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Direct Condensation Polymerization of Lactic acid

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SUMMARY: In order to synthesize the higher molecular weight poly(lactic acids) by direct condensation polymerization of lactic acid, dipentaerythritol was used as a chain branching agent. Poly(lactic acids) of high molecular weight, 67000(Mn), was obtained by using antimony trioxide catalyst with good color. This poly(lactic acids) showed Tg of 54.8 °C, Tm of 147 °C and cold crystallization temperature of 115 °C. The polymer could be melt processed into transparent films. Tensile modulus of 311 Kg/ mm^2, tensile strain of 21% and tensile strength of 12.41 Kg/ mm^2 were obtained for film collected at 400%/min and drawn 4 times.

Introduction

Lactic acid that can be made by chemical synthesis or by fermentation technique is nontoxic and harmless to animals, plants and human beings. Poly(lactic acid)s, which are polymers of lactic acid, can be easily hydrolyzed in the presence of moisture. Due to these properties, poly(lactic acid)s have been used in biodegradable medical applications[1-6)] such as suture or staples for surgery, sustained release polymers for drug delivery, etc., as well as in agricultural applications for soil treatment including herbicides, soil disinfectants, and the like.

In recent years, poly(lactic acid)s have attracted commercial interest for solving environmental pollution problems caused by plastic wastes. The application of poly(lactic acid)s have been extended for use as general purpose biodegradable polymeric materials for packaging materials, food containers, coating materials, and so forth. The polymeric materials for these uses must have a high molecular weight in order to provide the desired strength to the resulting products.

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Two processes for preparing a poly(lactic acid)s have been known in the arts. One is the ring-opening polymerization of lactide$^{7)}$. This process involves two steps: the conversion of lactic acid feed stock to lactide and the polymerization of lactide to give poly(lactic acid)s product. This process is complicated, and time and labor consumptive. But relatively high molecular weight poly(lactic acid)s could be obtained. The another process is the direct condensation polymerization of lactic acid. This process is relatively simpler than that mentioned above, but it has a defect in that the resulting polymers has a low molecular weight and thus, shows poor physical properties which are not useful as a general purpose biodegradable material. The direct condensation methods as a more economical process has been studied for many years by many scientist, but high molecular weight polymer could not be synthesized because of the unfavorable equilibrium to high polymer in the usual condensation reaction conditions. Recently, a group of Mitsui Toatsu Chemicals, Japan, reported their success in obtaining high molecular weight PLLA by the direct condensation polymerization of lactic acid in solution$^{8)}$. Also scientist of Helsinki Univ., Finland, have been studied the direct condensation polymerization of lactic acid. They increased the molecular weight by joining lactic acid prepolymer chain together using diisocyanate as a chain extender$^{9)}$.

For the modifications of physical properties of poly(lactic acid)s, we already synthesized star-shaped poly(lactic acid)s by ring-opening polymerization of lactide$^{10)}$. The star-shaped poly(lactic acid)s could be synthesized to have a higher molecular weight than linear poly(lactic acid)s did under certain conditions. This concept that the higher molecular weight poly(lactic acid)s could be synthesized by star-shaped architecture was introduced to the direct condensation polymerization of lactic acid. Multifunctional hydroxyl compounds were used as star-shaping agent. The star-shaped polymer in this article means the polymer in which many polymeric chains are attached to a polyfunctional substance in a radial arrangement.

Experimental part

Materials

Pharmaceutical grade L-lactide acid (LA) from Purac was a 90% aqueous solution of the monomer that was minimum 95% optically pure. Antimony trioxide (Sb_2O_3), tin oxide (SnO), dipentaerythritol with 99+% purity, respectively, were purchased from Aldrich Chemical co. and used without purification. All other chemicals and solvents were of analytical grades and used without further purification.

Measurements

The structure of polymers was analyzed by means of a Varian 300 MHz ^{1}H-NMR(Gemini-300) apparatus in deuterated chloroform solution and by an Alpha Centauri FT-IR (Mattson Instruments) apparatus. The intrinsic viscosity of the polymers was measured in chloroform at 25 °C using an Ubbelohde viscometer. Gel permeation chromatography (GPC) measurements were carried out at 35 °C using a Waters ALC/GPC 150C equipped with micro-styragel columns and calibrated with polystyrene standards, which covered a MW range of 1,000- 1,000,000. Chloroform was used as eluent at a flow rate of 1.0 ml/min. Differential scanning calorimeter (DSC) was performed on a Du Pont Thermal Analyzer 2000 using a heating rate of 20 °C/min in a nitrogen atmosphere. Second heating runs were carried out after sample had been quenched from the melt.

