Preparation and Characterization of Inclusion Complexes between Methylated Cyclodextrins and Poly(tetrahydrofuran)

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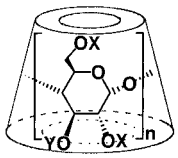
ABSTRACT: Binding properties of poly(tetrahydrofuran) (PTHF) to methylated cyclodextrins (CDs) in aqueous solutions were studied by turbidity titration and ^{1}H NMR measurements. PTHF, which has a low solubility in water, was dissolved in water on addition of 2,6-di-*O*-methyl-*β*-CD (DM-*β*-CD) and DM-α-CD. 2,3,6-tri-*O*-methyl-*β*-CD (TM-*β*-CD) and TM-α-CD did not solubilize PTHF. When PTHF was mixed with aqueous solutions of DM-*β*-CD and TM-*β*-CD, the inclusion complexes crystallized after several days. 1,4-Butanediol (monomer model) and PTHF ($M_w = 250$) did not form crystalline complexes with methylated CDs. The yields of the complexes of PTHF with methylated *β*-CDs increased with increasing molecular weight of PTHF and reached a maximum at about $M_w = 1000$. The complexes were characterized by ^{1}H NMR, solid-state ^{13}C NMR, powder X-ray, and FT-IR measurements.

Introduction

It is well-known that native cyclodextrins (CDs)[1−5] form inclusion complexes with various low molecular weight compounds. Recently, we found that CDs form crystalline complexes with macromolecules such as poly(ethylene glycol) (PEG),[6,7] poly(tetrahydrofuran) (PTHF),[8] and poly(propylene glycol) (PPG).[9,10] When the polymer is mixed with an aqueous solution of CD, the mixture immediately becomes turbid to give crystalline CD−polymer complexes. The selectivity of the macromolecular recognition of CDs is high. X-ray diffraction and ^{13}C cross-polarization magic angle spinning (CP/MAS) NMR measurements showed that CD molecules of CD−polymer complexes are in a channel type structure, and polymer chains are included in the cylinders of CDs. Later, CDs were found to form complexes not only with hydrophilic polymers but also with hydrophobic polymers, such as polyesters,[11] polyamides,[12] and polyisobutylene.[13] It was shown that the formation of the network of intermolecular hydrogen bonding between OH groups of CDs is important for the complex formation.

We have expanded the investigation of the complex formation between CD and polymers to the substituted CD system. Methylated CDs (Chart 1) are simple and important CD derivatives. The properties of methylated CDs are significantly different from those of native CDs. For example, the water-solubility of *β*-CD is 1.85 g/100 mL at 25 °C, whereas that of 2,6-di-*O*-methyl-*β*-CD (DM-*β*-CD) is 60 g/100 mL. Therefore, methylated CDs are expected to solubilize hydrophobic polymers in water more efficiently than native CDs, so that spectroscopic studies on the interaction between CDs and hydrophobic polymers might be possible in aqueous solutions. In addition, though the water solubility of *β*-CD increases with increasing temperature, that of DM-*β*-CD decreases. So it might be possible to obtain complexes between methylated CDs and hydrophobic polymers by heating the solutions. It is interesting to compare macromolecular recognition of native CDs to that of modified CDs. Previously, we focused on the complex formation between methylated CDs and PPG. PPG ($M_w = 4000$) is only slightly soluble in water. The solubility of PPG in water significantly increases on addition of DM-*β*-CD, and then the inclusion complexes crystallize. The interactions between DM-*β*-CD and PPG in water were studied by turbidity titration and NMR relaxation experiments. 2,3,6-Tri-*O*-methyl-α-CD (TM-α-CD), TM-*β*-CD, and DM-α-CD neither solubilize PPG in water nor form a precipitated complex with PPG.

Chart 1. Methylated CDs



	DM-α-CD	TM-β-CD	DM-β-CD
Number of glucose units	6	7	7
X	CH_3	CH_3	CH_3
Y	H	CH_3	H

No strong interactions between methylated CDs (DM-α-CD, DM-*β*-CD, TM-α-CD, and TM-*β*-CD) and hydrophilic PEG could be monitored in water by NMR methods. On addition, a clear aqueous solution of methylated CD and PEG did not give any precipitates even after 2 months. These results showed that methylated CDs have different properties of macromolecular recognition from native CDs. In comparison with native CDs having many hydroxy groups, weak hydrogen bonding between methylated CDs might show effects on the construction of channel-type complexes of methylated CDs. Other hydrophilic polymers, such as poly(vinyl alcohol) and poly(vinyl pyrrolidone), did not give crystalline complexes with methylated CDs. However, we found that methylated CDs selectively form inclusion complexes with hydrophobic polymers, such as PPG, PTHF, poly(propylene), and poly(ethylene). These results indicate that the hydrophobic interaction between methylated CDs and polymers is one of the most important factors for complexation.

