

## High Molecular Weight Poly(L-lactide) Synthesized in Supercritical Fluids

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### Introduction

Supercritical carbon dioxide (scCO<sub>2</sub>) is a viable 'green' alternative and can be removed without trace. Moreover, it has been demonstrated that scCO<sub>2</sub> is a promising alternate reaction medium for polymerization. However, its widespread use has been restricted due to its limited solvent power, which reduces possible homogeneous polymerizations to an extremely narrow range. Thus far, most studies have focused on heterogeneous-phase polymerizations and on the development of new 'CO<sub>2</sub>-philic' materials (substance with a high affinity for CO<sub>2</sub> solution at lower pressures).<sup>1</sup> However, in many cases, solutions to the use of expensive 'CO<sub>2</sub>-philic' materials and their later removal are needed. A number of studies have reported upon the ROP of cyclic esters in scCO<sub>2</sub>. While an increase in yield and molecular weight (MW) in the presence of the stabilizer has been reported, all MWs obtained were lower than 50 000 g/mol. Recently, we found that supercritical chlorodifluoromethane (scR22) can be successfully utilized as a solvent for the ROP of L-LA,<sup>2</sup> wherein the polymerization proceeds in a homogeneous state in scR22 and results in high PLLA molecular weights. An attractive feature of chlorodifluoromethane (R22) is its lower ozone depleting potential than chlorofluoromethane, and in fact it is used in medical application.<sup>3</sup>

Much of the recent work in using supercritical fluids (SCFs) for polymer composite. Polymer nanocomposite is broadly defined to include a material consisting of two immiscible phases of which one is a polymeric material and one is present as a dispersed phase (or domain) with a nanoscale feature in at least one dimension. The nanoclay is a layered silicate which can be exfoliated into platelets with nanometer thickness and aspect ratios on the order of 10<sup>3</sup>. The application of supercritical fluids to the preparation of composites is through one of two approaches: in-situ polymerization of the dispersed phase in a SCF swollen polymer matrix, or dispersive mixing of the nanoscale phase into the polymer matrix using the SCF to reduce the matrix viscosity and/or nucleate nanoscale bubbles in the material. This paper presents our investigations into the effects of reaction conditions and reactant concentrations on monomer conversion and PLLA molecular weight, in the stannous octoate initiated polymerization of L-LA in scR22. Also, we prepared PLA/clay nanocomposite.

### Experimental

#### Materials

L-Lactide (L-LA) was purchased from Purac Biochem BV (Gorinchem, The Netherlands). It was recrystallized from ethyl acetate and dried in a vacuum (0.2 mmHg) over P<sub>4</sub>O<sub>10</sub>. Tin(II)bis(2-ethylhexanoate) (Sn(Oct)<sub>2</sub>) (Sigma Chemical Co., St. Louis, MO, 99%) and 1-dodecanol (DoOH) (Aldrich, 99.5%) were purified by distillation under reduced pressure and dissolved in dry toluene. R22 was purchased from the Solvay Gas Co. and had a certified purity of 99.99 wt.-%, and used as received. Toluene was dried by refluxing over the benzophenone-Na complex and distilled in a nitrogen atmosphere just prior to use. CDCl<sub>3</sub> (Aldrich, 99.5 atom % D) was used as received.

#### Polymerization Procedure in Supercritical R22

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 (3.0 g), DoOH solution (0.3 mL of a 0.11 M solution in toluene;  $3.3 \times 10^{-2}$  mol of DoOH), and Sn(Oct)<sub>2</sub> solution (0.43 mL of a 0.12 M solution in toluene;  $5.2 \times 10^{-5}$  mol of Sn(Oct)<sub>2</sub>) were added to the cell. The toluene was removed under vacuum, the

reactor heated to 50 °C, and purged with nitrogen for 5 min. When the reactor was cooled to room temperature, it was evacuated for 2 h using a liquid nitrogen cooled trap and then purged with nitrogen for an additional 10 min. The cell was then disconnected from the nitrogen line, evacuated, and connected to the R22 feed system. The cell was filled with liquid R22 to ca. 30 bar at 50 °C by using an air-driven gas compressor (Maximator Schmidt Kranz & Co. GmbH) and then gradually heated to 110 °C to achieve a pressure of 200 bar. Polymerization was allowed to proceed for the predetermined times. After the polymerization, the reactor was cooled to room temperature, and R22 was vented through a needle valve into chloroform in order to collect both unreacted monomer and polymer. To quantify L-LA conversions, the cell was rinsed with chloroform in order to dissolve traces of polymer and monomer. Both chloroform solutions were then poured into a large volume of cold methanol. The precipitated PLLA was recovered by filtration and dried under vacuum at room temperature. Monomer conversion was determined gravimetrically

### Results & Discussion

#### Effect of Time

A series of L-LA polymerizations initiated by Sn(Oct)<sub>2</sub> ([LA]<sub>0</sub>/[Sn]<sub>0</sub> = 200) were carried out in scR22 at 130 °C and 300 bar, where [LA]<sub>0</sub> is the initial L-lactide concentration and [Sn]<sub>0</sub> is the initial Sn(Oct)<sub>2</sub> concentration. The reaction time dependences of monomer conversion and PLLA MW growth are shown in Figure 1. The monomer conversion increased to ca. 70% on increasing the reaction time to 1 h. The molecular weight of the product also increased to ca. 160 000 g/mol over the same period. However, a further increase in the polymerization time to 4 h had little effect on either monomer conversion or on PLLA MW. Pasch et al.<sup>14</sup> reported that PS calibrated GPC measurements overestimate the actual molecular weights of aliphatic polyesters by 50-100% (depending on their structures and molecular weights). Therefore, the actual MWs of PLLA are expected to be less than those determined by GPC.

