Inclusion Complexation and Formation of Polypseudorotaxanes between Poly[(ethylene oxide)-*ran*-(propylene oxide)] and Cyclodextrins

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Received July 2, 2001

Cyclodextrins (CDs) are a series of cyclic oligosaccharides composed of 6, 7, or 8 D(+)-glucose units linked by α-1,4-linkages and named α-, *β*-, or *γ*-CD, respectively. The geometry of CDs gives a doughnut-shaped hydrophobic cavity having a depth of ca. 7.0 Å and an internal diameter of ca. 4.5 Å for α-, ca. 7.0 Å for *β*-, and ca. 8.5 Å for *γ*-CD.[1] They have been extensively studied in supramolecular chemistry as host molecules capable of including guest molecules ranging from low molecular weight organic/inorganic compounds to polymers.[1,2]

Recently, polypseudorotaxanes formed by macrocycles threading over a polymer chain have attracted much interest.[2−14] A large number of reports have been published on formation of polypseudorotaxanes, i.e., inclusion complexes with necklace-like supramolecular structures between cyclodextrins and various homopolymers or block copolymers.[2,7−14] The size correlation between the cross-sectional areas of polymer chains and the cavities of CDs plays an important role in the inclusion complex formation. Poly(ethylene oxide) (PEO) and oligoethylene (OE) of various molecular weights form inclusion complexes with α-CD to give crystalline polypseudorotaxanes in high yields, but not with *β*-CD and *γ*-CD.[7] Conversely, poly(propylene oxide) (PPO) can form inclusion complexes with *β*-CD and *γ*-CD in high yields, but not with α-CD.[8] The assumption is that the PPO chain is too large to penetrate the inner cavity of α-CD.[8c] There is also preferential inclusion. *β*-CD would selectively include the PPO block of the triblock copolymer poly(ethylene oxide)-*block*-poly(propylene oxide)-*block*-poly(ethylene oxide) (PEO-*b*-PPO-*b*-PEO) to form a polypseudorotaxane,[9] while α-CD selectively includes the PEO blocks of PEO-*b*-PPO-*b*-PEO.[10b] With the most spacious *γ*-CD, even a double-stranded inclusion complex with PEO with modified bulky end groups can be formed.[11]

In this study, we report the unexpected observation that poly[(ethylene oxide)-*ran*-(propylene oxide)] [P(EO-*r*-PO)] can form inclusion complexes with α-CD as well as *γ*-CD to give polypseudorotaxanes in high yields. Although there are propylene oxide (PO) units randomly placed in the polymer backbone, the copolymer still can penetrate the smallest cavity of α-CD to form inclusion complexes. The phenomenon is interesting in light of the fact that PPO homopolymer could not penetrate α-CD to form any crystalline inclusion complex. It seems that the α-CD molecules may overcome the energy barrier in passing over a PO unit or short PO segment and then form a stable inclusion complex with EO units of the copolymer. This is the first observation of inclusion complexation and polypseudorotaxanes formation between a random copolymer and a cyclodextrin.

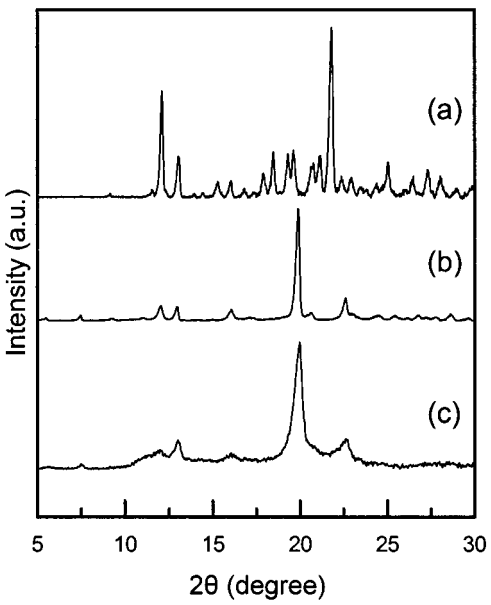

Figure 1. X-ray powder diffraction patterns for the α-CD−propionic acid complex (a), α-CD−PEO (M_n 1000) complex (b), and α-CD−P(EO-*r*-PO)-2500 complex (c).

