Preparation and Characterization of Inclusion Complexes of Polyisobutylene with Cyclodextrins

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ABSTRACT: β-Cyclodextrin (β-CD) and γ-cyclodextrin (γ-CD) formed inclusion complexes with polyisobutylene (PIB) of various molecular weights to give stoichiometric compounds in crystalline states. α-Cyclodextrin (α-CD) did not form complexes with PIB of any molecular weight. The yields of the complexes with β-CD decreased with an increase in the molecular weight of PIB. In contrast, the yields of the complexes with γ-CD increased with an increase in the molecular weight and the complexes were obtained almost quantitatively with PIB of molecular weight 1350. The chain-length selectivity is reversed between β-CD and γ-CD. The inclusion complexes were isolated and found to be 3:1 (monomer unit:CD). The complexes were characterized by IR, ^{1}H NMR, ^{13}C NMR, ^{13}C CP/MAS NMR, ^{13}C PST/MAS NMR spectra, and X-ray (powder), thermal, and elemental analyses. The structures of the complexes are discussed.

Introduction

Cyclodextrins (CDs) are a series of cyclic oligosaccharides consisting of six to eight glucose units linked by α-1,4 linkages. They are called α-, β-, and γ-CD respectively. They form inclusion complexes with a variety of low molecular weight compounds.[1] Previously, we reported that α-cyclodextrin (α-CD) formed complexes with poly(ethylene glycol) (PEG) of various molecular weights to give crystalline compounds in high yields,[2] although β-CD did not form complexes with PEG of any molecular weight. However, we found that β-CD and γ-CD formed complexes with poly(propylene glycol) (PPG) to give crystalline complexes in high yields,[3] although α-CD did not form complexes with PPG of any molecular weight. The cross-sectional area of polymers correlates with the size of the CD with which it forms a complex.[4] Moreover, we and others have prepared polyrotaxanes in which many α-CDs or crown ethers were threaded on a polymer chain.[5]

More recently, we found that CDs form complexes not only with hydrophilic polymers but also with hydrophobic oligomers and polymers, such as oligoethylene[6] and polyisobutylene (PIB).[7] α-CD formed complexes with oligoethylene (OE), although β- and γ-CD did not form complexes with OE. On the contrary, β- and γ-CD formed complexes with PIB, although α-CD did not form complexes with PIB of any molecular weight. Now we have studied the complex formation of β-CD and γ-CD with PIB in detail. The complex formation is chain-length dependent and stoichiometric. This paper describes in detail the formation of inclusion complexes of cyclodextrins with PIB.

Results and Discussion

Selectivity of Complex Formation. Previously, we reported that α-CD formed complexes with poly(ethylene glycol) (PEG) and oligoethylene (OE) of various molecular weights to give crystalline compounds, although β-CD and γ-CD did not form complexes with PEG and OE. A PEG or OE chain fits well into the cavity of α-CDs. However, α-CD did not form complexes with PIB of any molecular weight. Instead, when PIB was added to saturated aqueous solutions of γ-CD under sonication, the solution became turbid and the complexes were formed as crystalline precipitates.

Table 1. Formation of Solid-State Complexes between Cyclodextrins and Hydrophobic Polymers/Oligomers with Various Chain Sectional Areas

			yield (%)		
polymer/oligomer	structure	mol wt	α-CD	β-CD	γ-CD
OE(20)	—CH_2CH_2—	563	63	0	0
squalane	—$CH_2CH(CH_3)CH_2CH_2$—	423	0	62	24
PIB	—$CH_2C(CH_3)_2$—	∼800	0	8	90

Table 1 shows the complex formation of three hydrophobic oligomers/polymers with cyclodextrins. OE, which has the smallest cross-sectional area, selectively forms a complex with α-CD (diameter of the cavity: 4.5 Å) in high yield, while squalane, which has the larger cross-sectional area, selectively forms complexes with β-CD (diameter of the cavity: 7.0 Å) and γ-CD (diameter of the cavity: 8.5 Å). It is of interest that PIB, which has dimethyl groups on a main chain, does not form complexes with α-CD but forms complexes with γ-CD. These results indicate that the relative sizes of the cavities of cyclodextrins and the cross-sectional areas of the polymers are important in the complex formation.

