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Stereocomplex Formation between Enantiomeric Poly(lactic acid)s. 4. Differential Scanning Calorimetric Studies on Precipitates from Mixed Solutions of Poly(D-lactic acid) and Poly(L-lactic acid)

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ABSTRACT: Polymer blends of poly(D-lactic acid) (PDLA) and poly(L-lactic acid) (PLLA) were obtained by precipitation from their 1 g/dL methylene chloride mixed solutions into methanol under stirring and studied by differential scanning calorimetry (DSC). The DSC results showed that the racemic crystallization (stereocomplex crystallization) between PDLA and PLLA occurred in preference to the crystallization of each homopolymer, irrespective of the molecular weight of poly(lactic acid), in contrast to the polymer blends obtained by casting the mixed solutions of PDLA and PLLA with high molecular weights. However, when the mixed solution from PDLA and PLLA with a high molecular weight was poured into the nonsolvent without stirring or at 5 g/dL, the formation of racemic crystallites was greatly reduced and the homopolymer crystallites were formed in addition to the racemic crystallites. These results strongly suggest that the racemic crystallization does not take place in dilute solutions but during the precipitation process. The racemic crystallite has 1.4 kcal/mol as the enthalpy of fusion when the PDLA concentration in the mixed solution approaches zero.

Introduction

Poly(lactic acid) (PLA) has stereoisomers: poly(D-lactic acid) (PDLA), poly(L-lactic acid) (PLLA), and poly(DL-lactic acid) (PDLLA). PDLA and PLLA are mirror images of one another in their structure and both are crystallizable, whereas PDLLA is an amorphous and optically inactive polymer. The unit cell of PLLA is found to be pseudoorthorhombic with an assumed 10_3 helical conformation.[1]

We have already reported that the crystallites of the stereocomplex are formed upon mechanical blending of PDLA and PLLA[2] and have studied the gelation through the stereocomplex formation in concentrated solutions by viscometry and NMR spectroscopy.[3] Similar stereocomplex formation has been reported on many other blends from isotactic D and L polymers.[4–13] The PLA stereocomplex is found to possess a racemic crystalline structure, where PDLA and PLLA chains are packed side by side with a D monomer unit to L monomer unit ratio of 1:1.[14,15] Loomis et al. studied the racemic crystallized materials for medical use[16–21] and estimated the critical lactate unit needed for formation of the PLA racemic crystallites to be about 10 on the basis of the result of blending random copolymers of L-lactide/ϵ-caprolactone with random copolymers of D-lactide/ϵ-caprolactone.[21] For the formation of racemic crystallites, PDLA and PLLA molecules must crystallize through only intermolecular interaction, in contrast to the homopolymer crystallization, which would take place through both intra- and intermolecular interactions of PDLA or PLLA. Several physical means are known to promote the intermolecular interaction for the formation of more stable crystallites. They include polymer solidification by cooling a polymer melt, increase of the polymer concentration of a polymer solution until drying, and precipitation of a polymer by pouring the solution into the nonsolvent. These processes are utilized in melt, dry, and wet spinning, respectively.

In a previous work we investigated the PLA stereocomplex formation through the drying process, but it was not by dry spinning but by casting a polymer solution to obtain films.[22] In order to get high-strength polymeric materials, it is generally favorable to employ high molecular weight polymers. However, when a mixed solution of PDLA and PLLA, both with high molecular weights, was cast, the homopolymer crystallites were predominantly formed and a long aging time was needed on the solution to obtain a film containing only the racemic crystallites.[22] In the present work the racemic crystallization through precipitation of PDLA and PLLA from their mixed solutions with the nonsolvent was studied in an attempt to more readily obtain the PLA stereocomplex materials. Influences of the stirring of nonsolvent, the PDLA/PLLA blend ratio, the polymer molecular weight, the kind of solvent, and the solution concentration on the formation of racemic crystallites will be described.