Polymerization of L-lactic acid

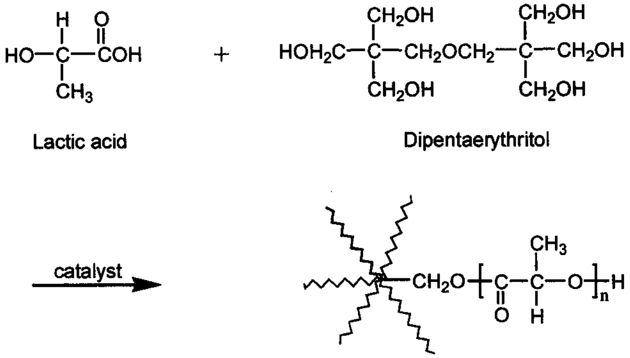
150 g of a 90 % aqueous L-lactic acid solution and various amount of dipentaerythritol (DIPET) were added to a 4-neck flask equipped with a thermometer, a condenser, and a N_2 inlet tube. The mixture was dehydrated by heating it in a nitrogen stream, while stepwise varying the temperature and the pressure from 105 °C and 350 mmHg to 150 °C and 30 mmHg. After removing about 38 g of water, 0.1 g of Sb_2O_3 was added. The resulting mixture was then polycondensated at an elevated temperature of 200 °C under a reduced pressure of 3 to 5 mmHg. The viscosity of the reaction system increased as the

polycondensation proceeded. After heating for 27 hr under reduced pressure, 106 g of a colorless polymer was obtained. The molecular weight of the resulting polymer was found to be 49,000.

Results and Discussion

In general, the polycondensation of lactic acid proceeds stepwise in a similar manner to the esterification of a diacid with a diol. The molecular weight of the resulting polymer increases in proportion to the reaction time. During the polycondensation, an amount of water is produced as a by-product, which hydrolyzes the resulting polymer, and thus, decreases the molecular weight of the polymer. Therefore, it is very important to choose a method to remove the water formed effectively from the reaction system. A variety of dehydration techniques have been known which include, for example, increasing the stirring rate during the reaction, using much reduced pressure, and introducing a nitrogen gas flow. However, these techniques have fundamental limitations as a method to remove water, because the viscosity of the reaction system increases with the increase in the molecular weight of the resulting polymer. Therefore, it is a key point to reduce the viscosity of the reaction system as much as possible in order to obtain a high molecular weight of polymers. The star-shaped polymer has been known in the art and is reported to have a lower melting viscosity than that of linear chain polymers of the same molecular weight[11)]. The poly(L-lactic acid)s, PLLA, in a star-shape, which show a lower melting viscosity, enable efficient removing the water formed during the reaction.

In principle, two processes are available for preparing a star form of PLLA, namely, a direct polymerization of lactic acid using a multi-functional reagent, and a two-step process comprising preparing a straight chain PLLA followed by coupling. Among these, the former process is preferred to produce the star-shaped PLLA. In this study, we used the former process to obtain higher molecular weight PLLA by direct condensation polymerization, and dipentaerythritol (DIPET) having six primary hydroxyl group was used as the multifunctional branching monomer. (Scheme 1)



Scheme 1

The reaction mechanism for forming the star-like molecular structure depends on the difference in the reactivities of polyhydroxyl compounds and lactic acid used in the reaction. In the initial stage of the reaction, all primary hydroxyl groups of polyhydroxyl compounds are first reacted with lactic acid to form a small star-shaped structure. The molecular chains grow while maintaining their star-shaped structure by the subsequent reaction of lactic acid, resulting in the desired polymer in a star form having a high molecular weight. This type of reaction is expected to have a higher reaction rate in the growth of molecular weight when it is compared with that of linear polymer at the same conversion of reaction. The results of polymerization are summarized in Table 1. The polymerization was conducted in bulk with continuous stirring. The preferred polymerization temperature was in the range of 170 – 220 °C. When the temperature was below 170 °C, the reaction takes place slowly. Above 220 °C the products became dark brown.

