Blends of Aliphatic Polyesters. I. Physical Properties and Morphologies of Solution-Cast Blends from Poly(DL-lactide) and Poly(ε-caprolactone)

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SYNOPSIS

Effects of the mixing ratio of poly(DL-lactide) (PDLLA) and poly(ε-caprolactone) (PCL) on the thermal and mechanical properties and morphologies of the solution-cast blends were investigated by differential scanning calorimetry (DSC), polarizing microscopy, tensile tests, and dynamic mechanical analysis. The presence of amorphous PDLLA did not disturb crystallization of PCL over the PDLLA content [X_{PDLLA} = PDLLA/(PCL + PDLLA)] from 0.1 to 0.9 and allowed PCL to form spherulites over X_{PDLLA} ranging from 0.1 to 0.6. The spherulite radius was larger for the blends than for the nonblended PCL. Phase separation occurred for the blends with X_{PDLLA} between 0.1 and 0.9. T_m of PCL remained unchanged in the X_{PDLLA} range up to 0.6 but decreased at X_{PDLLA} above 0.6, whereas the crystallinity of PCL was constant around 60%, irrespective of X_{PDLLA}. The tensile strength (σ_B), the yield stress (σ_Y), the Young's modulus (E), and the storage modulus (G') of the blends increased monotonously with X_{PDLLA} if σ_B at X_{PDLLA} = 0 and 0.6 and σ_Y at X_{PDLLA} = 0.6 were excluded. Elongation-at-break (ε_B) of PDLLA increased dramatically, while ε_B of PCL decreased remarkably when a small amount of the other component was added. Equations and parameters predicting σ_Y, E, and G' of the PCL-PDLLA blends were proposed as a function of X_{PDLLA}. © 1996 John Wiley & Sons, Inc.

INTRODUCTION

Recently, much attention has been paid to degradable aliphatic polyesters such as poly(L-lactide) (PLLA), poly(D-lactide) (PDLA), poly(DL-lactide) (PDLLA), poly(glycolide), poly(β-hydroxybutyrate), poly(ε-caprolactone) (PCL), and their copolymers because they are biodegradable in the human body as well as in the earth. For their practical applications, however, they should have proper properties with respect to mechanical strength, degradation, and drug release, depending on their application purposes. PLLA, PDLA, and PDLLA are in the glassy state at room temperature with T_g around 50°C,[1-5] while PCL is in the rubbery state at room temperature with T_g around −60°C.[6-10]

Random and block copolymers of lactide and ε-caprolactone have been utilized for regulating the degradation rate,[9,11-13] mechanical properties,[9,10] and drug release profiles.[10,14] On the other hand, simple physical blending between two of these polymers may also produce biodegradable materials having a variety of physical properties. Indeed, the following blend pairs from PLLA, PDLA, PDLLA, and PCL have been investigated:

1. PLLA and PDLLA;[15-17]
2. PLLA and poly(L-lactide-co-glycolide);[18,19]
3. PLLA and poly(L-lactide-co-ε-caprolactone);[18,19]
4. PDLA and D-lactide-rich poly(lactide);[15]
5. PDLA and poly(D-lactide-co-glycolide);[20]
6. PCL and poly(L-lactide-co-glycolide);[19]
7. PLLA and PDLA;[15,20-36]
8. PDLA and L-lactide-rich poly(lactide);[15]

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Table I Molecular Characteristics of the Polymers

	$[\eta]$ (dL/g)	$\bar{M}_v$ (g/mol)	M_n (g/mol)	M_w (g/mol)	M_w/M_n
PDLLA	1.95	1.33×10^5	2.00×10^5	3.25×10^5	1.63
PCL	1.45	1.20×10^5	1.38×10^5	2.66×10^5	1.93

9. PLLA and poly(D-lactide-b-ε-caprolactone);[37] and

10. PDLA and poly(L-lactide-co-glycolide).[20]

Blends 1–6 are different from those of blends 7–10 in that the latter blends form stereocomplex (racemic crystallites) between the L-lactide monomer sequences and the D-lactide monomer sequences.[29,30] Blends 1–6 have been studied mostly on the degradation and drug release properties but not on the mechanical properties.[18,19]

Recently Domb showed that a blend from PDLLA and PCL, both of a low molecular weight (M_W = 2000), formed a homogeneous phase both in solution and melt blending.[38] However, there have been few reports on blends from high molecular weight PDLLA and PCL. Cha and Pitt concluded on the basis of no change in the crystallinity of PCL (M_n = 7.6 × 10⁴) in the presence of PLLA (M_n = 2 × 10⁴) that they were immiscible when solution-cast blends were compression-molded.[19]

The purpose of this work is to study the effects of polymer mixing ratio on the mechanical and thermal properties and morphology of solution-cast blends from PDLLA and PCL. In this work, blends were obtained by solution casting instead of melting of mixed polymers because melting at high temperatures causes degradation of aliphatic polyesters and transesterification between them.

EXPERIMENTAL

Materials

PDLLA and PCL were synthesized with the method reported previously.[39] DL-lactide was purchased from Tokyo Kasei Kogyo Co. Ltd., Tokyo, Japan, and purified by repeated recrystallization using ethyl acetate as solvent. ε-Caprolactone was purchased from Nakarai Tesque Co. Ltd., Kyoto, Japan, and purified by distillation under a reduced pressure. Ring-opening polymerization was performed for DL-lactide and ε-caprolactone in bulk at 140°C for 10 and 72 h, respectively, using stannous octoate (0.03 wt %) as the polymerization catalyst.[40] The resulting polymer

was purified by reprecipitation using acetone and methylene chloride as the solvent for PDLLA and PCL, respectively, and methanol as the precipitant for both the polymers.