The selectivity in complex formation of polymers with cyclodextrins is different from their complex formation with low molecular weight compounds. Since a polymer chain has many binding sites, each CD is able to recognize each binding site.

Effects of Molecular Weight of PIB on the Complex Formation. Figure 1 shows the yields of the complexes of CDs with PIB as a function of the molecular weight of PIB. The yields are based on the starting amount of CD and the stoichiometry of CD to PIB as described below. Saturated aqueous solutions of CD and PIBs (liquid; 3 equiv as monomer units to CD) were used. The yields of the complexes of PIB with γ-CD increased with an increase in the molecular weight of PIB. The complexes were obtained almost quantitatively with PIB of molecular weights 800 and 1350 with

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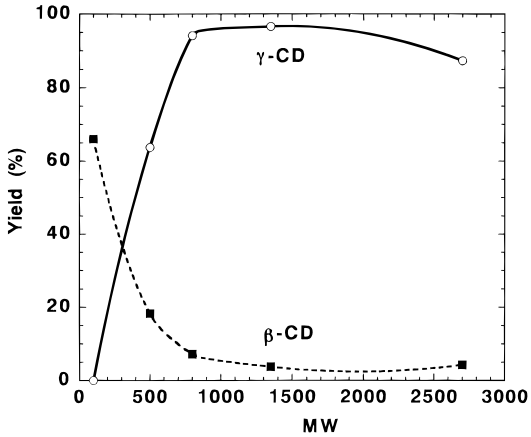

Figure 1. Yields of the complexes of β-CD and γ-CD with PIB as a function of the molecular weight of PIB.

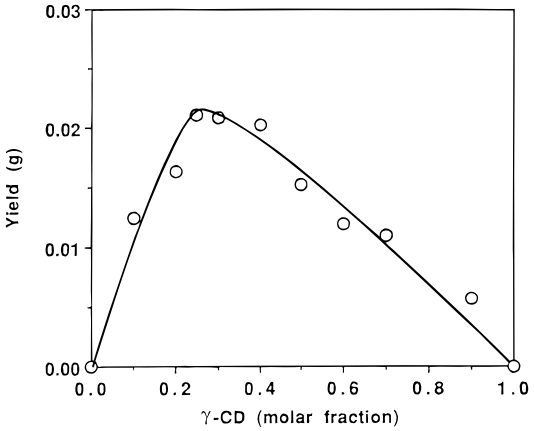

Figure 2. Continuous variation plots for the complex formation between γ-CD and PIB (MW = 1350). The sum of the initial concentration of γ-CD and PIB was fixed at 10^{-4} M.

γ-CD. In contrast, the yields of the complexes of PIB with β-CD decreased with an increase in the molecular weight of PIB. The chain-length selectivities are reversed between β-CD and γ-CD. γ-CD did not form complexes with the low molecular weight analogs, such as 2,2-dimethylbutane and 2,2,4-trimethylpentane. β-CD formed a complex with 2,2,4-trimethylpentane in high yield and with 2,2-dimethylbutane in moderate yield. This behavior is different from the complex formation between β-CD and PPG, where the yields increase with increasing molecular weight and reach a maximum at molecular weight 1000 and then decrease with increasing molecular weight. This may be due to the fact that PIB is more hydrophobic and thicker than PPG owing to the dimethyl groups of the main chain. α-CD did not form complexes with PIB of any molecular weight, although it formed complexes with oligoethylene of various molecular weights to give crystalline complexes in high yields. An α-CD cavity is too small for PIB to penetrate due to steric hindrance by dimethyl groups on the main chain.

Figure 1 shows that a minimum chain length of PIB is required for the formation of crystalline complexes with γ-CD. The same phenomenon was observed in the formation of crystalline complexes of PEG with α-CD. This is thought to be characteristic of crystalline complex formation between polymers and cyclodextrins, reflecting the importance of cooperative effects in the complex formation. The cooperation is thought to result from the fact that a single polymer chain has many binding sites which include cyclodextrin molecules. The neighboring cyclodextrin molecules bound on a polymer chain interact with each other by forming hydrogen bonds. This view is consistent with the fact that PIB does not form crystalline complexes with 2,6-di-*O*-methyl-γ-CD and water-soluble γ-CD polymer. These compounds are thought to be unable to include a PIB chain to form crystalline complexes, because they cannot form hydrogen bonds due to the lack of hydroxyl groups.

