Solid Polyrotaxanes of Polyethylene Glycol and Cyclodextrins: The Single Crystal X-ray Structure of PEG−*β*-cyclodextrin[†]

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The application of supramolecular principles to the construction of complex objects by "bottom up" approaches, includes, besides the use of coordination and hydrogen bonds, π stacking, and so forth, the establishment of mechanical linkages as exemplified by knots, catenanes and rotaxanes.[1] In the last instance, one molecule is threaded onto another,[2] or in the case of polyrotaxanes, many molecules are threaded onto a long "axle".[3] In solution, the ends of the axle need to be capped to prevent unthreading. The inclusion of polymers in the toroidal cavity of cyclodextrins to give polyrotaxanes is seen as a particularly powerful way to build larger objects such as molecular tubes[4a] and may well serve as platforms for the construction of molecular machines.[4b]

Much characterization work has been carried out to confirm the rotaxane character of the products of the reaction of polymeric glycols with cyclodextrins; however, confirmatory structural information is still lacking.[3,4,6] Here we report the first single-crystal structural analysis of a polymeric glycol−cyclodextrin polyrotaxane, that of poly(ethylene glycol) and *β*-cyclodextrin, **1**. It is worth noting that the literature[4,5] quite generally states that ethylene glycol oligomers do not bind to *β*-cyclodextrin, and hence one is left to conclude that rotaxanes do not form from these components. We show that it is relatively straightforward to produce the solid polyrotaxanes of PEG,[7] as, evidently, complex formation in solution is not a prerequisite for solid polyrotaxane synthesis. Other unexpected CD rotaxanes, such as that of PEG with *γ*-cyclodextrin,[8] become available by the method described here, or by related techniques.

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(7) Crystals of the title material were grown from poly(ethylene glycol), water (1:1), and *β*-cyclodextrin (solid) in an oven at ~70 °C over a period of approximately 1 month. The crystals are stable at room temperature for several hours.

(8) Crystals of the polyrotaxane with *γ*-cyclodextrin were grown as in (7); crystals are in the form of tetragonal prisms, space group $P4_22_12$, $a = 23.37$ Å, $c = 23.91$ Å.
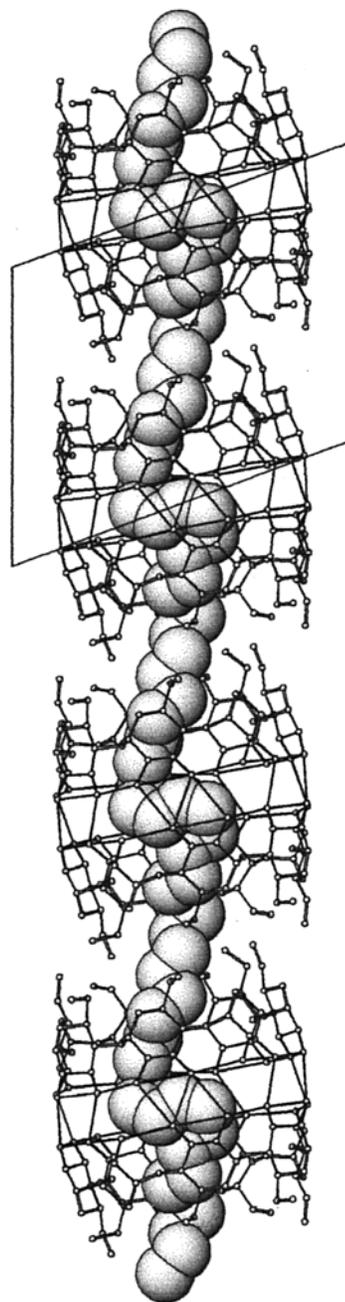

Figure 1. The poly(ethylene glycol) molecule threading through four unit cells. The hydrogen bonds between pairs of connected head-to-head cyclodextrin molecules are shown. The view is along the *b* axis, with the hydrogen atoms omitted.