The viscosity-average molecular weight ($\bar{M}_v$) of the polymers was determined from the intrinsic viscosity (η) using the following equations reported for PDLLA by Schindler and Harper[41] and for PCL by Koleske and Lundberg.[42]

$$[\eta] = 2.21 \times 10^{-4} \, \bar{M}_v^{0.77}$$

(PDLLA in chloroform at 25°C)   (1)

$$[\eta] = 9.94 \times 10^{-5} \, \bar{M}_v^{0.82}$$

(PCL in benzene at 30°C)   (2)

M_W and M_n were evaluated using a Tosoh GPC system with TSK-GEL columns ($GMH_{XL} \times 2$) and polystyrene as standard. Molecular characteristics of the polymers are given in Table I.

Blend films were prepared with a solution casting method using methylene chloride as cosolvent. Methylene chloride solutions having different PDLLA and PCL contents were prepared at a total polymer concentration of 1.0 g/dL and then cast onto flat glass plates, followed by solvent evaporation at room temperature for approximately 1 week. To avoid reaching a dried state of quasi-equilibrium, the solvent evaporation was performed very slowly as reported in previous papers (ca. 1 week).[15,20,23] The resulting films were dried in vacuo for 1 week and stored at room temperature for more than 1 month so that equilibrium could be attained. Differential scanning calorimetry (DSC), tensile tests, and dynamic mechanical relaxation tests were performed on the samples of 50 μm thickness, while the morphology study was performed on those of 25 μm thickness.

Measurements

The glass transition and melting temperatures (T_g and T_m, respectively) and the enthalpy of fusion (ΔH_m) of the blends were determined with a Shimadzu DT-50Q differential scanning calorimeter equipped with a liquid nitrogen quenching system.

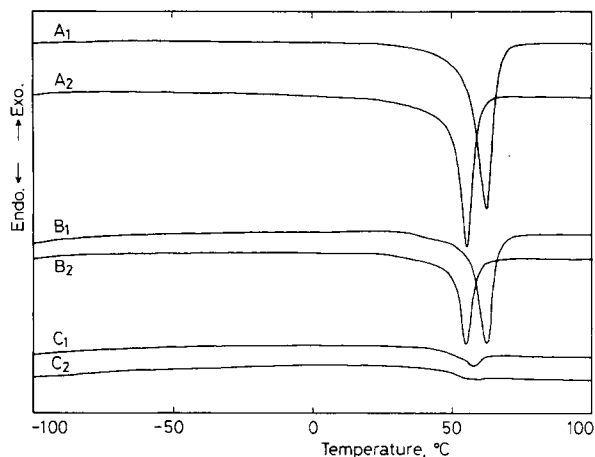**Figure 1** DSC thermograms of the equimolar blend and nonblended PDLLA and PCL: (A_1) nonblended PCL (1st run); (A_2) nonblended PCL (2nd run); (B_1) equimolar blend (1st run); (B_2) equimolar blend (2nd run); (C_1) nonblended PDLLA (1st run); (C_2) nonblended PDLLA (2nd run).

For the first run, the samples were cooled to ca. $-140°C$ and then heated to $100°C$ under a nitrogen gas flow at a rate of $10°C/min$, while the second run was performed on the sample used for the first run under the same condition as the first run after quick quenching from 100 to ca. $-140°C$. T_g, T_m, and ΔH_m were calibrated using indium as the standard. The glass transition temperature of PCL in the blends could not be evaluated accurately because its transition was too small. In addition, the glass transition of PDLLA (ca. $50°C$) and melting of PCL (ca. $60°C$)[43,44] were overlapped in the DSC thermogram. We evaluated the transition enthalpy from the area surrounded by DSC original spectrum and the extrapolated line of the baseline after transition. The crystallinity of PCL ($x_{c,PCL}$) was calculated under the assumption that the enthalpy of glass transition of the blends per gram of PDLLA was constant and the same as that of nonblended PDLLA ($\Delta H_{g,PDLLA} = 4$ and 0 J/g of PDLLA for first and second runs, respectively). Under this assumption, $x_{c,PCL}$ was calculated for different PDLA contents (X_{PDLLA}) by the following equations.

$$x_{c,PCL} (\%) = (\Delta H_t - \Delta H_{g,PDLLA} \cdot X_{PDLLA})$$
$$\cdot 100/[(1 - X_{PDLLA}) \cdot 142] \quad (3)$$

$$X_{PDLLA} (w/w) = PDLLA/(PCL + PDLLA) \quad (4)$$

where ΔH_t (J/g of polymer) is the enthalpy of overall transition including the glass transition enthalpy of PDLLA and melting enthalpy of PCL, and 142

(J/g of PCL) is the melting enthalpy of PCL with 100% crystallinity reported by Crescenzi et al.[44]

Morphology of blend films was studied with a Zeiss polarizing microscope. Films of 25 μm thickness exhibited a morphology very similar to those of 50 μm. Since the optical contrast of 25 μm films was much clearer than that of 50 μm, the photos of 25 μm films alone will be shown below.

Tensile properties of blend films were measured at $25°C$ and 50% relative humidity using a tensile tester at a crosshead speed of 100%/min. The initial length of the specimen was always kept to 20 mm. The dynamic mechanical analysis of blends was performed using Orientec Rhovibron DDV-01FP at 35 Hz and a heating rate of $4°C/min$.

