Preparation and Characterization of Inclusion Complexes of Aliphatic Polyesters with Cyclodextrins

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ABSTRACT: Cyclodextrins (CDs) were found to form inclusion complexes with aliphatic polyesters $[-O(CH_2)_xOCO(CH_2)_4CO]_n$ (where $x = 2$, 3, or 4) to give crystalline compounds. α- and γ-CD formed complexes with these polyesters in high yields, although β-CD gave complexes in moderate yields. Although the yields of the complexes of α-CD with poly(trimethylene adipate) (PTA) ($x = 3$) and poly(1,4-butylene adipate) (PBA) ($x = 4$) decreased with increasing molecular weight, α-CD formed complexes with poly(ethylene adipate) (PEA) ($x = 2$) in high yields even at higher molecular weights. The yields of the complexes of γ-CD with these polyesters showed a maximum at the molecular weight of 1000. The complexes were isolated and characterized by FTIR, ^{1}H NMR, ^{13}C CP/MAS NMR spectra, and X-ray diffraction studies. The inclusion modes are discussed.

Introduction

Cyclodextrins (CDs) are a series of cyclic oligosaccharides consisting of six to eight glucose units linked by α-1,4 bonds. They are called α-, β-, and γ-CD, respectively. Since CDs were discovered, a large number of inclusion complexes of CDs with various low molecular weight compounds have been prepared and characterized.[1] However, there were few reports on the formation of inclusion complexes of CDs with polymers until recent years.

Recently, much attention has been directed toward interlocked molecules, such as rotaxanes, catenanes, and polyrotaxanes.[2] Main-chain polyrotaxanes containing crown ethers[3] and cyclodextrins (CDs)[4,5] and side-chain polyrotaxanes[6] have been prepared and characterized. We reported that CDs formed complexes with hydrophilic polymers such as poly(ethylene glycol),[7] poly(propylene glycol),[8] and poly(methyl vinyl ether).[9] More recently, we found that CDs formed complexes with hydrophobic oligomers and polymers, such as oligoethylene[10] and polyisobutylene.[11] These polymers are stable and difficult to be used as biodegradable polymers because of their C−C or C−O ether bonds in the main chain formed by addition polymerizations of vinyl monomers or ring-opening polymerizations of epoxides.

There have been no reports on the formation of inclusion complexes of CDs with polymers obtained by condensation polymerizations, such as polyesters and polyamides, except for the examples of the inclusion polymerization of monomer complexes with CDs.[12] Recently, Tonelli et al. reported that poly(ϵ-caprolactone) formed clathrate type complexes with urea.[13] Chenite and Brisse reported that polyesters formed complexes with urea.[14] It is of interest if biodegradable polymers, such as poly(ϵ-caprolactone), poly(hydroxybutylate), and poly(alkylene adipate)s are included in the biodegradable framework, like cyclodextrins. We found that linear aliphatic polyesters form complexes with cyclodextrins to give crystalline compounds. We have briefly reported the complex formation of poly(ϵ-caprolactone) with α-CD.[15] Here we report the preparation and characterization of inclusion complexes of CDs with aliphatic polyesters $[-O(CH_2)_xOCO(CH_2)_4CO]_n$ (where $x = 2$, 3, or 4) in detail.

Results and Discussion

Complex Formation between Aliphatic Polyesters and CDs. Previously, we reported that α-CD formed complexes with poly(ethylene glycol)[7] and oligoethylene (OE)[10] of various molecular weights to give crystalline compounds, although β-CD and γ-CD did not form complexes with PEG and OE under the same conditions. A PEG or OE chain fits well into the cavity of α-CDs. Molecular modeling of linear aliphatic polyesters, $[-O(CH_2)_xOCO(CH_2)_4CO]_n$ (where $x = 2$, 3, or 4) suggested that the polymer chains in either all-trans or kink conformations are slim enough to fit in the α-CD cavity. Recently, Tonelli et al. made the urea inclusion complex of poly(ϵ-caprolactone) and Brisse et al. reported that the aliphatic polyesters formed complexes with urea.[13,14] The diameter of the urea channel is estimated to be 5.5 Å, which is close to that of the α-CD cavity.