Table 1. Condensation polymerization of L-lactic acid at 200 °C (amount of lactic acid: 135g, Sb_2O_3: 0.2g).

Mole ratio [LA]/[DIPET]	Reaction Time (hour)	Mv[a)]	Mn[b)]	Mw[b)]	MWD[b)]
—[c)]	0.5	458	114	136	1.2
—	1	764	345	503	1.46
—	2	1600	775	2900	3.73
—	3	3500	2700	6800	2.52
—	4	5900	8100	16200	1.99
—	7	13800	25700	42500	1.65
—	10	16000	25900	50200	1.94
—	24	17100	31100	58400	1.88
1800	2	773	196	626	3.19
1800	5	1900	1100	4000	3.54
1800	7	3000	3300	9200	2.79
1800	9	4900	6600	16400	2.49
1800	23	42200	39400	134600	3.41
1800	28	45100	45700	224000	4.9
1800	32	56600	67600	388000	5.74

a) Mv was calculated from $[\eta] = 3.48\times10^{-4}Mv^{0.75}$
b) GPC data (polystyrene calibrated)
c) In absence of DIPET.

Fig. 1 shows a typical curve indicating the increase of viscosity with reaction time with or without DIPET. The molecular weight of a polymer slowly increases upon initiation of the polymerization. But after 5 hour, the increase of the molecular weight of the star-shaped PLLA is much faster than that of the corresponding linear PLLA. Such a high molecular weight of the star-shaped PLLA is a distinctive feature in view that the PLLA obtained by the conventional polycondensation technique shows a lower molecular weight. These results reveal that the process of the present work can produce a PLLA having a higher molecular weight in a facile and economically efficient manner as compared with the conventional techniques. From GPC data in Table 1, linear PLLA showed a molecular weight distribution ranging form 1.5 to 2 with unimodal distribution, while star-shaped PLLA showed a molecular weight distribution ranging form 3 to 5 with bimodal distribution. This is a typical demonstration of the branched structure of the PLLA.

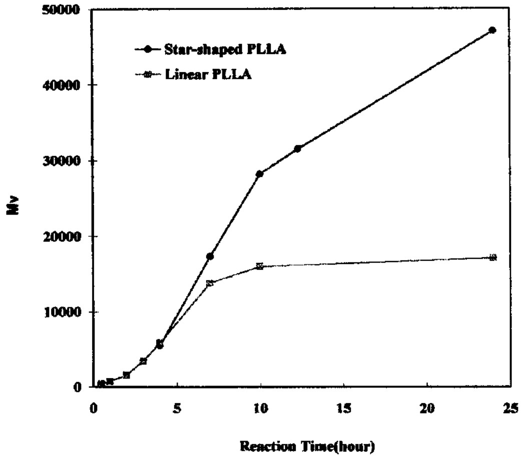


Fig. 1. Plot of molecular weight as a function of polymerization time for linear and star-shaped PLLAs.

Various kind of catalyst can be used as the polycondensation catalyst for lactic acid. The representative examples of such catalysts include stannous chloride, stannous oxide, tetraphenyl tin, tin powder, isopropyltitanate, tetrachlorotitanate, titanium-n-butoxide, antimony oxide, antimony chloride, lead oxide, calcium oxide, aluminum oxide, iron oxide, calcium chloride, zinc acetate, p-toluene sulfonic acid, and so forth. Table 2 shows the molecular weight of PLLA polymerized with these catalysts. When titanate catalysts were used, the higher molecular weight PLLA was obtained whereas obtained polymers showed dark color. SnO showed a similar result. Sb_2O_3, which is well known as an active catalyst in the esterification reaction, showed the higher molecular weight PLLA. Although catalytic activity was less than titanate catalysts, the obtained PLLA had a good color.

Table 2. The molecular weight of star-shaped PLLA's polymerized at 200 °C with various kind of catalyst.