Experimental Section

Materials. PDLA and PLLA were synthesized with the previously reported method.[23] Methyl D-lactate with an optical purity of 97% was supplied by Daicel Chemical Industries, Ltd., Japan, and hydrolyzed to D-lactic acid. L-Lactic acid with an optical purity of 98% was purchased as a 90 wt % aqueous solution from CCA Biochem bv, The Netherlands. The following polymer synthesis was performed in the same manner for both PDLA and PLLA. The oligomeric PLA's prepared by the condensation polymerization of lactic acid were thermally decomposed to yield the lactide monomers. Ring-opening polymerization was performed for each of the lactides in bulk in the temperature range from 140 to 220 °C using stannous octoate as the polymerization catalyst.[24] The resulting polymer was purified by the reprecipitation method using methylene chloride and methanol as the solvent and nonsolvent, respectively.

The viscosity-average molecular weight ($\bar{M}_v$) of polymers was determined from their intrinsic viscosity, $[\eta]$, in chloroform at

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Table I
Polymerization Conditions and Molecular Characteristics of the Synthesized Polymers

	polymerization conditions			polymer		
code no.	SO,[a] wt %	temp, °C	time, h	$[\eta]$, dL/g	$\bar{M}_v$	$[\alpha]^{25}_D$, deg
D1	0.03	140	10	0.27	4.9×10^3	+153
D2	0.03	220	5	0.92	2.6×10^4	+154
D3	0.03	220	0.5	1.70	6.1×10^4	+154
D4	0.03	140	0.3	2.79	1.2×10^5	+156
D5	0.03	140	10	6.15	3.6×10^5	+153
L1	0.003	140	81	0.36	7.3×10^3	-147
L2	0.03	140	5	0.96	2.8×10^4	-153
L3	0.03	160	5	1.71	6.2×10^4	-151
L4	0.03	140	10	3.01	1.3×10^5	-153
L5	0.03	140	10	6.16	3.6×10^5	-153
L6	0.03	140	10	6.98	4.2×10^5	-157

[a] Stannous octoate.

25 °C with an Ubbelohde viscometer using the equation[25]

$$[\eta] = 5.45 \times 10^{-4} \bar{M}_v^{0.73} \qquad (1)$$

The specific optical rotation of polymers, $[\alpha]$, was measured in chloroform at a concentration of 1 g/dL at 25 °C using a Perkin-Elmer polarimeter 241 at a wavelength of 589 nm. Characteristics of the polymers used in this work are listed in Table I, together with the polymerization conditions. The optical rotation $[\alpha]^{25}_D$ in chloroform was approximately +150° for PDLA and -150° for PLLA, in good agreement with the reported value.[26]

Complex polymer blends were obtained by the following precipitation method. Methylene chloride solutions (1 g/dL) were prepared from each of the polymers. Five milliliters of the solution of PDLA was mixed with that of PLLA, and the polymer was then precipitated with 500 mL of methanol at room temperature. Stirring using a tip of a 10-mm radius and a 70-mm length was carried out at a rate of approximately 200 rpm for 0.5 h to force the PDLA and PLLA chains to collide with each other and to effectively remove the solvent from the precipitate. The filtrated precipitate was further desolvated by using fresh methanol, followed by drying in vacuo for approximately 1 week and annealing at 140 °C in an atmosphere of nitrogen for 1 h prior to subjecting it to differential scanning calorimetry (DSC). As the precipitates from PDLA and PLLA with low molecular weights were dispersed in methanol, they were purified by centrifugation at 5000 rpm. In addition to methylene chloride, chloroform, benzene, and dioxane were used as solvents for comparison.

Measurements. The melting temperature and the enthalpy of fusion of PLA precipitates were measured by using a Shimadzu DT-50 DSC apparatus. Heating was performed under a constant flow of nitrogen gas at a rate of 10 °C/min. The temperature and the enthalpy of fusion were calibrated by using indium as the standard.