When an aqueous solution of α-CD was added to the polyester above the melting temperature of the polymer and agitated by ultrasound for 10 min, the solution became turbid and complexes were formed as crystalline precipitates. All the polyesters, PEA, PTA, and PBA of molecular weight 840−1000 formed complexes with CDs. α- and γ-CD formed complexes with these polymers in high yields, although β-CD gave complexes in moderate yields. These results are in contrast to those of the complex formation of CDs with poly(ethylene glycol)[7] and with oligoethylene.[10] Poly(ethylene glycol) and oligoethylene formed complexes only with α-CD. This is due to the fact that these polyesters are more hydrophobic than poly(ethylene glycol) and have ester groups that can form hydrogen bonds with the hydroxyl groups of CDs.

Figure 1 shows the yields of the complexes of the polyesters with α-CD as a function of the molecular weight of the polyesters. The yields are based on the starting amount of CD and the stoichiometry of CD to the polymers, as described in the next section. Saturated aqueous solutions of CD and excess amounts of the polymer were used. The yields of the α-CD complex

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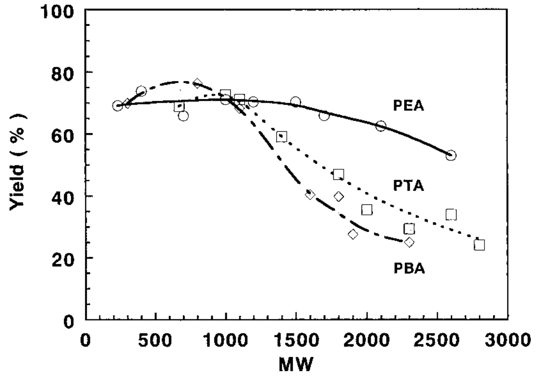

Figure 1. Yields of the complexes of α-CD with PEA, PTA, and PBA as a function of the molecular weight of the polymers.

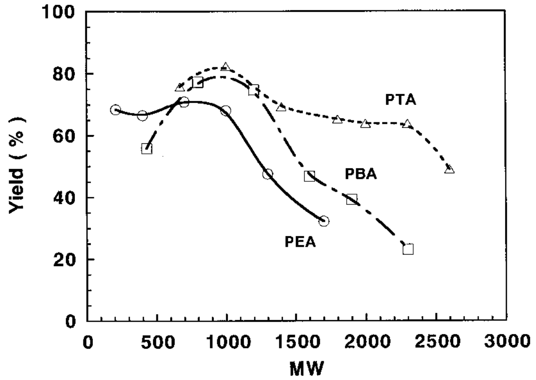

Figure 2. Yields of the complexes of γ-CD with PEA, PTA, and PBA as a function of the molecular weight of the polymers.

with poly(trimethylene adipate) (PTA) and poly(1,4-butylene adipate) (PBA) decreased as the molecular weight increased. It is in contrast to the cases for the complex formation between CDs and hydrophilic polymers, such as poly(ethylene glycol) (PEG)[7] and poly(oxytrimethylene) (POX).[16] In these cases, the yield increased with an increase in the molecular weight and then reached saturation (PEG) or decreased with increasing molecular weight (POX).

Although the yields of the complexes of α-CD with PTA and PBA decreased with increasing molecular weight, poly(ethylene adipate) (PEA) formed complexes with α-CD in high yields even with higher molecular weights. This is due to the fact that PEA with ethylene glycol units is more hydrophilic than the other polymers. PTA and PBA are more hydrophobic than PEA, so CDs are difficult to diffuse onto the polymer chains.

Figure 2 shows the yields of the complexes of the polyesters with γ-CD as a function of the molecular weight of the polyesters. The yields of the complexes of γ-CD with these polyesters showed a maximum at the molecular weights of 800−1000. These results are similar to those on the complex formation between poly(propylene glycol) with γ-CD. But it is in contrast to the case of the complex formation of polyisobutylene (PIB) with γ-CD. In this case the yields of the complexes with γ-CD increased with increasing molecular weight and reached saturation at about the molecular weight of 1000. This result suggests that the inclusion mode of the complex between these polyesters and γ-CD is different from that between PIB and γ-CD. It is interesting that PTA forms complexes with γ-CD even at higher molecular weights, although the yields of the complex of PEA and PBA with γ-CD decreased with increasing molecular weight. These results are in sharp contrast to those of the α-CD complexes (Figure 1). In this case PEA forms complexes with α-CD even at higher molecular weights although the yields of the complex of PTA showed a decrease with an increase in the molecular weight. These results suggest that the inclusion modes of α-CD and γ-CD complexes are different.

