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# Polymerization of aqueous lactic acid to prepare high molecular weight poly(lactic acid) by chain-extending with hexamethylene diisocyanate

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## Abstract

In order to synthesize the high molecular weight poly(lactic acid) [PLA], Hexamethylene diisocyanate [HDI] was used as a chain extender connecting the terminal group of polymers. Poly(lactic acid) of high molecular weight, 76000 ($M_w$) and 33000 ($M_n$), was obtained by using antimony trioxide catalyst after chain-extending with HDI. Without chain-extending, the molecular weight of PLA was about 7000 ($M_n$). $T_m$ in the 2nd-scan DSC thermogram was not found when PLA was chain-extended with HDI. In order to check the degree of crystallization of polymers, annealing of these polymers was carried out at 120 °C. Peaks of XRD (X-Ray Diffraction) were sharpened as the duration of annealing was lengthened. The analysis of polymers reacted with HDI by $^1$H-NMR showed the broad peaks at 1.32 and 3.14 ppm assigned to HDI units. The molecular weight of polymers increased with the increase in the mole ratio of -NCO/-OH.

## Introduction

The availability of biocompatible and biodegradable polymers has promoted major advances in the biomedical field. A few synthetic polymers, such as poly(-ε-caprolactone) [PCL], polylactide [PLA], and polyglycolide [PGA] are known for their usefulness in medicine (1).

Until now, high molecular weight PLA was synthesized by a ring-opening polymerization of the cyclic diester of lactic acid which is called as a lactide (2,3). However, the cost of this process is high due to the complexity of the process. While polycondensation of lactic acid is a low cost process because cheap lactic acid in liquid phase is polymerized. However, as the molecular weight of PLA becomes high, it is difficult to remove the water in order to obtain high molecular weight PLA. When the reaction temperature was increased to promote the removal of water, the high molecular weight polymer can not be synthesized because of the decomposition reaction at high

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temperature (4). Chain extender to connect the end groups of PLA was used to increase the molecular weight of prepared polyester. The effective chain extenders in the reaction with polyesters were found to be ethylene carbonate, heterocyclic compound and diisocyanate (5).

In this work, the molecular weight of PLA prepared by direct polycondensation of lactic acid was increased by adding chain extender at the last stage of polycondensation. The chain extender reacted with the terminal group (-OH) of polymer to increase the molecular weight. Hexamethylene diisocyanate [HDI] was used as a chain extender.

## Experimental

**Polymerization** : L-lactic acid of 90 % aqueous solution was used as a monomer. 40 g of L-lactic acid and 20 mg of various catalysts were added to three neck flask (250 ml). The mixture of reactants was stirred by mechanical stirrer. The reactor was immersed in an oil bath at 160 °C, then the reactor was flushed with dry $N_2$ at a rate of 120-130 ml/min for 6 hr. The polycondensation reaction was proceeded under vacuum for 18 hr.

The final vacuum in the reactor was kept at 0.1-0.3 torr. After this polycondensation reaction, 1 ml of HDI was added to the reactor and reacted with resulting polymer under nitrogen atmosphere at 160 °C for 10 min. The reaction product was dissolved in 100-150 ml of $CHCl_3$ and precipitated in the excess of methanol. The precipitated PLA was isolated by filtration and dried at room temperature under vacuum.

**Analysis of Polymer** : Intrinsic viscosities were determined in chloroform at 30 °C. The viscometer is 46460-50 Tube Cannon-Fenske. The molecular weights were measured in chloroform solution at 35 °C with GPC (Waters 150-CV). The column configuration consisted of four columns of 500, $10^3$, $10^4$ and $10^5$Å. The molecular weight of polymer was estimated according to the polystyrene calibration curve. DSC measurements were performed with a Dupont TA 2000 scanned at the rate of 10 °C/min. A 2nd-scan DSC spectrum was recorded after the sample was quenched to room temperature. $^1$H-NMR spectra were recorded in $CDCl_3$ with 300 MHz NMR spectrometer (Bruker AMX-300). X-ray diffraction patterns were recorded with an X-ray diffractometer (Rikaku D/MAX-III) with CuKα radiation.