Results

1. Effect of Stirring. DSC thermograms of the precipitates obtained at different stirring rates are given in Figure 1. The polymer pair used is D5–L5 with the equimolar mixing ratio. As reported elsewhere, the DSC peak at 180 °C corresponds to fusion of the homopolymer crystallites, while the peak at 230 °C corresponds to fusion of the racemic crystallites (stereocomplex crystallites).[2] As is apparent, the area of the melting peak for the homopolymer crystallites is much larger than that of racemic crystallites when the precipitate was obtained without any shearing force (0 rpm). On the contrary, only the melting peak of the racemic crystallites is seen for the precipitates obtained under stirring. The enthalpy of fusion of racemic crystallites (ΔH_{f2}) evaluated from Figure 1 increases from 5 (at 0 rpm) to 45 J/g of polymer (200 rpm), whereas that of homopolymer crystallites (ΔH_{f1}) decreases from 47 (0 rpm) to 0 J/g of polymer (50 rpm). This result shows that vigorous mixing during precipitation promotes the racemic crystallization. The stirring rate was fixed a 200 rpm in the following experiments.

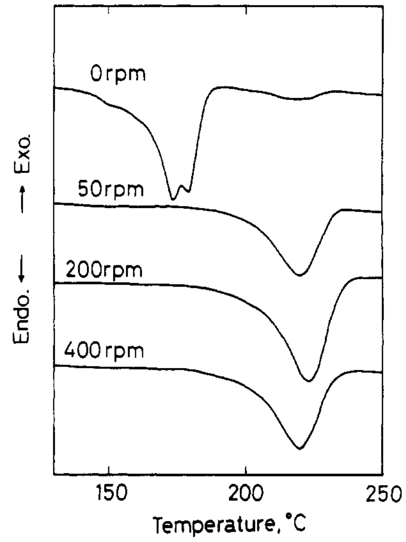

Figure 1. Stirring effects on DSC thermograms of the precipitates from mixed solutions of D5 and L5 ($X_D = 0.5$; methylene chloride, 1 g/dL).

2. Effect of Blend Ratio. Figure 2 shows DSC thermograms of the precipitates obtained from the 1 g/dL methylene chloride solution of a PDLA and PLLA mixture with various PDLA contents (X_D), which are defined as

$$X_D = \mathrm{PDLA}/(\mathrm{PDLA} + \mathrm{PLLA}) \qquad (2)$$

The pair of PLA used in this study is D5–L5. It is clearly seen that the precipitates of the homopolymer, PDLA ($X_D = 1$) or PLLA ($X_D = 0$), give a single endothermic peak around 180 °C, whereas another additional peak is observed in the vicinity of 230 °C for the blend polymers. When X_D approaches 0.5, the DSC peak around 180 °C becomes broader and finally vanishes, while only the peak around 230 °C remains. The melting temperatures of the homopolymer crystallites (T_{f1}) and the racemic crystallites (T_{f2}), estimated from Figure 2, are plotted as a function of X_D of the mixed polymers in Figure 3. Apparently, T_{f2} remains almost constant, independent of X_D in the range of 0.1–0.9, whereas T_{f1} decreases as X_D approaches 0.5, probably because the homopolymer crystallites become smaller and finally disappear. Thus, it is obvious that the most favorable X_D for the formation of racemic crystallites is 0.5, similar to the crystallization by the casting method.[22] For this reason, we fixed X_D always at 0.5 in the following experiments.

