactic acid) (PLA) is a promising biodegradable polymer based on renewable resources. This paper describes scale-up studies to synthesize high molecular weight PLA (>100'000 g/mol) in five steps from commercial lactic acid. The first four steps of this process consist of synthesizing a highly pure precursor, lactide, which can be converted into a high molecular PLA by ring opening polymerization (ROP). We produced PLA with a molecular weight of 109'000 g/mol using this strategy.

Keywords: Lactic acid · Lactide · Poly(lactic acid) · Ring opening polymerization

Introduction

The earth's oil reserves are declining. Today around 4% of the world oil production is used for the synthesis of polymers.[1] Substitutes for fossil-based plastics must be found. PLA, a bio-based, biodegradable and biocompatible thermopolymer is a bright and concrete alternative.

PLA is produced from renewable resources (Fig. 1). Carbohydrates extracted from plants or wastes are fermented to lactic acid. The fermentation route by the bacteria *Lactobacillus* leads mainly to pure L-lactic acid.[2]

Because of the chirality of lactic acid, PLA exists in different enantiomeric forms: L-PLA (PLLA), D-PLA (PDLA) or DL-
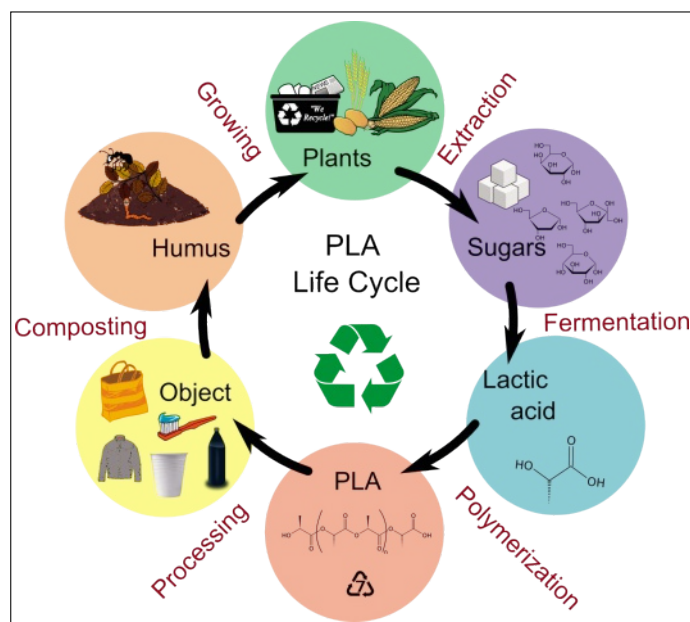

Fig. 1. Life cycle of PLA.

PLA (PDLLA). PLA is semi-crystalline if more than 85–88% of the monomers are enantiomerically pure. Below this purity, it is amorphous and has a lower melting temperature. Semi-crystalline PLA has a melting temperature between 170–180 °C and a glass transition temperature between 55 and 60 °C. The properties of PLA also depend on its molar mass. Amorphous low molecular weight DL-PLA is used for medical applications such as drug release where good degradability is required while high molecular weight L-PLA (>100'000 g/mol) is used in packaging where good thermomechanical properties are crucial.[3,4]

As shown in Fig. 2, there are several routes from lactic acid that lead to PLA. Lactic acid can be directly converted to PLA by polycondensation. However this route forms low molecular weight PLA because of the difficulty to remove water produced during the reaction. As the molecular weight increases, the viscosity of the mixture also increases and it becomes more difficult to eliminate water. The presence of water shifts the esterification equilibrium reaction toward the lower molecular weight polymer.

