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Notes

Inclusion Complexation of Cyclodextrins with Polyglycol in Mixed Guest Systems

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Abstract : The inclusion complexations of α-, β- and γ- cyclodextrins (CDs) with the polyglycols, such as poly(ethylene glycol) (PEG), poly(propylene glycol) (PPG) and poly(butylene glycol) (PBG) by competitive reaction in the presence of two guest molecules were investigated. The selective complexation of CDs with the polyglycols in two guest systems were found and corresponding crystalline complexes formed were characterized by ^{1}H-NMR, ^{13}C CP/MAS NMR, and powder X-ray analysis. As consequences, α- and β-CDs formed selective crystalline complexes with PEG and PPG by competitive reaction, respectively, while γ-CD formed complexes with both of PPG and PBG. The stoichiometry of formed complexes with CDs are 2:1 (monomer unit : CD).

Introduction

Cyclodextrins (CDs) are cyclic oligosaccharides formed by an α-1,4-linkages of glucopyranose units.[1-6] The most commonly used oligosaccharides are α-, β- and γ-CDs with six, seven and eight glucopyranose units, respectively. These compounds possess a hydrophilic exterior, which makes them soluble in water, and an interior cavity, which is less polar than water. The α-, β- and γ-CDs have approximate inner cavity diameters of 5.0, 7.8 and 9.5 Å, respectively. CDs were discovered a century ago[7,8] and have been studied extensively as models for enzyme active sites to mimic enzyme activities and to understand the mechanism of molecular recognition.[3-5]

A great number of inclusion complexes of CDs with low molecular weight molecules like organic compounds were characterized. Therefore, these properties enable CDs to incorporate guest molecules on the basis of size and hydrophobicity. More recently, Harada *et al.*[9-14] reported not only on the complexation of CDs with hydrophilic polymers such as poly(ethylene glycol) (PEG), poly(propylene glycol) (PPG) and poly(methyl vinyl ether), and hydrophobic polymers such as oligoethylene and poly(isobutylene) in single guest systems, but also on the interactions of guest moieties attached on a polymer chain with CDs.

There have been no reports, however, on the formation of inclusion complexes of CDs with the polymer by competitive complex reaction in the presence of two guest molecules. We found that CDs form selectively crystalline complexes with the polyglycols in two guest systems such as PEG/

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PPG, PPG/poly(butylene glycol) (PBG) and PEG/PBG systems. The complexes formed were characterized by ^{1}H-NMR, ^{13}C CP/MAS NMR, and X-ray (powder) analysis. In this paper, the selective formation of CD complexes with polyglycols in competitive reaction and characterization of these inclusion complexes are discussed.

Experimental

Materials. CDs were obtained from Nakarai Tesque Inc. and used after drying at 100°C under vacuum. PEG, PPG and PBG were purchased from Aldrich. DMSO-d_6 used as solvent in NMR measurements was obtained from Aldrich.

Measurements. ^{1}H-NMR spectra were recorded at 300 MHz in DMSO-d_6 on a Jeol JNM-LA300 spectrometer. Chemical shifts were referenced to the solvent value (δ 2.50 for DMSO). ^{13}C CP/MAS NMR spectra were measured at 75 MHz on a Jeol JNM-LA 300 spectrometer with spinning rate of 5.5-6.0 kHz. CP spectra were acquired with a 4 ms proton 90° pulse, a 1 ms contact time, and a 5 s repetition time. X-ray diffraction patterns for powdered samples were obtained on a Rigaku diffractometer under the following conditions: target Cu, voltage 40 kV, current 4 mA, count range 2000 cps and scanning speed 5°/min.

Preparation of the Inclusion Complexes of CDs with Polyglycols. The binary mixtures of polyglycols each containing PEG (0.1g)/PPG (0.1g), PPG (0.1g)/PBG (0.1g) and PEG (0.1g)/PBG (0.1g) were put into individual glass tubes. An aqueous solution of α-, β- and γ-CDs (40~60 mL) containing 1.0 g of CDs were added to the tubes containing binary mixture of polyglycols at room temperature, and the mixture ultrasonically agitated for 20 min and then allowed to stand overnight at room temperature. The precipitated products were collected by centrifuge, dried under vacuum up to 100 °C, washed with H_2O, and dried under vacuum up to 100 °C to give the CD complexes. The yields were calculated on the basis of 2:1 (glycol unit : CD) stoichiometry.