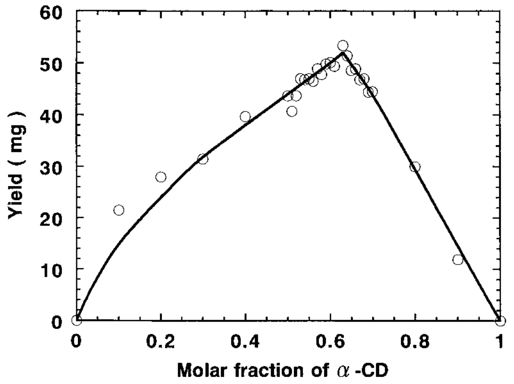

Figure 3. Continuous variation plot for complex formation between α-CD and PEA (MW = 530).

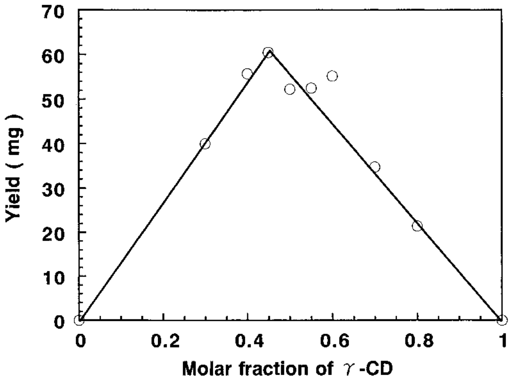

Figure 4. Continuous variation plot for complex formation between γ-CD and PEA (MW = 700).

Stoichiometries of the Complexes. Figure 3 shows a continuous variation plot (Job plot) for the complex formation between PEA and α-CD. The plots show a maximum at 0.62 of the α-CD fraction, indicating that two cyclodextrins bind 1.3 monomer units of the polyesters. The inclusion complexes were isolated by centrifugation and filtration. The ^1H NMR spectra of the complexes confirm the stoichiometry. The length of 1.3 monomer units of PEA corresponds to twice the height of α-CD.

Figure 4 shows a continuous variation plot for the complex formation between PEA and γ-CD. The plots show a maximum at 0.43 of γ-CD fraction, indicating that γ-CD forms complexes with PEA with a 1:1.5 stoichiometry: a single cyclodextrin binds 1.5 monomer units of PEA. The stoichiometry was confirmed by the ^1H NMR spectra of the complexes. γ-CD accommodates twice as much PEA in the cavity than α-CD. The diameter of the γ-CD cavity is 8.5−9 Å, which is twice as large as that of α-CD (4.5 Å). But the height of the cavity of γ-CD is the same as those of α-CD and β-CD (7 Å), which corresponds to the length of half of the monomer unit. Molecular model studies indicate that the γ-CD cavity is large enough to accommodate two chains of the polymer, whereas the α-CD cavities are too small to do this.

Figure 4 also shows a shoulder at 0.6 molar fraction of γ-CD, indicating that a single chain complex also formed when there is an excess amount of γ-CD in the system.

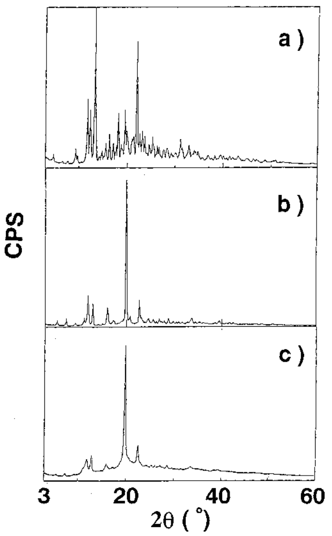

Figure 5. X-ray diffraction patterns for the α-CD−propionic acid complex (a), α-CD−poly(ethylene glycol) complex (b), and α-CD−PEA complex (MW = 1200) (c).

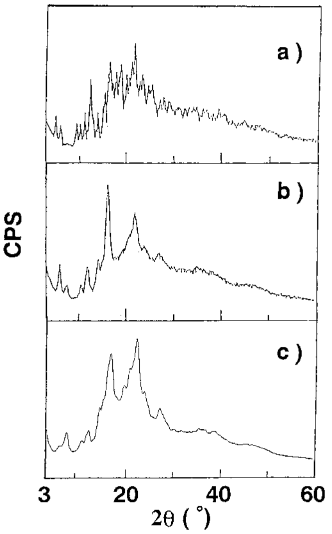

Figure 6. X-ray diffraction patterns for γ-CD (a), the γ-CD−poly(propylene glycol) complex (b), and the γ-CD−PEA complex (MW = 700) (c).

