

Synthesis of Lactide from Oligomeric PLA: Effects of Temperature, Pressure, and Catalyst

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Abstract : Lactide was produced from oligomeric PLA by back-biting reaction of the OH end groups. For optimization of the reaction conditions, the effects of temperature, pressure, PLA molecular weight, and catalyst type on the lactide synthesis were examined. The fraction of D,L-lactide decreased with increasing temperature. Among the various Sn-based catalysts, the D,L-lactide fraction was maximized when SnO was used. A higher yield with lower racemization was observed at lower pressure. The conversion of PLA was maximized at an oligomeric PLA molecular weight of ca. 1380. The yield of lactide increased but the fraction of D,L-lactide decreased with increasing molecular weight. The highest conversion with the lowest racemization degree was obtained at a catalyst concentration of 0.1 wt%. The lactide was more sensitive to racemization because of the entropic effect.

Keywords: poly(lactic acid), D,L-lactide, meso-lactide, catalysts, depolymerization, racemization, deprotonation.

Introduction

Because many petrochemical-based polymers are not environmentally friendly, research attention has focused on the development of biodegradable polymers as replacements. Poly(lactic acid) (PLA) is a well known biodegradable polymer that has found a number of applications in industry in the form of plastics, fibers, etc.¹⁻⁴ It was believed until 1995 that it was difficult to obtain a high molecular weight PLA using the conventional, direct condensation reaction, due to the resulting depolymerization reaction.⁵ Many researchers have investigated the synthesis of high molecular weight PLA, only to conclude that such a process would not be economically viable.⁶ The most industrially acceptable PLA synthetic process so far reported proceeds via lactide formation. In this process, the lactic acid monomer is first polymerized to oligomeric PLA, depolymerized to lactide, and then re-polymerized to attain a high molecular weight by a ring opening mechanism.⁷⁻¹² The formation of the lactide is regarded as one of the most important processes in this overall mechanism, since the optical purity of the lactide significantly affects the quality of the final prod-

uct.¹³

Various catalyst systems have been used to maximize the yield in lactide production, while minimizing the racemization. Among the many possible catalyst systems, Sn-based catalysts are usually considered to be the most efficient for the synthesis of lactide, because of the following three advantages. First, they result in a low degree of racemization at high temperature.¹⁴⁻¹⁶ Second, their toxicity is extremely low compared to that of other heavy metal catalysts. Third, the purification procedure used to remove them from PLA is well known.¹⁷ The purpose of the present work is to provide information about the preparation of lactide with a high yield and high optical purity. We also investigated how the yield and degree of racemization of lactide were affected by the reaction pressure, temperature, catalyst type, and the molecular weight of the oligomeric PLA.

Experimental

Materials. L-lactic acid was purchased from Purac Co. (Barcelona, Spain). Three types of Sn-based catalysts - stannous oxide (SnO, Aldrich, Milwaukee, WI, USA), stannous octoate (SnOct₂, Aldrich), and stannous chloride (SnCl₂, Aldrich) - were used for the preparation of lactide. All of

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these materials were used without further purification.

Synthesis of Prepolymer. The aqueous solution of L-lactic acid (90 wt%) was dehydrated to produce oligomeric PLA at 200°C without catalysts under a nitrogen atmosphere for 6 hrs using a 1,000 mL reaction vessel equipped with a Dean-Stark trap. In order to obtain oligomeric PLA with different molecular weights, the prepolymer synthesis reaction was conducted at different pressures ranging from 10 to 20 torr. The molecular weight of oligomeric PLA was determined as previously described.¹⁸

Synthesis of Lactide. A 1,000 mL four-necked flask was equipped with a mechanical stirrer and a thermometer. This reactor was connected to a distillation column (2 cm ID × 30 cm length) filled with stainless steel packing materials. The prepolymer produced was charged into the flask and mixed with a predetermined amount of the Sn-based catalyst. The flask was heated and reduced at a predetermined temperature and pressure, in order for the crude lactide to be expelled by distillation and collected in the receptacle. The receptacle was placed in an oil bath kept at about 90°C in order to prevent the crude lactide from solidifying. The distillation reaction was completed in two hours. Nuclear magnetic resonance spectroscopy (NMR, 500 MHz, Varian, USA) was used to analyze the crude lactide. For the NMR measurements, the samples were dissolved in a solvent consisting of chloroform (CDCl₃) with tetramethylsilane (TMS) as a standard.