Stoichiometry of the Complexes. The yield of the complexes of PIB with γ-CD increased with an increase in the amount of PIB added to the aqueous solution of γ-CD. The saturation of the formation of the complexes was observed. The results indicate that the complex formation is stoichiometric. Figure 2 shows continuous variation plots for the formation of complexes of PIB with γ-CD. The plots show a maximum at the molar fraction of 0.25, suggesting that a CD interacts with three residues of the PIB chain.

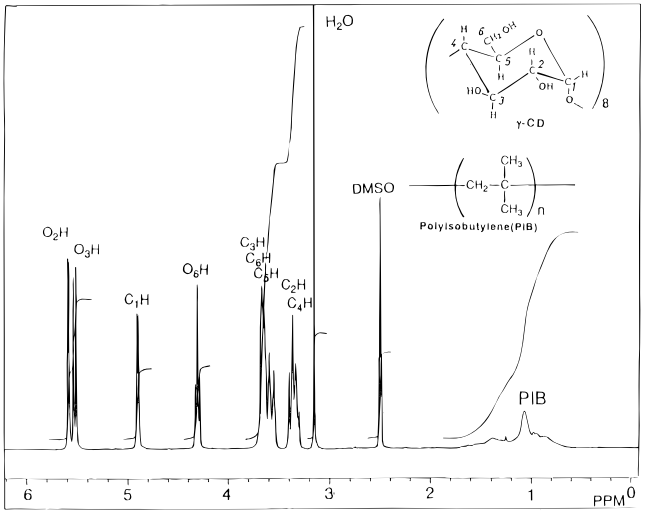

Figure 3. 270 MHz ^{1}H NMR spectra of the complexes of PIB (MW = 800) with γ-CD in DMSO-d_6.

The complexes were isolated by centrifugation and filtration and washed with water to remove uncomplexed CD, dried, and then washed with tetrahydrofuran to remove nonincluded PPG. Figure 3 shows the ^{1}H NMR spectra of the complex between γ-CD and PIB of molecular weight 800. Comparing the integral of the peak of CD(1H) and that of the methyl group on PIB, three monomer units were found to bind to a γ-CD molecule. It should be noted that the stoichiometries are always 3:1 (monomer unit:CD) whatever the ratio of interacting CD and PIB.

Properties. The complexes of γ-CD with PIB are sparingly soluble in water. The solubilities are too low to determine the quantitative solubility of inclusion compounds. This is in contrast to the complexes of poly(methyl vinyl ether) (PMeVE) with γ-CD,[8] which are soluble in a large amount of water or by heating. This is owing to the fact that PIB is more hydrophobic than PMeVE. The complexes are soluble in dimethyl sulfoxide and dimethylformamide. The X-ray diffraction studies (powder) show that all the complexes are crystalline, in spite of the fact that PIB is liquid.

Thermogravimetric measurements of the complexes show that they decompose above 320 °C, i.e., at a temperature higher than that for nonincluded γ-CD, which melts and decomposes below 310 °C, indicating that complexation with PIB stabilizes γ-CD.

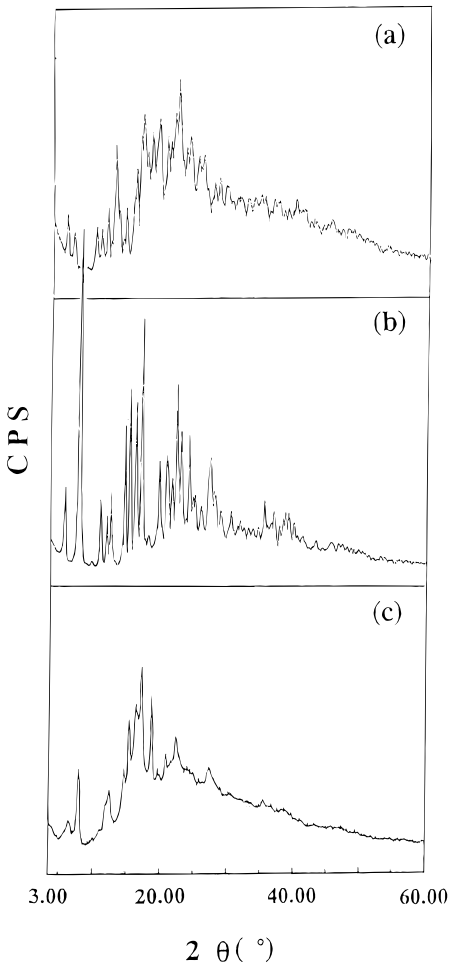

Figure 4. X-ray diffraction patterns for γ-CD (a), γ-CD-1-propanol complex (b), and γ-CD−PIB (MW = 800) complex (c).