Results and Discussion

Selectivity of Complex Formation by Competitive Reaction. To explore the influence of structural variation in the complexation upon selectivity, the complex formations of α-, β- and γ-CDs with the polyglycols by competitive reactions were examined. Table I gives the yields of the CD complexes formed with polyglycols in binary guest systems.

In PEG/PPG system, PEG which has no side-chain selectively formed a complex only with α-CD, while PPG having methyl side-chain selectively formed crystalline complexes with β- and γ-CD in 60% and 35% yields, respectively. The yield of crystalline α-CD complex with PPG is higher than that of γ-CD complex. These results are similar to those of the complex formation of the CDs with PPG in single guest systems reported by Harada.[8] This is due to that PPG chain fit well into the cavity of β-CD by comparing with γ-CD.

When the saturated aqueous solutions of α-, β- and γ-CDs were added to PPG/PBG system, formed complexes of β- and γ-CDs with PPG and PBG, respectively, while α-CD did not give any complex with PPG or PBG. This result can be explained that the cavity of α-CD is too small for PPG or PBG to penetrate due to steric hindrance by methyl or ethyl groups attached on the main chain. Even the γ-CD which has the largest cavity formed limited amounts of crystalline complexes

Table I. Competitive Precipitation (%yield) for Crystalline Complexes of CDs with Binary Polyglycols

Binary Mixture of Polyglycol	Yield (%)		
	α-CD	β-CD	γ-CD
PEG/PPG	10% / a	a / 60%	a / 35%
PPG/PBG	a / a	65% / a	19% / 23%
PEG/PBG	13% / a	a / a	a / 11%

a : Means not detected by ^{1}H NMR.

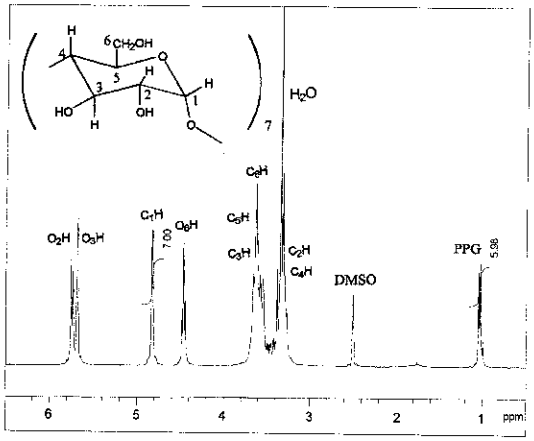


Figure 1. ^{1}H-NHR spectrum of complex of PPG with β-CD in DMSO-d_6.

with PPG and PBG in 19% and 23% yields, respectively. These results indicate that γ-CD can not form crystalline complex selectively in PPG/PBG system, which is attributed to the larger cavity rather than side-chain group of polyglycol. In contrast, β-CD selectively formed complex with PPG in higher yield (65%) than γ-CD and not with PBG. It is noteworthy that PPG with suitable side-chain group can be included in cavity of β-CD.

In PEG/PBG system, α-CD formed selectively a complex with PEG while α-CD formed crystalline complex with PBG. As shown in above results, these phenomena indicate that the relative sizes of the cavities of CDs and shapes of the polymers are important in both of the single and the competitive complex reaction.

NMR techniques are especially important to confirm the stoichiometry of CD complexes with polyglycols. Figure 1 shows the well-separated ^{1}H-NMR spectrum for β-CD complex with PPG in DMSO-d_6. The resonance at δ 4.82 is assigned to the proton attached to C1 from β-CD and the multiplet at δ 1.03 indicates the methyl protons from PPG. Comparing the peak intensities for C1 (7H, 1H × 7) of β-CD and methyl group (6H, 3H × 2) of PPG, it is found that two monomer units of PPG bind to one β-CD molecule. So it is obvious that the stoichiometry of the complex is 2:1 (monomer units of PPG : β-CD). Also, α- and γ-CD complexes with PEG or PBG were found to