Results and Discussion

Six samples of PLA, with number average molecular weights of 350, 600, 980, 1,380, 2,180 and 3,100 g/mol were prepared. The synthetic scheme used for the preparation of lactide is illustrated in Figure 1. The lactide was produced

from oligomeric PLA by back-biting reaction of the OH end groups.¹⁹ In this reaction, the carbon atom in the carbonyl group of PLA is attacked by the OH end group, which is in a partially positive-charged state due to its interaction with the SnO catalyst. As the chain length of the oligomeric PLA is shortened to the extent that the lactide is produced, the polymerization reaction rate decreases with increasing molecular weight of the oligomeric PLA.

Figure 2 shows the typical NMR spectrum of lactide measured during its synthesis. The signals in the NMR spectrum were assigned to the chemical structure of lactide, as shown in Figure 2.⁵ The CH₃ signal of D,L-lactide was observed at 1.70 ppm, but that of meso-lactide at 1.72 ppm. The methyl signal of meso-lactide was shifted downfield than that of D,L-lactide due to higher deshielding effect. The fractional amount of D,L- and meso-lactide in the product were calculated by comparing the integral areas of these signals.^{5,20}

Figure 3 shows the effect of the catalyst on the % conversion of PLA at different temperatures when the depolymerization reaction was conducted using PLA with a molecular weight of 600 g/mol, at a reaction pressure of 20 torr and a catalyst concentration of 0.1 wt%. The crude lactide contains D-lactide, L-lactide, meso-lactide, and other impurities such as lactic acid, lactic acid dimer (lactoyllactic acid) and water. D,L-lactide means a minute amount of D-lactide in addition to L-lactide, because even when L-lactic acid is used as the raw material for the synthesis of the crude lactide, the lactic acid inevitably undergoes racemization. The % crude lactide in product increased with increasing temperature, because the depolymerization reaction rate increased with increasing temperature. Using the catalyst doubled the % crude lactide in product and the conversion varied slightly according to the catalyst type. The conversion of PLA was in the following order : SnCl₂ > SnOct₂ > SnO, due

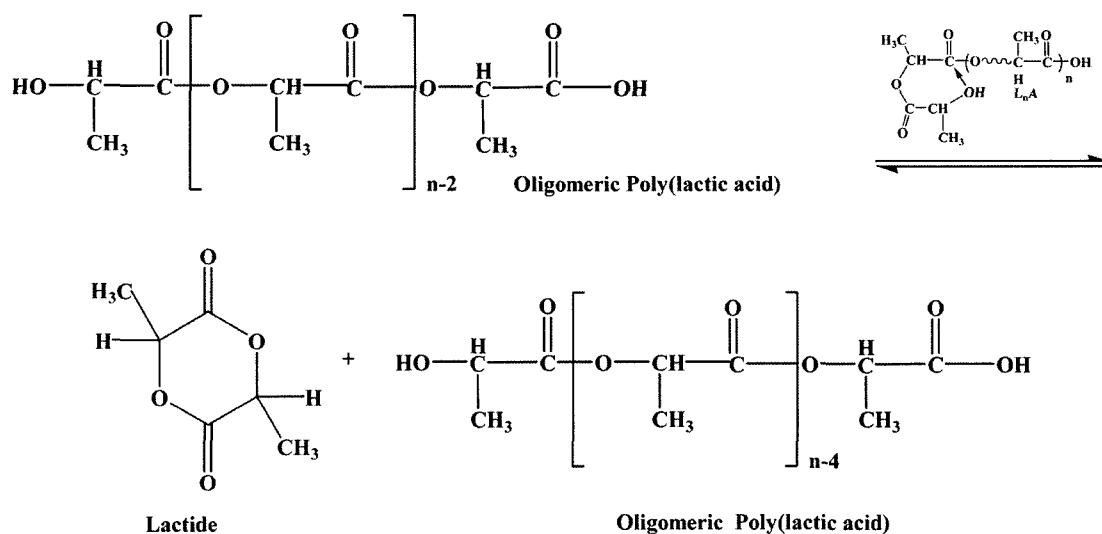


Figure 1. Scheme for the preparation of lactide from oligomeric PLA through a back biting process.

