Morphological Change of Poly (ε-caprolactone) with a wide Range of Molecular Weight via Formation of Inclusion Complex with α-Cyclodextrin

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ABSTRACT: The effect of molecular weight of poly(ε -caprolactone) (PCL) on the formation and stability of inclusion complexes (ICs) between α -cyclodextrin (α -CD) and PCL was investigated by FTIR, WAXD, and DSC measurements. ICs between α -CD and PCLs with a wide range of number-average molecular weight, $M_n = 1.21 \times 10^4 - 1.79 \times 10^5$, were prepared by mixing the aqueous solution of CD and acetone solution of PCL followed by stirring at 60 °C for 1h and at the room temperature for 1 day. FTIR, WAXD, and DSC measurement showed the PCL chains were included into the α -CD cavity, and the crystallization of PCL was suppressed in the α -CD cavity. Stoichiometry and yield of each IC varied with the molecular weight of guest PCL, and the effect of IC formation on the crystallization behaviour of guest polymer decreased with the increase of molecular weight of guest polymer. ©2005 Wiley Periodicals, Inc. J Polym Sci Part B: Polym Phys 43: 1433–1440, 2005

Keywords: cyclodextrin; hydrogen bond; inclusion complex; polyester

INTRODUCTION

Cyclodextrins (CDs) are a series of cyclic oligosaccharides composed of at least six $(1\rightarrow 4)$ linked α -D-glucopyranosyl residues. In order of increasing number of D-glucopyranosyl residues, from 6 to 8, they are termed α -CD, β -CD, and γ -CD, respectively. Their shape is like a hollow truncated cone, and they have no hydroxyl group inside their cavity. Therefore, the hydrophobicity of their cavity gives an ability to include hydrophobic molecules inside their cavity.^{1–6} Recently, it was found that CDs form crystalline inclusion complexes (ICs) with biodegradable polyesters. Harada et al.^{7–9} found that linear aliphatic polyesters, such as poly(ε -caprolactone) (PCL),

poly(ethylene adipate) (PEA), poly(trimethylene adipate) (PTA), and poly(1,4-butylene adipate) (PBA), form crystalline inclusion complexes with CDs. Huang et al.¹⁰ observed that the PCL and poly(ethylene oxide) (PEO) chains were included inside the channels formed by α -CD, and Shuai et al.¹¹ have reported the partial inclusion of poly(3-hydroxybutyrate) [P(3HB)] chain into CDs. There are some reports on the effect of IC formation on the state and physical properties of polymer included inside the CD cavity. Tonelli et al.¹² have investigated the effect of CD IC formation on the miscibility of poly(L-lactic acid)(PLLA)/PCL blend, and on the morphology of the PLLA-PCL copolymer obtained from diblock copolymerisation.¹³

Because several aliphatic polyesters were biodegradable and biocompatible, they constitute a very important class of biomaterials of growing interest in the field of biomedical applications, especially as matrices for controlled drug deliv-

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ery systems.¹⁴ In the biodegradable polyester family, poly(ε -caprolactone) (PCL) is one of the well-known representatives whose synthesis and properties have been extensively studied.^{15–17}

PCL has high flexibility while its tensile strength and melting point are low.¹³ There have been several reports about the formation of IC between CDs and PCL by Harada et al.^{7,8} and Tonelli et al.¹⁸ Harada et al. have investigated the formation and the structure of α -CD-PCL IC by using low molecular weight PCL samples $(M_n = 5.3 \times 10^2 - 3.0 \times 10^3)$ as the guest polymer.