PTHF is a hydrophobic linear polyether. We report here the complex formation between PTHF and methylated CDs. We found that the solubility of PTHF in water increases at low concentrations of DM-*β*-CD and DM-α-CD. However, at high concentrations of DM-*β*-CD and DM-α-CD, the solubility decreases to give crystalline inclusion complexes. TM-*β*-CD also forms crystalline complexes with PTHF. The crystalline complexes between methylated CDs and PTHF were characterized by ^{1}H NMR, solid ^{13}C NMR, powder X-ray, and FT-IR experiments.

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Experimental Section

Materials. Poly(tetrahydrofuran)s (PTHFs) (M_w = 250, 650, 1000, 2000, and 2900) were purchased from Aldrich. 1,4-Butanediol was purchased from Wako Pure Chemical Industries, Ltd. 2,6-Di-*O*-methyl-β-CD (DM-β-CD) and 2,3,6-tri-*O*-methy-β-CD (TM-β-CD) were purchased from Nacalai Tesque Ltd. DM-α-CD was kindly supplied from Nippon Food Chemical Ltd. TM-α-CD was purchased from Cyclolab R&D Lab. D_2O, and DMSO-d_6 was obtained from Aldrich.

Measurements. Absorption spectra were recorded on a Shimadzu UV-2001 spectrometer at room temperature. ^{1}H NMR experiments on DMSO-d_6 solutions were carried out on a JEOL EX-270 NMR spectrometer operating at 270 MHz. Chemical shifts of ^{1}H NMR spectra in DMSO-d_6 at 303 K were referenced to the solvent value (δ = 2.50 ppm). Powder X-ray diffraction patterns were taken by Cu Kα irradiation with a Rigaku RAD-ROC X-ray diffractometer (voltage, 40 kV; current, 100 mA; scanning speed, 3°/min). ^{13}C cross-polarization magic angle spinning (CP/MAS) and pulse saturation transfer/MAS (PST/MAS) spectra were recorded at 75.6 MHz on a Chemagnetics JMN-CMX300W spectrometer at room temperature. Chemical shifts were referenced to external hexamethylbenzene (δ = 17.36 ppm). FT-IR measurements were performed on a Jusco FT/IR-410 spectrometer by the KBr method.

Preparation of DM-β-CD−PTHF Complex. PTHF (20 mg) was added to a DM-β-CD saturated aqueous solution (DM-β-CD, 1.2 g; distilled water, 2.00 mL), and then the mixture was sonicated for 30 min. The turbid solution was allowed to stand for 5 days. The products precipitated were collected by centrifugation, dried under vacuum, washed with a small portion of distilled water, and dried under vacuum to give the DM-β-CD−PTHF complexes.

DM-β-CD−PTHF650. Yield: 6% (based on CD) (72 mg); 27% (based on PTHF). ^{1}H NMR (270 MHz, DMSO-d_6): δ = 4.97 (d, 7H, C(1)H of DM-β-CD), 4.95 (s, 7H, O(3)H of DM-β-CD), 3.70 (t, 7H, C(3)H of DM-β-CD), 3.56 (s, 7H, C(3)H of DM-β-CD), 3.50 (s, 21H, O(2)CH_3 of DM-β-CD), 3.25 (s, 21H, O(6)CH_3 of DM-β-CD), 1.50 (m, 4H × 1.3, C−methylene H of PTHF). IR (KBr, cm^{-1}): 3420 (vs, ν_{OH}), 2928 (s, ν_{CH}), 1158, 1090, 1051 (vs, ν_{CO}). Anal. Calcd for $(C_{56}H_{98}O_{35})_1(C_4H_8O)_{1.3}(H_2O)_{1.7}$: C, 50.49; H, 7.74. Found: C, 50.47; H, 7.59.

DM-β-CD−PTHF1000. Yield: 10% (based on CD) (120 mg); 42% (based on PTHF). ^{1}H NMR (270 MHz, DMSO-d_6): δ = 4.97 (d, 7H, C(1)H of DM-β-CD), 4.95 (s, 7H, O(3)H of DM-β-CD), 3.71 (t, 7H, C(3)H of DM-β-CD), 3.56 (s, 7H, C(3)H of DM-β-CD), 3.50 (s, 21H, O(2)CH_3 of DM-β-CD), 3.25 (s, 21H, O(6)CH_3 of DM-β-CD), 1.50 (m, 4H × 1.2, C−methylene H of PTHF). IR (KBr, cm^{-1}): 3416 (vs, ν_{OH}), 2928 (s, ν_{CH}), 1158, 1090, 1051 (vs, ν_{CO}). Anal. Calcd for $(C_{56}H_{98}O_{35})_1(C_4H_8O)_{1.2}(H_2O)_{1.7}$: C, 50.41; H, 7.72. Found: C, 50.38; H, 7.63.