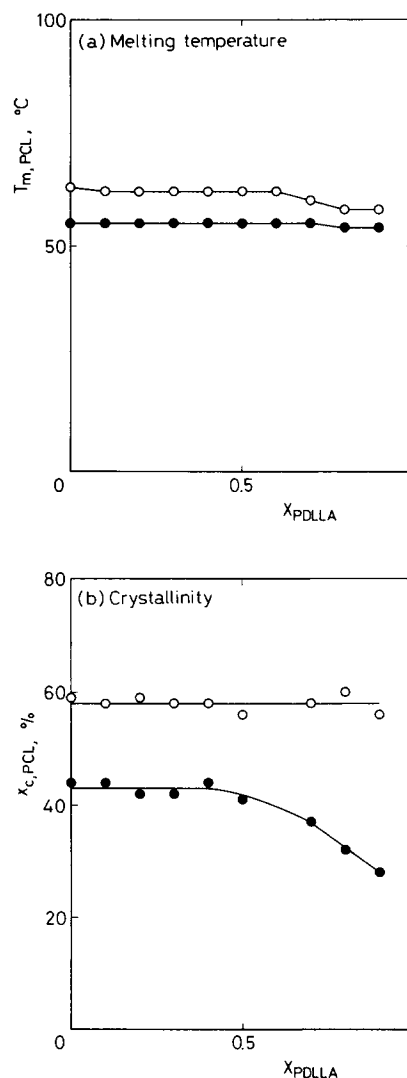**Figure 2** Melting temperature [$T_{m,PCL}$; (a)] and crystallinity [$x_{c,PCL}$; (b)] of PCL in the blends as a function of X_{PDLLA}: (O) 1st run; (●) 2nd run.

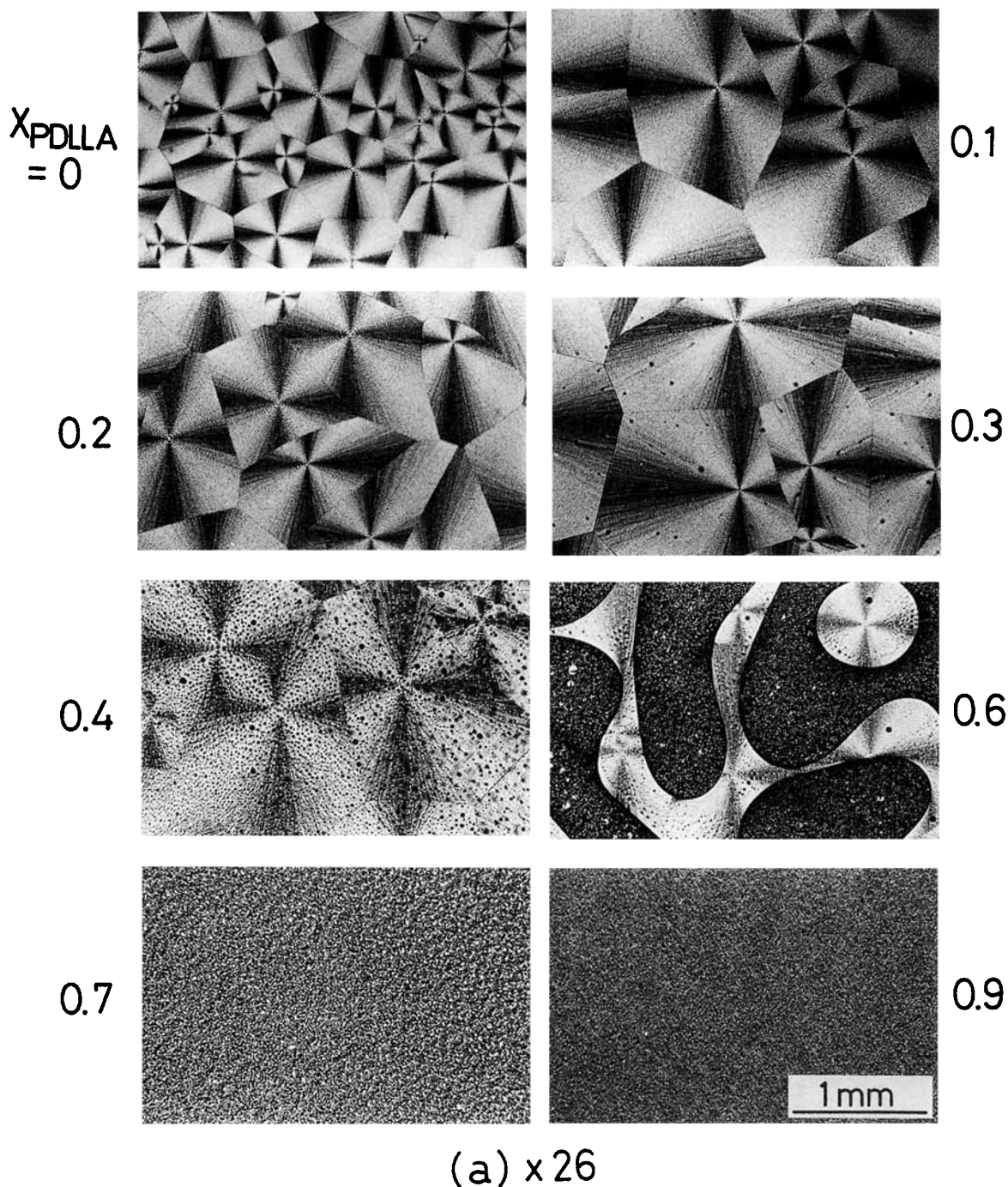**Figure 3**   Photomicrographs of the blends with different X_{PDLLA} [×26; (a)] and magnification for X_{PDLLA} = 0.7 [×105; (b)].