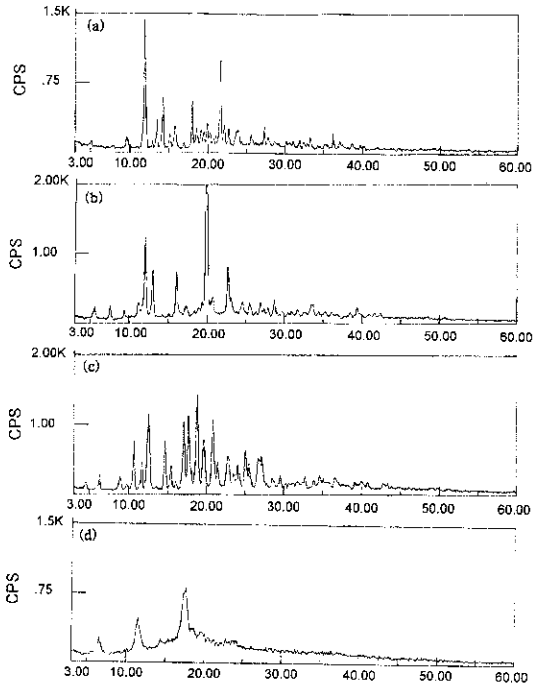
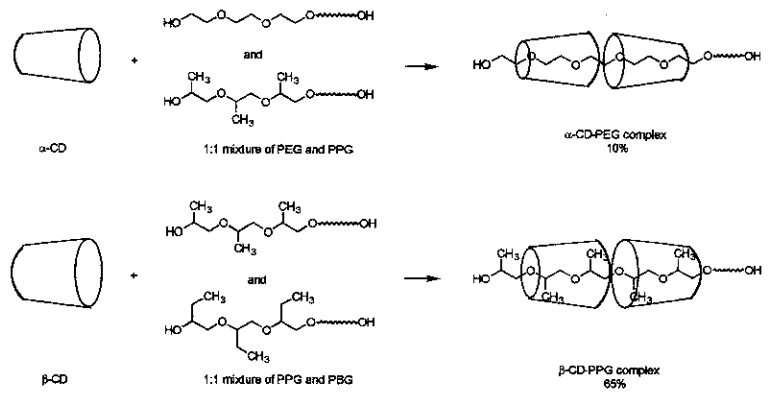


Figure 2. X-ray diffraction patterns (a) α-CD, (b) α-CD-PEG complex, (c) β-CD and (d) β-CD-PPG complex.

have the same stoichiometry of 2:1 (monomer units : CD).

Binding Models of the Complexes. Figure 2 shows the X-ray powder patterns of α-, β-CD and their complexes with PEG and PPG. According to Harada *et al.*[9,12] crystalline type of CD complexes with the variation of molecular lengths of guest can be classified by two groups: one is cage type, and the other is channel type. The former is crystalline type for CD complexes with small molecular such as propionic acid, and the latter is for CD complexes with long chain molecular such as valeric acid and oligo ethylene.

In comparing our results with cage type, the X-ray powder pattern show that the CD complexes are crystalline, and different from those of free CDs, even more different from that of the complex of α-CD with small molecule, which has been reported as the cage type. The patterns of these complexes with PEG, PPG and PBG containing to long chain are more similar to that of the complex with *p*-nitroacetanlide,[12] which has been proved to have a column structure by X-ray study of a single crystal of the complex.



Scheme I. Specific inclusion complexations of CDs with polyglycols and proposed structures of the CD-polyglycol complexes.