Binding Modes of the Complexes. Figure 4 shows the X-ray pattern of γ-CD (a) and the complexes of γ-CD with 1-propanol (b) and with PIB (MW = 800) (c). Saenger et al. reported that the structures of the inclusion complexes of CDs with low molecular weight compounds can be classified as "cage type" or "channel type".[9] The patterns show that all the complexes are crystalline and the pattern of the PIB complex is different from that of free γ-CD, but similar to that of the complex with 1-propanol, which has been proved to have a column structure by the X-ray study of a single crystal of the complex.[10] Although relative intensities of each peak are different, the diffraction data (2θ) are similar to each other. The characteristic peak at 8° can be observed for the complex of γ-CD with PIB as well as for the complex with 1-propanol, although γ-CD does not show the peak. These results indicate that in the PIB complexes with γ-CD, the CD exhibits a different packing from that in free γ-CD, which has cage type structures, and has channel structures as in the complex with 1-propanol.

Figure 5 (I) shows the ^{13}C-CP/MAS NMR spectrum of the γ-CD with PIB (MW = 1000) and Figure 5 (II) shows that of γ-CD. γ-CD assumes a less symmetrical conformation in the crystal when it does not include a guest in the cavity. In this case, the spectrum shows resolved C-1 and C-4 resonances from each of the α-1,4-linked glucose residues. On the other hand, in the spectrum of the γ-CD−PIB complex, each carbon of glucose can be observed in a single peak. These results indicate that γ-CD adopts a symmetrical conformation

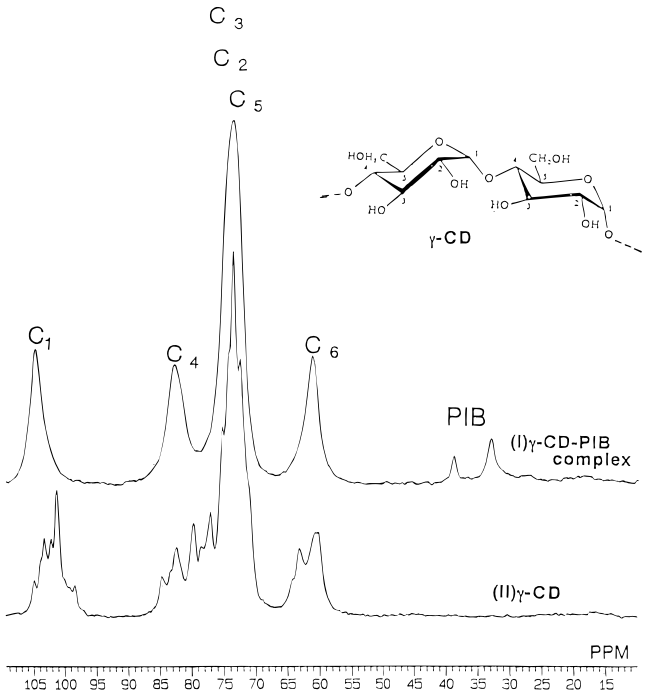

Figure 5. ^{13}C-CP/MAS NMR spectra of γ-CD−PIB complex (I) and γ-CD (II).

