초임계유체에서의 L-Lactide 개환 중합

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Ring-Opening Polymerization of L-Lactide in Supercritical Fluid

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Introduction

The polymerization of homopolymer and copolymers of lactide has been studied to a great extent because of an interest in using these biodegradable and biocompatible polymers in a wide variety of biomaterial applications. Polymerization can occur either in bulk or solution; bulk polymerization is desired when the end product is intended for medical application. On the other hand, solution polymerization with methylene chloride, chlorobenzene, benzene, or toluene as solvents, is not preferred because the solvent must thoroughly be removed before use. The use of supercritical CO_2 (sc CO_2) as a solvent for polymerization is attractive because the product may be easily collected from solution after processing. Unfortunately, many polymers beyond specific fluoropolymers, polysiloxanes and a recently studied series of aliphatic polyesters have limited solubility in sc CO_2, leading to low molecular weights (MWs) and making the range of possible homogeneous polymerizations extremely narrow. On the other hand, it was observed that high MW PLLA (MW=300,000) were soluble in sc HCFC-22 at 110 ^oC and 180 bar. PLLA exhibited an LCST phase behavior in HCFC-22, due to the specific interaction between the hydrogen atom in the HCFC-22 and the ester group in the polymers.

Here we describe the conversion and molecular weight of PLLA produced via a homogeneous polymerization in sc HCFC-22 with respect to time, reaction temperature, reaction pressure and total concentration.

Experimental Section

Materials. L-Lactide (L-LA) was purchased from Purac Biochem BV (Gorinchem,

The Netherland). They were recrystallized from ethyl acetate and dried in vacuum (0.2 mmHg) over P_4O_{10}. Tin(II)bis(2-ethylhexanoate) ($Sn(Oct)_2$) (Sigma Chemical Co., St. Louis, MO, 99%) and 1-dodecanol (Aldrich, 99.5%) were purified by distillation under reduced pressure and dissolved in dry toluene. HCFC-22 was purchased from Solvey Gas Co. (USA), and its certified purity was 99.99 wt %. It was used as received without further purification. Toluene was dried by refluxing over benzophenone-Na complex and distilled under nitrogen atmosphere just prior to use. $CDCl_3$ (Aldrich, 99.5 atom % D) was used as received.

Polymerization Procedure in Supercritical HCFC-22 (Typical Example). The high-pressure schematized in Figure 1. Polymerization was conducted in a 52 mL stainless steel high-pressure cell equipped with a magnetic stirring bar and an electrically heating mantle. L-LA (2.85 g), initiator solution (0.3 mL of a 0.11 M solution in toluene; 1.54×10^{-3} mol of 1-dodecanol) and catalyst solution (0.4 mL of a 0.12 M solution in toluene; 2.37×10^{-3} mol of $Sn(Oct)_2$) were added into the cell. The toluene was removed under vacuum for a few minutes. The cell was then connected to the nitrogen purge and HCFC-22 feed system. The reactor was heated to 50 °C and purged with nitrogen for 5 min. While cooling to room temperature, it was evacuated for a few hours via a trap cooled by liquid nitrogen. And then it was purged with nitrogen for an additional 10 min. The cell was filled with liquid HCFC-22 to ca. 30 bar at 50 °C by an air-driven gas compressor (Maximator Schmidt Kranz & Co. GMBH) and then gradually heated to 110 °C to achieve a pressure of 200-205 bar. Polymerization was allowed to proceed for 10 hrs. The reactor was then cooled to 25 °C, and the HCFC-22 was vented through a needle valve. To quantify the LA conversion, the cell was rinsed with $CHCl_3$ in order to dissolve traces of polymer. This polymer solution was poured into cold methanol; the precipitated PLLA was recovered by filtration and dried under vacuum at 25 °C overnight to constant weight. The monomer conversion was determined gravimetrically(62 %). M_n was determined by GPC.