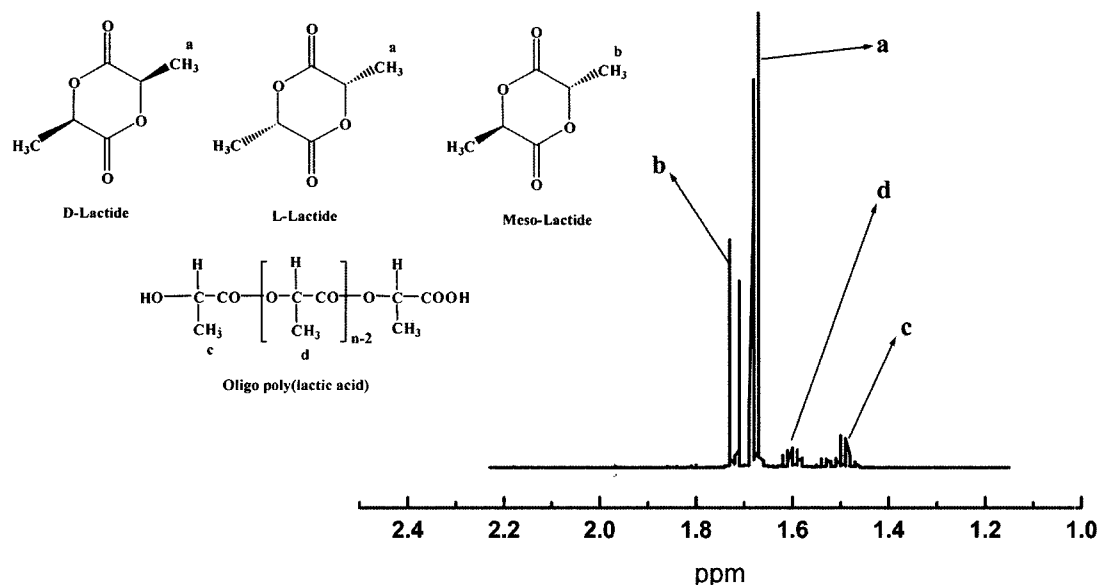


Figure 2. ^1H NMR spectra of lactide and oligomeric PLA in the crude lactide.

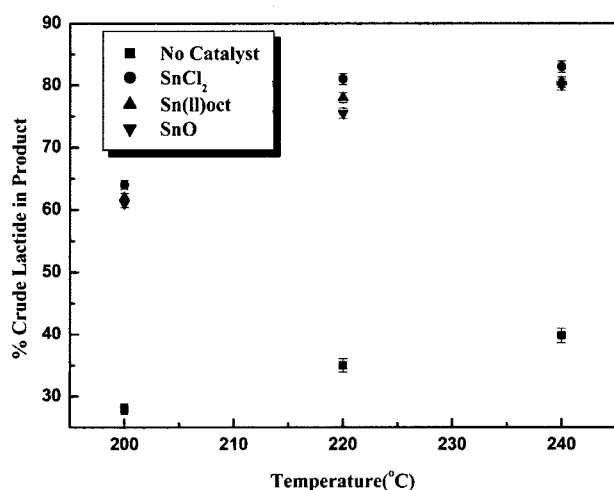


Figure 3. Variation of % crude lactide in product as a function of reaction temperature for different catalyst systems using no catalyst (■), SnCl_2 (●), Sn(II)oct (▲), and SnO (▼), respectively.

to the difference in the solubility of the catalysts, with SnO being the most insoluble.⁵ The % crude lactide in product was expressed by (1):

$$\% \text{ crude lactide in product} = \frac{\text{Amount of crude lactide produced (g)}}{\text{Amount of PLA charged in the reactor (g)}} \times 100 (\%) \quad (1)$$

Figure 4 shows the variation of (a) the lactide yield and

(b) the D,L-lactide fraction during the lactide production. The lactide yield and the D,L-lactide fraction were defined in this contribution by eqs. (2) and (3):

$$\text{Lactide yield (\%)} = \frac{\text{Amount of lactide(D,L-and meso-lactide) produced (g)}}{\text{Amount of crude lactide produced (g)}} \times 100 (\%) \quad (2)$$

$$\text{D,L - lactide fraction (\%)} = \frac{\text{Amount of D,L-lactide produced (g)}}{\text{Amount of lactide(D,L-and meso-lactide) produced (g)}} \times 100 (\%) \quad (3)$$

Both the lactide yield and D,L-lactide fraction decreased with increasing temperature. The D,L-lactide fraction decreased when the Sn-based catalysts were used. This result was explained in terms of the deprotonation of lactide. Lactide is highly sensitive to weak bases, because the α -proton is highly acidic.²¹⁻²³ The end group (e.g. octoate, chloride, or oxide) of each catalyst is basic which enables it to deprotonate lactide easily, as shown in Figure 5(a). The D,L-lactide fraction was slightly higher when SnO was used among Sn-based catalysts. This deprotonation process was accelerated by increased temperature. Deprotonation is the main route for racemization, which occurs as the proton abstracted from one face of lactide is added to the opposite face of the same molecule, as shown in Figure 5(b).