The crystals[7] of **1** were monoclinic,[9] space group *C*2, *Z* = 4, with the unit cell parameters $a = 18.726$ Å, $b = 24.475$ Å, $c = 15.398$ Å, $\beta = 110.5°$. The structure consists of a poly(ethylene glycol) chain threaded through hydrogen-bonded head-to-head dimers with one CD for every three monomeric C_2H_4O units (Figure 1). The polymer chain is highly disordered about the axis of the channel that passes through a stack of CD dimers. The proposed geometry[3,4] for the α-CD−PEG polyrotaxane shows a CD threaded tightly on the polymer chain with two C_2H_4O segments per CD. For *β*-CD−PEG, periodicity between guest and host is achieved in a different way, as there are three C_2H_4O segments per CD. This occurs because the polymer chain "bunches up" in the central, wide part of the H-bonded dimer,

whereas in the toroidal cavity itself and between adjoining CD tail sections the chain is extended. We have noted this space before as being suitable for including large hydrophobic guest species such as pyrene.[10]

Only two of the primary hydroxyls in the cyclodextrin molecule are disordered, each over two positions with site occupancies of 0.64 and 0.36. The disordering of the primary hydroxyls is less pronounced than for cyclodextrin compounds with octanol and hexanol guest molecules present inside and between host molecules,[10] perhaps because of the lower mobility of the polymer. Each of the secondary cyclodextrin hydroxyls is hydrogen-bonded to secondary hydroxyls both in the same and in the neighboring molecule in the head-to-head cyclodextrin dimers, thus forming a network of hydrogen bonds.

The space between the columns of cyclodextrin molecules is filled with water molecules (not shown) that are disordered over several possible positions, with site occupancies from 0.2 to 1.0. There are eight water molecules per cyclodextrin molecule. Each is hydrogen-bonded to other water molecules, thus forming a three-dimensional network. Some of the water molecules form hydrogen bonds with the hydroxyls of the cyclodextrin molecule.

The symmetry of the guest molecule does not match the crystallographic symmetry. Whereas the center of the cavity formed by the β-CD head-to-head dimer lies on a 2-fold axis,

the polymer molecule inside the channel has no such symmetry. Within the dimer cavity the polymer fragment is disordered over two sets of sites that are not symmetry related. Each set of sites has an additional symmetry related set within the cavity, giving an overall site occupancy of 0.25. Continuity of the polymer at the unit cell boundaries is achieved by linking one of the sets of sites in one unit cell to the second set in neighboring unit cells. All C−C and C−O distances and angles in the poly(ethylene glycol) molecule were fixed, but free rotation around the C−C and C−O bonds was allowed. The resulting conformation of the polymer shows that only parts of the molecule have trans or gauche configurations, with the torsion angles varying from 9 to 179°.

The minimum intermolecular distances derived generally are equal to the sum of the van der Waals radii, indicating that specific interactions between host and guest molecules are absent. The two influences on the overall conformation of the polymer molecule are likely to be, on one hand, the need to minimize intramolecular steric interactions and, on the other hand, space filling of the cyclodextrin channel by maximizing the guest−host van der Waals contacts.

At this point we also comment on the synthesis of the PEG−β-cyclodextrin polyrotaxane by noting that the successful synthesis of the title compound required the use of an excess of PEG and only small amounts of water. On the other hand, on slow cooling from PEG and excess water, only β-CD hydrate crystals resulted in significant yield. Therefore, the synthesis really is a conversion of solid β-CD, via limited amounts of dissolved β-CD, to the solid polyrotaxane. These observations open the door to the synthesis of numerous other less traditional solid CD polyrotaxanes via slow conversion from the CD hydrates at somewhat elevated temperatures, or even by hydrothermal treatment.

(9) Diffractometer Bruker SMART CCD; MO Kα radiation ($\lambda = 0.71073$ Å); temperature of measurement, −100 °C; empirical formula: $C_{48}H_{98}O_{46}$; crystal size = 0.2 × 0.3 × 0.4 mm, monoclinic crystal system, space group $C2$, $a = 18.726(2)$ Å, $b = 24.475(3)$ Å, $c = 15.398(2)$ Å, $\beta = 110.479(2)°$, $V = 6611.1(1)$ Å^3, $Z = 4$, $\rho_{calc} = 1.418$ Mgm^{-3}; $2\theta_{max} = <57.5°$, ω scan mode, absorption coefficient = 0.128 mm^{-1}); reflections collected: 24779, independent reflections: 9231 (R(int) = 0.0925). SHELXTL suite of programs was used to refine the structure (Sheldrick, G. M. *Acta Crystallogr.* **1990**, *A46*, 467−473) All non-hydrogen atoms were refined anisotropically by full-matrix least-squares on F^2, hydrogen atoms were placed in calculated positions and allowed to ride on the parent atoms. No corrections were made for polarization or absorption. Data/restraints/parameters 9231/1/1252, goodness-of-fit on $F^2 = 0.984$, final R indices [$I > 2\sigma(I)$] $R1 = 0.069$, $wR^2 = 0.155$, R indices (all data), $R1 = 0.119$, $wR^2 = 0.183$, largest diff. peaks and holes 0.45 and −0.31 eÅ^{-3}.

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