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Preparation and structures of supramolecules between cyclodextrins and polymers

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Contents

Abstract

Cyclodextrins (CDs) form inclusion complexes with various polymers with high selectivities to give crystalline compounds. α-CD formed complexes with poly(ethylene glycol) (PEG) and oligoethylene in high yields, although β-CD did not form complexes with PEG. However, β-CD formed complexes with poly(propylene glycol) (PPG). Although α-CD did not form complexes with polyisobutylene (PIB) and poly(methyl vinyl ether) (PMVE), γ-CD formed complexes with PIB and PMVE. There is a good correlation between the sectional areas of the polymers and the sizes of the CDs. The stoichiometries, properties, and structures of the

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complexes are discussed. The yield of the complexes increased with increasing molecular weight. Polyrotaxanes, in which many cyclodextrins are threaded on a poly(ethylene glycol) chain, were prepared by capping the chain ends of the polymers in the complexes with bulky groups.

Keywords: Supramolecules; Cyclodextrins; Polymers

1. Introduction

In recent years, much attention has been focused on molecular recognition of low molecular weight compounds [1]. Crown ethers [2], cryptands [3], cyclophanes [4], and calixarenes [5] have been extensively used as host molecules. However, the guests recognized by these host molecules have been limited to small molecules and simple ions, such as lithium, sodium, potassium, chloroform, and benzene. Host molecules which can recognize and respond sensitively to larger and more complicated compounds and even polymers are required.

In biological systems such as enzymes–substrates, antigen–antibodies, DNA, RNA, and cell adhesion systems, however, macromolecular recognition, that is, recognition of macromolecules by macromolecules, plays an important role in constructing supramolecular structures and maintaining their lives [6]. However, there have been no approaches toward macromolecular recognition by artificial host–guest systems.

Since cyclodextrins were discovered, a great number of reports (more than 10 000 papers) have been published on cyclodextrins. However, studies on the inclusion properties of cyclodextrins were limited to those with low molecular weight compounds [7–9]. Cyclodextrins are cyclic molecules consisting of six to eight glucose units linking through α-1-4-glycosidic linkages. They are called α-, β-, and γ-cyclodextrin (CD), respectively. They are known to form inclusion complexes with a wide variety of low molecular weight compounds, ranging from nonpolar hydrocarbons to polar carboxylic acids and amines. There have been no reports on the complex formation of cyclodextrins with polymers when we started our work in early 1980s. Therefore, we have started our project on complex formation between polymers and cyclodextrins.

There have been some examples in which a monomer was polymerized in situ within a cyclodextrin complex. Ogata et al. prepared hexamethylene diamine complexes of β-CD [10]. Polyamides were obtained by condensation of dibasic acid chlorides and the inclusion complexes of the diamine. Maciejewski reported the polymerization and copolymerization of vinylidene chlorides as adducts with β-CD [11]. There are some reports which suggest interactions between cyclodextrins and some polymers in aqueous solutions. Kitano et al. reported that cyclodextrins show some effects on the critical micelle concentrations of some micelle-forming surfactants [12]. Iijima et al. studied diffusion of cyclodextrin in the presence of poly(styrenesulfonate) in aqueous solutions and reported that there are some interactions between cyclodextrin and the polymer [13].

There have recently been reports by Gibson et al. describing the formation of supramolecular complexes bewteen crown ethers and oligomers [14].

Table 1
Complex formation of CDs with hydrophilic polymers

Polymer	Structure	MW	Yield (%)		
			α-CD	β-CD	γ-CD
PVA	$-(CH_2CH(OH))$	22000	0	0	0
PAAm	$-(CH_2CH(CONH_2))$	10000	0	0	0
PEG	$-(CH_2CH_2O)-$	1000	92	0	trace
PPG	$-(CH_2CH(CH_3)O)$	1000	0	96	80
PMVE	$-(CH_2CH(OCH_3))$	20000	0	0	80

2. Complex formation between cyclodextrins and hydrophilic polymers [15]

We tested whether cyclodextrins would form complexes with some water-soluble nonionic polymers. Table 1 shows the results of the formation of complexes of cyclodextrins with some nonionic polymers. We found that cyclodextrins did not form complexes with some nonionic water-soluble polymers (such as poly(vinyl alcohol) (PVA) and polyacrylamide (PAAm)) by the same procedure as that for low molecular weight compounds. However, we found that α-CD forms crystalline complexes with poly(ethylene glycol) (PEG) in high yield.

2.1. Complex formation of α-cyclodextrin with poly(ethylene glycol) [16]

When aqueous solutions of PEG were added to a saturated aqueous solution of α-CD at room temperature the solution became turbid and the complexes were formed as precipitates when the average molecular weight of PEG was more than 200. [17]

2.1.1. Rates of complex formation

While preparing the complexes of α-CD with PEG we found that the rate of complex formation depends on the molecular weight of PEG. Fig. 1 shows the effects of molecular weights on the rate of turbidity development after mixing the saturated α-CD solution and PEG solution. The figure clearly shows that PEG of molecular weight 1000 forms complexes most rapidly. This may be partly due to the fact that the number of end groups decreases as the molecular weight increases. Addition of the PEG solution to a saturated aqueous solution of β-CD did not cause any change in solution.