This deprotonation operation took place exclusively for

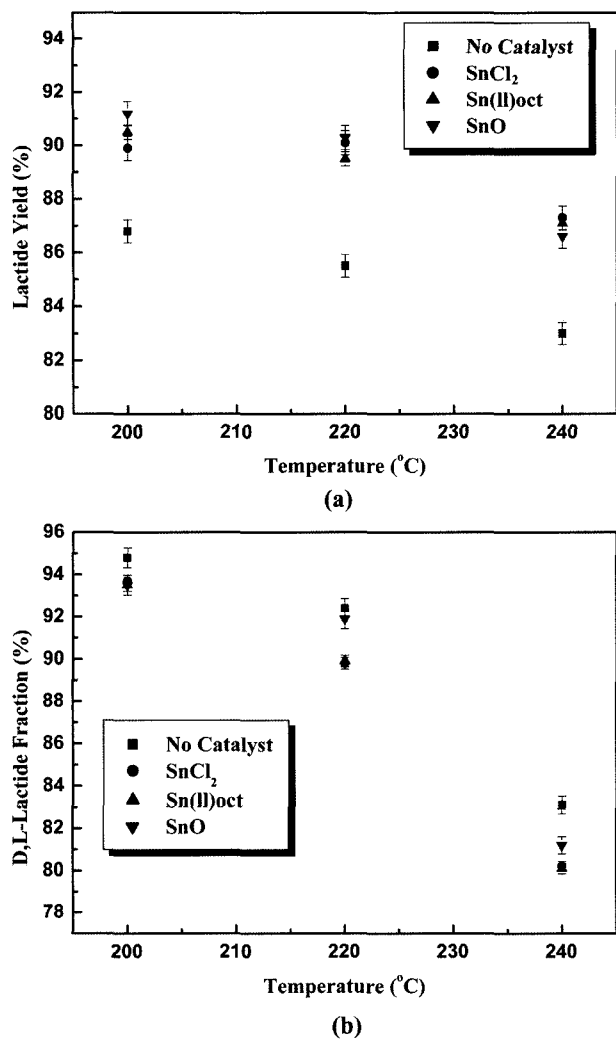


Figure 4. Variation of (a) lactide yield and (b) D,L-lactide fraction as a function of reaction temperature for different catalyst systems using no catalyst (■), SnCl₂ (●), Sn(II)oct (▲), and SnO (▼), respectively.

lactide, and not for oligomeric PLA. In the case of oligomeric PLA, the electron pairs on the anion resulting from deprotonation are delocalized and this generates a partial π -bond, as shown in Figure 5(a). As this partial π -bond prevents rotation, this configuration is unfavorable for oligomeric PLA from the entropic point of view. In the case of lactide, the deprotonation is sterically favorable, as the rotation is hindered due to the small ring size.²¹

Figure 6 shows the pressure dependence of the % conversion of PLA when the reaction was carried out using PLA with a molecular weight of 600 g/mol. The reaction temperature was 220 °C and 0.1 wt% SnO was used as a catalyst. The % crude lactide in product increased from 48 to 81% as the pressure was decreased from 100 to 10 torr. The lactide was eliminated from the reactor immediately after it was formed at the lower pressure, thus increasing the conversion.