RESULTS

Differential Scanning Calorimetry

Figure 1 shows DSC thermograms of first and second runs for the equimolar blend and the nonblended PDLLA (DLLA homopolymer) and PCL (CL homopolymer). The transition observed around 50 and 60°C on the first run is the glass transition of PDLLA[1-5] and the melting of PCL,[43,44] respectively. Clearly, the melting peak of PCL in the blend is quite similar to that of the nonblended PCL in shape and position both for the first and second runs, though the melting peak on the first run in the blend as well as in the nonblended PCL shifts to lower temperature on the second run. The absence of PCL
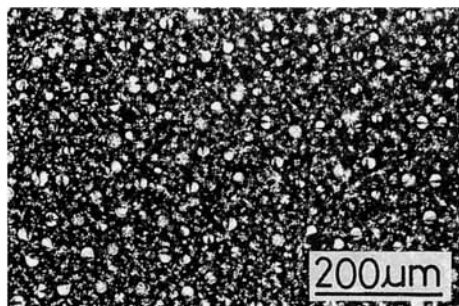
(b) $X_{PDLLA} = 0.7$, $\times 105$

Figure 3 *(Continued from the previous page)*

crystallization peak on the second scanning both for the blend and the nonblended PCL suggests that PCL rapidly crystallized during quenching from the melt with liquid nitrogen. The difference in the DSC spectrum between the first and the second scan may be ascribed to the larger lamella thickness of PCL in the spherulites formed by prolonged drying of the cast blend films rather than to that of the PCL spherulites of the second run formed during quenching with liquid nitrogen.

Figure 2 shows the melting temperature [$T_{m,PCL}$ (°C)] and the crystallinity [$x_{c,PCL}$ (%)] of PCL in blends with different X_{PDLLA} for the first and second runs. The $x_{c,PCL}$ value for $X_{PDLLA} = 0.6$ is not given in Figure 2(b) because large domains of 1 mm size were formed in the films, which made the $x_{c,PCL}$ estimation from DSC difficult. As is evident from the result of first run, $T_{m,PCL}$ is almost constant for X_{PDLLA} between 0 and 0.6 but lowers from 62 to 58°C when X_{PDLLA} further increases from 0.6 to 0.8. On the other hand, $x_{c,PCL}$ remains constant around 60% for X_{PDLLA} between 0 and 0.9, in contrast with the solution-cast blend from amorphous PDLLA and crystallizable PLLA, which formed no crystallite at ratios of PDLLA/(PLLA + PDLLA) above 0.8.[45]

During the second DSC run of the sample quenched from the melt to a lower temperature than the glass transition of PCL, the scanning curves showed a melting peak but no crystallization peak, irrespective of X_{PDLLA}. This indicates again that rapid crystallization of PCL occurred in the blend films during quenching with liquid nitrogen. This rapid crystallization of the nonblended PCL during quenching is in good agreement with the result reported by Koleske and Lundberg.[6] As is apparent from Figure 2(a), $T_{m,PCL}$ of the second run remains constant for all the blends, although lower than that of the first run. On the other hand, as is seen in Figure 2(b), $x_{c,PCL}$ of the second run is smaller than

that of the first run for all the blends and is constant for X_{PDLLA} between 0 and 0.4 but decreases when X_{PDLLA} is above 0.5.

Morphology

Figure 3 shows photomicrographs of blends with different X_{PDLLA}. PCL spherulites (light domains) are clearly observed for the blends with X_{PDLLA} between 0 and 0.4 but become more disordered with the increasing X_{PDLLA}, finally disappearing or becoming very small when X_{PDLLA} is above 0.7. The largest radius of spherulites is approximately 0.5 mm at $X_{PDLLA} = 0$ (nonblended PCL) and 1 mm at X_{PDLLA} between 0.1 and 0.4. The spherulite density (SD) decreases dramatically when X_{PDLLA} changes from 0 to 0.1 but remains almost constant for X_{PDLLA} between 0.1 and 0.4. The SD value calculated from Figure 3(a) is given in Table II. To compare the SD of the blends with that of the nonblended PCL, SD was normalized to unit area of PCL using the following equation:

normalized SD (number/mm^2)

$$= \text{nonnormalized SD}/(1 - X_{PDLLA}) \quad (5)$$

The normalized SD is given in Table II.

It is seen in Figure 3 that phase separation occurs for the blends with X_{PDLLA} at least between 0.3 and 0.7 during solvent evaporation of the mixed solution of PDLLA and PCL. Dark round spots with the average size of 50 μm are observed in the PCL spherulites for the blend films of $X_{PDLLA} = 0.3$ and 0.4, while a large number of small PCL crystallite assemblies and continuous dark domain are noticed for the blends with $X_{PDLLA} = 0.6$ and 0.7. The dark round spots must be composed of amorphous PDLLA and contain practically no PCL because no PCL crystallite is observed in the dark round regions and no decrease in $x_{c,PCL}$ is observed for the blends.