Two random copolymers, P(EO-*r*-PO)-2500 and P(EO-*r*-PO)-12000, with number-average molecular weights of 2500 and 12 000, respectively, were purchased from Aldrich. According to the manufacturer, both copolymers have 80 mol % content of PEO and 20 mol % of PPO. They are both liquid at room temperature and are completely miscible with water. Their compositions are represented as $EO_{42}PO_{11}$ for P(EO-*r*-PO)-2500 and $EO_{205}PO_{52}$ for P(EO-*r*-PO)-12000. When aqueous solutions of P(EO-*r*-PO) or bulk P(EO-*r*-PO) were added into an aqueous solution of cyclodextrin followed by sonication at room temperature, the solutions gradually became turbid, and inclusion complexes were formed as crystalline precipitates when α-CD or *γ*-CD was used, while no complexes were formed when *β*-CD was used. The complexes, i.e., polypseudorotaxanes formed between P(EO-*r*-PO) copolymers and α-CD or *γ*-CD, were isolated by filtration or centrifugation, washed with water, and dried under vacuum. The polypseudorotaxanes dissolved gradually when they were added into a large amount of water, indicating that the complex formation is reversible, and the polypseudorotaxanes are in equilibrium in solution with their components.

Figure 1 shows the X-ray powder diffraction patterns of α-CD−P(EO-*r*-PO)-2500 complex and other inclusion complexes of α-CD with propionic acid and PEO of molecular weight 1000. In Figure 1a, the pattern of α-CD−propionic acid complex represents a cage-type structure of α-CD inclusion complexes.[15] In Figure 1b, the pattern of α-CD−PEO complex with a number of sharp reflections and the main one at $2\theta = 19.4°$ ($d =$

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10.1021/ma011129b CCC: $20.00
Published on Web 11/21/2001

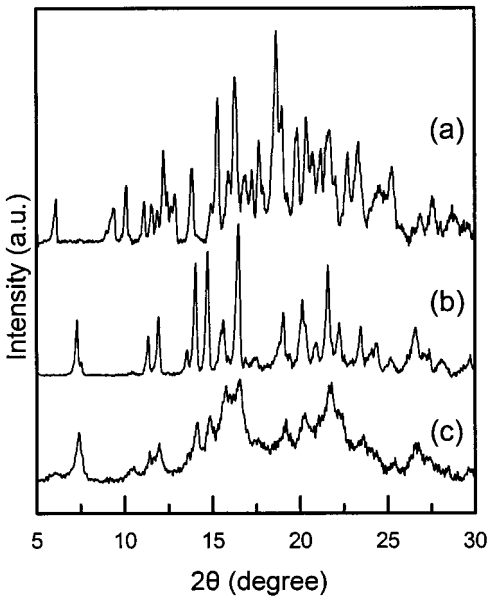

Figure 2. X-ray powder diffraction patterns for γ-CD (a), γ-CD−PPO (M_n 1000) complex (b), and γ-CD−P(EO-*r*-PO)-2500 complex (c).

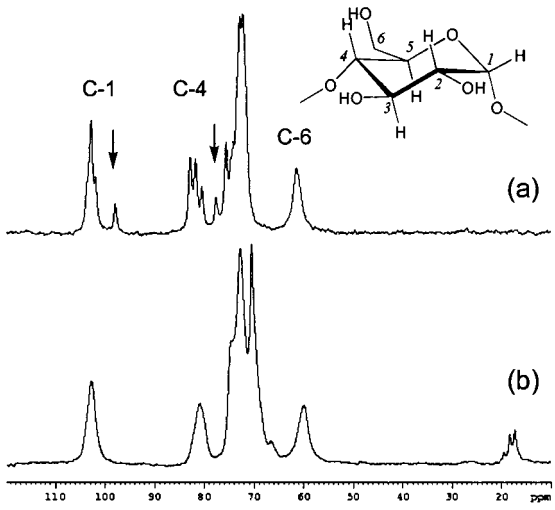

Figure 3. ^{13}C CP/MAS NMR spectra of uncomplexed α-CD (a) and α-CD−P(EO-*r*-PO)-2500 complex (b). The arrows show the resolved resonances for C-1 and C-4 adjacent to a single conformationally strained glycosidic likage.

