# Site-Selective Complexation of Amphiphilic Compounds by Cyclodextrins

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(Received February 21, 2000; CL-000176)

Cyclodextrins (CDs) have been found to form inclusion complexes with Triton X in a site-selective manner; α-CD binds an ethylene glycol chain specifically and β-CD binds a hydrophobic end group (an iso-octylphenyl group and a phenyl group) specifically.

Site-selective complexation plays an important role in constructing supramolecular structures in biological systems and in chemical processes.[1] Some viruses and organelles, for example, are formed by molecular assemblies through site-selective binding of polymers. Some enzymes recognize specific sites of proteins and DNA. Site-selectivities or regio-selectivities are also of importance in chemical synthesis. Site-selective complexation should play an important role in the construction of artificial supramolecular structures in polymeric systems. There are few reports on the site-selective complexation shown by polymeric systems.

Previously, we reported that α-cyclodextrin (α-CD) forms complexes with poly(ethylene glycol) (PEG) to give stoichiometric complexes in a crystalline state.[2] β-CD did not form complexes with PEG of any molecular weight. However, β-CD formed complexes with poly(propylene glycol)(PPG),[3] although α-CD does not form complexes with PPG. Recently, we have found that β- and γ-CD form complexes with poly(isobutylene) (PIB), which has much larger cross sectional area than PEG and PPG, although α-CD does not form complexes with PIB.[4] Furthermore, we and Wenz et al. prepared polyrotaxanes in which many CDs are threaded on a polymer chain.[5-7]

Now we found that CDs recognize specific sites of a polymer chain to give complexes. We used a series of Triton X molecules as amphiphilic guest compounds, which have a PEG chain and an *iso*-octyl group through a benzene ring. We found that α-CD formed complexes with Triton X to give solid compounds. On the other hand β-CD did not form solid complexes with Triton X. However, β-CD was found to bind hydrophobic end groups to give soluble complexes in water. α-CD recognizes a PEG chain of Triton X and β-CD recognizes hydrophobic end groups of the molecule. CDs show site-selectivities.

When aqueous solutions of Triton X with a long PEG chain were added into the saturated aqueous solution of α-CD, the solution became turbid and the complexes were formed as a solid state. On the other hand, the addition of Triton X into the aqueous solution of β-CD did not give any solid complexes. However, there is a possibility that β-CD forms soluble complexes with Triton X in water, because β-CD formed complexes with *iso*-octylphenol to give crystalline complexes. Therefore, we measured the solubilities of β-CD in the presence of Triton X and some nonionic water-soluble polymers. If β-CD forms soluble complexes with polymers in water, the solubilities of β-CD should increase on addition of polymers. PEG and some other polymers did not cause any effects on the solubilities of β-CD. In contrast, the solubilities of β-CD increased more than twice in the presence of Triton X and N. These results suggest that β-CD forms complexes with Triton molecules in solution and does not form complexes with other polymers including PEG. Quantitative studies on the effects of Triton X on the solubilities of β-CD show that two β-CD molecules bind a single Triton X molecule. The dissociation constant of the complex is $2.4 \times 10^{-3}$ M.

Therefore we measured the UV absorption spectra and the circular dichroism spectra in the presence of CDs. Figure 1(a) shows the absorption spectra of Triton X-405 in the absence and presence of β-CD. α-CD did not cause any effects on the UV absorption spectrum of Triton X. In contrast, the absorption band around 250–290 nm split in two peaks on addition of β-CD, indicating that a benzene ring of Triton X is placed in a less polar environment than in water, although a benzene ring of Triton X is not included in α-CD cavity. Figure 1(b) shows the circular dichroism spectrum of Triton X-405 in the presence of β-CD. No induced Cotton effects have been observed in the presence of α-CD. The spectrum shows a large minus Cotton effects in the absorption range 250–290 nm on Triton X in the presence of β-CD. These results indicate that a benzene ring of