Table II Spherulite Density (SD) of the Blends with Different X_{PDLLA}

X_{PDLLA}	Nonnormalized SD (Number/mm^2)	Normalized SD[a] (Number/mm^2)
0	4.9	4.9
0.1	0.9	1.0
0.2	1.3	1.6
0.3	0.9	1.3
0.4	0.9	1.5

[a] Normalized SD = nonnormalized SD/(1 − X_{PDLLA}).
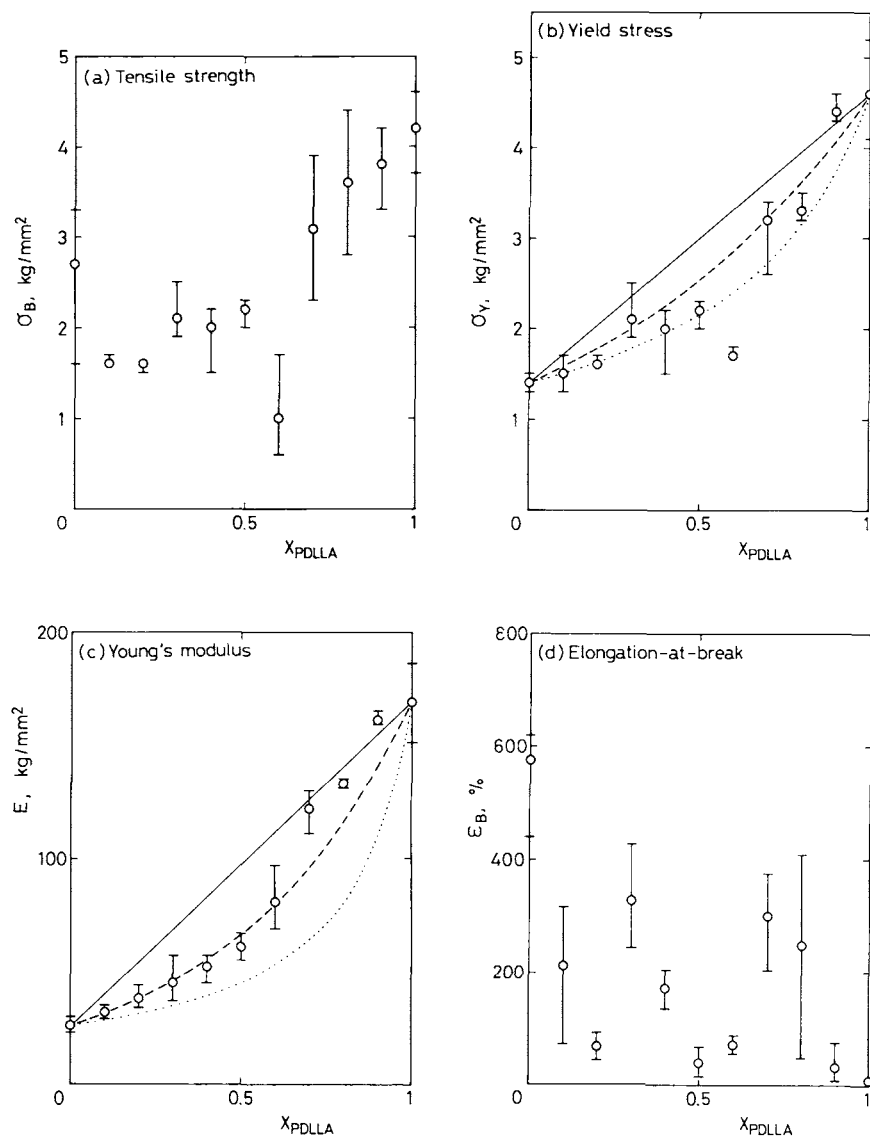
Figure 4 Tensile strength [σ_B; (a)], yield stress [σ_Y; (b)], Young's modulus [E; (c)], and elongation-at-break [ε_B; (d)] of the blends as a function of X_{PDLLA}: (———) calculated using eq. (6) with $n = 1$; ($\cdots\cdots$) calculated using eq. (6) with $n = -1$; (----) calculated using eq. (7).

Tensile Properties

Tensile strength (σ_B), yield stress (σ_Y), Young's modulus (E), and elongation-at-break (ε_B) of the blend films are plotted as a function of X_{PDLLA} in Figure 4. The modulus increases monotonously with an increase in X_{PDLLA} with larger slopes for X_{PDLLA} above 0.5 than those of X_{PDLLA} below 0.5. Both σ_B and σ_Y show a behavior similar to E, if σ_B for $X_{\mathrm{PDLLA}} = 0$ and 0.6 and σ_Y for $X_{\mathrm{PDLLA}} = 0.6$ are excluded. The highest ε_B is observed at $X_{\mathrm{PDLLA}} = 0$, and the lowest at $X_{\mathrm{PDLLA}} = 1$, while relatively small ε_B values are found at $X_{\mathrm{PDLLA}} = 0.2$ and 0.5. Clearly, ε_B of PCL decreases remarkably when a

small amount of PDLLA is added, whereas ε_B of PDLLA shows a dramatic increase upon addition of a small amount of PCL. This result is similar to that of blends from glassy poly(β-hydroxybutyrate) and rubbery PCL.[46]