To use biodegradable polymers as practical polymeric materials, they should be reasonably satisfactory in mechanical properties¹⁹ and controllable biodegradability.²⁰ It is well known that the mechanical properties, such as tensile strength. elongation, tensile and impact strength of the polymers vary more or less with the morphology and the crystallinity.²¹ Also, the biodegradability of crystalline polymer is known to depend on the crystallinity as well as on the crystalline microstructure.²²⁻²⁶ Therefore, if the CD IC formation affect the crystallization of the guest polymer, the CD IC formation is expected to affect subsequently the mechanical property and biodegradability of aliphatic polyesters. From this viewpoint, in the present work, we focused on the changes in the crystallization behavior of PCLs with different molecular weight through the formation of IC. So far as we know, it is the first report on the morphological change of polyester with a wide range of molecular weight $(M_n = 1.21 \times 10^4 - 1.79 \times 10^5)$ through the formation of IC with CD.

EXPERIMENTAL

Materials

Poly(ε -caprolactone)(PCL) samples, supplied by the courtesy of Daicel Chemical Co., Japan, were used after precipitation in ethanol from chloroform solution. Highly pure α -cyclodextrin sample was generously supplied by Nihon Shokuhinn Kagaku Co., and it was dried in vacuum at 90 °C for 8 h before use.

IC Sample Preparation

To prepare the inclusion complexes between α -cyclodextrin and PCLs, α -CD (5 g) and PCL (0.5 g) were dissolved in water (50 mL) and ace-

tone (100 mL), respectively. Then, the polymer solution was added dropwise to the α -CD solution at 60 °C under vigorous stirring. After stirring at 60 °C for 1 h, the mixture was cooled to room temperature and stirred further for 1 day. The precipitated products were collected by filtration, washed with acetone and water, and then dried under vacuum at room temperature for 2 days.

Molecular Weight Measurements

Molecular weight of PCL sample was measured by a Tosoh HLC-8020 GPC instrument with a Tosoh SC-8010 controller and a refractive detector. Polystyrene standards with narrow molecular weight distribution were used to construct a calibration curve. The number-average and weight-average molecular weight (M_n, M_w) and polydispersity (M_w/M_n) were calculated through a SC-8010 data processor.

¹H NMR Measurement

¹H NMR measurements were accomplished to estimate the stoichimetry of each IC, that is, the molar ratio of α -CD and monomeric repeating unit of PCL. ¹H-NMR spectra were recorded in DMSO- d_6 solution of IC at 80 °C on a JEOL GSX270 FT-NMR spectrometer.

FTIR Measurement

FTIR measurements were carried out on a Spectra 2000 single-beam IR spectrometer (Perkin-Elmer, Tokyo, Japan) under N₂ purging. All the spectra were recorded at a resolution of 4 cm⁻¹ and with an accumulation of 16 scans. PCL samples for FTIR measurements were prepared by 1.5 wt % chloroform solution on the surface of a silicon wafer. The FTIR spectra were observed after the solvent was completely evaporated. In the cases of ICs, samples for the measurements were prepared by dispersing the powder of ICs in KBr and compressing the mixtures to form disks.

Curve Fitting

A curve-fitting program was used to resolve the carbonyl vibration band of PCL in the IR spectra into amorphous and crystalline fraction. This program is based on the least-squares parameter adjustment criterion using the Gauss-Newton iteration procedure. This fit adjusts the peak position, the lineshape (a Gaussian frac-

Sample	PCL1	PCL2	PCL3	PCL4	PCL5
$\overline{ {M_{ m n}} (imes 10^4) } \ {M_{ m w}} (imes 10^4) \ {M_{ m w}} / {M_{ m n}}$	$1.21 \\ 2.18 \\ 1.80$	2.99 5.99 2.00	$4.13 \\ 6.77 \\ 1.64$	$8.30 \\ 13.9 \\ 1.67$	$17.9 \\ 27.4 \\ 1.53$

Table 1. The Molecular Weight of PCL SamplesUsed as the Guest Polymer of IC

tion whereby zero represents a pure Lorentzian and unity represents a pure Gaussian), and the peak width and the height in such a way that a best fit is obtained.