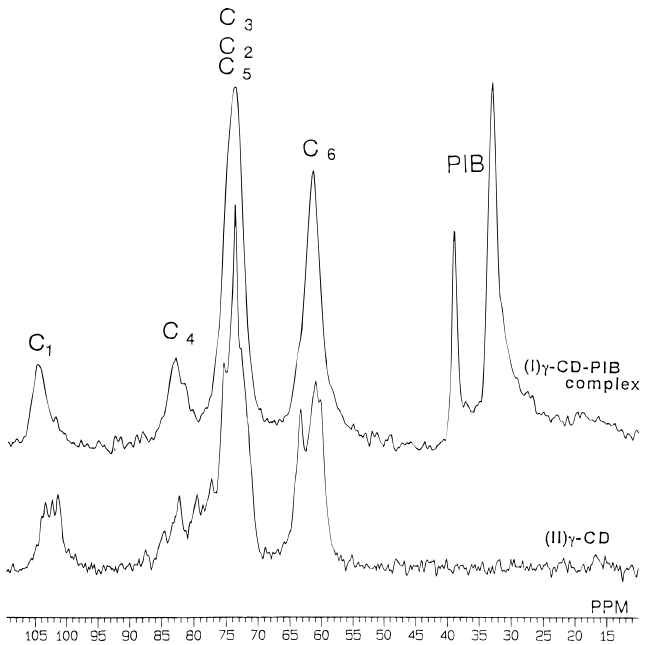

Figure 6. ^{13}C-PST/MAS NMR spectrum of γ-CD−PIB complex (I) and γ-CD (II).

and each glucose unit of γ-CD is in a similar environment. The X-ray studies of single crystals showed that γ-CD adopted a symmetrical conformation when it included guests in the cavities.[11] CP/MAS NMR spectra of complexes and uncomplexed cyclodextrins are consistent with the results of X-ray studies. Therefore, a PIB chain is thought to be included in the cavities of cyclodextrins. Figure 6 (I) shows the ^{13}C PST/MAS solid state NMR spectrum of the γ-CD−PIB complex, which gives stronger signals of relatively mobile carbons of the sample than ^{13}C CP/MAS NMR. The relative intensities of the peaks of PIB to those of γ-CD in Figure 6 (I) are much stronger than those in Figure 5 (I), indicating that the PIB chain is not so rigid as γ-CD in the complex. These results are consistent with the view that γ-CD molecules form a channel, forming the crystal frame of

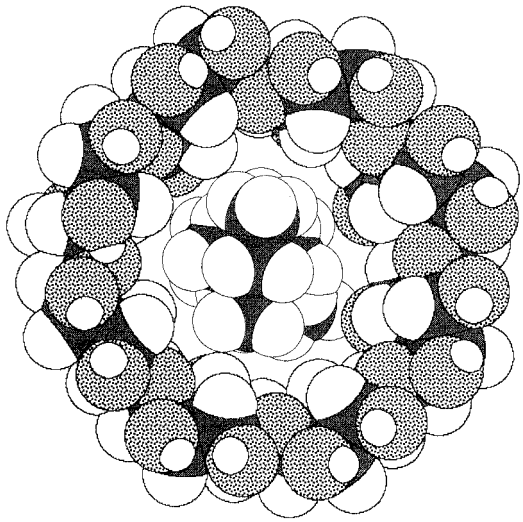

Figure 7. Proposed structure of the complex between γ-CD and PIB.

the complexes. Molecular model studies show that PIB chains are able to penetrate γ-CD cavities, while the PIB chain cannot penetrate α-CD cavities owing to the hindrance of dimethyl groups on the main chain. Model studies further indicate that the single cavity accommodates three isobutylene units. The inclusion complex formation of polymers with cyclodextrins is entropically unfavorable. However, formation of the complexes is thought to be promoted by hydrogen bond formation between cyclodextrins. Therefore, the head-to-head and tail-to-tail arrangement, which results in a more effective formation of hydrogen bonds between cyclodextrins, is thought to be the most probable structure. Such a structure was proved by X-ray studies on a single crystal of the complex between γ-CD and 1-propanol. Figure 7 shows a proposed structure of the complex between γ-CD and PIB.