Enthalpies of fusion at T_{f1} (ΔH_{f1}) and at T_{f2} (ΔH_{f2}), estimated from Figure 2, are shown in Figure 4. Appar-

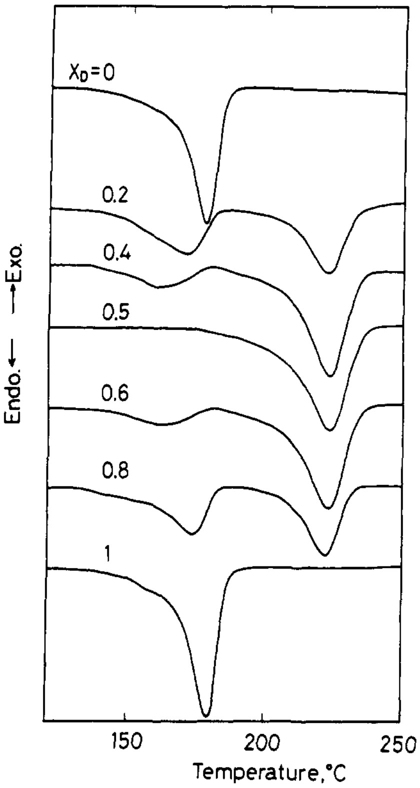

Figure 2. DSC thermograms of the precipitates from mixed solutions of D5 and L5 at various X_D (methylene chloride, 1 g/dL).

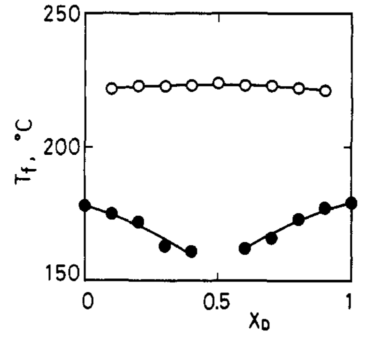

Figure 3. T_{f1} (●) and T_{f2} (○) of the precipitates from mixed solutions of D5 and L5 as a function of X_D (methylene chloride, 1 g/dL).

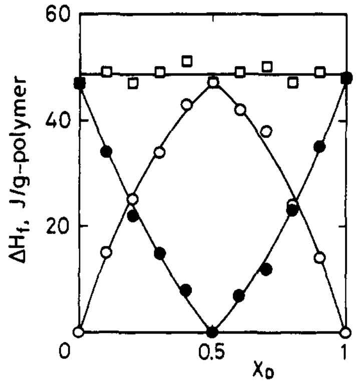

Figure 4. ΔH_{f1} (●), ΔH_{f2} (○), and their sum (□) for the precipitates from mixed solutions of D5 and L5 as a function of X_D (methylene chloride, 1 g/dL).

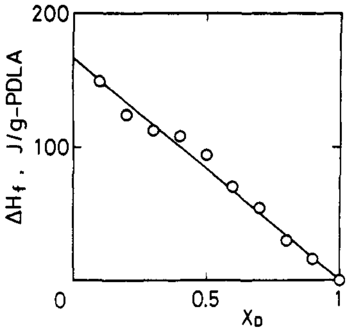

Figure 5. ΔH_{f2} per gram of PDLA calculated from the result of Figure 4 as a function of X_D.

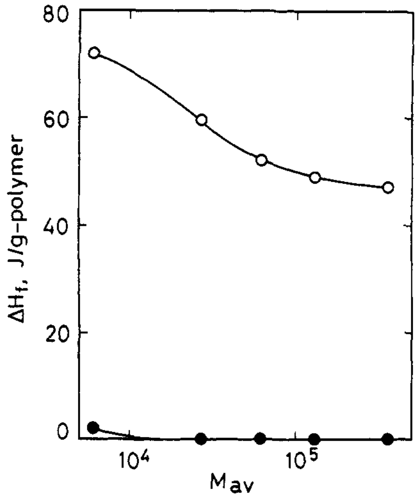

Figure 6. ΔH_{f1} (●) and ΔH_{f2} (○) of the precipitates from mixed solutions of PDLA and PLLA with similar molecular weights as a function of the average molecular weight of PDLA and PLLA (M_{av}) (X_D = 0.5; methylene chloride, 1 g/dL).