#### Effect of Temperature

The effect of temperature on monomer conversion and PLLA MW was investigated in a series of polymerizations conducted at temperatures ranging from 90 to 150 °C and at a constant pressure of 200 bar. In all of these experiments, the ratio of monomer to R22 concentration was held constant at 12.4 wt.-%. Increasing the reaction temperature from 90 to 130 °C resulted in increased monomer conversion from 11.5 to 72.2%. The MWs of the resulting product also increased from 18 000 to 77 000 g/mol over the same temperature range. However, a further increase in the polymerization temperature to 150 °C resulted in a slightly reduced monomer conversion and MW to 70.9% and 76 000 g/mol, respectively. This may have been due to thermal depolymerization reactions and catalyst instability at the elevated temperature of 150 °C for 10 h in scR22. Such reductions in MW and monomer conversion were consistent with the thermal degradation, described elsewhere for Sn(Oct)<sub>2</sub> catalyzed lactone polymerization.<sup>15</sup> Teyssié et al. observed similar MW limitation behavior in aluminum isopropoxide initiated polymerization of lactides in toluene. They attributed their result to inter- and intramolecular transesterification reactions at higher temperature than 70 °C. The MWD was rather narrow at low temperature, but increased as the temperature increased.

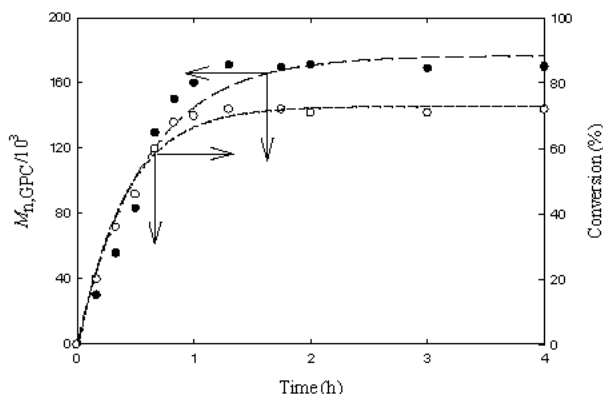


Figure 1. Relation between monomer conversion (o) and poly(L-lactide) molecular weight (•) by GPC at different times. Polymerization conditions:  $[LA]_0 = 0.4$  mol/L,  $[LA]_0/[Sn]_0 = 200$ , at 130 °C and 300 bar in scR22.

### Effect of Initiator

The effects of 1-dodecanol (DoOH) and  $Sn(Oct)_2$  concentration on the monomer conversion and the PLLA MW were investigated in a series of polymerizations conducted at various initiator concentrations. When the initial  $Sn(Oct)_2$  concentration was held constant ( $[Sn]_0 = 0.99 \times 10^{-3}$  mol/L) and the initial DoOH concentration increased, the MW of PLLA gradually reduced from 75 000 to 11 000 g/mol. When the initial  $Sn(Oct)_2$  concentration increased and initial DoOH concentration was held constant ( $[DoOH]_0 = 1.84 \times 10^{-3}$  mol/L), then the MW of PLLA ranged from 38 500 to 34 000 g/mol. Thus, the MW of PLLA was found to be independent of the initial  $Sn(Oct)_2$  concentration. A slight reduction in MW on increasing the initial  $Sn(Oct)_2$  concentration is attributed to the presence of adventitious impurities in the  $Sn(Oct)_2$ . Our previous study on the polymerization of L-LA initiated by  $Sn(Oct)_2$  in scR22, provided direct spectroscopy evidence of tin covalently bound to the polyester chain end ( $—Sn—OR$ ). This observation suggested that  $Sn(Oct)_2$  is not the initiator, rather that tin-alkoxide forming from DoOH and  $Sn(Oct)_2$  serves as the initiating species in scR22, which is consistent with previous reports, whereby  $Sn(Oct)_2$  initiated the polymerization of  $\epsilon$ -caprolactone in THF solution or in bulk.

### Effect of Monomer and Solvent Concentrations

The R22 concentration was varied from 13.0 to 59.4% w/v (for a 52 mL reaction cell) with respect to the L-LA concentration (a constant 0.13 mol/L) in order to investigate the effect of the R22 concentration upon the PLLA produced. Increased R22 concentration resulted in a reduced monomer conversion and PLLA. In detail, for an R22 concentration of 13.0% w/v the monomer conversion and the PLLA MW were 81.2% and 88 500 g/mol, respectively. At an R22 concentration of 59.4% w/v, however, oligomer was obtained. Thus, this series of experiments showed that the monomer conversion and the PLLA MW depended on the R22 concentration. When the L-LA concentration was increased from 0.17 to 1.07 mol/L and the R22 concentration was held constant (at 51.5% w/v), the monomer conversion and the PLLA MW gradually increased to 80.2% and 86 500 g/mol, respectively. This could be explained by intermolecular interaction between solvent and propagating active species. There should be preferential solvation of the tin alkoxide by R22, thereby increasing the solvent concentration at the tin alkoxide. Increased scR22 concentration and/or decreased L-LA concentration made competing interaction between monomer and R22 for coordination to tin alkoxide shift toward in favor of R22-tin alkoxide coordination. As a consequence the hindered nucleophilic attack of L-LA on tin-alkoxide would lead to low degree of polymerization. The MWD also increased on increasing the L-LA concentration.

### Conclusion

Supercritical chlorodifluoromethane can be successfully utilized as a solvent for the ring-opening polymerization of L-LA. This process has several advantages versus traditional polymerization in organic solvents or in scCO<sub>2</sub> for the preparation of PLLA. First, it enables the synthesis of high molecular weight PLLA. Second, the supercritical solvent used in this study is non-flammable, and can be completely separated from the polymer by depressurization.

### References

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