Wide-Angle X-ray Diffraction (WAXD)

WAXD measurement was carried out on a RU-200 X-ray diffractometer (Rigaku Co., Tokyo, Japan) operated at 40 kV and 200 mA. Nickelfiltered Cu K_{α} radiation ($\lambda = 0.154$ nm) was used. WAXD patterns were recorded in the 2θ range of 5–55° with the scanning speed of 1.0°/min at room temperature. Solution cast samples for WAXD measurements of pure PCL were prepared by evaporating a 3 wt % chloroform solution on a Petri dish, and powder samples were used for the measurements of α -CD and ICs.

Differential Scanning Calorimetry (DSC)

The melting and crystallization behavior were investigated by employing a Pyris Diamond DSC (PerkinElmer Co., Tokyo, Japan). An indium standard was used for calibration, and nitrogen was used as the purge gas. The weights of all samples for the measurements were from 4 to 5 mg. The samples were firstly heated from 0 to 120 °C at the heating rate of 10 °C/min (first scan), melted at 120 °C for 2 min, and then cooled from 120 to 0 °C at the cooling rate of 10 °C/min. The melting ($T_{\rm m}$) and crystallization temperature ($T_{\rm c}$) were taken as the peak of the melting endotherm in the heating scan and crystallization exotherm in the cooling scan, respectively.

The glass transition temperature $(T_{\rm g})$ was, measured by using a DSC 220 system connecting with a workstation SSC5300 (SEIKO Instrument Co., Tokyo, Japan). The weights of all samples for the measurements were from 4 to 5 mg. The samples were first melted at 120 °C for 2 min, rapidly quenched to -100 °C with liquid nitrogen, and then heated again to 120 °C at a heating rate of 20 °C/min (second scan). T_g was taken as the peak top of DDSC (the differentiation of DSC) curve obtained from the second heating scan.

RESULT AND DISCUSSION

In this research, five kinds of PCL with different molecular weight were used as the guest polymer of ICs. The molecular weights of respective PCLs were shown in Table 1. The formation of α -CD-PCL IC was probed by WAXD, DSC, and FTIR measurements. As shown below, all measurements showed that PCL chains with a wide range of molecular weight were included into the α -CD cavity with forming ICs.

Figure 1 shows the yield and the host (α -CD) guest (polyester) stoichiometry of each IC as a function of the molecular weight of PCL. The stoichiometry, that is, the molar ratio of CD and the monomeric repeating unit of PCL in each IC was investigated by ¹H NMR measurements. It was shown that both the yields and the amounts of CD attached to the PCL chains decreased as the molecular weight of guest polymer increased. This result is identical to that in the previous report by A. Harada's group,^{7,8} where the low molecular weight PCL samples (M_n) $= 5.3 \times 10^2 - 3.0 \times 10^3$) were used as the guest polymers of α -CD lCs. Because one of the main driving forces for CD IC formation is the hydrophobic interaction, $^{1-4,27,28}$ it is expected that the existence of the carbonyl group could exhibit a negative effect on the formation of CD IC. Moreover, for the CD IC formation of polyester with the higher molecular weight, CDs should travel the longer distance on the polyester chain with



Figure 1. The yields of ICs (\bullet), and the molar ratios of α -CD and repeating monomer unit of PCL in the ICs (\blacksquare), as a function of the molecular weight of PCL, respectively.



Figure 2. Wide-angle X-ray diffraction patterns of (a) PCL1, (b) PCL2, (c) PCL3, (d) PCL4, (e) PCL5, (f) α -CD, (g) α -CD-PCL1 IC, (h) α -CD-PCL2 IC, (i) α -CD-PCL3 IC, (j) α -CD-PCL4 IC, (k) α -CD-PCL5 IC.

passing through more amounts of the carbonyl groups. Therefore, the decreases in both the yield and the amount of CD in each IC were due to the fact that it is more difficult to displace the α -CD molecule from the chain end to the middle part of the long polymer chain as the chain length of the guest polymer became longer.