ently, X_D that gives the maximum ΔH_{f2} and the minimum ΔH_{f1} is again 0.5. The increase in ΔH_{f1} accompanying the larger X_D deviation from 0.5 suggests that the homopolymer present in excess cannot participate in the formation of racemic crystallites but aggregates by itself into the form of homopolymer crystallites. It is interesting to point out that the sum of ΔH_{f1} and ΔH_{f2} remains almost constant, regardless of X_D. This may be an indication that the racemic crystallites already formed do not hinder the subsequent homopolymer crystallization. Figure 5 shows ΔH_{f2} per gram of PDLA as a function of X_D. The values were calculated from Figure 4 using the following equation:

$$\Delta H_{f2}\ (\text{J/g of PDLA}) = \Delta H_{f2}\ (\text{J/g of polymer})/X_D \qquad (3)$$

It is clear that ΔH_{f2} per gram of PDLA increases linearly with the decreasing X_D. This suggests that the PDLA molecules can participate more effectively in the racemic crystallites as the counterpart of PDLA exists in larger excess.

3. Effect of Molecular Weight. 3-1. Similar Molecular Weights. The molecular weight dependence of the formation of racemic crystallites was investigated for the PDLA and PLLA pairs with similar molecular weights. Figure 6 shows ΔH_{f1} and ΔH_{f2} of the precipitates obtained from the mixed solutions of PDLA and PLLA as a function of the arithmetic mean of their molecular weight (M_{av} = $[\bar{M}_v(\text{PDLA}) + \bar{M}_v(\text{PLLA})]/2$). The pairs employed here are D1-L1, D2-L2, D3-L3, D4-L4, and D5-L5. As is seen, ΔH_{f1} is negligibly small in comparison with ΔH_{f2} for all the pairs to reveal that only the racemic crystallites are formed in the blended precipitates. The ΔH_{f2} value decreases with the increasing molecular weight of PLA and the highest ΔH_{f2} is observed for the PLA pair of the lowest molecular weight. However, it should be stressed that the racemic crystallites were generated even from the polymer pair having such a high molecular weight as 3.6×10^5. This is in marked contrast to the polymer blends

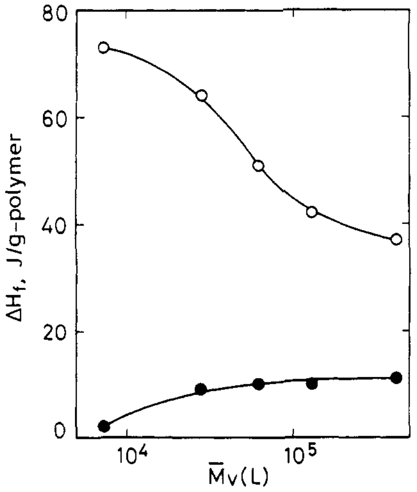

Figure 7. ΔH_{f1} (●) and ΔH_{f2} (○) of the precipitates from mixed solutions of D1 and PLLA with various molecular weights as a function of molecular weight of PLLA [$\bar{M}_v$(L)] (X_D = 0.5; methylene chloride, 1 g/dL).

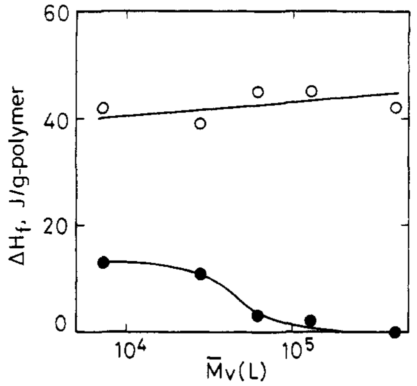

Figure 8. ΔH_{f1} (●) and ΔH_{f2} (○) of the precipitates from mixed solutions of D5 and PLLA with various molecular weights as a function of molecular weight of PLLA [$\bar{M}_v$(L)] (X_D = 0.5; methylene chloride, 1 g/dL).

obtained by casting the mixed solutions.[22]