Currently, the only reported direct route to synthesize high molecular weight PLA is by an azeotropic dehydrative
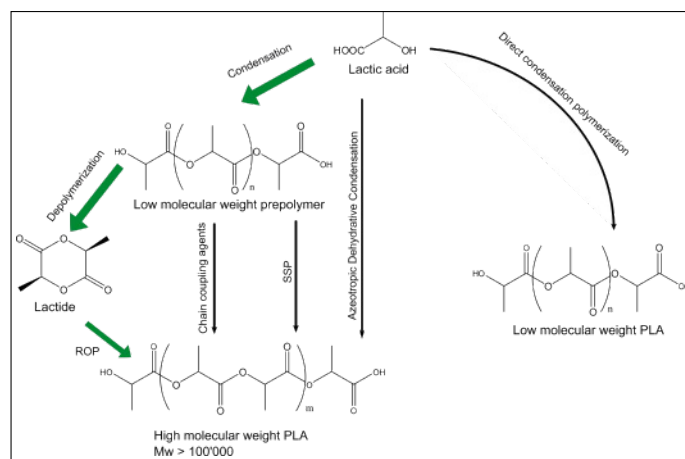

Fig. 2. Synthetic routes to PLA. The bold green path is the route we chose to synthesize PLA.

condensation.[5–7] The drawback of this method is the use of a solvent. The Chinese company Mitsui Toatsu Chemicals has patented such a process.[8]

It is also possible to first synthesize a low molecular weight prepolymer and then follow one of several pathways that lead to high molecular weight PLA. Chain coupling agents can be added to increase the molecular weight of PLA obtained by polycondensation, though attention has to be paid to the biodegradability and biocompatibility of the agents used.

Another route is the combination of melt and solid polycondensation (solid state polymerization, SSP). Polymers with molecular weight up to 500'000 g/mol have been produced by this method, which is usually considered as a green process with regard with the 'low' temperature used (180 °C) and the solvent-free process.[9,10]

The most common route is through lactide, a cyclic dimer of lactic acid. By ring opening polymerization (ROP) of lactide,
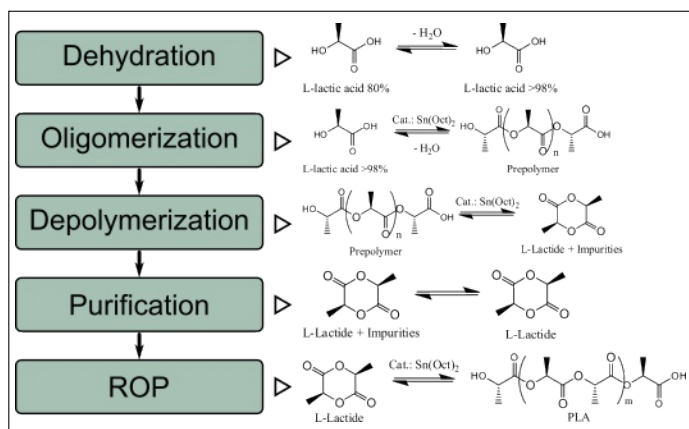
Fig. 3. EIA-FR five step process for the production of high molecular weight PLA.

no water is formed and it is possible to produce high molecular weight PLA. The majority of the industrial producers have chosen this route, for instance NatureWorks, the world leader in the manufacture of PLA with 140'000 metric tons per year in 2011.[11]

The EIA-FR has been active for several years in the development of an industrial process for the production of PLA. This article aims to present the five-step process we developed for the synthesis of high molecular weight PLA (Fig. 3) using the lactide route.

Experimental

Materials

L-Lactic acid FCC 80 was purchased from Purac. Tin octoate 95%, potassium tert-butoxide 99.99%, ethyl acetate >99.5%, acetone >99.5%, 2-propanol 99.5% and Hydranal®-methanol dry were purchased from Sigma-Aldrich and toluene (pure) was obtained from Brenntag.

Synthesis Process

Dehydration of lactic acid 80% is performed using a short path distillation (SPD) unit KDL5 from UIC GmbH at a pressure of 50 mbar and a temperature of 120 °C. Dehydrated lactic acid is oligomerized in batch at a pressure of 100 mbar and a temperature of 170 °C with 1% tin octoate as catalyst to yield a prepolymer with a degree of polymerization (DP) between 8 and 12. A reactive distillation is performed in the SPD unit at 250 °C and 5 mbar and 2% of tin octoate to form lactide. Raw lactide is purified by crystallization up to a purity of 99.9%. A batch polymerization of lactide is done in 2 hours at 170 °C and atmospheric pressure in a glass reactor with 0.04% tin octoate as catalyst.