## Results and Discussion

**Polymerization**: Zinc acetate, dibutyltinoxide (DBTO) and antimony trioxide ($Sb_2O_3$) were well known as a catalyst in the transesterification reaction. These catalysts were evaluated in the polycondensation reaction of lactic acid. Table 1 shows the molecular weight of PLA polymerized with these catalysts. When $Sb_2O_3$ was used, the highest molecular weight was obtained. The DSC thermogram for PLA-3 was shown in the Figure 1. $T_m$ (melting point) is 151 °C as shown in the first scan of DSC thermogram. $T_g$ (glass temperature) and $T_c$ (crystallization temperature) was 51 °C and 106 °C,

Table 1. The molecular weights of PLA's polymerized at 160 °C and chain-extended with HDI.

| Sample No. | Catalyst | [NCO]/[OH]* | $M_n$ | $M_w$ | $M_n/M_w$ |
|---|---|---|---|---|---|
| PLA-1 | Zinc acetate | - | 4300 | 6000 | 1.40 |
| PLA-1-HDI | Zinc acetate | 2.53 | 9100 | 14000 | 1.55 |
| PLA-2 | DBTO | - | 6600 | 10100 | 1.54 |
| PLA-2-HDI | DBTO | 3.87 | 24000 | 57000 | 2.35 |
| PLA-3 | $Sb_2O_3$ | - | 7000 | 11000 | 1.58 |
| PLA-3-HDI | $Sb_2O_3$ | 4.11 | 33000 | 76000 | 2.31 |

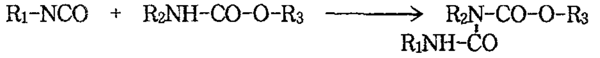
* : Mole ratio of -NCO to -OH

respectively as shown in the 2nd-scan. Two $T_m$'s at 144 °C and 151 °C are observed in the 2nd-scan.

**Effect of chain extender** : The $M_n$ of resulting polymer was increased by 2-4 times as HDI reacted with PLA as shown in the Table 1. It can be thought that two isocyanate groups of HDI react with end group (-OH) of PLA to increase the molecular weight by twice in the manner as shown in reaction ① in the following. However, the increment of molecular weight by HDI reaction was more than twice as shown in the Table 1. The excess amount HDI can react with the other end group (-COOH) and/or react with the urethane group to form a branch known as a allophanate reaction (6) as shown in the following (reaction ②).

$$2\ \mathrm{H}\text{-}\left[\mathrm{O\text{-}CHCH_3\text{-}CO}\right]_n\text{-}\mathrm{OH} + \mathrm{OCN\text{-}(CH_2)_6\text{-}NCO} \longrightarrow$$

$$\mathrm{HO}\text{-}\left[\mathrm{CO\text{-}CHCH_3\text{-}O}\right]_n\text{-}\mathrm{CO\text{-}NH\text{-}(CH_2)_6\text{-}NH\text{-}CO}\text{-}\left[\mathrm{O\text{-}CHCH_3\text{-}CO}\right]_n\text{-}\mathrm{OH}$$ ①



$$\mathrm{R_1\text{-}NCO} + \mathrm{R_2NH\text{-}CO\text{-}O\text{-}R_3} \longrightarrow \underset{\substack{|\\ \mathrm{R_1NH\text{-}CO}}}{\mathrm{R_2N}}\mathrm{\text{-}CO\text{-}O\text{-}R_3}$$ ②

Allophanate reaction is the reaction of -NCO with urethane bond formed by reaction of -NCO with -OH. $M_w/M_n$ of PLA-1 is smaller than that of the others. When the ratio of [NCO] to [OH] was low, the reaction of HDI with terminal -OH of PLA mainly occurred. However, side reaction of HDI to form a branch structure increased as the ratio of [NCO] to [OH] increased. The molecular weight of branched polymer formed by allophanate reaction was broad resulting in the larger polydispersity. $M_w$ of 75900 was obtained by using $Sb_2O_3$ as a catalyst, when the ratio of [NCO] to [OH] is 4.11.

**Crystallinity** : DSC thermogram of PLA-3-HDI is shown in Figure 2. $T_m$ of PLA-3-HDI was 145 °C in the 1st-scan. Unlike PLA-3, $T_c$ and $T_m$ of PLA-3-HDI were not observed in the 2nd-scan. This suggests that the crystallization rate of

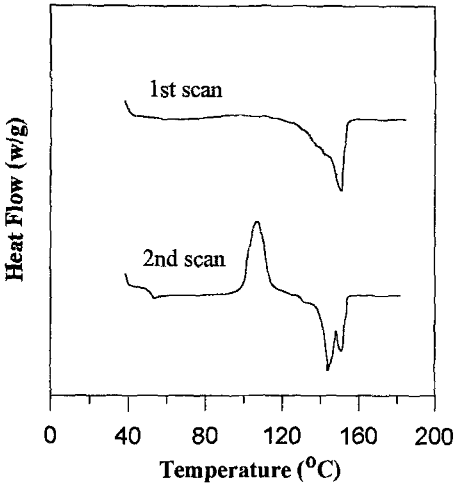


Figure 1. DSC thermogram of PLA-3 at a heating rate of 10 °C/min.