3-2. Dissimilar Molecular Weights. ΔH_{f1} and ΔH_{f2}, calculated from the DSC endothermic peaks of the precipitates from the mixed solutions of D1 and PLLA of various molecular weights, are plotted as a function of the molecular weight of PLLA [$\bar{M}_v$(L)] in Figure 7. The polymer pairs employed are D1–L1, D1–L2, D1–L3, D1–L4, and D1–L6. It is clearly seen that ΔH_{f2} is much larger than ΔH_{f1} for all the molecular weights of PLLA, again supporting the assumption that the racemic crystallites are preferentially formed in the precipitate. ΔH_{f2} decreases and ΔH_{f1} increases with the increasing $\bar{M}_v$(L), probably because of more difficult crystallization of D1 with PLLA having higher molecular weights, resulting in enhanced homopolymer crystallization with the increasing molecular weight difference between PDLA and PLLA.

The pairs of a high molecular weight PDLA and different molecular weight PLLA were also investigated for their crystallization. They include D5–L1, D5–L2, D5–L3, D5–L4, and D5–L6. Figure 8 shows the results. It is seen that the racemic crystallization preferentially takes place, irrespective of the molecular weight of PDLA and PLLA or the molecular weight difference between PDLA and PLLA, similar to the finding in Figure 7. ΔH_{f1} increases and ΔH_{f2} decreases with the decreasing $\bar{M}_v$(L) or the increasing molecular weight difference between PDLA and PLLA. The increased ΔH_{f1} and the decreased ΔH_{f2} with the increase in the molecular weight difference between PDLA and PLLA in Figure 8 are also similar to the result in Figure 7, where PDLA with a low molecular weight was employed. The lower ΔH_{f2} than that in Figure 7 must be due to the high molecular weight of PDLA used.

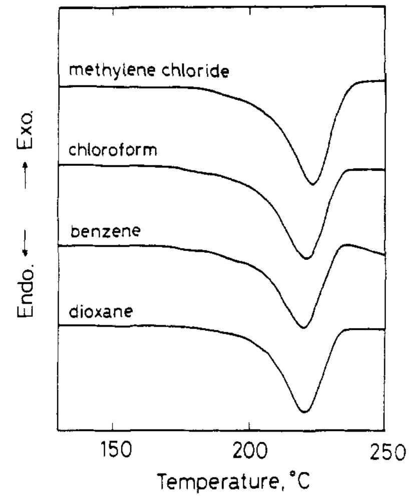

Figure 9. Solvent effects on DSC thermograms of the precipitates from mixed solutions of D5 and L5 (X_D = 0.5).

Table II
T_{f1}, T_{f2}, ΔH_{f1}, and ΔH_{f2} of Blends from D5 and L5 Solutions in Various Solvents

solvent	T_{f1}, °C	T_{f2}, °C	ΔH_{f1}, J/g of polymer	ΔH_{f2}, J/g of polymer
methylene chloride	-	224	0	47
chloroform	-	221	0	42
benzene	-	220	0	40
dioxane	-	221	0	45

4. Effect of Solvent. Figure 9 shows DSC thermograms of the polymer blends precipitated from the mixed solutions of D5 and L5 in different solvents. In the case of benzene, the PLA solutions were prepared at 0.1 g/dL and 60 °C and cooled to room temperature prior to mixing the solutions. The solubility of PLA with high molecular was so low in benzene that we could not prepare the 1 g/dL homogenous solution even on raising the temperature. The themograms given in Figure 9 show similar curves, irrespective of the solvent used, especially around T_{f2}. This insignificant effect of solvent on the racemic crystallization is similar to the finding on the blends obtained by the solution-casting method,[22] suggesting that the racemic crystallites are not yet formed in solution but during the precipitation process. T_{f1}, T_{f2}, ΔH_{f1}, and ΔH_{f2} detemined from Figure 9 are summarized in Table II. It is seen that, despite the relatively high molecular weight of employed polymers, only the racemic crystallization occurs, almost independent of the solvent used.