Analysis

Water content in lactic acid and lactide was measured by a Karl Fischer titration using a 756 KF from Metrohm with Hydranal®-Coulomat AD as titration solution.

NMR analyses were performed using a Bruker Ultra Shield 300 (300 MHz). The DP of oligomers was evaluated by ^{1}H-NMR in DMSO by dividing the integral of the peak corresponding to the CH$_3$ of the repeating unit of the prepolymer ($\delta = 5.2$ ppm) by the integral of the peak corresponding to the CH$_3$ of an end unit ($\delta = 4.2$ ppm or $\delta = 4.96$ ppm). The purity of the products (lactic acid and lactide) was also checked by NMR.

Enantiomeric purity was determined by GC-FID with a GC 8000 Top from CE Instruments equipped with a Cyclodex-B

column (30 m × 0.25 mm × 0.25 μm) from Agilent. The oven was programmed to remain at 150 °C for 10 minutes, followed by a 50 °C/min ramp to 250 °C, where it remained for an additional 1 minute. The carrier gas was helium with a flow rate of 1.5 mL/min and a split flow of 1:20.

The residual acid content in lactide was quantified by a non-aqueous titration by potassium tert-butoxide in methanol with a Solvotrode from Metrohm.

Molecular weights and polydispersity of PLA were determined by gel permeation chromatography (GPC) using a 1525 Binary HPLC pump from Waters equipped with a differential refractometer detector (Waters 410) and three columns in series: Phenogel Linear/Mixe 5μ, Phenogel 10^{3}Å 5μ and Phenogel 10^{5}Å 5μ. The detector and the columns are heated to 35 °C. The calibration curve is obtained with 6 standards of polystyrene.

Thermal stability of PLA was evaluated by thermogravimetric analysis (TGA) with a TGA/SDTA 851e LF1100 from Mettler-Toledo under a nitrogen atmosphere (100 mL/min). All analyses were run in a aluminum oxide pan 70 μL from 25 °C to 300 °C with a heating rate of 10 °C/min.

Melting and glass transition temperature were measured by differential scanning calorimetry (DSC) using a DSC820 from Mettler-Toledo under a nitrogen atmosphere (100 mL/min) in fully closed aluminum crucibles of 40 μL. The analyses were carried out from 30–200 °C with a heating rate of 10 °C/min. Two runs of heating were made on each sample with a rapid cooling in-between to eliminate the thermal history of the polymer. Only the second scan was evaluated. The glass transition temperature was taken at the inflexion point of the heat capacity change, while the melting point at the maximum of the peak corresponding to the fusion.

Results and Discussion

Commercial lactic acid usually contains large amounts of water (10–50%) which has to be removed. For this dehydration we used a short path distillation installation (SPD). Dehydration of 13 kg of lactic acid containing 21% of water gave lactic acid with a residual water content of 1.4% with 94% yield.

Lactide is commonly synthesized from low molecular weight PLA of a degree of polymerization (DP) comprised between 8 and 25. This low molecular weight PLA can be produced by polycondensation of dehydrated lactic acid.[12,13] Typically a catalyst is added to the prepolymer and the produced lactide is distilled off.

We conducted oligomerization by a batch reaction of 0.7–4 kg. Eight hours were necessary to reach a suitable DP, which can be easily determined by ^{1}H-NMR measurements. We aimed for a DP of 8 < DP < 12. We carried out this reaction with and without catalyst – as expected longer reaction time was needed without catalyst to reach a DP of approx. 10 (Fig. 4). For batches of 4 kg the reaction times were longer than for 0.7 kg because of the poorer mixing efficiency.

Depolymerization was carried out continuously on the SPD installation. Lactide was distilled off the reaction mixture. The raw lactide obtained contained some low molecular weight prepolymers, lactic acid and water. Yields of this reaction reached 95–97% for 80–90% of purity (determined by ^{1}H-NMR).

To produce high molecular weight PLA, lactide has to be very pure (>99.9%). Therefore an efficient removal of water and residual acids is crucial for the quality of PLA. Moreover, if PLA with high cristallinity is needed, the content of meso-lactide (<0.1%) has to be as low as possible. The residual water content should be below 0.01% and the acidity below 10 mEq/kg.