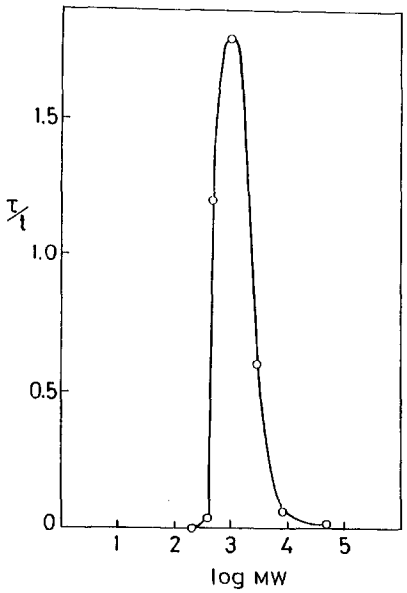

Fig. 1. Effects of molecular weight on the rate of turbidity development after mixing the saturated α-CD and PEG solutions.

2.1.2. Effects of the molecular weight of polymers on the yields of the complexes [18]

The complexes were isolated by filtration or centrifugation. Fig. 2 shows the yields of the complexes of α-CD with PEG of various molecular weights. The yields are calculated on the basis of 2 : 1 (ethylene glycol unit : α-CD) stoichiometry, as discussed in the following section. α-CD did not form complexes with the low molecular weight analogs ethylene glycol, diethylene glycol, and triethylene glycol. α-CD formed complexes with PEG of molecular weight >200. The yields were found to increase with

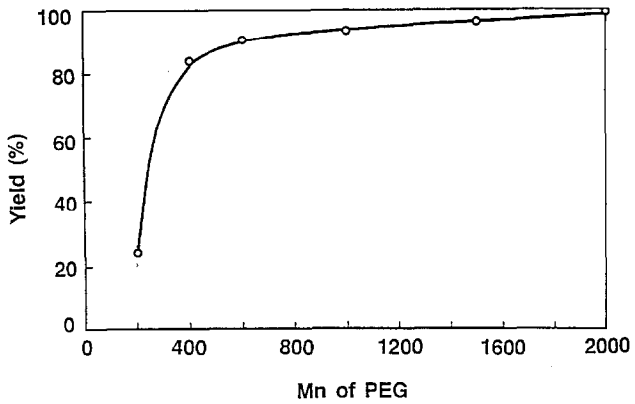

Fig. 2. Yields of the complexes of α-CD with PEG as a function of the molecular weight of PEG.

increasing molecular weight. The complexes were obtained almost quantitatively with PEG of molecular weight >1000. β-CD did not form complexes with PEG of any molecular weight. Although PEG of molecular weight >1000 formed complexes with α-CD slowly, they gave high yields after several hours.

This observation that a minimum PEG length is required for the formation of stable cyclodextrin complexes shows the importance of cooperativity in complexation and is similar to the formation of PEG complexes with hydrogen-donor polymers such as poly(acrylic acid).

2.1.3. *Stoichiometries of the complexes*

The complex formation of α-CD with PEG was studied quantitatively. Fig. 3 shows the yields of the complexes of α-CD with PEG of average molecular weight 600 as a function of added PEG. The yields increased linearly when the amount of PEG added was small and leveled off at a molar ratio of 2:1 (ethylene glycol unit:CD). These results indicate that the complex formation is stoichiometric. The saturation values show that more than 90% of the α-CD was consumed by the complex formation with PEG. The continuous variation plots for the complexation between α-CD and PEG also suggest that the stoichiometries of the complexes are all 2:1. The stoichiometries were confirmed by the ^{1}H NMR spectrum. Fig. 4 shows the ^{1}H NMR spectrum of the complex of PEG-600 with α-CD. It should be noted that the stoichiometries of the complexes are always 2:1 even if α-CD and PEG are mixed in any ratio. The length of two ethylene glycol units corresponds to the depth of the cavity of α-CD.

Carbohydrate polymers such as dextran and pullulan did not form insoluble complexes with PEG. Amylose and dextrin also did not form insoluble complexes with PEG. Glucose, methyl glycoside, maltose, and maltotriose did not form

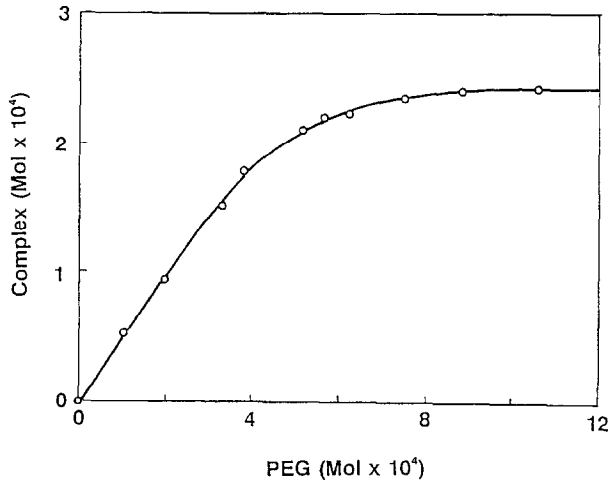

Fig. 3. Amount of α-CD-PEG complexes as a function of added PEG (MW=600). A total amount of 2 ml of saturated aqueous solution of α-CD was used.

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