Polymer Characterization. Molecular weight and molecular weight distribution were determined by gel permeation chromatography (GPC) using a Waters150-C equipped with a Waters 510 fluid unit and a Waters 410 differential refractometer. A combination of three Shodex microstyragel columns with molecular weight exclusion limits of 1500/70000/400000 $g \cdot mol^{-1}$ was used. The column were eluted by $CHCl_3$ (flow rate of 1.0 mL/min at 30 °C) and calibrated with polystyrene standards over a MW range of 1,000 ~ 350,000. NMR spectra were recorded at 25 °C using Varian Unity Plus 300 MHz spectrometer in $CDCl_3$ for ^1H NMR. TMS used as an internal shift

reference.

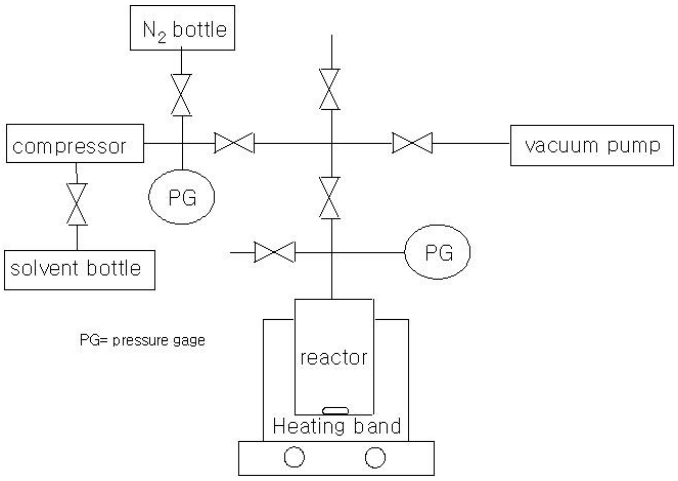

Figure 1. Schematic diagram of experimental apparatus used in the study

Result and Discussion

Table 1. Ring opening polymerization of L-LA in supercritical HCFC-22 at 110 °C, 200-205 bar, $[LA]_0/[I]_0$=650 and $[LA]_0/[Cat]_0$=422. Total concentration (monomer weight/cell volume) is 0.06 (g/mL) and weight ratio of L-LA to HCFC-22 is 12.4 wt%. I is 1-dodecanol as initiator.

entry	react time (min)	conv (%)	$M_{n,GPC}$ $\times 10^{-3}$ (g/mol)	$M_{n,calc}$ $\times 10^{-3}$ (g/mol)	MWD	# of phase
1	240	20.0	17.1	18.9	1.47	1
2	360	30.9	30.8	29.1	1.46	1
3	480	34.8	35.7	32.8	1.35	1
4	600	38.8	39.4	36.5	1.55	1
5	750	49.2	45.9	46.2	1.38	1
6	1000	58.8	72.1	55.5	1.52	1
7	1200	62.6	80.2	55.8	1.60	1
8	1400	66.1	89.4	62.1	1.71	1
9	2880	66.0	80.3	62.0	1.80	1
10	3360	66.5	87.1	62.4	1.78	1

$M_{n,calc} = M_I + [M]_0/[I]_0 \times M_{LA}(conv/100)$

The use of sc HCFC-22 as a solvent for the polymerization of PLLA was attractive because sc HCFC-22 is nontoxic and could easily be separated from the polymer by depressurization. PLLA could, therefore, be synthesized in solution but remain free of residual organic solvents to yield a high-purity polymer intended for biomedical

application.

Copolymerization was carried out with L-LA by ring-opening polymerization. $Sn(Oct)_2$ was selected for this investigation because it has been approved for use as a food additive and is the most widely used catalyst for PLLA in biomedical application. All polymerizations were conducted in solution with continuous stirring. During the polymerization of L-LA, conversion, M_n and molecular weight distribution (MWD), determined by GPC, continues to increase with time, as seen in table 1. The conversion at polymerization temperature of 110 °C increased from 20.0 to 64.1 % on increasing the reaction time from 240 to 1400 min, respectively. M_n also increased from 17,000 to 89,000 g/mol on the same time range. However, increasing the polymerization time to 3360 min did not result in a further increase in conversion and M_n. The molecular weight distribution (MWD), which is rather narrow at low conversion, increases as the reaction progress. This broadening of the MWD may be due to slow initiation compared to propagation and/or to intermolecular and intramolecular trans-esterification reaction typical of all tin-based systems. The experimental $M_{n,GPC}$ is higher than the value calculated from the ratio of the monomer to initiator concentration.

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