Complex Formation Between Cyclodextrin and Poly(propylene glycol)

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β- and γ-cyclodextrin form complexes with poly(propylene glycol) of various molecular weights to give crystalline compounds in high yields, although they do not form complexes with propylene glycol, dipropylene glycol, nor tripropylene glycol; α-cyclodextrin does not form complexes with poly(propylene glycol).

Although cyclodextrins (α-, β-, and γ-CD) form inclusion complexes with a great number of low molecular weight compounds, both organic[1] and inorganic,[2] there are few reports on the interactions of CDs with polymers. We have found that β-CD and γ-CD formed complexes with poly(propylene glycol) (PPG) of various molecular weights to give crystalline compounds in high yields.

When PPG was added to a saturated aqueous solution of β-CD at room temperature and with sonication, the solution became turbid and the complexes were obtained as precipitates. This is the first observation that β-CD forms complexes with polymers in the solid state.

Table 1 shows the results of the preparation of the complexes of cyclodextrins with poly(propylene glycol) of various molecular weights. α-CD did not form complexes with PPGs of any molecular weight. β-CD forms inclusion complexes with PPG when the average molecular weight of PPG is more than 400. The complex was obtained almost quantitatively with PPG of molecular weight 1000 and the yields decrease with the increase in the molecular weight of PPG. γ-CD also forms complexes with PPG in high yields even when the molecular weight of PPG is low (400—725).

The complex formation of β-CD with PPG was studied quantitatively. The amount of complex formed increases with an increase in the amount of PPG added to the aqueous solution of β-CD. The saturation observed indicates a stoicheiometric complexation. From the initial slope, the two propylene glycol units were found to be bound to a single β-CD molecule. The continuous variation plots for the formation of the complex between PPG and β-CD are maximum at 0.33, indicating the 2:1 stoicheiometry. The stoicheiometry was further confirmed by the use of ^{1}H NMR spectroscopy. The NMR spectrum of the complex shows the methyl protons of PPG (3-H × 2) and C-1-H protons of β-CD(7-H) in a 6:7 ratio. The length of the two propylene glycol units corresponds to the depth of the β-CD cavity (*ca.* 7 Å).[3]

Table 1. Preparation of complexes of CD with PPG.

	Yield(%)	
M_w	β-CD[a]	γ-CD[b]
dipropylene glycol	0	0
tripropylene glycol	0	0
400	1	76
425	27	74
725	84	77
1000	96	80
2000	50	31
3000	32	20
4000	27	15

[a] CD saturated solution 5 ml, PPG 20 mg; [b] CD saturated solution 1 ml, PPG 20 mg, sonication 10 min and allowed to stand 1 h at room temperature.

The complexes dissolve when heated in water. The addition of an excess amount of benzoic acid, which is thought to be a competitive inhibitor,[4] to the suspension of the complex resulted in solubilization of the complex when the molecular weight of PPG is low (725). Thus, the formation of the complex seems to be reversible.

The complexes were isolated by filtration or centrifugation, washed and dried. The inclusion complexes are thermally stable. Thermogravimetric analysis shows that they decompose >320 °C, although β-CD melts and decomposes <310 °C.

The *X*-ray powder pattern shows that the complexes are crystalline and the patterns are different from those of the complexes with small molecules, such as propionic acid or propanol, indicating that the complexes of β-CD and PPG are not isomorphous with the so-called cage structure.[5]

Molecular-model studies show that PPG chains are able to penetrate β-CD cavities, while the PPG chain cannot pass through the α-CD cavity owing to the hindrance of the methyl group on the main chain. These views are in accordance with our results that β-CD formed complexes with PPG but α-CD did not form complexes with PPG. Model studies indicate further that the single cavity accommodates two propylene glycol units. Studies of the detailed structure of the complex are now in progress.

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