Dynamic Mechanical Properties

The storage modulus (G') and loss tangent (tan δ) of blends with different X_{PDLLA} are plotted as a function of temperature in Figure 5. We could not measure G' and tan δ at temperatures above 50°C due to very high elongations of the films. G' of the
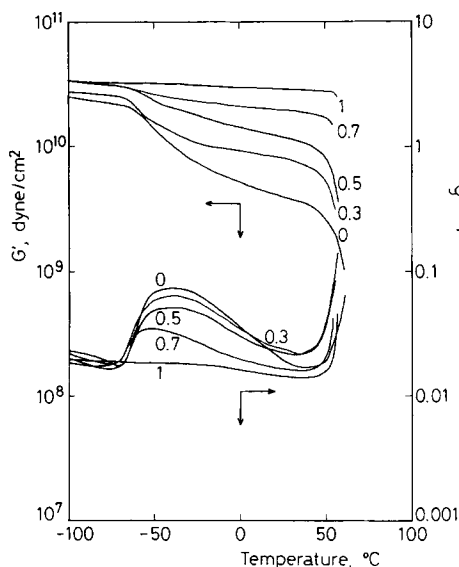
Figure 5 Storage modulus (G') and loss tangent (tan δ) of the blends with different X_{PDLLA}.

nonblended PCL decreases monotonously above $-60°C$, and a dramatic decrease occurs above $60°C$. Tan δ has a broad peak around $-40°C$ and a dramatic increase above $50°C$. The transitions around -60 and $50°C$ are assigned to the glass transition and the melting of PCL, respectively, as demonstrated by Koleske and Lundberg[6] and Wada et al.[10] On the other hand, G' and tan δ of the nonblended PDLLA remain unvaried below $50°C$, whereas G' decreases and tan δ increases markedly above $50°C$. The transition around $50°C$ is assigned to the glass transition of the nonblended PDLLA, as reported elsewhere,[3] by Migliaresi et al.,[4] and also by Celli and Scandola[5] for the nonblended isotactic PLLA.

G' and tan δ of the blends with $X_{PDLLA} = 0.3$, 0.5, and 0.7 are similar to those of the nonblended PCL, except that the peak height of tan δ around $-40°C$ and the slope of G' above $-40°C$ decreases with the increasing X_{PDLLA}. The G' value of the blends at temperatures between T_g of PCL and PDLLA increases monotonously with X_{PDLLA}. No effect of blending with PDLLA is observed on the glass transition and melting temperatures of PCL. This is in contrast with miscible blends of PCL with PVC,[6] nitrocellulose,[47] or phenoxy,[47] where T_g of the blends fit well with the Fox expression[48] to suggest that PCL and PDLLA are phase-separated. G' of the blends at $25°C$ is plotted as a function of X_{PDLLA} in Figure 6. As is evident, G' of the blends increases monotonously with the increasing X_{PDLLA}. Such a dependence of G' on X_{PDLLA} is observed over the temperature range between -60 and $60°C$.

DISCUSSION

As demonstrated in Figures 1-3 and 5, DSC, polarizing microscopy, and dynamic mechanical analysis suggest that mixing of PDLLA and PCL solutions undergoes phase separation after the solvent evaporation. In addition, polarizing microscopy has revealed that PCL could form spherulites in the blends with the decreased normalized SD when X_{PDLLA} was between 0.1 and 0.4. If PDLLA and PCL were phase-separated perfectly before PCL spherulite nucleus formation and PDLLA had simply a volume-filling effect as a diluent, the normalized SD at $X_{PDLLA} = 0.1$ would not decrease so significantly but would remain almost constant, irrespective of X_{PDLLA}. The addition of PDLLA must have affected the formation of the PCL spherulite nuclei, similar to aliphatic polyesters blended with a small amount of poly(vinyl butyral) or poly(vinyl chloride)[49] and to solution and melt blends of PDLLA and PLLA.[45,16,17] A decrease in the normalized SD by addition of PDLLA suggests that phase separation must have taken place during the spherulite formation or crystallization of PCL in the blends. When PDLLA was a minor component ($X_{PDLLA} = 0.3$ and 0.4), PDLLA molecules excluded during the crystallization and spherulite growth of PCL would assemble themselves to form dark spots in PCL spherulites, as observed by polarizing microscopy. When PDLLA was a major component ($X_{PDLLA} \geq 0.7$), PCL molecules formed small crystallite assemblies surrounded by a continuous PDLLA dark domain. This was also observed as a phase-separated structure by polarizing microscopy. In spite of these results, we cannot conclude that PCL is immiscible with PDLLA be-
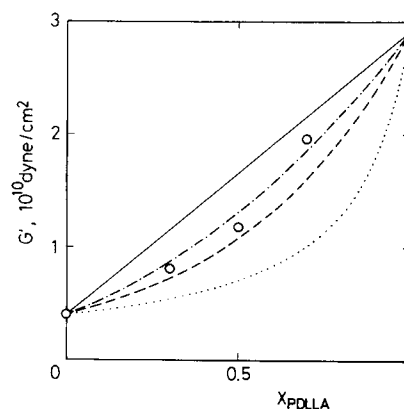

Figure 6 Storage modulus (G') of the blends at $25°C$ as a function of X_{PDLLA}: (——) calculated using eq. (6) with $n = 1$; (– · – ·) calculated using eq. (6) with $n = 0.4$; (· · · ·) calculated using eq. (6) with $n = -1$; (----) calculated using eq. (7).

Table III   The Range of X_{PDLLA} Fitting Eq. (6) and (7) for Mechanical Properties of the Blends

	Equation (6)			Equation (7)
	n = -1	n = 0.4	n = 1	
σ_Y	$0 \leqq X_{\text{PDLLA}} \leqq 0.5$			$0.7 \leqq X_{\text{PDLLA}} \leqq 1$
E			$0.7 \leqq X_{\text{PDLLA}} \leqq 1$	$0 \leqq X_{\text{PDLLA}} \leqq 0.6$
G'		$0 \leqq X_{\text{PDLLA}} \leqq 1$		

cause there is the probability that the cosolvent molecules have induced the phase separation during solvent evaporation.