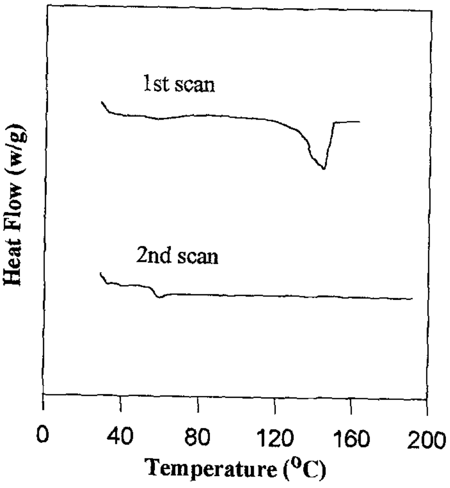


Figure 2. DSC thermogram of PLA-3-HDI at a heating rate of 10 °C/min.

PLA-3-HDI is much slower than that of PLA-3 because of the formation of branch structure by the allophanate reaction. $T_m$ of PLA-3-HDI accords with the lower $T_m$ of two $T_m$'s of PLA-3. In order to investigate the crystallinity of PLA-3-HDI, PLA-3-HDI was annealed at 120 °C after melting at 170 °C to remove crystallinity. $T_m$'s at 140 °C and 147 °C were observed in DSC thermogram after annealing at 120 °C for two hours. The peak area of $T_m$ of 140 °C decreased and that of $T_m$ of 147 °C increased as the annealing time increased. This suggests that crystal structure of PLA-3-HDI was converted very slowly from imperfect structure to perfect structure. Figure 4 shows XRD pattern of PLA-3-HDI. PLA-3 shows the sharpest and most intense peak at $2\theta$ of 16.7° (020 reflection). Other peaks were appeared at 14.8° (101 reflection), 19.1° (023 reflection) and at 22.3° (121 reflection) (7). These peaks of PLA-3-HDI became sharper and the intensity increased as increasing the annealing time. However, the crystallinity even after 24 hr-annealing is less than PLA-3. The presence of allophanate branching decreased the crystallinity.

**$^1$H-NMR** : Figure 5 shows the $^1$H-NMR spectrum of PLA-3 (A) and PLA-3-HDI (B). Both spectra exhibited the signal of methine group at 5.15 ppm (a) and the signal of methyl group at 1.55 ppm (c). The signal at 4.4 ppm (b) characteristic of the hydrogen of methine group next to a hydroxyl end group was found. However, the signal at 4.4 ppm was not observed in the spectrum of PLA-3-HDI because HDI reacted with hydroxyl end group. The chemical shift of hydrogen of the urethane bond formed by reaction of HDI with hydroxyl end group, was observed at 6.27 ppm (d) (8). The broad signals at 1.32 ppm (f) and 3.14 ppm (e) in the spectrum of PLA-3-HDI were assigned to the unit of HDI in the polymer chain (9). The intensity ratio of the signal corresponding to urethane to the signal of HDI unit was not 1 : 2. This can be explained by the fact that the hydrogen in the urethane bond was reacted with other

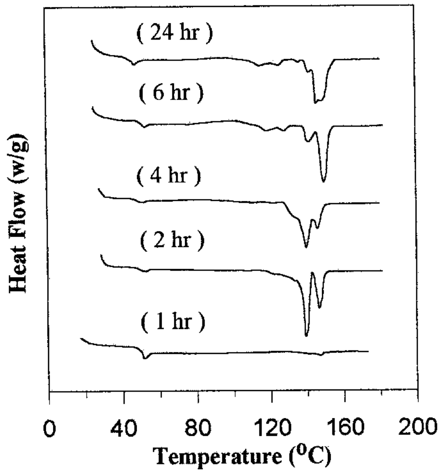


Figure 3. DSC thermogram of PLA-3-HDI as a function of annealing time at 120 °C. (The number in the parenthesis indicates the time of annealing.)

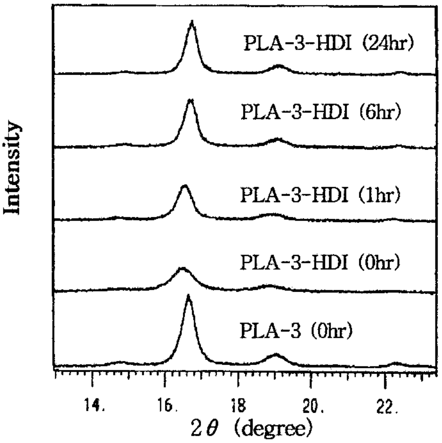


Figure 4. XRD of PLA-3 and PLA-3-HDI as a function of annealing time. (The number in the parenthesis indicates the time of annealing.)

polymer chain by allophanate reaction to form branch structure.