Binding Modes of the Complexes. Figure 5 shows the X-ray powder patterns of the α-CD−propionic acid complex (a), α-CD−PEG (MW = 1000) (b), and the α-CD−PEA complex (c). The X-ray powder patterns show that the complexes are crystalline and the pattern of the α-CD−PEA complex is similar to that of the complexes between α-CD and PEG, which have been reported to have a columnar structure (Figure 5b), and is different from that of the complex between α-CD and propionic acid, which has been reported to have a cage type structure (Figure 5a). Therefore, the complex of PEA with α-CD assumes a columnar structure rather than a cage type structure. The other complexes of α-CD with PTA and PBA showed the same results.

Figure 6 shows the X-ray powder patterns of γ-CD (a), the γ-CD−PPG (MW = 1000) complex (b), and the γ-CD−PEA complex (c). The pattern of the γ-CD−PEA complex is similar to that of the complexes between γ-CD and PPG, which has a columnar structure (Figure 6b), and is different from that of γ-CD, which has a cage type structure (Figure 6a). Therefore, the complex of PEA with γ-CD also assumes a columnar structure.

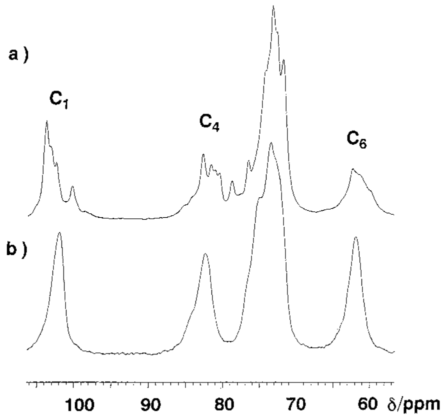

Figure 7. ^{13}C CP/MAS NMR spectra of α-CD (a) and the α-CD-PEA (MW = 1200) complex (b).

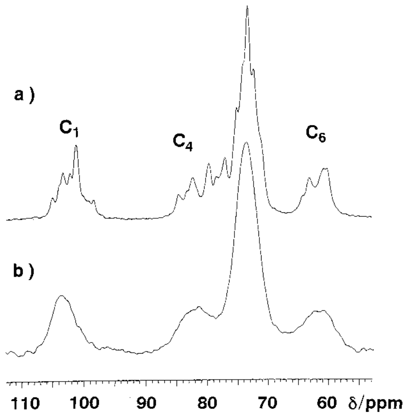

Figure 8. ^{13}C CP/MAS NMR spectra of γ-CD (a) and the γ-CD−PEA (MW = 700) complex (b).

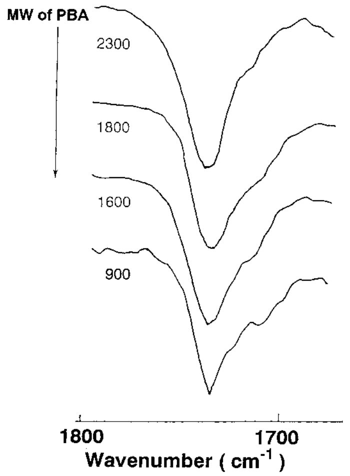

Figure 9. FT-IR spectra of α-CD−PBA complexes.

The ^{13}C CP/MAS NMR spectra of the complexes show that CD adopts a symmetrical cyclic conformation in the complex, although CD assumes a less symmetrical conformation in the crystal when it does not include a guest in the cavity (Figures 7 and 8). A polymer chain is thought to be included in the cavities of CDs.

Figure 9 shows the FTIR spectra of the complexes of PBA with α-CD in the ester carbonyl region. As the molecular weight of PBA decreases, that is, the density of CDs in the complex increases, the band at 1735 cm^{-1} becomes sharp with the appearance of new peaks at 1725 cm^{-1}, which can be assigned to hydrogen-bonded carbonyl stretching. This result indicates that some of the ester carbonyl groups of the included polymer form

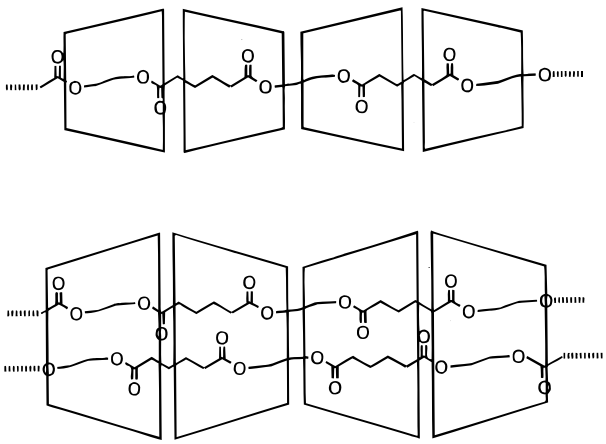

Figure 10. Proposed structure of the α-CD−PEA and γ-CD−PEA complexes.

hydrogen bonds with the hydroxyl groups of the cyclodextrins.