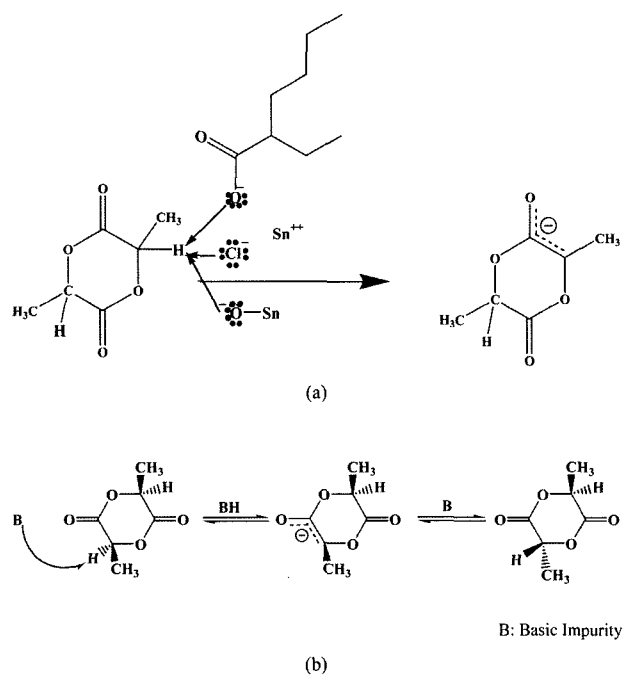


Figure 5. Schematic illustration of (a) the deprotonation of lactide by basic end groups of each catalyst (e.g. octoate, chloride, and oxide), and (b) the racemization of lactide via deprotonation.

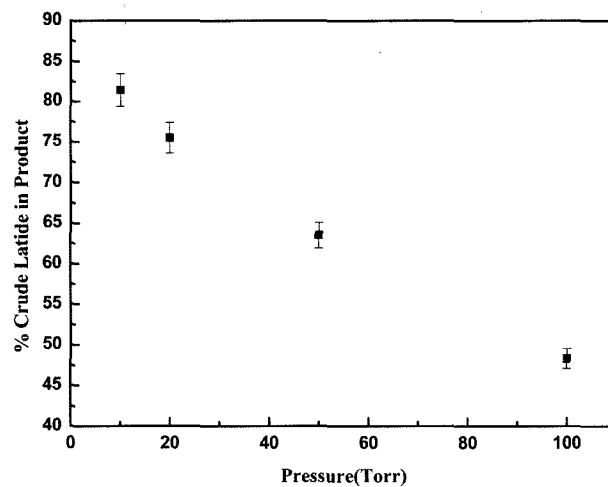


Figure 6. Variation of % crude lactide in product as a function of pressure.

Figure 7 shows the effect of pressure on the lactide yield and D,L-lactide fraction. The lactide yield increased from 89.2 to 91.5%, whereas the D,L-lactide fraction decreased from 94 to 85.2%, when the pressure decreased from 100 to 10 torr. This is probably because the elimination of basic impurities such as water was accelerated at a lower pressure, thereby considerably decreasing the amount of racemization that occurred.

Figure 8 shows the effect of the PLA molecular weight on

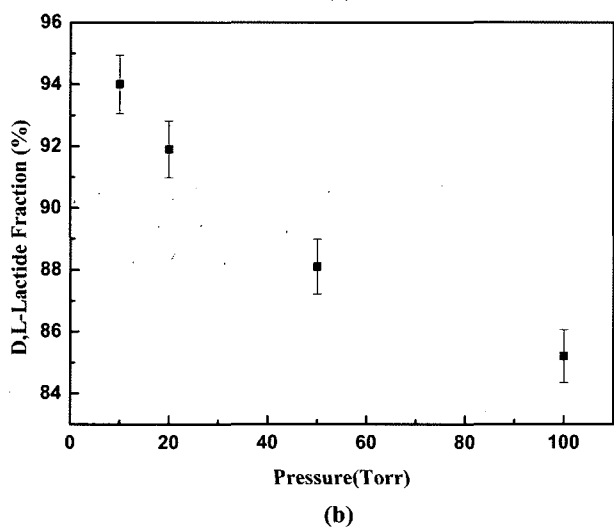
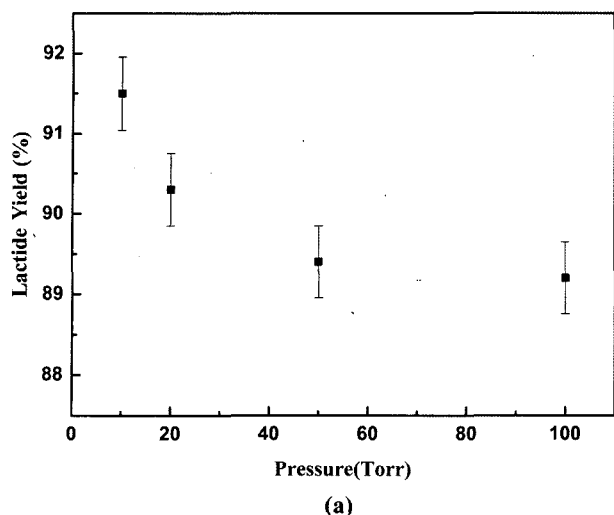


Figure 7. Variation of (a) lactide yield and (b) D,L-lactide fraction as a function of pressure.