DM-β-CD−PTHF2000. Yield: 10% (based on CD) (120 mg); 42% (based on PTHF). ^{1}H NMR (270 MHz, DMSO-d_6): δ = 4.97 (d, 7H, C(1)H of DM-β-CD), 4.95 (s, 7H, O(3)H of DM-β-CD), 3.71 (t, 7H, C(3)H of DM-β-CD), 3.56 (s, 7H, C(3)H of DM-β-CD), 3.50 (s, 21H, O(2)CH_3 of DM-β-CD), 3.25 (s, 21H, O(6)CH_3 of DM-β-CD), 1.50 (m, 4H × 1.2, C−methylene H of PTHF). IR (KBr, cm^{-1}): 3419 (vs, ν_{OH}), 2928 (s, ν_{CH}), 1157, 1090, 1051 (vs, ν_{CO}). Anal. Calcd for $(C_{56}H_{98}O_{35})_1(C_4H_8O)_{1.2}(H_2O)_{1.2}$: C, 50.73; H, 7.70. Found: C, 50.70; H, 7.65.

Preparation of Solid TM-β-CD−PTHF Complex. PTHF (20 mg) was added to a TM-β-CD aqueous solution consisting of 0.45 g of TM-β-CD and 2.00 mL of distilled water, and then the mixture was sonicated for 30 min. The turbid solution was allowed to stand for 7 days. The products precipitated were collected by centrifugation, dried under vacuum, and washed with a small portion of distilled water. The products were dried under high vacuum to give the TM-β-CD−PTHF complexes.

TM-β-CD−PTHF650. Yield: 29% (based on CD) (130 mg); 76% (based on PTHF). ^{1}H NMR (270 MHz, DMSO-d_6): δ = 5.05 (d, 7H, C(1)H of TM-β-CD), 3.69 (m, 14H, C(3)H and C(5)H of TM-β-CD), 3.50 (s, 21H, O(2)CH_3 of TM-β-CD), 3.39 (s, 21H, O(3)CH_3 of TM-β-CD), 3.24 (s, 21H, O(6)CH_3 of TM-β-CD), 1.51 (m, 4H × 2.3, C−methylene H of PTHF). IR (KBr, cm^{-1}): 2929 (s, ν_{CH}), 1162, 1141, 1109, 1074, 1038 (vs, ν_{CO}). Anal. Calcd for $(C_{63}H_{112}O_{35})_1(C_4H_8O)_{2.3}(H_2O)_1$: C, 53.75; H, 8.27. Found: C, 53.71; H, 8.21.

TM-β-CD−PTHF1000. Yield: 31% (based on CD) (140 mg); 100% (based on PTHF). ^{1}H NMR (270 MHz, DMSO-d_6): δ = 5.05 (d, 7H, C(1)H of TM-β-CD), 3.69 (m, 14H, C(3)H and C(5)H of TM-β-CD), 3.50 (s, 21H, O(2)CH_3 of TM-β-CD), 3.39 (s, 21H, O(3)CH_3 of TM-β-CD), 3.24 (s, 21H, O(6)CH_3 of TM-β-CD), 1.51 (m, 4H × 2.9, C−methylene H of PTHF). IR (KBr, cm^{-1}): 2928 (s, ν_{CH}), 1162, 1141, 1109, 1074, 1038 (vs, ν_{CO}). Anal. Calcd for $(C_{63}H_{112}O_{35})_1(C_4H_8O)_{2.9}(H_2O)_{1.5}$: C, 53.79; H, 8.36. Found: C, 53.80; H, 8.20.

TM-β-CD−PTHF2000. Yield: 21% (based on CD) (95 mg); 79% (based on PTHF). ^{1}H NMR (270 MHz, DMSO-d_6): δ = 5.05 (d, 7H, C(1)H of TM-β-CD), 3.69 (m, 14H, C(3)H and C(5)H of TM-β-CD), 3.50 (s, 21H, O(2)CH_3 of TM-β-CD), 3.39 (s, 21H, O(3)CH_3 of TM-β-CD), 3.24 (s, 21H, O(6)CH_3 of TM-β-CD), 1.51 (m, 4H × 3.3, C−methylene H of PTHF). IR (KBr, cm^{-1}): 2929 (s, ν_{CH}), 1162, 1141, 1110, 1075, 1038 (vs, ν_{CO}). Anal. Calcd for $(C_{63}H_{112}O_{35})_1(C_4H_8O)_{3.3}(H_2O)_{0.2}$: C, 54.77; H, 8.37. Found: C, 54.75; H, 8.41.