Molecular modeling studies show that a PBA chain is able to penetrate α-CD cavities. Model studies further indicate that the length of the polymer chain included in α-CD corresponds to the height of α-CD. γ-CD includes twice as much polymer chain in the cavity than α-CD. Figure 10 shows proposed structures of the complexes of PEA with α-CD and γ-CD.

Now we are studying the complex formation of various polyesters and polyamides with CDs and the structures of the complexes in detail. In addition, we are studying degradation of the polyesters in the complexed form in comparison with their uncomplexed states. The details will be published later.

Experimental Section

Materials. Cyclodextrins (α-, β-, and γ-CD) were obtained from Nacarai Tesque Inc. and used after drying under vacuum with P_2O_5. Poly(ethylene adipate) (PEA), poly(trimethylene adipate) (PTA), and poly(butylene adipate) (PBA) were prepared from adipoyl chloride and glycols as follows.

Preparation of Aliphatic Polyesters. Linear aliphatic polyesters were prepared by condensation polymerization between adipoyl chloride and alkylene glycols in $CHCl_3$ under N_2 flow. The obtained polydisperse samples were fractionated by gel permeation chromatography on Sephadex LH-20 (eluent: methanol or THF).

The molecular weight was measured by GPC (eluent: THF) calibrated by a polystyrene standard. The M_w/M_n of PAAs is 1.01−1.10. PEA: ^{1}H NMR (DMSO-d_6, 270 MHz) δ 4.20 (s, 4H, oxymethylene H of PEA), 2.31 (m, 4H, α-methylene H of PEA), 1.52 (m, 4H, β-methylene H of PEA). PTA: ^{1}H NMR (DMSO-d_6, 270 MHz) δ 4.01 (t, 4H, oxymethylene H of PTA), 2.30 (m, 4H, α-methylene H of PTA), 1.88 (m, 2H, methylene H of PTA), 1.53 (m, 4H, β-methylene H of PTA). PBA: ^{1}H NMR (DMSO-d_6, 270 MHz) δ 4.02 (m, 4H, oxymethylene H of PBA), 2.29 (m, 4H, α-methylene H of PBA), 1.60 (m, 4H, methylene H of PBA), 1.53 (m, 4H, β-methylene H of PBA). Table 1 shows the molecular weights and the polydispersity (M_w/M_n) of the polyesters used in this experiment.

Preparation of the Inclusion Compounds. Aliphatic polyester (20 mg) was put into tubes with heating above the melting temperature. A saturated aqueous solution of CD (1.0−2.0 mL) was added, and the mixtures were ultrasonically agitated for 10 min with heating and then allowed to stand overnight at room temperature. The precipitated products were collected by centrifugation, dried under vacuum up to 100 °C, washed with THF, and then dried under vacuum to give the polymer complex.

Table 1. M_w and M_w/M_n of PAAs

PEA		PTA		PBA	
M_w	M_w/M_n	M_w	M_w/M_n	M_w	M_w/M_n
2400	1.04	2800	1.02	2300	1.03
2100	1.02	2600	1.02	1900	1.04
1700	1.04	2300	1.02	1800	1.03
1500	1.04	2000	1.02	1600	1.03
1200	1.05	1800	1.02	1100	1.02
1000	1.09	1400	1.05	900	1.04
700	1.10	1000	1.03	840	1.02
400	1.01	670	1.06	750	1.04
230	1.05			290	1.03

Measurements. GPC determination was carried out with a Tosoh CCP &8010 system (columns: G3000HXL and G2000-HXL). ^{1}H NMR spectra were recorded at 270 MHz in DMSO-d_6 and D_2O on a JEOL EX-270 spectrometer. Chemical shifts were referenced to the solvent values (δ 2.50 for DMSO-d_6 and δ 4.70 for HOD). Powder X-ray diffraction patterns were taken by using Cu Kα radiation with a Rigaku RAD-ROC diffractometer. ^{13}C CP/MAS NMR spectra were measured on a JEOL GSX-400 NMR spectrometer with a single contact time of 1 ms and spinning rates of 5.5 and 6.4 kHz.

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