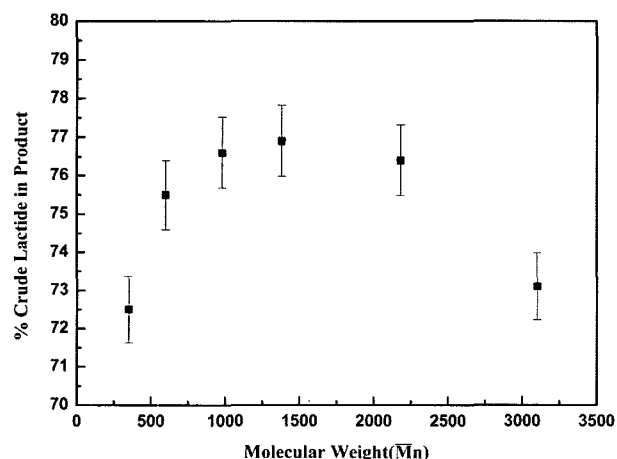


Figure 8. Variation of % crude lactide in product as a function of molecular weight of oligomeric PLA.

the % conversion of PLA. The reaction was conducted at 220°C and 20 torr with 0.1 wt% SnO catalyst, which increased the % crude lactide in product to a maximum of 77% at a PLA molecular weight of 1,380 g/mol. Since the SnO catalyst interacts with the oxygen atom in the carbonyl group of PLA, the electron pair on the carbon atom is slightly shifted toward the oxygen atom. Since the carbon in the carbonyl group becomes positively charged, it is easily attacked by the OH group in PLA. When the molecular weight of the oligomeric PLA was decreased from 1,380 g/mol, the % crude lactide in product decreased because the interaction between the SnO and the carbonyl oxygen atom is hindered as the Sn atom is surrounded by OH groups. The decreased PLA molecular mobility reduced the PLA conversion at a high PLA molecular weight (high viscosity). The concentration of hydroxyl groups decreased with increasing PLA molecular weight. Thus, the conversion of PLA decreased as back-biting reaction decreased at this high molecular weight range. Fig-

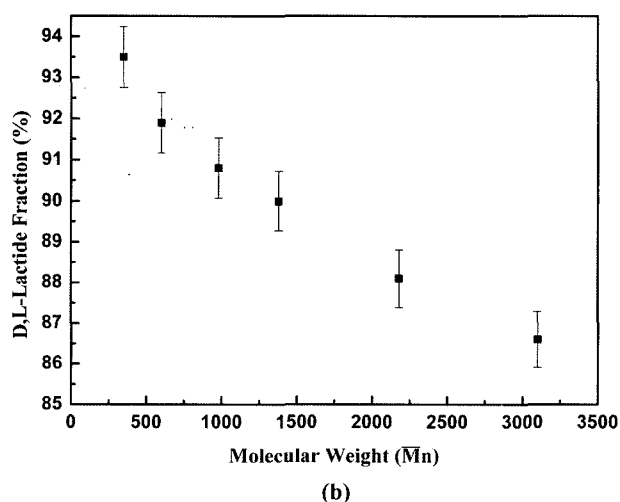
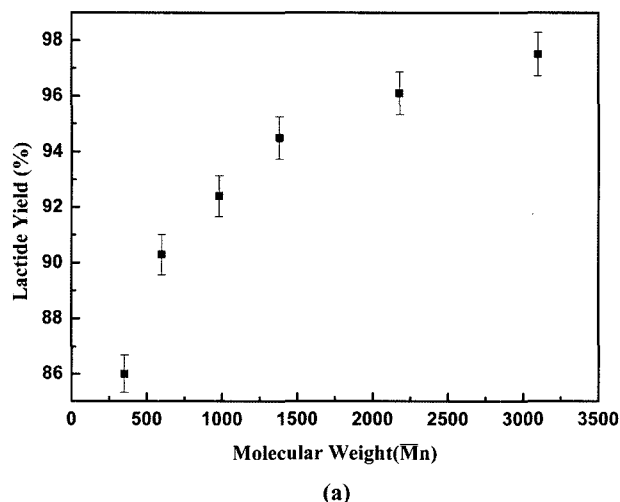


Figure 9. Variation of (a) lactide yield and (b) D,L-lactide fraction as a function of molecular weight of oligomeric PLA.