The WAXD patterns of α -CD, pure PCLs, and respective ICs were shown in Figure 2. A series of peaks were detected for α -CD powder. The prominent peaks were located at 9.9, 12.2, 14.5, 19.5, and 21.9, almost identical to the results as found in the previous reports.^{11,13} The characteristic peaks of crystalline phase for PCLs were observed at 20.8 and 23.8, regardless of their molecular weight.

The WAXD patterns of α -CD-PCL ICs strongly support the formation of IC. Although the relative intensity of each peak is different, two strong peaks at 20 and 22.5° are present in the diffraction patterns of all ICs. These two peaks, very different from those of both pure α -CD and PCL, are well known to be the characteristics of α -CD-based IC crystals adopting the channel structure.²⁹ It is known that CDs have channel structure upon forming IC with polymer because of the long-chain nature of polymers.¹⁸ In the channel structure, the CD rings are stacked on the top of each other to produce cylindrical central cavities, while pure CDs form the cage structure where the CD cavity is closed on both sides by adjacent molecules.¹⁸



Figure 3. The first heating DSC curves of (a) PCL1, (b) PCL2, (c) PCL3, (d) PCL4, (e) PCL5, (f) α -CD, (g) α -CD-PCL1 IC, (h) α -CD-PCL2 IC, (i) α -CD-PCL3 IC, (j) α -CD-PCL4 IC, (k) α -CD-PCL5 IC.

It is notable that the characteristic peaks of PCLs were observed in the WAXD patterns of all ICs except for α -CD-PCL1 IC, indicating that the crystalline region of PCL existed in the ICs.

The existence of crystalline phase of PCL in the α -CD-PCL ICs is also confirmed by the thermal analysis as shown below.

The melting behavior, glass transition, and crystallization behavior of each IC were investigated by employing DSC. The first and the following cooling scan DSC curves are shown in Figures 3 and 4, respectively. As shown in



Figure 4. The cooling DSC curves of (a) PCL1, (b) PCL2, (c) PCL3, (d) PCL4, (e) PCL5, (f) α -CD, (g) α -CD-PCL1 IC, (h) α -CD-PCL2 IC, (i) α -CD-PCL3 IC, (j) α -CD-PCL4 IC, (k) α -CD-PCL5 IC.

Figure 3, no melting peak was observed in the first heating scan of α -CD, and the melting peaks of pure PCLs were observed at almost the same temperature, about 59 °C, regardless of molecular weight. In the cases of pure PCLs, the value of melting enthalpy (ΔH) decreased with the increase of molecular weight of PCL, indicating the molecular weight dependence of crystallinity.³⁰ The decrease in crystalline fraction with increase of the molecular weight is considered to be due to increased chain entanglements.²¹ Upon formation of ICs, however, the intensity of melting peak of PCLs remarkably decreased, and the value of ΔH was larger as the molecular weight of guest polymer was higher. From this result, it is shown that the crystallization of PCL was remarkably suppressed in the α -CD cavity and the suppression was more prominent when the molecular weight of guest polymer was lower. This phenomenon is considered to be due to the different stoichiometry among each of ICs. If there is less amount of α -CD threaded onto the PCL, it is natural that more parts of polymer chain would be located outside the α -CD cavity, which can form the crystalline phase.

The crystallization behavior during DSC cooling scan of respective ICs (Fig. 4) also supports the partial inclusion of PCL chains with higher molecular weight into the α -CD cavity. No crystallization peak was observed in the cooling scan of α -CD and the crystallization peak of PCL1, PCL2, PCL3, and PCL4 was detected at about 31 °C. The crystallization of PCL5 was detected at about 29 °C, a little but clearly lower temperature than the crystallization temperature of the other pure PCLs, indicating that its crystallization was depressed by increased chain entanglements. Except for PCL5, the crystallization peaks observed in the cooling scan for pure PCLs disappeared in the cooling scan DSC curves of corresponding ICs, indicating that the crystallization of the PCL was almost entirely suppressed in the α -CD cavity.