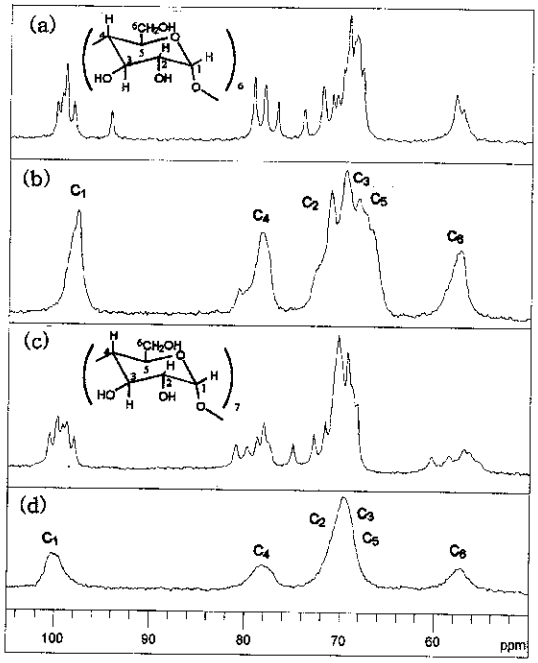


Figure 3. ^{13}C CP/MAS spectra of (a) α-CD, (b) α-CD-PEG complex, (c) β-CD and (d) β-CD-PPG complex.

Figure 3 shows the ^{13}C CP/MAS NMR spectra of the α-, β-CD and their complexes with PEG and PPG. The free α-CD appears at 99.8, 98.3, 98.0 and 93.8 ppm for C1, and 79.5, 78.2 and 76.3 ppm for C4, respectively, although an α-CD consists of six units of glucose which are attributed to the conformationally strained α-1,4-linked glucose.

On complexation the separated peak patterns for C1 and C4 resonance from α-CD vanished and collapsed to broad singlets, attributable to α-CD adopts more a symmetrical conformation than free α-CD, and each glucose units of α-CD in the complex are in a similar environment. In case of free β-CD and β-CD complex, similar spectral behavior to α-CD and its complex was observed even though the polymer chain included in cavity and cavity size of CD are different.

Overall, the ^{13}C CP/MAS NMR spectra of complexes and free CDs are consistent with the results of X-ray studies to give the proposed structures of α-CD-PEG and β-CD-PPG complexes in head-to-head or tail-to-tail fashion[9] by the specific complex formation shown in Scheme I.

In conclusion, α- and β-CDs formed complexes with PEG or PPG to give crystalline complexes by competitive reaction, while γ-CD formed complexes with PPG and PBG, which consist of a mixture, formed complexes with CDs in the stoichiometry of 2:1 (monomer unit : CD) to give crystalline complexes.

References

(1) J. Szejtli and T. Osa, in *Comprehensive Supra-molucular Chemistry,* Pergamon, Oxford, 1996, Vol. 3.
(2) J. H. Jung, C. Takehisa, Y. Sakata, and T. Kaneda, *Chem. Lett.*, 147 (1996).
(3) A. Ruebner, J. G. Moser, D. Kirsch, B. Spengler, S. Andrees, and S. Roehrs, *J. Incl. Phenom.*, **20**, 35 (1998).
(4) T. Hanawa, E. Yonemochi, T. Oguchi, Y. Nakai, and K. Yamamoto, *J. Incl. Phenom.*, **15**, 91 (1993).

(5) R. Bonomo, V. Cucinita, F. D Allessandro, G. Impellizzeri, G. Maccarrone, and E. Rizzarelli, *J. Incl. Phenom.*, **15**, 167 (1993).
(6) B.-L. Poh and Y. M. Chow, *J. Incl. Phenom.*, **14**, 85 (1992).
(7) M. L. Bender and M. Komiyama, *Cyclodextrin Chemistry*, Springer-Verlag, Berlin, 1978.
(8) J. Szeltle, *Cyclodextrins and Their Inclusion Complexes*, Akademiai Kiado, Budapest, 1982.
(9) A. Harada, M. Okada, J. Li, and M. Kamachi, *Macromolecules*, **28**, 8406 (1995).
(10) A. Harada, T. Nishiyama, Y. Kawaguchi, M. Okada, and M. Kamachi, *Macromolecules*, **30**, 7115 (**1997**).
(11) A. Harada, S. Suzuki, M. Okada, and M. Kamachi, *Macromolecules*, **29**, 5611 (1996).
(12) A. Harada, J. Li, and M. Kamachi, *Bull. Chem. Soc. Jpn.*, **26**, 5698 (1993).
(13) J. Li, A. Harada, and M. Kamachi, *Macromolecules*, **67**, 2808 (1994).
(14) A. Harada, *Functional Materials*, **18**, 16 (1998).