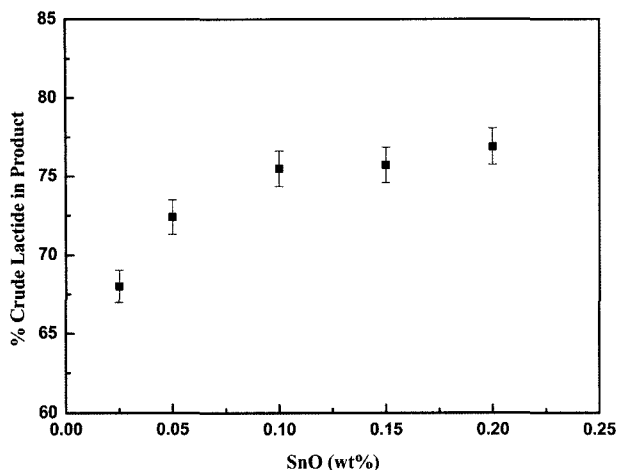


Figure 10. Variation of % crude lactide in product as a function of SnO catalyst.

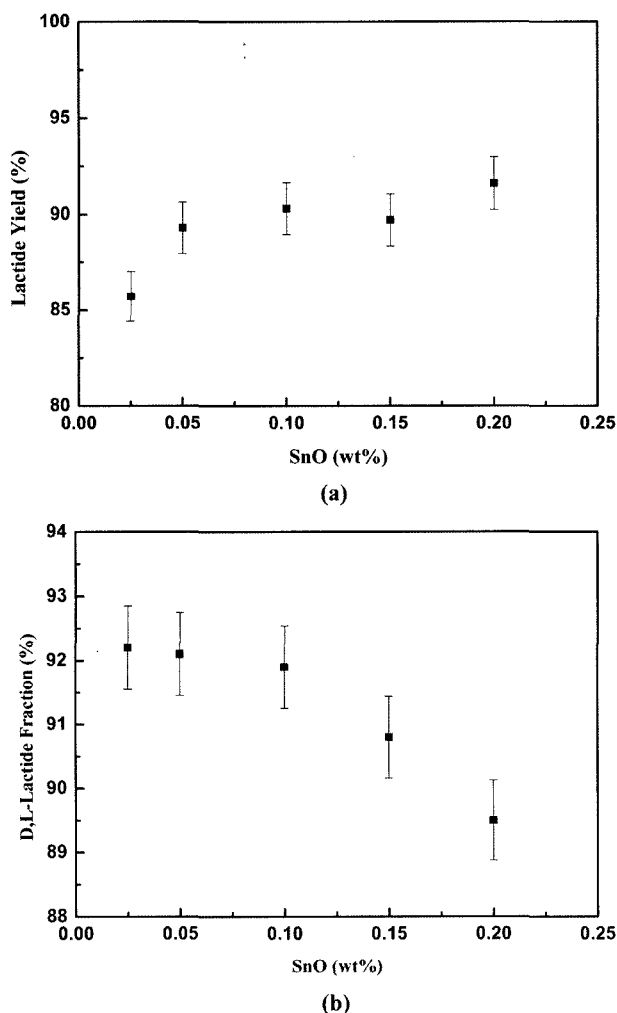


Figure 11. Variation of (a) lactide yield and (b) D,L-lactide fraction as a function of SnO catalyst.

ure 9 shows the variation of the lactide yield and D,L-lactide fraction when different molecular weights of PLA were used. The lactide yield increased as the concentration of the other impurities decreased at higher PLA molecular weight. But D,L-lactide fraction decreased with increasing molecular weight of PLA. This is because the chain cleavage associated with the thermal stress takes place more easily at higher molecular weights of PLA. The chain cleavage usually occurs at the alkyl-oxygen or acyl-oxygen bond in the PLA. Cyclization at the chain terminal after the chain cleavage possibly produces meso-lactide.²⁴

Figure 10 shows the effect of the catalyst concentration on the % conversion of PLA when the depolymerization reaction was carried out for the PLA with a molecular weight of 600 g/mol at 220°C and 20 torr. The % crude lactide in product increased from 67 to 77% as the SnO concentration was increased from 0.025 to 0.2 wt%. The higher conversion obtained at a higher SnO concentration may have been due to the higher reaction kinetics. Figure 11 shows the variation of the lactide yield and D,L-lactide fraction during the lactide production. The fraction of D,L-lactide decreased from 92.2 to 89.5% as the SnO concentration was increased from 0.025 to 0.2 wt% because the higher catalyst concentration increased the incidence of side reactions.