Preparation of Solid DM-α-CD−PTHF Complex. PTHF (20 mg) was added to DM-α-CD aqueous solution consisting of 0.6 g of DM-α-CD and 2.00 mL of distilled water, and then the mixture was sonicated for 30 min. The turbid solution was allowed to stand for 1 month. The products precipitated were collected by centrifugation, dried under vacuum, and washed with a small portion of distilled water. The products were dried under high vacuum to give the DM-α-CD−PTHF complexes.

DM-α-CD−PTHF650. Yield based on CD: <1%. ^{1}H NMR (270 MHz, DMSO-d_6): δ = 4.97 (m, 12H, C(1)H and O(3)H of DM-α-CD), 3.95−3.60 (m, 12H, C(3)H and C(5)H of DM-α-CD), 3.56 (s, 6H, C(3)H of DM-α-CD), 3.48 (s, 18H, O(2)CH_3 of DM-α-CD), 3.24 (s, 18H, O(6)CH_3 of DM-α-CD), 1.50 (m, 4H × 4, C−methylene H of PTHF). IR (KBr, cm^{-1}): 3427 (vs, ν_{OH}), 2931 (s, ν_{CH}), 1155, 1089, 1051 (vs, ν_{CO}).

Turbidimetric Titration. Methylated CD was dissolved in distilled water (2.00 mL). PTHF (20 mg) was added to the aqueous solution, and then the mixture was sonicated for 20 min. Turbidities were measured by transmittance (%) at 800 nm using an absorption spectrometer.

NMR Analysis of D_2O Solutions. PTHF (10 mg) was added to a DM-β-CD (0.46 g) (or DM-α-CD (0.10 g)) solution in D_2O (1.00 mL). The solution was stirred overnight and bubbled with N_2 gas. NMR measurements were carried out on a JEOL EX-270 spectrometer at 298 K, operating at 270 MHz for ^{1}H nuclei and 67.9 MHz for ^{13}C. Chemical shifts were referenced to external 3-(trimethylsilyl)propionic acid sodium salt (DSS).

Results and Discussion

When a CD aqueous solution was sonicated with PTHF, the mixture immediately became turbid and then gave precipitated complexes. In a similar manner, PTHF (M_w = 650) (PTHF650) (20 mg) was added to an aqueous solution of methylated CD (2.00 mL of distilled water) and agitated by sonication for 20 min. The changes of the turbidity of the mixtures of PTHF650 and solutions of methylated CD were studied by turbidity titration experiments (Figure 1). The turbidity of the TM-β-CD−PTHF650 system increased with time. On the other hand, the transmittance of the DM-α-CD and DM-β-CD systems apparently increased. PTHF650 was dissolved in a water phase on addition of DM-β-CD or DM-α-CD. We could not observe interactions between TM-α-CD and PTHF. These results obviously show that PTHF650 was bound to DM-α-CD, TM-β-CD, and DM-β-CD in a water phase.

To investigate modes of interactions between methylated CDs and PTHF, we used a PTHF derivative (PTHF9An) (Chart 2). 9-Anthracene end groups are larger than the cavity sizes of the methylated CDs. When PTHF9An was mixed with aqueous solutions of

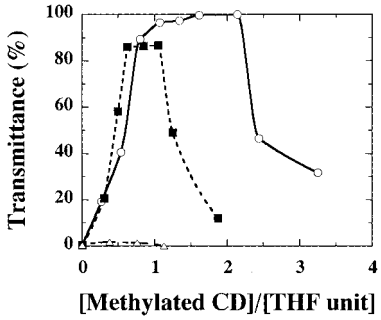


Figure 1. Effects of the concentrations of methylated CDs on transmittance of PTHF650−water system: (○) DM-*β*-CD; (■) DM-α-CD; (△) TM-*β*-CD.

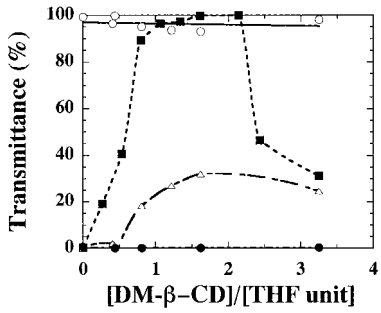
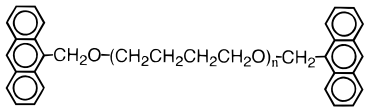


Figure 2. M_w dependency of turbidity of PTHF at various concentrations of DM-*β*-CD: (○) PTHF250; (■) PTHF650; (△) PTHF1000; (◆) PTHF2000; (●) PTHF2900.