Plots of mechanical properties of the PCL-PDLLA blends as a function of X_{PDLLA} yielded monotonous curves at least for σ_Y, E, and G', as seen in Figures 4(b) and (c), and Figure 6. The dependence of the mechanical properties on X_{PDLLA} can be accounted for quantitatively if we use the following equations proposed by Nielsen[50,51] for polymer blends system.

$$P(X_{\text{PDLLA}})^n = X_{\text{PDLLA}} \cdot P(\text{PDLLA})^n$$
$$+ (1 - X_{\text{PDLLA}}) \cdot P(\text{PCL})^n \quad (6)$$
$$\log P(X_{\text{PDLLA}}) = X_{\text{PDLLA}} \cdot \text{Log } P(\text{PDLLA})$$
$$+ (1 - X_{\text{PDLLA}}) \cdot \text{Log } P(\text{PCL}) \quad (7)$$

where $P(X_{\text{PDLLA}})$ is a physical property of PCL-PDLLA blends at a given X_{PDLLA}, while $P(\text{PCL})$ and $P(\text{PDLLA})$ express a physical property of the nonblended PCL and PDLLA, respectively. Equation (6) becomes identical to eq. (7) when n approaches 0. Equation (7) is known as logarithmic rules of polymer blends. Equation (6) represents a series and a parallel model when $n = -1$ and 1, respectively. The curves calculated using eq. (6) with $n = -1$ and 1 and eq. (7) are given in Figures 4(b) and (c). As can be seen, the σ_Y values obtained for X_{PDLLA} below 0.5 are in agreement with those calculated using eq. (6) with $n = -1$, while σ_Y for X_{PDLLA} above 0.7 agree with those calculated using eq. (7). On the other hand, E for X_{PDLLA} below 0.6 are in agreement with those predicted by eq. (7), while E for X_{PDLLA} above 0.7 agree with those calculated using eq. (6) with $n = 1$. The results are summarized in Table III. It should be stressed that the agreement of the experimental values with those calculated using eq. (6) and (7) does not support the validity of application of the simplified models to our system.

The G' values calculated using eq. (6) with -1, 0.4, and 1 and eq. (7) are given in Figure 6. They are roughly in agreement with the observed values,

similar to σ_Y and E. The observed G' shows better agreement with that calculated when the eq. (6) with $n = 0.4$ is used. In contrast with these polymer blends, G' of copolymers from DL-lactide and ε-caprolactone showed a minimum at a DL-lactide/ε-caprolactone ratio around 4/6, although T_g decreased monotonously with an increase in the ε-caprolactone content in the copolymers.[9,10] This denotes that T_g of the copolymers is not directly correlated with the mechanical properties of the copolymers.

The discontinuous dependence of σ_B and σ_Y on X_{PDLLA} at 0.6 can be explained in terms of lacking in a continuous phase for this blend due to formation of large domains observed at $X_{\text{PDLLA}} = 0.6$ by polarizing microscopy. A significant decrease in σ_B and ε_B of PCL by the addition of a small amount of PDLLA seen in Figures 4(a) and (d) must be related to disordering of the spherulite structure of PCL by the added PDLLA molecules. If we exclude some deviation of the observed data from the data calculated, it may be concluded that simple physical mixing of PCL with PDLLA can produce blends with a wide variety of physical properties without the help of copolymerization of CL and DLLA monomers.

REFERENCES

1. A. M. Reed and D. K. Gilding, Polymer, 20, 1459 (1979).
2. B. Kalb and A. J. Pennings, Polymer, 21, 607 (1980).
3. K. Jamshidi, S.-H. Hyon, and Y. Ikada, Polymer, 29, 2229 (1988).
4. C. Migliaresi, D. Cohn, A. De Lollis, and L. Fambri, J. Appl. Polym. Sci., 43, 83 (1991).
5. A. Celli and M. Scandola, Polymer, 33, 2699 (1992).