5. Effect of Solution Concentration. The dependence of racemic crystallization on the polymer concentration of mixed solution was insignificant for the polymer pairs of low molecular weights. However, the polymer concentration effect was observed for the high molecular weight PDLA and PLLA pairs. ΔH_{f1} and ΔH_{f2} of the precipitates from the mixed solution of D5 and L5 in methylene chloride are plotted in Figure 10 as a function of polymer concentration. As it was quite difficult to mix the concentrated solution of D5 with that of L5 into a homogenous solution because of its high viscosity, their 2.5 and 5 g/dL solutions were prepared by solvent evaporation of the 1 g/dL mixed solution of D5 and L5. The experiment was not performed for the polymer concentration below 0.001 g/dL because of the difficulty of collecting the precipitate dispersed in a great amount

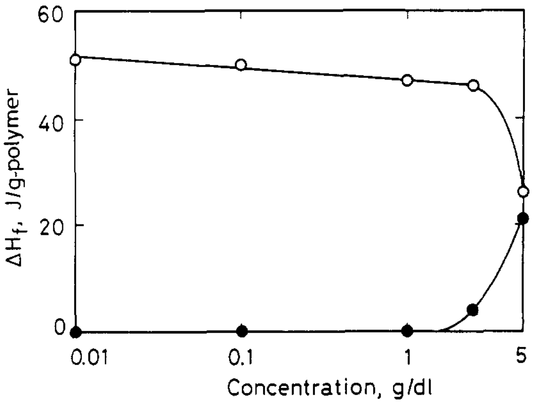

Figure 10. ΔH_{f1} (●) and ΔH_{f2} (○) of the precipitates from mixed solutions of D5 and L5 at various concentrations ($X_D = 0.5$; methylene chloride).

of nonsolvent. As is apparent from Figure 10, the ΔH_{f2} change is not remarkable in the polymer concentration range from 0.01 to 2.5 g/dL but drastically occurs from 46 to 26 J/g of polymer above 2.5 g/dL. On the other hand, ΔH_{f1} is absolutely zero over the polymer concentration range from 0.01 to 1 g/dL and rapidly increases as the polymer concentration becomes higher than 2.5 g/dL. Almost the same amount of homopolymer crystallites as that of the complex ones was formed at 5 g/dL. The effect of solution concentration is reproducible at a higher concentration above 2.5 g/dL.

Discussion

In our previous DSC study on the cast films from PDLA and PLLA, it was found that the homopolymer crystallites were predominantly formed in comparison with the racemic crystallites, so far as both PDLA and PLLA had a high molecular weight such as 1 × 10^5.[22] In the casting process, the polymer concentration was allowed to gradually increase from 1 g/dL to the infinite concentration to produce a dry film containing no solvent. Once the racemic crystallites were formed from PDLA and PLLA at a high concentration, they were no more soluble in the solvent used for casting even by either raising the solution temperature or diluting the solution with the solvent. Thus, the preferable formation of the homopolymer crystallites in the cast films from the high molecular weight PDLA and PLLA pairs reveals that microscopic phase separation must have occurred in the course of condensation of the cast solution. In other words, microscopic phase separation into the PDLA-rich and the PLLA-rich regions seems to have occurred in the solution of the polymer pairs of high molecular weight during the solution condensation, resulting in microscopic fractuation of X_D from 0.5 in solution. This is a favorable condition for the homopolymer crystallization.

Also in the precipitation process, such microscopic phase separation is likely to take place as the nonsolvent molecules diffuse into the polymer solution, at least, unless any stirring is given to the mixture of the solution and the nonsolvent. This is depicted in Figure 11a. As is evident from Figure 1, stirring is needed for the racemic crystallization to take place when the precipitation method is employed for blending the polymer pairs of high molecular weights. Without stirring, the PLA molecules may go into the microscopically phase-separated state, as the nonsolvent gradually diffuses into the PLA solution. Consequently, the homopolymer crystallites may be predominantly formed in the separated phases during precipitation without vigorous stirring, similar to the solution casting.