Chart 2. PTHF9An



methylated CDs, no change was observed. It was suggested that methylated CDs thread on a PTHF chain through small polymer ends to form inclusion complexes.

A. Interactions in Water. Figure 1 shows the solubilizing effects of methylated CDs on PTHF650 observed by turbidity experiments. We studied M_w dependency of the interaction between DM-*β*-CD and PTHF (Figure 2). PTHF250 did not show any changes in the turbidity on addition of DM-*β*-CD. The solubility of PTHF650 increases with increasing concentration of DM-*β*-CD. The mixture gave a clear solution at about a 1.5 ratio of [DM-*β*-CD]/[PTHF650]. However, the transmittance of DM-*β*-CD−PTHF650 solutions decreases at higher [DM-*β*-CD]. Only a part of the PTHF1000 is dissolved in an aqueous solution by DM-*β*-CD. PTHFs (M_w = 2000 and 2900) are insoluble in water even in the presence of DM-*β*-CD. A PTHF with a high M_w is too hydrophobic to be solubilized effectively in a water phase containing DM-*β*-CD. A similar M_w dependency was observed in the case of the DM-α-CD−PTHF system (Figure 3). Both DM-*β*-CD and DM-α-CD solubilized PTHF650 effectively. Addition of TM-*β*-CD did not increase the solubility of PTHF of various M_ws, and the mixtures gave precipitates after 7 days.

We studied the interactions between DM-CDs and PTHF in D_2O at 25 °C by ^1H and ^{13}C NMR spectroscopy. In the absence of CD, the ^1H resonance of methylene H of PTHF at 1.60 ppm is a multiplet. On addition of DM-α-CD, the signal of PTHF was broadened and slightly shifted downfield. Addition of DM-*β*-CD also caused both broadening and downfield shift ($\Delta\delta$ = +0.04−0.05 ppm)

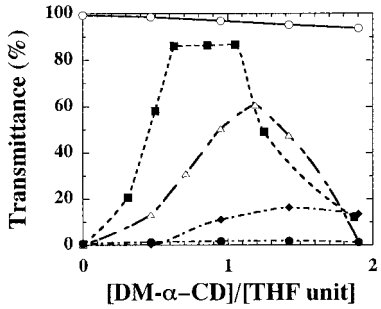


Figure 3. M_w dependency of turbidity of PTHF at various concentrations of DM-α-CD: (○) PTHF250; (■) PTHF650; (△) PTHF1000; (◆) PTHF2000; (●) PTHF2900.

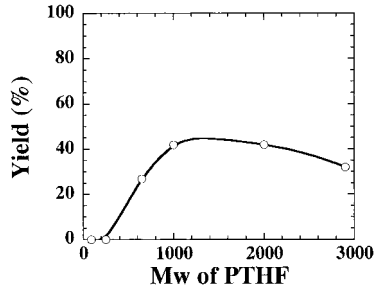


Figure 4. Yields of the complexes of DM-*β*-CD with PTHF as a function of M_w of PTHF. Yields are calculated based on PTHF.

of PTHF signals. Addition of DM-CDs caused broadening of the ^{13}C resonances of PTHF. These spectral changes are slight, but it should be noted that there are no changes in the spectra of PEG on addition of CDs and methylated CDs. The spectral changes indicate that PTHF is included in the cavities of DM-*β*-CD or DM-α-CD to form hydrophilic complexes.

B. Crystallization of Inclusion Complexes. DM-*β*-CD. DM-*β*-CD−PTHF650 solutions became turbid at a high concentration of DM-*β*-CD. We found that this behavior results from crystallization of DM-*β*-CD−PTHF650 complexes. When PTHF was mixed with a saturated DM-*β*-CD solution, crystalline precipitates formed after 3 days. Figure 4 shows the effects of the molecular weight of PTHF on the yields of the complexes. 1,4-Butanediol (monomer model) and PTHF250 did not give any crystalline complexes. The yields of the complexes increased with increasing M_w of PTHF. PTHF2900 is so hydrophobic that it does not interact effectively with DM-*β*-CD in water. ^1H NMR measurements of the crystalline complexes were carried out in DMSO-d_6. The ^1H NMR spectrum of the complex from a DM-*β*-CD−PTHF650 solution shows signals of DM-*β*-CD and PTHF650 (Figure 5). We found that the stoichiometry of the precipitates is always in a ratio of about 1:1−1.5 (DM-*β*-CD: THF unit), even if DM-*β*-CD and PTHF are mixed in any ratio. The stoichiometry is in good agreement with that of the α-CD−PTHF complex. The stoichiometries of DM-*β*-CD−PTHF aggregates are independent of M_w in the range of 650 to 2000.