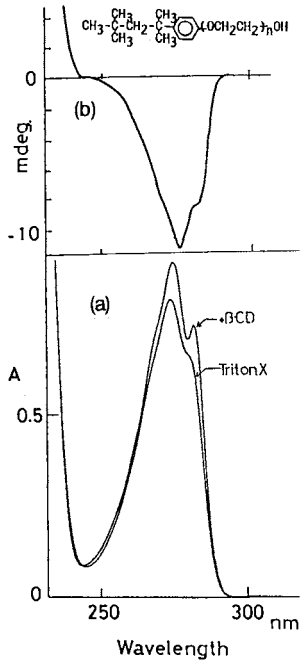


**Figure 1.** UV absorption spectra of Triton X-405 ($10^{-4}$ M) in the absence and presence of β-CD ( $10^{-2}$ M) (lower) and circular dichroism spectrum of Triton X-405 in the presence of β-CD ($10^{-2}$ M) (upper).

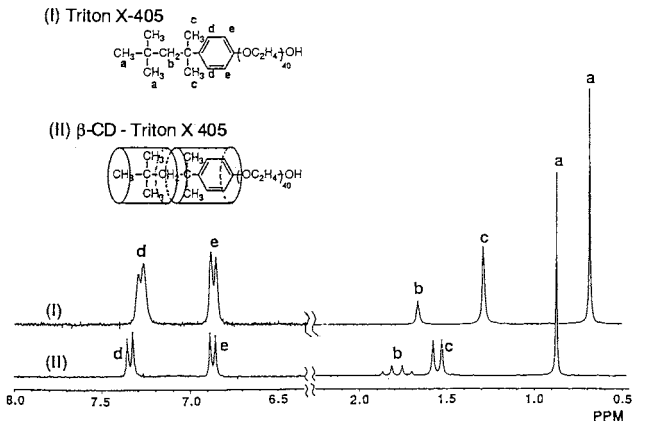


**Figure 2.** $^1$H-NMR Spectra of Triton X-405 in the absence (I) and presence (II) of β-CD in $D_2O$.

Triton X is placed in a chiral β-CD cavity with a definite orientation, although it is not included in the α-CD ring. All the spectroscopic measurements were carried out under the critical micelle concentrations (CMC) of Triton X.

Figure 2 shows the $^1$H NMR spectra of Triton X-405 in the absence and presence of β-CD. α-CD did not show any effects on the NMR spectra of Triton X. In contrast, signals of hydrophobic chains of Triton X shifted toward lower fields on addition of β-CD although signals of PEG do not change. Peaks of benzene protons became sharp and shifted to lower fields. Methyl groups close to the benzene ring split in doublet and the methylene group appears as quartet, indicating that Triton X molecules exist as rotamers in β-CD cavities. These results indicate that not only a benzene ring but also aliphatic groups are included in β-CD rings. Therefore we propose a structure of the complex between β-CD and Triton X as shown in Figure 3. In the complex between α-CD and Triton X, a PEG chain is included in the tunnel formed by α-CDs as a similar fashion to those as we previously showed in the complexes between α-CD and PEG. On the other hand in the complex between β-CD and Triton X, only hydrophobic end groups were included in the two β-CD rings. Complex formation of CDs with some non-ionic surfactants has been reported.[8-10] Interactions of CD polymers with some non-ionic polymers[11] and ionic polymers[12] have been reported. Dual complexation of low molecular weight compounds has been reported.[13-15]

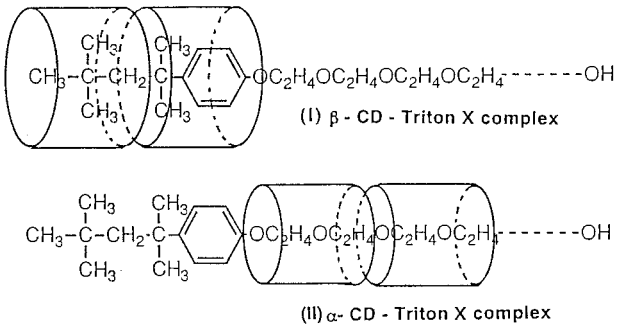


**Figure 3.** Proposed Structures of β-CD-Triton X complex (I) and α-CD-Triton X complex (II).

In conclusion CDs recognize specific sites of a polymer chain, form unique supramolecular structures, and show site-selectivities as shown in the biological systems.

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