**Reaction time and molecular weight** : 3 ml of HDI was added to the PLA polymerized at 160 °C. PLA reacted with HDI at 160 °C for longer than 20 min was not dissolved in chloroform. As time of reaction with HDI increased, the degree of swelling increased and solubility in chloroform decreased. The reaction of HDI with urethane bond produced the branch and crosslink structure. However, at 140 °C, polymer reacted with HDI was dissolved well in chloroform even though the reaction

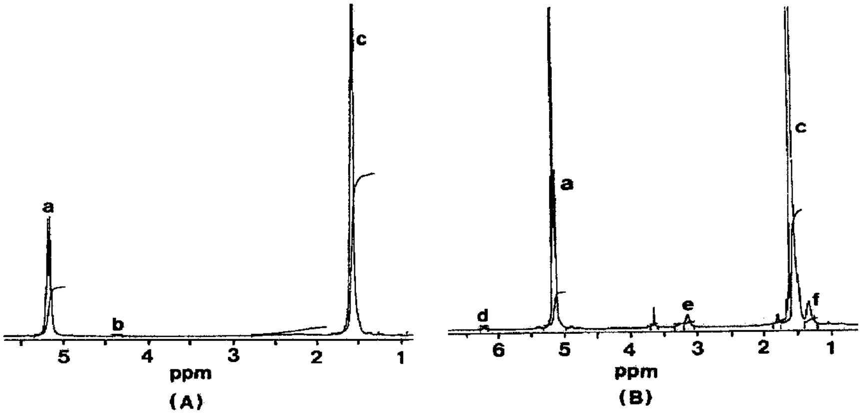


Figure 5. $^1$H-NMR spectrum of PLA-3 (A) and PLA-3-HDI (B).

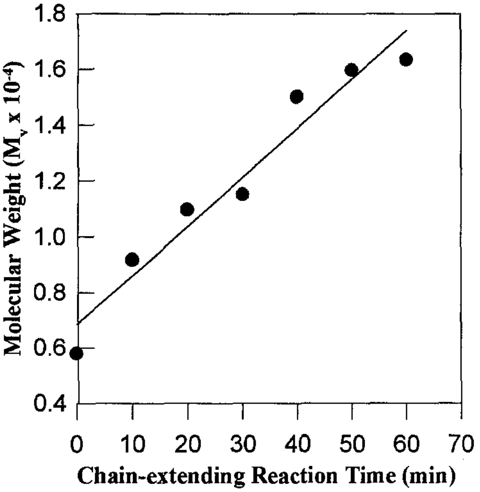


Figure 6. The increase of molecular weight with chain-extending reaction time at 160 °C.

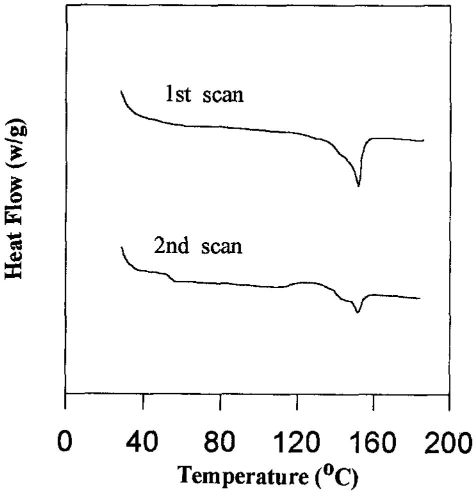


Figure 7. DSC thermogram of PLA reacted with HDI at 140 °C for 60 min.

was proceeded longer than 20 min. Figure 6 shows that molecular weight of polymer increased with the increase of reaction time after addition of 3 ml of HDI. The increment of molecular weight of polymer chain-extended at 140 °C is not as large as that of polymer chain-extended at 160 °C. Figure 7 shows the DSC thermogram of polymer produced by reaction of HDI at 140 °C for 60 min. $T_m$ was shown in the 2nd-scan. It can be concluded from this result that the reaction of HDI with PLA producing the branch and crosslink structure decreased at lower reaction temperature. If the reaction time and temperature increase, PLA of high molecular weight can be obtained because of formation of branch structure. However, branching and crosslinking reaction should be reduced to improve the biodegradability of polymer, because the crosslinking and branching reduced the biodegradability.

## Conclusion

The molecular weight of PLA was increased by reaction of HDI with OH group of PLA. The $T_m$ of PLA reacted with HDI was not found in the 2nd scan of DSC because of the slow rate of crystallization. By annealing the PLA reacted with HDI at 120 °C, chain-extended PLA crystallized slowly. The formation of branched structure caused the slow crystallization. The reaction temperature and time controls the formation of allophanate group. $^1$H-NMR spectrum shows that the -NCO group of HDI has reacted with the hydroxyl group which is the end-group of PLA.

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