The impurities were removed by crystallization. We tested several solvents (Table 1) and toluene showed the best results in
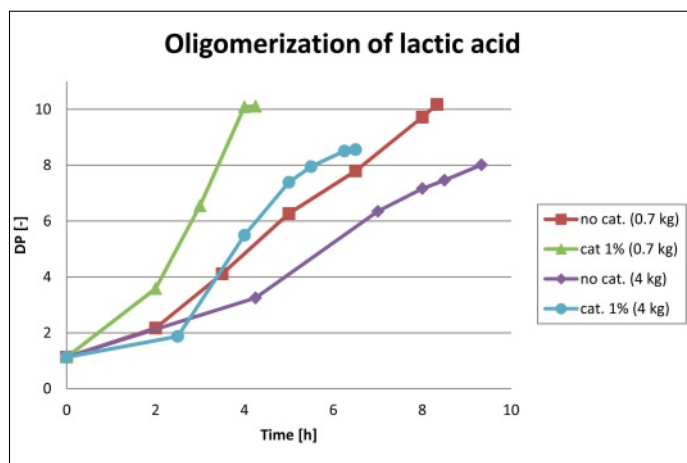
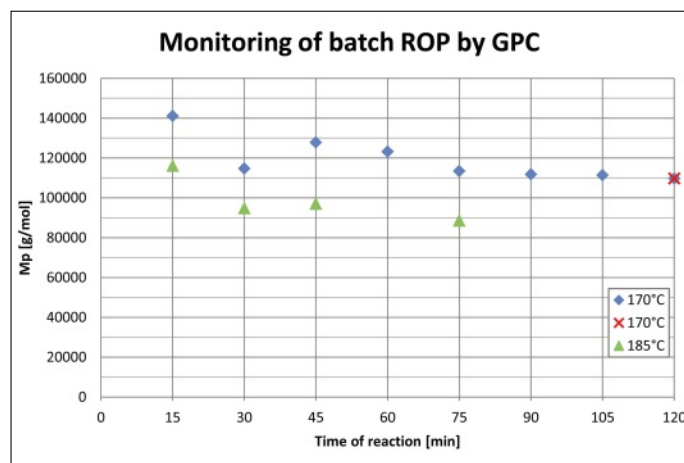Fig. 4. Degree of polymerization (DP, determined by ¹H-NMR) over time for different oligomerization reactions.

Fig. 5. Monitoring of molar mass (Mp) over time for batch polymerizations at 170 °C (blue tiles and red cross) and 185 °C (green triangle).

Table 1. Results of crystallization of lactide in various solvents.

Solvent	Yield [%]	Purity[a] [%]	Water content[b] [%]	meso-lactide[c] [%]
Raw Lactide	*–*	*84*	*0.14*	*2.75*
Toluene	74	94	0.06	0.35
Acetone	33	93	0.16	0.33
2-propanol	80	96	0.15	0.37
Ethyl acetate	70	91	0.14	0.48

[a]Determined by 1H-NMR; [b]Determined by Karl Fischer titration; [c]Determined by GC

Fig. 6. TGA curves for PLA synthesized at 170°C for different samples taken at 15, 30, 60 and 120 minutes during batch ROP.

terms of yield, purity, water content and meso-lactide content. 2-Propanol showed also good results but it reacted with lactide when the mixture was heated to reflux. Crystallization in acetone shows a poor yield and in ethyl acetate the purity obtained after one crystallization is lower than for toluene and isopropanol.

Therefore we chose toluene as the crystallization solvent. Two successive crystallizations are necessary to reach an acceptable purity of lactide for a total yield of 61%.

ROP of lactide is commonly performed with tin octoate (tin 2-ethylhexanoate) as catalyst.[5] We carried out batch ROP in a simple glass reactor. The mixture catalyst and lactide was agitated with a magnet and left to react for 2 hours. The magnet stops agitating few minutes after the beginning of the reaction. At the end of the polymerization PLA becomes nearly solid and it becomes laborious to recover it.