4.57 Å) represents the channel-type structure of crystalline necklace-like polypseudorotaxanes of α-CD and PEO,[7c,15] which is totally different from that of the α-CD−propionic acid complex. The pattern of α-CD−P(EO-*r*-PO)-2500 complex (Figure 1c) is similar to that of α-CD−PEO complex, but different from that of α-CD−propionic acid complex, suggesting that the α-CD−P(EO-*r*-PO)-2500 polypseudorotaxane is isomorphous with the channel-type structure formed by the α-CD−PEO complex.

The X-ray powder diffraction pattern of γ-CD−P(EO-*r*-PO)-2500 complex is shown in Figure 2, as compared with those of γ-CD and inclusion complex of γ-CD with PPO homopolymer. Similar to the observation with α-CD, the pattern for the γ-CD−P(EO-*r*-PO)-2500 complex (Figure 2c) resembles that of the polypseudorotaxane formed by γ-CD and PPO, i.e., the γ-CD-PPO complex (Figure 2b), which is known to display a channel-type structure,[8c] and differs from that of γ-CD (Figure 2a), a cage-type structure.[16]

Figure 3 shows the ^{13}C CP/MAS NMR spectra of uncomplexed α-CD and α-CD−P(EO-*r*-PO)-2500 complex. The α-CD molecule is known to assume a less symmetrical conformation in the crystalline uncomplexed state.[17] In this case, the spectrum shows resolved C-1 and C-4 resonances. Especially, resonances for C-1 and C-4 adjacent to a single conformationally strained glycosidic linkage are observed in the spectrum.[18] In contrast, the resolved resonances disappear in the spectrum of the α-CD−P(EO-*r*-PO)-2500 complex, and each carbon of the glucose unit is observed as a single peak. The results indicate that the α-CD molecules in the polypseudorotaxane adopt a symmetrical conformation, and each glucose unit of α-CD is in a similar environment,[7c] which further supports the formation of an inclusion complex between P(EO-*r*-PO) and α-CD.

The stoichiometry of the polypseudorotaxanes was studied using ^{1}H NMR spectroscopy. Figure 4 shows the ^{1}H NMR spectra of α-CD−P(EO-*r*-PO)-2500 and α-CD−P(EO-*r*-PO)-12000 complexes in D_2O. A comparison between the integral intensities of peaks for α-CD and those for P(EO-*r*-PO) gives the compositions of the polypseudorotaxanes. The ratios of α-CD to a single copolymer chain were found to be ca. 22 for the α-CD−P(EO-*r*-PO)-2500 complex and ca. 102 for the α-CD−P(EO-*r*-PO)-12000 complex. Considering the compositions of the two copolymers, the molar ratio of EO unit to α-CD is 2:1 for both polypseudorotaxanes. This matches perfectly the stoichiometry of the α-CD−PEO complexes reported previously.[7c] The results indicate that in the α-CD−P(EO-*r*-PO) polypseudorotaxanes only the EO segments are closely included by α-CD molecules, while probably the PO units randomly placed in the copolymer chain are uncovered. On the basis of this observation, we can hypothesize the mechanism of the inclusion complex formation between α-CD and P(EO-*r*-PO). Although a PO segment is too large for α-CD to form a stable inclusion complex, the molecular motion of both α-CD and a PO unit or short PO segment is flexible enough to overcome the energy barrier caused by an α-CD molecule encountering a PO unit or short PO segment when the α-CD molecule is threaded by the P(EO-*r*-PO) chain. Consequently, the P(EO-*r*-PO) chain can penetrate the α-CD cavity freely, and then stable inclusion complex "segments" are formed between α-CD and EO units of P(EO-*r*-PO). This is also in accordance with the broadening X-ray powder pattern for the α-CD−P(EO-*r*-PO) complexes (Figure 1c), which shows the α-CD−P(EO-*r*-PO)-2500 complex has a lower crystallinity than the stoichiometric α-CD−PEO complex, most likely caused by the uncovered PO units that "break up" and shorten the channels in the α-CD−P(EO-*r*-PO) polypseudorotaxane. It remains to be determined what is the minimum PO segment length that would thwart the "skip-over" of α-CD. Work is also in progress to understand why complex formation between the P(EO-*r*-PO) copolymers and β-CD failed.