X-ray diffraction studies of methylated CDs and their complexes with low molecular weight compounds have been reported.[14,15] In Figure 6, the powder X-ray diffraction pattern of the DM-*β*-CD−PTHF complex is different from that of free DM-*β*-CD.[16] The crystal packing of the DM-*β*-CD−PTHF complex was compared with those of model DM-*β*-CD complexes, for example, DM-*β*-CD−*p*-nitrophenol and −*p*-iodophenol complexes.[17,18] In these DM-*β*-CD complexes, DM-*β*-CD

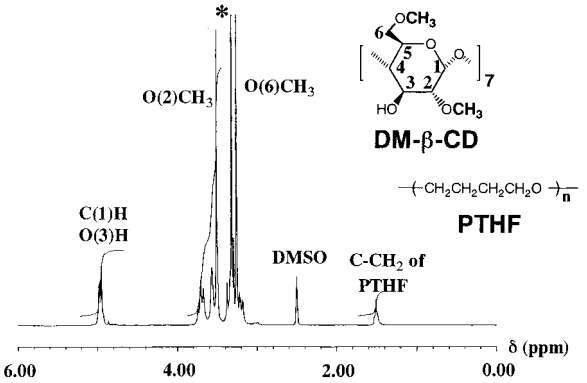


Figure 5. ^{1}H NMR spectrum of DM-β-CD−PTHF650 complex in DMSO-d_6 at 30 °C.

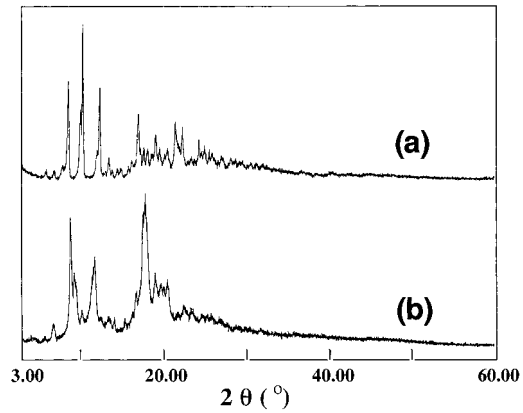


Figure 6. Powder X-ray diffraction patterns of DM-β-CD (a) and the DM-β-CD−PTHF650 complex (b).

molecules do not form a column structure, and the O(2) and O(3) side of the DM-β-CD cavity is blocked by the neighboring DM-β-CD. These packed DM-β-CDs cannot include a polymer chain. In fact, X-ray measurements did not give any similarity of crystal structures between DM-β-CD−PTHF and DM-β-CD complexes with the low molecular weight compounds. We found that the crystal structure of the DM-β-CD−PTHF complex is different from those of DM-β-CD with low molecular weight compounds and is typical for the DM-β-CD−polymer system.

The solid-state ^{13}C resonances of C(1) and C(4) of CD give information about the CD crystal structure such as conformations of glycosidic linkages and the packing state. Figure 7 shows ^{13}C cross-polarization magic angle spinning (CP/MAS) NMR spectra of DM-β-CD and the DM-β-CD−PTHF650 complex. The C(1) region of free DM-β-CD was dispersed, showing that the structure of a DM-β-CD ring is asymmetric. The chemical shifts of the C(1) peaks were 102.3 and 101.7 ppm. However, the C(1) resonance of DM-β-CD−PTHF complex is a sharp singlet (δ = 102.7 ppm). Although the spectral changes are slight, the difference cannot be ignored. These results showed that the structure of DM-β-CD including PTHF is symmetric. Hall and his co-worker[19] reported that the ^{13}C resonances of DM-β-CD showed no strong multiplicity changes after complexation with small guest molecules, such as benzene, toluene, and biphenyl etc. Inoue[20−22] and Veregin[23] reported that the ^{13}C single peak of C(1) of CD complex with low molecular weight compounds is caused by the crystal packing of CD molecules in a "channel-type". It was also supported by our previous works that CD−polymer complexes in a channel-type gave single signals for C(1) and C(4) in

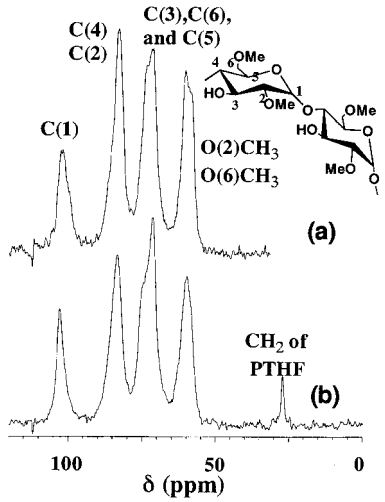


Figure 7. ^{13}C CP/MAS NMR spectra of DM-β-CD (a) and the DM-β-CD−PTHF650 complex (b).