Experimental Section

Materials. β-Cyclodextrin and γ-cyclodextrin were obtained from Nakarai Tesque Inc. and used after drying at 80 °C under vacuum with P_2O_5. 2,6-Di-*O*-methyl γ-cyclodextrin and 2,3,6-tri-*O*-methyl β-cyclodextrin were obtained from Nihon Shokuhin Kako Co. 2,2-Dimethylbutane and 2,2,4-trimethylpentane were purchased from Nakarai Tesque Inc. PIBs of average molecular weights 500, 800, 1350, and 2700 were purchased from Polyscience. The average molecular weights of the various polymer samples were found by GPC to be within the specification given by the suppliers. Water-soluble γ-CD polymer was prepared by the reaction of γ-CD with epichlorohydrin by a method similar to that of the β-CD polymer.[12] Dimethylformamide (DMF) (Nakarai Tesque Inc.) was purified with reduced pressure distillation from molecular sieves (4A) under a nitrogen atmosphere. Tetrahydrofuran (THF) (Nakarai Tesque Inc.) was fractionally distilled from CaH_2 under a nitrogen atmosphere. DMSO-d_6, $CDCl_3$, and D_2O used as solvents in the NMR measurements were obtained from Aldrich.

Measurements. ^{1}H NMR spectra of the complexes were recorded at 270 MHz on a JEOL JNM EX-270 NMR spectrometer. Chemical shifts were referred to the solvent values (δ = 2.50 for DMSO). ^{13}C CP/MAS and PST/MAS NMR spectra were measured at 100 MHz on a JEOL JNM GSX-400 NMR spectrometer with a sample spinning rate of 5.5 kHz at room temperature. CP spectra were acquired with a 4 ms proton 90 pulse, a 1 ms contact time, and a 5 s repetition time. Powder X-ray diffraction patterns were taken by using Cu Kα radiation with a Rigaku RAD-ROC X-ray diffractometer (voltage, 40 kV; current, 40 mA; scanning speed, 3° min^{-1}). IR spectra of the complexes were measured with a JASCO DP/F-3 spectrometer.

Preparation of the Inclusion Complexes of Polyisobutylenes with γ-CD. PIBs (20.0 mg) were put into tubes. A saturated aqueous solution of γ-CD (1.00 mL) was added at room temperature, and the mixtures were ultrasonically agitated for 10 min and then allowed to stand overnight at room temperature. The products that precipitated were collected by centrifugation, dried under vacuum up to 100 °C, washed with THF, and then dried under vacuum up to 100 °C to give the complexes.

***γ*-CD−PIB800.** Yield: 94%. ^{1}H-NMR (DMSO-d_6, 270 MHz): δ 5.74−5.69 (m, 16H, O(2)H and O(3)H of γ-CD), 4.89 (d, 8H, C(1)H of γ-CD), 4.49 (t, 8H, O(6)H of γ-CD), 3.63−3.52 (m, 24H, C(3)H, C(5)H and C(6)H of γ-CD), 3.38−3.27 (m, 16H, C(2)H and C(4)H of γ-CD), 2.00−0.60 (m, 24H, methyl H and methine H of PIB). ^{13}C-NMR (DMSO-d_6, 67.9 MHz): δ 101.84 (C(1) of γ-CD), 81.08 (C(4) of γ-CD), 73.07 (C(2) of γ-CD), 72.75 (C(3) of γ-CD), 72.33 (C(5) of γ-CD), 60.15 (C(6) of γ-CD). IR (KBr, cm^{-1}): 3411 (vs, ν_{OH}), 2952, 2932 (s, ν_{CH}), 1158, 1080, 1028 (vs, ν_{CO}). Anal. Calcd for $C_{60}H_{104}O_{40}\cdot 7.5H_2O$: C, 45.03; H, 7.49. Found: C, 45.04; H, 7.32.

***β*-CD−PIB500.** Yield: 18%. ^{1}H-NMR (DMSO-d_6, 270 MHz): δ 5.70−5.64 (m, 14H, O(2)H and O(3)H of β-CD), 4.84 (d, 7H, C(1)H of γ-CD), 4.41 (t, 7H, O(6)H of β-CD), 3.64−3.55 (m, 21H, C(3)H, C(5)H, and C(6)H of β-CD), 3.38−3.27 (m, 14H, C(2)H and C(4)H of β-CD), 2.00−0.60 (m, 64H, methyl H and methine H of PIB). IR (KBr, cm^{-1}): 3409 (vs, ν_{OH}), 2957, 2930 (s, ν_{CH}), 1156, 1080, 1030 (vs, ν_{CO}). Anal. Calcd for $C_{74}H_{134}O_{35}\cdot 1.7H_2O$: C, 55.05; H, 8.58. Found: C, 55.09; H, 8.99.

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