6. J. V. Koleske and R. D. Lundberg, *J. Polym. Sci., Part A-2,* **7,** 795 (1969).
7. A. Schindler, R. Jeffcoat, G. L. Kimmel, C. G. Pitt, M. E. Wall, and R. Zeidinger, in *Contemporary Topics in Polymer Science,* E. M. Pearce and J. R. Schaefgen, Eds., Plenum, New York, Vol. 2, 1977, p. 251.
8. C. G. Pitt, A. R. Jeffcoat, R. A. Zweidinger, and A. Schindler, *J. Biomater. Res.,* **13,** 497 (1979).
9. S.-H. Hyon, W.-I. Cha, and Y. Ikada, *Polym. Prepr. Japan,* **39,** 2319 (1990).
10. R. Wada, S.-H. Hyon, and Y. Ikada, *Pharm. Res.,* **8,** 1292 (1991).
11. C. G. Pitt, M. M. Gratzl, G. L. Kimmel, J. Surles, and A. Schindler, *Biomaterials,* **2,** 215 (1981).
12. X. D. Feng, C. X. Song, and W. Y. Chen, *J. Polym. Sci., Polym. Lett. Ed.,* **21,** 593 (1983).
13. T. Nakamura, S. Hitomi, T. Shimamoto, S.-H. Hyon, Y. Ikada, S. Watanabe, and Y. Shimizu, in *Biomaterials and Clinical Applications,* A. Pizzoferrato, P. G. Marchetti, A. Ravaglioli, and A. J. C. Lee, Eds., Elsevier Science Publishers B.V., Amsterdam, 1987, p. 75.
14. C. G. Pitt, R. A. Jeffcoat, A. Schindler, and R. A. Zweidinger, *J. Biomed. Mater. Res.,* **13,** 497 (1979).
15. H. Tsuji and Y. Ikada, *Macromolecules,* **25,** 5719 (1992).
16. H. Tsuji and Y. Ikada, *J. Appl. Polym. Sci.,* **58,** 1793 (1995).
17. H. Tsuji and Y. Ikada, *Polym. Prepr. Japan,* **43,** 1193 (1994).
18. Y. Cha and C. G. Pitt, *J. Controlled Release,* **7,** 69 (1988).
19. Y. Cha and C. G. Pitt, *Biomaterials,* **11,** 108 (1990).
20. H. Tsuji and Y. Ikada, *J. Appl. Polym. Sci.,* **53,** 1061 (1994).
21. Y. Ikada, K. Jamshidi, H. Tsuji, and S.-H. Hyon, *Macromolecules,* **20,** 904 (1987).
22. H. Tsuji, F. Horii, S.-H. Hyon, and Y. Ikada, *Macromolecules,* **24,** 2719 (1991).
23. H. Tsuji, S.-H. Hyon, and Y. Ikada, *Macromolecules,* **24,** 5651 (1991).
24. H. Tsuji, S.-H. Hyon, and Y. Ikada, *Macromolecules,* **24,** 5657 (1991).
25. H. Tsuji, S.-H. Hyon, and Y. Ikada, *Macromolecules,* **25,** 2940 (1992).
26. H. Tsuji, F. Horii, M. Nakagawa, Y. Ikada, H. Odani, and R. Kitamaru, *Macromolecules,* **25,** 4114 (1992).
27. H. Tsuji, Y. Ikada, S.-H. Hyon, Y. Kimura, and T. Kitao, *J. Appl. Polym. Sci.,* **51,** 337 (1994).
28. H. Tsuji and Y. Ikada, *Macromolecules,* **26,** 6918 (1993).
29. T. Okihara, M. Tsuji, A. Kawaguchi, K. Katayama, H. Tsuji, S.-H. Hyon, and Y. Ikada, *J. Macromol. Sci. Phy.,* **B30**(1&2), 119 (1991).
30. T. Okihara, A. Kawaguchi, H. Tsuji, S.-H. Hyon, Y. Ikada, and K. Katayama, *Bull. Inst. Chem. Res., Kyoto Univ.,* **66,** 271 (1988).
31. G. L. Loomis, J. R. Murdoch, and K. H. Gardner, *Polym. Prepr., Am. Chem. Soc. Div. Polym. Chem.,* **31**(2), 55 (1990).
32. G. L. Loomis and J. R. Murdoch, U.S. Pat. 4,719,246 (1988).
33. G. L. Loomis and J. R. Murdoch, U.S. Pat. 4,766,182 (1988).
34. G. L. Loomis and J. R. Murdoch, U.S. Pat. 4,800,219 (1989).
35. G. L. Loomis and J. R. Murdoch, U.S. Pat. 4,902,515 (1990).
36. G. L. Loomis and J. R. Murdoch, U.S. Pat. 4,981,696 (1991).
37. P. J. Dijkstra, A. Bulte, and J. Feijen, *Proceedings of the 17th Annual Meeting of the Society for Biomaterials,* May 1–5, 1991, Scottsdale, AZ, Society for Biomaterials, Algonquin, IL, p. 184.
38. A. J. Domb, *J. Polym. Sci., Part A: Polym. Chem.,* **31,** 1973 (1993).
39. W. R. Sorensen and T. W. Campbell, *Preparative Methods of Polymer Chemistry,* Wiley, New York, 1961.
40. S.-H. Hyon, K. Jamshidi, and Y. Ikada, in *Polymers as Biomaterials,* S. W. Shalaby, A. S. Hoffman, B. D. Ratner, and T. A. Horbett, Eds., Plenum, New York, 1984, pp. 51–65.
41. A. Schindler and D. Harper, *J. Polym. Sci., Polym. Chem. Ed.,* **17,** 2593 (1979).
42. J. V. Koleske and R. D. Lundberg, *J. Polym. Sci., Part A-2,* **7,** 897 (1969).
43. H. Bittiger and R. H. Marchessault, *Acta Crystallogr.,* **B26,** 1923 (1970).
44. V. Crescenzi, G. Manzini, G. Calzolari, and C. Borri, *Eur. Polym. J.,* **8,** 449 (1972).
45. H. Tsuji and Y. Ikada, submitted to *J. Appl. Polym. Sci.*
46. S. Imagawa, M. Harada, T. Urakami, A. Iwamoto, and Y. Tokiwa, *Polym. Prepr. Jpn.,* **42,** 3712 (1993).
47. G. L. Brode and J. V. Koleske, *J. Macromol. Sci., Chem.,* **A6**(6), 1109 (1972).
48. T. G. Fox, *Bull. Am. Phys. Soc.,* **2,** 123 (1956).
49. H. D. Keith, F. J. Padden, and T. P. Russell, *Macromolecules,* **22,** 666 (1989).
50. L. E. Nielsen, *Mechanical Properties of Polymers and Composites,* Marcel Dekker, New York, 1974.
51. L. E. Nielsen, *Predicting the Properties of Mixtures: Mixture Rules in Science and Engineering,* Marcel Dekker, New York, 1978.