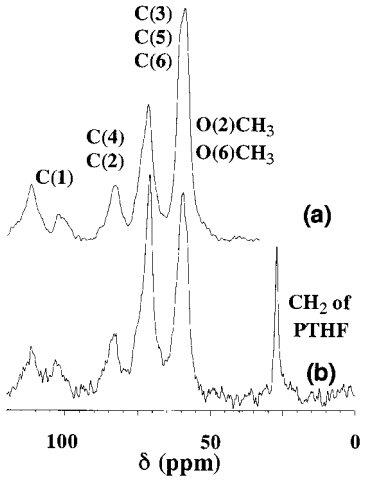


Figure 8. ^{13}C PST/MAS NMR spectra of DM-β-CD (a) and the DM-β-CD−PTHF650 complex (b).

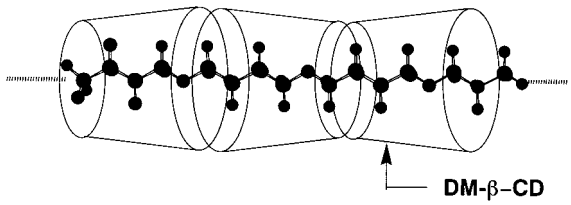


Figure 9. Proposed structure of the complex between DM-β-CD and PTHF.

the ^{13}C CP/MAS spectra. We proposed that the crystal structure of DM-β-CD−PTHF650 complex adopts a channel type in which DM-β-CD molecules are stacked along PTHF chain to form a symmetric channel-type structure. Figure 8 shows ^{13}C pulse saturation transfer (PST)/MAS NMR spectra of DM-β-CD and the DM-β-CD−PTHF650 complex. In ^{13}C PST/MAS NMR spectra, carbons of the flexible region give strong signals. The ^{13}C signal of PTHF (δ = 27.2 ppm) is so sharp and strong that PTHF chains in DM-β-CD cavities are probably flexible. Figure 9 shows a proposed structure of the crystalline DM-β-CD−PTHF complex.

TM-β-CD. When a mixture consisting of PTHF and TM-β-CD was allowed to stand at room temperature for 7 days, crystalline complexes slowly formed. It took longer for the TM-β-CD−PTHF complex to form crystals than for DM-β-CD−PTHF (5 days). Figure 10 shows the

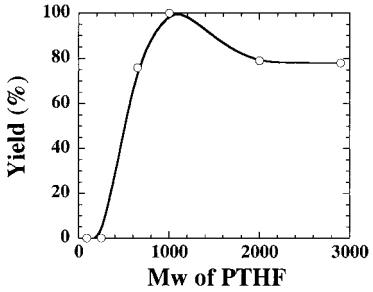


Figure 10. Yields of the complexes of TM-β-CD with PTHF as a function of M_w of PTHF. Yields are calculated based on PTHF.

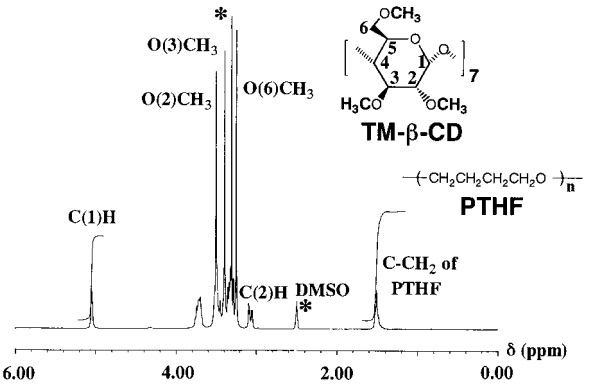


Figure 11. ^{1}H NMR spectrum of TM-β-CD−PTHF650 complex in DMSO-d_6 at 30 °C.

results of crystalline complex formation of TM-β-CD with PTHF of various molecular weights. It is clear that Figure 10 gives a tendency similar to that observed in Figure 4. The yield is the highest at M_w = 1000 for PTHF. TM-β-CD shows chain-length selectivity.