Catalyst	Reaction Time (hour)	Yield	Mv	Color
p-Toluene sulfonic acid	20	80	14400	medium
Sb_2O_3	27	93	48000	good
SnO	12	80	48000	poor
Sn	16	85	35000	poor
Stannous octoate	20	71	16700	medium
Dibutyl tin oxide	20	60	12000	medium
Tetraphenyl tin	71	80	17000	medium
Titanium-n-butoxide	47	60	67000	poor
Titanium isopropoxide	55	85	47000	poor
$Zr(OBu)_4$	20	70	14200	Medium

The PLLA samples were analyzed using ^1H NMR and FT-IR spectroscopies. The NMR and FT-IR spectra of the linear and star polymers were not so much different to each other, as expected. For the characterization of structural differences between linear and star PLLAs, their thermal behavior as well as their mechanical properties were investigated.

Table 3 shows thermal data of PLLAs. Tg of linear and star-shaped PLLA were observed at 52.9 °C and 54.8 °C respectively. Star-shaped PLLA has a lower melting point (147 °C) compare to ring opening polymerized linear PLLA, while condensation polymerized linear PLLA has no melting point. Also the cold crystallization temperature was shown at 115 °C, which was compared with 102 °C of ring opening polymerized linear PLLA. The lower melting point and higher cold crystallization of star-shaped PLLA is another typical demonstration of the branched structure of the PLLA. From TGA thermograms of PLLA in nitrogen, linear PLLA started to decompose at about 219 °C, indicating relatively poor thermal stability than star-shaped PLLA.

Table 3. Physical property of linear and star-shaped PLLA.

	Linear	Star
Intrinsic viscosity	0.52	1.28
Mv	17100	56800
Mn$^{a)}$	31100	67600
Mw$^{a)}$	58400	388000
MWD$^{a)}$	1.88	5.37
Tg (°C)	52.9	54.8
Tcr (°C)	102	115
Tm (°C)	-	147.4
Td (°C)$^{b)}$	219.2	239.9

a) GPC data (polystyrene calibrated)
b) Temperature at 5% weight loss.

Tensile strength and ultimate elongation of PLLAs were evaluated from films, which was made by hot melt pressing followed by drawing of melt pressed sheets. Star-shaped PLLAs were successfully processed into strong film, whereas linear PLLAs were not processed due to the lower molecular weight of polymer. Drawing of films at different speeds and ratios were performed at 80 °C. The mechanical data for uniaxial and biaxial drawn star-shaped PLLA films are summarized in Table 4. As expected, the higher the drawing speed of film, the higher strain and strength was obtained. Film collected at 400%/min and drawn 4 times reached a tensile strength of 12.41 Kg/ mm^2, a tensile strain of 21% and tensile modulus higher than 300 Kg/ mm^2. The high molecular weight PLLA has good mechanical strength and optical clarity comparable to commercial polystyrene. Considering that the molecular weight of polymers prepared in this study were not high enough compared to the commercial polylactide (~Mn 130,000), the prepared PLLAs exhibited good tensile strength and modulus values.

Table 4. PLLA film drawing at 80°C

Mode	Draw ratio (%)	Draw rate (%/min)	Strain at break (%)	Stress at break (kg/mm^2)	Strain at peak (%)	Stress At peak (kg/mm^2)	Young`s Modulus (kg/mm^2)
Uniaxial	400	167	21.820	2.944	4.500	6.861	235.4
Uniaxial	400	244	16.420	2.091	5.083	7.735	250.0
Uniaxial	400	325	22.820	8.773	14.150	11.020	271.1
Uniaxial	400	400	21.920	8.655	19.450	12.410	311.1
Uniaxial	200	475	18.900	1.770	4.808	5.649	187.2
Uniaxial	300	475	13.400	2.263	4.850	6.551	244.1
Uniaxial	400	475	25.62	3.814	10.140	7.594	246.8
Uniaxial	500	475	15.620	7.192	9.850	9.832	286.6
Biaxial	300X300	3300	4.175	4.488	3.638	4.699	196.6
Biaxial	400X400	3300	13.850	3.702	3.550	5.467	217.9

Conclusion

Moderate to high molecular weight PLLA was prepared by direct condensation polymerization. The polymer could be melt processed into transparent films. The PLLA according to the present works shows an excellent tensile strength, which is attributed to its high molecular weight. Thus, it can be widely used as a general-purpose biodegradable material, sustained release matrix for drug or agrochemical delivery, as well as films for packaging and agricultural use

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