Conclusions

Lactide was produced from oligomeric PLA by back-biting reaction of the OH end groups. In the lactide preparation, the temperature had a more significant effect on the conversion of PLA and the degree of racemization than the type of Sn-based catalyst. A higher PLA conversion and lower racemization were obtained at a lower pressure. The conversion of PLA was maximized when the molecular weight of the oligomeric PLA was 1,380. The yield of lactide increased but the fraction of D,L-lactide decreased with increasing molecular weight. Catalyst levels above 0.1 wt% significantly decreased the fraction of D,L-lactide. Lactide is more sensitive to racemization than oligomeric PLA because the former is deprotonated more easily due to favorable entropy change.

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References

- (1) P. Mainilvarlet, R. Rahm, and S. Gogolewski, *Biomaterials*, **18**, 257 (1997).
- (2) W. Hoogsteen, A. R. Postema, A. J. Pennings, and G. T. Brinke, *Macromolecules*, **23**, 634 (1990).
- (3) C. Bastioli, *Macromol. Symp.*, **135**, 193 (1998).
- (4) K.W. Kim and S. I. Woo, *Macromol. Chem. Phys.*, **203**, 2245 (2002).
- (5) S. I. Moon, C. H. Lee, M. Miyamoto, and Y. Kimura, *J.*

- Polym. Sci.: Part A; Polym. Chem.*, **38**, 1673 (2000).
- (6) K. Yamane, *et al.*, USP 6916939 (2005).
- (7) F. E. Kohn, J. W. A. Van Den Berg, V. D. Ridder, and J. Feijen, *J. Appl. Polym. Sci.*, **29**, 4265 (1984).
- (8) G. I. Shim, J. H. Kim, S. H. Kim, and Y. H. Kim, *Korea Polym. J.*, **5**, 19 (1997).
- (9) A. J. Nijenhuis, D. W. Grijpma, and A. J. Pennings, *Macromolecules*, **25**, 6419 (1992).
- (10) J. Zhang, Z. Gan, Z. Zhong, and X. Jing, *Polym. Int.*, **45**, 60 (1998).
- (11) K. A. M. Thakur, R. T. Kean, E. S. Hall, J. J. Kolstad, T. A. Lidgren, M. A. Doscotch, J. I. Siepmann, and E. J. Munson, *Macromolecules*, **30**, 2422 (1997).
- (12) K. A. M. Thakur, R. T. Kean, and E. S. Hall, *Anal. Chem.*, **69**, 4303 (1997).
- (13) P. R. Gruber, *et al.*, USP 2574073 (1993).
- (14) H. R. Kricheldorf and A. Serra, *Polym. Bull.*, **14**, 497(1985).
- (15) H. R. Kricheldorf and M. Sumbel, *Eur. Polym. J.*, **25**, 585 (1989).
- (16) D. R. Witzke, R. Narayan, and J. J. Kolstad, *Macromolecules*, **30**, 7075 (1997).
- (17) H. R. Kricheldorf and S. R. Lee, *Polymer*, **36**, 2995 (1995).
- (18) D. K. Yoo, D. S. Lee, and D. Kim, *Macromol. Res.*, **13**, 68 (2005).
- (19) H. P. Benecke, *et al.*, USP5332839 (1994).
- (20) M. Muller, *et al.*, USP 5214159 (1993).
- (21) H. R. Kricheldorf and I. Kreiser-Saunders, *Macromol. Chem.*, **191**, 1057 (1990).
- (22) H. R. Kricheldorf, I. Kreiser-Saunders, and C. Boettcher, *Polymer*, **36**, 1253 (1995).
- (23) H. R. Kricheldorf and D.-O. Damaru, *Macromol. Chem.*, **198**, 1753 (1997).
- (24) H. Tsuji, I. Fukui, H. Daimon, and K. Fujie, *Polym. Degrad. Stabil.*, **81**, 501 (2003).