We followed batch polymerization by GPC by taking samples with a glass rod every 15 minutes. We conducted this experiment at 170 °C and 185 °C. Both curves of polymerization showed the same trend. After 15 minutes of reaction, the polymer had the highest mass compared to the samples taken at any other times. The molar mass shows a minimum at 30 minutes and then tends to stabilize itself. By examining the pattern of the curve of molar mass over time, we suspect that this polymerization reaction first reaches a kinetic equilibrium where the highest mass of PLA is dominant before tending towards a thermodynamic equilibrium that forms PLA with the most stable molar mass (Fig. 5, Table 2).

We evaluated the thermal stability of the polymers by TGA (Fig. 6). For PLA synthesized at 170 °C, the sample taken at 15 minutes is the only one that shows a loss of mass starting at 80 °C. Furthermore, its loss of mass reaches a plateau around 200 °C before undergoing degradation. One can assume that this
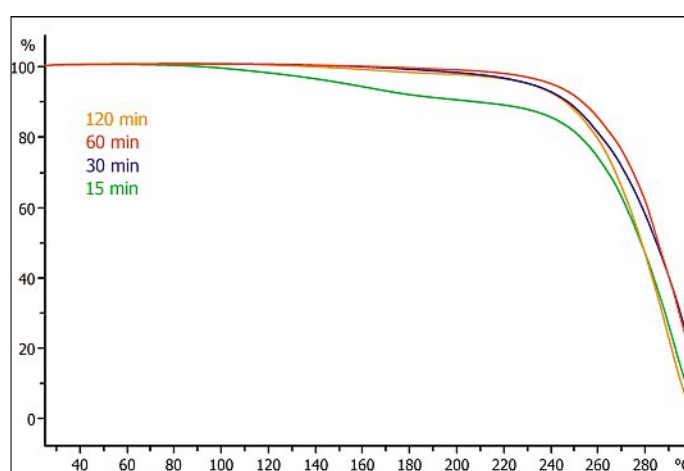
first loss of mass corresponds to unreacted lactide. Lactide is not observable in the other samples taken later in the polymerization reaction. This confirms the above theory of the polymerization that first reaches a kinetic equilibrium before a thermodynamic equilibrium.

We performed DSC analyses on some of the samples to determine glass and melting temperatures. Both the glass and melting temperatures are lower for the sample taken at 15 minutes than at 120 °C. PLA with higher molecular weight should show higher glass and melting temperatures[14] which is not the case here. This confirms that the polymerization is not complete at 15 minutes and that lactide was not fully converted into PLA.

Conclusion

We developed an efficient process to synthesize PLA. In five steps, commercial lactic acid 80% was converted into PLA of high molecular weight. A total yield of 54% was reached for this process. The use of a solvent was necessary only for the purification step which makes our process green because the solvent is recycled. We developed this process having in mind industrial production. We successfully produced high molecular weight PLA of 109'000 g/mol with a melting temperature of 171 °C and a glass transition temperature of 51 °C. However the batch polymerization remains problematic because of the

Table 2. Molar masses, melting and glass transitions temperatures for samples of PLA taken at different times during a batch polymerization reaction (Mp: most present molar mass; Mw: weight average molar mass; Mn: number average molar mass).

Time [min]	Mp[a] [g/mol]	Mw[a] [g/mol]	Mn[a] [g/mol]	Polydisper- sity[a]	Melting temperature[b] [°C]	Glass transition temperature[b] [°C]
15	141'116	172'663	140'164	1.24	167	42
30	114'719	132'458	88'278	1.50	–	–
45	127'796	138'081	83'131	1.66	–	–
60	123'195	139'211	90'155	1.54	–	–
75	113'483	129'058	80'703	1.60	–	–
90	111'853	128'706	84'121	1.53	–	–
105	111'435	130'382	84'451	1.54	–	–
120	109'759	125'942	80'040	1.57	172	54
120 bis	109'759	119'269	62'288	1.91	171	51

[a]Determined by GPC; [b]Determined by DSC

difficulty to recover PLA at the end of the reaction. We are currently working on an alternative continuous method.

[1] Total From oil and gas to polymers: integrated petrochemical operations spanning the globe *http://www.total.com/en/our-energies/oil/processing/our-skills-and-expertise/petrochemicals-940866.html*, accessed Sep 28, 2012.
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