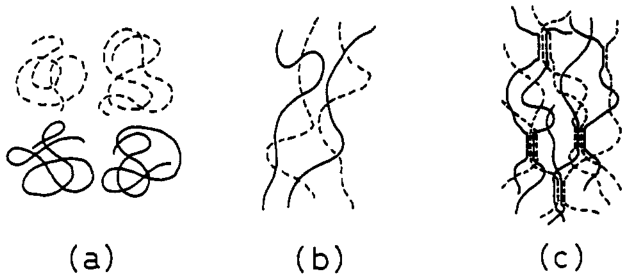

Figure 11. Mechanism of the racemic crystallization of PDLA and PLLA through precipitation (—: PDLA, - - -: PLLA): (a) without stirring, (b) under stirring, (c) racemic crystallization.

On the other hand, strong mixing between the polymer solution and the nonsolvent must take place quite quickly when stirred, so that the racemic crystallization between the dissimilar PLA chains will take place before the microscopic phase separation starts in solution. This may be one of the reasons for the preferential racemic crystallization which takes place, independent of the molecular weight, during the precipitation process under vigorous stirring. The well-mixed molecules may readily undergo the racemic crystallization. The molecular processes are schematically illustrated in parts b and c of Figure 11.

The other explanation for the preferential racemic crystallization under vigorous stirring is the following. The coils must interpenetrate those of the isomer for racemic crystallization to take place. Interpenetration between PDLA and PLLA both with high molecular weights is incomplete prior to crystallization under static condition because the coil is large, which leads to poor formation of the racemic crystallites. Stirring promotes interpenetration by elongating the coils and reducing a lateral dimension. Therefore, the racemic crystallites are formed preferentially.

It seems reasonable that one polymer component remaining in excess after the racemic crystallization will be inevitably involved in the subsequent homopolymer crystallization, when PDLA and PLLA are mixed together at a nonequimolar ratio. However, the reason is not clear to us why the racemic crystallization is suppressed while the homopolymer crystallization prevails, when there is a big difference in molecular weight between PDLA and PLLA, even if they are mixed at their equimolar ratio (Figures 7 and 8). One plausible reason for that is aggregation of the higher molecular weight component molecules by themselves upon contacting with the nonsolvent molecules before the lower molecular weight component molecules encounter them to form the racemic crystallites.

Finally, we roughly estimate the enthalpy of fusion of the racemic crystallites at $X_D \rightarrow 0$. As demonstrated in Figure 5, the racemic crystallinity seems to linearly increase with an increase in the PLLA amount in the mixed solution of PDLA and PLLA. Thus, extrapolation of X_D to zero gives 168 J/g of PDLA. As this value is based on PDLA only, the enthalpy of fusion of the racemic crystallites expressed in the conventional unit should be divided by a factor of 2. This gives 84 J/g of polymer or 1.4 kcal/mol as the enthalpy of fusion of the racemic crystallites at $X_D \rightarrow 0$. This must be very close to the enthalpy of fusion of the 100% racemic crystallites. The obtained value is much smaller than that reported by Loomis et al. (142 J/g of polymer).[21]

Conclusion

The thermodynamically stable racemic crystallization takes place in preference to the homopolymer crystallization, independent of the molecular weight of PDLA and PLLA, when precipitation of the blend polymers is carried out from their mixed solution at a low polymer concentration under vigorous stirring. This is in contrast to the solution casting, which failed in producing the racemic crystallites when both of the component polymers had a high molecular weight. It is likely that when the mixed solution comes into contact with the nonsolvent under stirring, association of the dissimilar polymer chains takes place very quickly before the solution goes into microscopic phase separation.

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Registry No. PDLA (homopolymer), 106989-11-1; PLLA (homopolymer), 26811-96-1; methylene chloride, 75-09-2; chloroform, 67-66-3; benzene, 71-43-2; dioxane, 123-91-1; PDLA (SRU), 26917-25-9; PLLA (SRU), 26161-42-2.