In the case of the α -CD-PCL5 IC, however, a small but clear crystallization peak of PCL was apparent at higher temperature than the crystallization temperature of pure PCL, indicating the presence of a part of polymer chain that can crystallize outside the CD cavity. It is notable that the crystallization temperature of the α -CD-PCL5 IC is higher than that of pure PCL5. It has been found that the incorporation of a small amount of α -CD can enhance the nucleation and crystallization of polyester.^{31,32} Therefore, it is thought that the crystallization of PCL chains located outside and inside the α -CD cavity was enhanced and suppressed, respectively.

In the second heating scan DSC curves (Fig. 5), no glass transition of α -CD was detected, and the glass transitions of pure PCLs were detected at almost the same temperature of about -62 °C, regardless of molecular weight. The glass transitions of PCL1, PCL2, PCL3, and PCL4, however, became unclear upon the formation of IC with α -CD. It can be inferred that the segmental mobility of the guest polymers severely limited in the α -CD cavity. In the case of α -CD IC of PCL5, however, a weak glass transition was detected at almost the same temperature as those of pure PCLs, indicating that some parts of polymer chain might remain outside the CD cavity and have the same segmental mobility as pure PCL, while the other parts are rigidly included in the α -CD cavity.

FTIR measurements for the respective ICs give us the more information about the phenomena of IC formation. FTIR spectra of the α -CD-PCL ICs were studied by comparing with those of pure PCLs and α -CD. As shown in Figure 6, FTIR spectra of the respective ICs indicate the coexistence of α -CD and PCLs. PCLs are characterized by the distinct carbonyl stretching bands(s, $v_{C=0}$) at 1735 cm⁻¹ and α -CD by the three intense bands at ll58 (antisymmetric v_s of the C–O–C glycosidic linkage), 1079, and



Figure 5. The second heating DSC curves of (a) PCL1, (b) PCL2, (c) PCL3, (d) PCL4, (e) PCL5, (f) α -CD, (g) α -CD-PCL1 IC, (h) α -CD-PCL2 IC, (i) α -CD-PCL3 IC, (j) α -CD-PCL4 IC, (k) α -CD-PCL5 IC. (The arrows indicate the glass transition.)



Figure 6. FTIR spectra of (a) PCL1, (b) PCL2, (c) PCL3, (d) PCL4, (e) PCL5, (f) α -CD, (g) α -CD-PCL1 IC, (h) α -CD-PCL2 IC, (i) α -CD-PCL3 IC, (j) α -CD-PCL4 IC, (k) α -CD-PCL5 IC.

1026 cm⁻¹ (coupled $v_{s(C-C/C-O)}$).³³ In the IR spectra of ICs, it was shown that the carbonyl stretching band of ICs became larger as the molecular weight of guest polymer grew higher, indicating the increase and decrease of relative contents of polymer and α -CD component, respectively, in the ICs. This result is consistent with that shown in the estimation of stoichiometry of ICs.

In Figure 7 the expanded carbonyl bands of ICs and pure PCLs are shown. It has been found that the IR carbonyl absorption band of pure PCL can be resolved into two components corresponding to the crystalline and noncrystalline amorphous phases,³⁴ and very indicative of the IC formation.^{35,36} When the α -CD-PCL IC is formed successfully, the PCL chains are located in the IC channels, and thus are not able to integrate to form the crystalline phase. Consequently, the crystalline carbonyl absorption of PCL disappears in the FTIR spectrum of ICs.^{35,36}

In this study, a curve-fitting program was used to resolve the carbonyl vibration band of PCL into two components, that is, the amorphous and the crystalline components. In the cases of inclusion complexes, the carbonyl band of each IC was resolved into three components, including the one arisen from the carbonyl group interacting with the hydroxyl group of CD through the hydrogen-bond in addition to the crystalline and the amorphous components.³⁶ The band of hydrogen-bonded component is partly overlapped with the hydroxyl band of water. In the case of α -CD PCL1 IC, as no melting behavior was observed by DSC measurement, the observed carbonyl absorption band was reasonably resolved into two components, that is, the amorphous and the hydrogen-bonded ones.