The stoichiometry of TM-β-CD−PTHF650 complex was found to be in a 1:2−2.5 ratio (TM-β-CD:THF unit) by the ^{1}H NMR spectrum (Figure 11). The proportion of the THF unit in TM-β-CD−PTHF complex increased with an increase in the M_w of PTHF. One possible reason is that the threading of TM-β-CD on a polymer chain is hindered due to the tight size fitting between PTHF and the TM-β-CD cavity in comparison with DM-β-CD. Molecular modeling studies indicated that interactions between the penetrated TM-β-CDs are weak due to a lack of hydrogen bonding between neighboring TM-β-CDs. Hydrophobic interactions and size fitting (van der Waals contacts) between PTHF and methylated CD are major driving forces for the complex formation.

We examined the structure of the TM-β-CD−PTHF650 complex by powder X-ray diffraction patterns (Figure 12). Powder X-ray analysis shows that the crystal packing of TM-β-CD−PTHF650 is obviously different from that of free TM-β-CD.[24] The TM-β-CD−*p*-iodophenol complex,[25] in which TM-β-CD is in a head-to-tail column, also gave different patterns for the powder X-ray diffraction. We carried out ^{13}C CP/MAS NMR measurements on the TM-β-CD−PTHF650 complex (Figure 13). The multiplet lines of C(1) of free TM-β-CD have their origin in differences in glucopyranosyl linkages. On the other hand, the resonance of C(1) of TM-β-CD−PTHF complex was simple. These spectral changes showed that TM-β-CD rings in the inclusion complex exist in a round shape because of insertion of PTHF into the CD cavities.

DM-α-CD. We found that the crystallization of DM-α-CD−PTHF complexes is very slow (about 1 month).

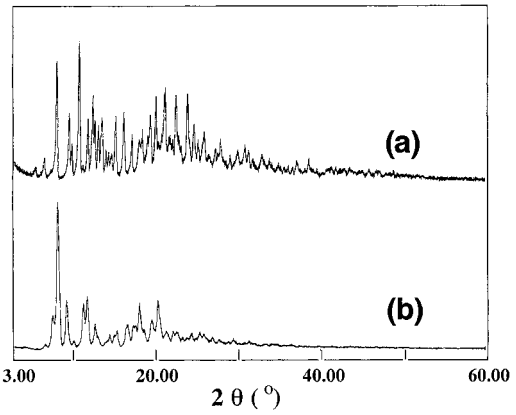


Figure 12. Powder X-ray diffraction patterns of TM-β-CD (a) and TM-β-CD−PTHF650 complex (b).

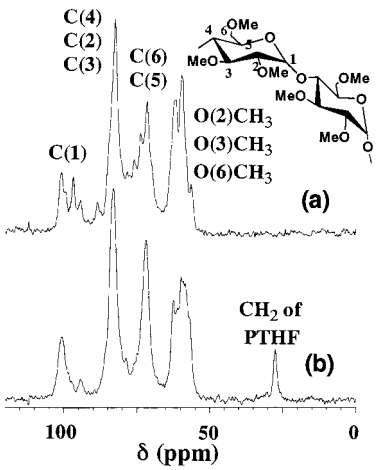


Figure 13. ^{13}C CP/MAS NMR spectra of TM-β-CD (a) and TM-β-CD−PTHF650 complex (b).

The yield of the DM-α-CD−PTHF650 complex was less than 1%. ^{1}H NMR analysis in DMSO-d_6 showed that the stoichiometry of DM-α-CD−PTHF650 complex was about 1:4 (DM-α-CD:THF unit). This stoichiometry is twice as large as that of DM-β-CD−PTHF650 complex. On the basis of powder X-ray diffraction pattern studies, it was showed that the crystal structure of DM-α-CD−PTHF650 complex is significantly different from that of free DM-α-CD.[26]

Conclusion

We found that PTHF forms inclusion complexes with DM-β-CD, TM-β-CD, and DM-α-CD to give crystalline complexes. Addition of DM-β-CD resulted in solubilization of hydrophobic PTHF in the water phase, and then the complexes crystallized. The stoichiometries of DM-β-CD−PTHF complexes were always 1:1−1.5 (DM-β-CD: THF unit) and showed good agreement with that of the respective α-CD−PTHF complex. ^{1}H NMR, powder X-ray, and solid-state ^{13}C NMR measurements indicated that many DM-β-CD molecules are threaded onto a PTHF chain to form a column structure. Dependency of the solubility of PTHF on concentrations of TM-β-CD could not be observed, whereas PTHF formed crystalline complexes with TM-β-CD after 7 days. The yields of crystalline DM-α-CD−PTHF complexes were low, because PTHF was solubilized in water on addition of DM-α-CD.

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