Crystal and Molecular Structure of a 2,6-Tetradeca-O-methyl-β-cyclodextrin–Adamantanol 1:1 Inclusion Complex

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Summary The first crystal structure to be determined for an inclusion complex in which a chemically modified cyclodextrin serves as the host reveals a host molecular conformation that retains many of the features of the parent molecule but provides an extended toroidal region in which larger hydrophobic substrate molecules can be accommodated.

$2,2',2'',2''',2'''',2''''',2'''''',6,6',6'',6''',6'''',6''''',6''''''$-TETRADECA-*O*-METHYL-β-CYCLODEXTRIN (**1**), Figure 1, has several properties of potential interest with respect to the behaviour of cyclodextrins in solution, to their catalytic activity,[1] and to the study of inclusion complexes in general. Knowledge of the conformation of (**1**) can also be expected to be of value in the possible development of its use as a solubilizer for hydrophobic substrate molecules (*e.g.* vitamins and prostaglandins). Crystals of the 1 : 1 inclusion complex between (**1**) and adamantanol were obtained by slow evaporation of an aqueous solution of (**1**) containing an excess of adamantanol.

Crystal data: $C_{56}H_{98}O_{35}\cdot C_{10}H_{16}O\cdot 12H_2O$, orthorhombic, space group $P2_12_12_1$, $a = 24{\cdot}210(9)$, $b = 19{\cdot}333(5)$, $c = 18{\cdot}266(6)$ Å (at *ca.* 120 K); $Z = 4$. Intensity data were measured with monochromatic Mo-K_α radiation for the cooled crystal. Of the 8061 unique reflections measured to a resolution of $2\theta_{max} = 50°$, 4838 were classified as observed $[I > 3\sigma(I)]$. To date, atomic co-ordinates and isotropic temperature factors for carbon and oxygen atoms have been refined with the observed data to give $R = 0{\cdot}142$.[2]†

The host-substrate complex (**2**) is shown in projection[3] in Figure 2. The conformation of (**1**) is similar to that of complexed β-cyclodextrin.[4] The orientation of the side chains containing the 6-*O*-methyl substituents extends the hydrophobic torus suggesting that (**1**) can accommodate considerably larger substrate molecules in a 1 : 1 host–substrate complex than can the parent compound. Based on a consideration of the van der Waals' radii, the height of

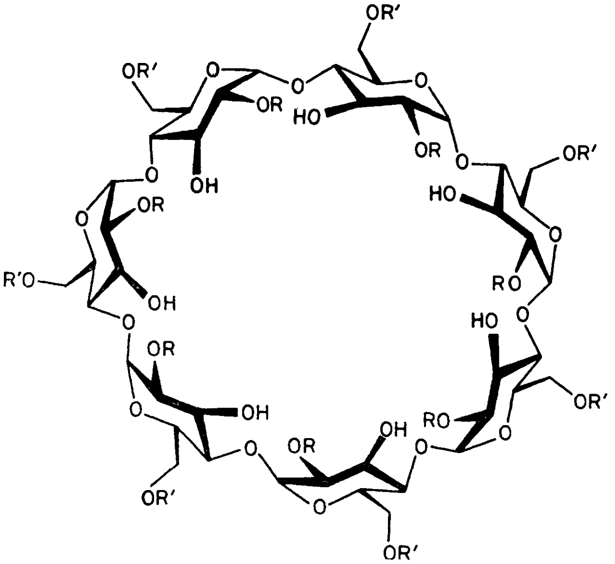

FIGURE 1. A schematic representation of the chemical structure of per-2,6-*O*-methyl-β-cyclodextrin (**1**). The substitured secondary hydroxy-groups are represented with R = Me and their primary analogues with R′ = Me.

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† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

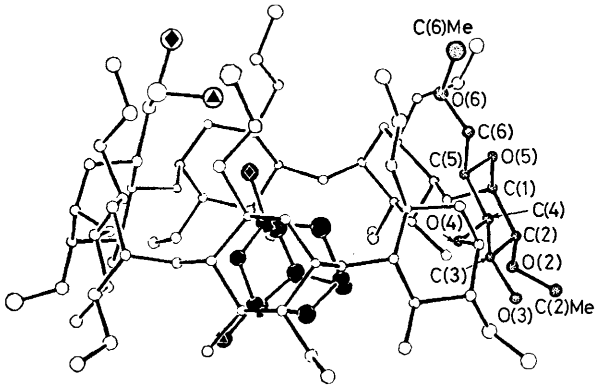

FIGURE 2. A projection of the per-2,6-*O*-methyl-β-cyclodextrin–adamantanol complex (**2**), with the substrate atoms as fully filled symbols. The atoms carrying the symbols ▲ and ◆ are disordered such that atoms with the same symbol are present simultaneously. The dotted symbols represent one glucose residue for which atom labelling has been given.

the torus is estimated to be 10—11 Å compared with *ca.* 9·5 Å for the parent.[5]

At the present stage in refinement of the crystal structure model of (**2**) the adamantanol substrate clearly appears to adopt two orientations in the torus. The hydroxy-moiety in one is directed toward the 'secondary,' O(2), face and in the other toward the primary, O(6), side. In both orientations, the hydroxy-moiety of the substrate is hydrogen-bonded to a water molecule but not directly to the host. The orientation of a C(6)-methyl group is correlated with the position of the adamantanol hydroxy-group as is illustrated by the special symbols in Figure 2.

Each methyl group of the secondary face is oriented away from the toroidal region (the $C_{1j}C_{2j}$–$O_{2j}C_{2j}^{Me}$ dihedral angle range is 81—133°). This conformation is particularly favourable for intramolecular hydrogen bonding between the 3-hydroxy-hydrogen atom and the oxygen atom of the 2-methoxy-moiety of the neighbouring glucose unit.

It is too early in the refinement process to analyse critically the interactions between water molecules, the host, and substrate. Presently, the asymmetric unit appears to contain twelve water molecules distributed over thirteen sites; the position of one water molecule is apparently closely correlated with the orientation of the adamantanol molecule.

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