The results, obtained from the FTIR and curvefitting analysis, were summarized in Table 2, compared with the estimation of yield and stoichiometry of ICs.

As shown in Figure 7 and Table 2, the strength of the crystalline components of the carbonyl absorptions of PCLs were remarkably decreased upon the formation of the ICs, and the carbonyl absorption bands of amorphous and hydrogen-bonded component were mainly detected in the IR spectrum of respective ICs. Although the carbonyl absorption bands of all PCLs showed quite similar changes upon forma-



Wavenumber/cm⁻¹

Figure 7. Expansion of the FTIR spectra of (a) PCL1, (b) PCL2, (c) PCL3, (d) PCL4, (e) PCL5, (f) α -CD-PCL1 IC, (g) α -CD-PCL2 IC, (h) α -CD-PCL3 IC, (i) α -CD-PCL4 IC, (j) α -CD-PCL5 IC. Ex: experimental result, Cr: crystalline component, Am: amorphous component, Hb: hydrogen-bonded component, OH: hydroxyl component (water).

			Relative Area Intensity (%) ^a					
			Pure State			IC		
Sample	Yield (g) of α -CD IC	Molar Ratio [α-CD]:[PCL monomeric unit]	Cr	Am	Hb	Cr	Am	Hb
PCL1	1.54	1:1.8	76	24	_	0	70	30
PCL2	1.36	1:2.4	61	39	_	5	68	27
PCL3	1.34	1:2.5	54	46	—	9	67	24
PCL4	1.13	1:3.9	53	47	_	13	67	20
PCL5	0.44	1:7.9	50	50	_	18	64	18

Table 2. The Effect of Molecular Weight of Polyester on the IC Formation

^a Cr, Am, and Hb: the relative area intensities of crystalline, amorphous, and hydrogen-bonded component, respectively, in the FTIR carbonyl band.

tion of ICs with α -CD, the degree of change in each IC was different with each other. The degrees of changes in the relative area fractions of the crystalline components in the carbonyl bands of respective PCLs increased with the decrease of the molecular weight of the guest PCL. This result is consistent with those of WAXD and DSC measurements in view of the fact that the degree of suppression for the crystallization of polyesters through IC formation varied inversely as the molecular weight of the guest PCL.

The hydrogen-bonded component of the carbonyl band gives us the information about the interaction between α -CD and polyesters in the IC formed. As the molecular weight of the guest PCL decreased, the portion of the hydrogenbonded component in the integrated intensity of the carbonyl band increased. This indicates that the IC formation was more strongly stabilized by the hydrogen-bond formed between the hydroxyl group of α -CD and the carbonyl group of PCL as the molecular weight of the guest PCL was lower. It can be deduced that more CD molecules attached to the polyester chain could be more effective in the suppression of crystallization of the guest polymer, and make more hydrogen- bond of the hydroxyl groups with the carbonyl groups of the guest polymer.

CONCLUSIONS

Inclusion complexes between α -CD and PCLs with a wide range of molecular weight were prepared by mixing the solution of α -CD and that of polyester, followed by stirring. The successful IC formation was confirmed by observing the channel structure of α -CD molecules and the significant reduction of crystalline region of the guest polymers in the ICs.

The stoichiometry of each IC indicate that the proportion of α -CD threaded onto the polyester through the IC formation increases as the molecular weight of the guest polymer decreases.

Upon the IC formation, PCL chains with the higher molecular weight are thought to be partially included in the α -CD cavity. That is, the crystalline region of PCL still remains outside the α -CD cavity, supported by detection of the melting peak, glass transition, and crystallization peak in DSC measurement.

The degree of suppression for the crystallization of guest polymer, and stabilization of IC formation by the hydrogen-bond increases with the decrease of the molecular weight of the guest polymer.

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