In summary, P(EO-*r*-PO) copolymers with PO units of 20 mol % have been found to form inclusion complexes with α-CD and γ-CD to give polypseudorotaxanes in high yields. Both polypseudorotaxanes are crystalline and assume a channel-type structure. The findings contradict the conventional wisdom that α-CD would not be large enough to thread over a PO unit. This may have intriguing implications in designing other cyclodextrin inclusion complexes and polypseudorotaxanes.

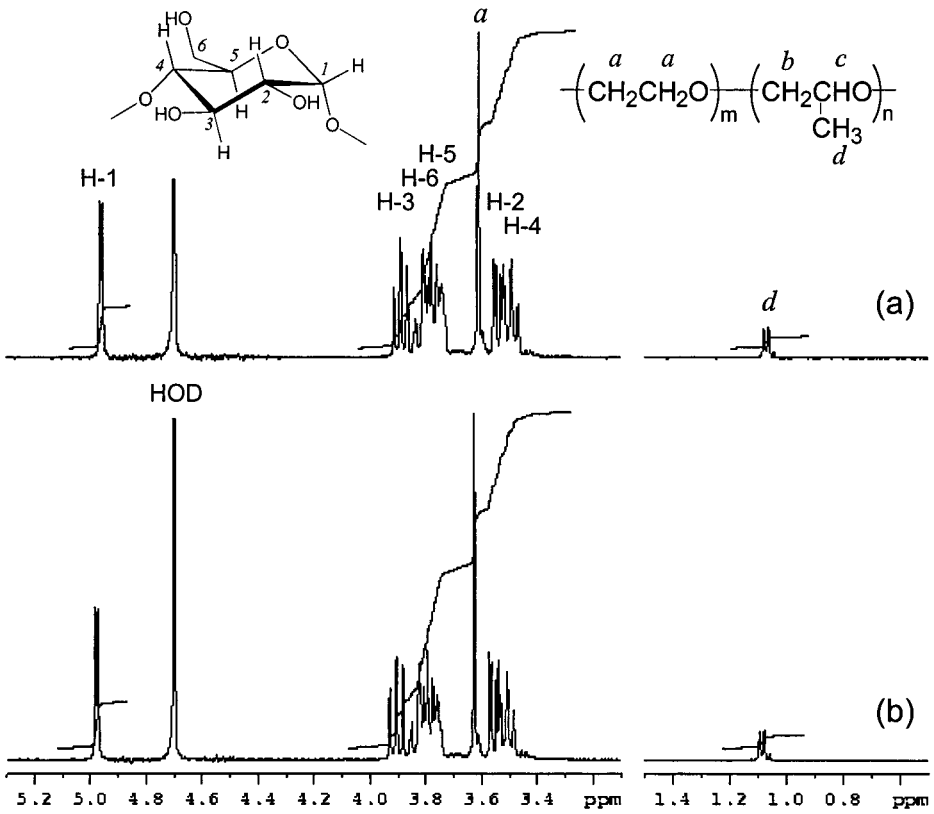

Figure 4. The 400 MHz ^{1}H NMR spectra of α-CD−P(EO-*r*-PO)-2500 complex (a) and α-CD−P(EO-*r*-PO)-12000 complex (b) in D_2O.

Acknowledgment. The authors gratefully acknowledge the financial support from the Institute of Materials Research and Engineering (IMRE), Singapore.

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MA011129B