# The Structure of the Cyclodextrin Complex. XVIII. Crystal Structure of β-Cyclodextrin-Benzyl Alcohol (1:1) Complex Pentahydrate

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The crystal structure of the β-cyclodextrin-benzyl alcohol (1:1) complex pentahydrate was determined by the X-ray diffraction method. The crystal is monoclinic with the space group $P2_1$, $Z=2$, $a=15.356(3)$, $b=10.101(2)$, $c=20.869(3)$ Å, and $\beta=109.90(1)°$. The structure was solved by an inspection of a Patterson map and a trial-and-error method combined with a rigid-body least-squares technique. The structure was refined using the block-diagonal least-squares method to an $R$-value of 0.066 for 5290 reflections ($\sin\theta/\lambda<0.63$). The β-cyclodextrin molecule is somewhat elliptically distorted from the regular heptagonal symmetry because of the inclusion of a planar molecule. One primary hydroxyl group shows a *gauche-trans* conformation, while the others are in a *gauche-gauche* conformation. The secondary hydroxyl groups form intramolecular O(2)-H···O(3′) or O(3′)-H···O(2) hydrogen bonds, which maintain the round structure of β-cyclodextrin. The guest benzyl alcohol molecule is fully enclosed within the host cavity. Water molecules are distributed in intermolecular spaces between β-cyclodextrin molecules. The phenyl group of the guest is located at the primary hydroxyl side of the cavity. The hydroxyl group occupies a position at the secondary hydroxyl side of the cavity, and forms hydrogen bonds with adjacent β-cyclodextrin molecules. β-Cyclodextrin molecules are stacked along the b axis to form a typical cage-type structure with a herringbone-like packing pattern.

Inclusion complexes of cyclodextrins with many pharmaceuticals, aromas, *etc.* have been successfully utilized in pharmaceutical and food industries.[1-4] Aralkyl alcohols are widely used antiseptics in pharmaceutical preparations. We have previously reported that aralkyl alcohols form inclusion complexes with cyclodextrins in water and in the solid state, using various techniques such as the solubility method, UV, CD, and $^1$H-NMR spectroscopies, and powder X-ray diffractometry.[5] In this study, we carried out a crystal- and molecular-structure determination of the β-cyclodextrin complex with benzyl alcohol to gain insight into the detailed geometry of the host-guest interaction in the solid state.

## Experimental

*Materials and Measurements.* β-Cyclodextrin and benzyl alcohol with a 1:1 molar ratio were dissolved in hot water. The solution was kept at room temperature. Then, the β-cyclodextrin-benzyl alcohol (1:1) complex pentahydrate was crystallized to a rod-like form. The crystal used in the X-ray diffraction experiment was sealed in a quartz capillary with a drop of mother liquor to prevent deterioration in air. Lattice parameters and diffraction intensities were measured on a Nicolet P3/F diffractometer with graphite-monochromated Cu $K\alpha$ radiation. The lattice constants were determined by a least-squares method using 25 reflections in the $2\theta$ range 40—45°. By using a $\theta$—$2\theta$ scan mode, 5290 independent reflections with $|F_o|\geqq 3\sigma(F)$ were collected up to 150° in $2\theta$. No correction was made for an absorption or extinction effect.

*Crystal Data*: $C_{42}H_{70}O_{35}\cdot C_7H_8O\cdot 5H_2O$, F.W. = 1333.2, monoclinic, space group $P2_1$, $Z=2$, $a=15.356$ (3), $b=10.101$ (2), $c=20.869$ (3) Å, $\beta=109.90$ (1)°, $V=3043.6$ (9) Å$^3$, $D_x=1.455$ g·cm$^{-3}$.

*Determination and Refinement of the Structure.* The orientation of the *pseudo* heptagonal axis of β-cyclodextrin was easily deduced from a Patterson map. The rotation around the *pseudo* heptagonal axis and the molecular position in the unit cell was determined from an $R$-map, which was calculated using a model structure of β-cyclodextrin with a seven-fold symmetry. The orientational and positional parameters of each glucose unit were corrected by a rigid-body least-squares method. After the refinement of the β-cyclodextrin structure by the block-diagonal least-squares method, benzyl alcohol and water molecules were found on Fourier and difference-Fourier maps. The block-diagonal least-squares refinement of the structure, including 85 hydrogen atoms, achieved an $R$-value of 0.066. The quantity minimized was $\sum\omega(|F_o|-|F_c|)^2$, with $\omega=1.0$ for all the reflections. Final atomic parameters and $B_{eq}$ values are given in Table 1. Tables of observed and calculated structure

Table 1. Atomic coordinates (×10$^4$) and $B_{eq}$ values ($B$/Å$^2$) of non-hydrogen atoms

| | $x$ | $y$ | $z$ | $B_{eq}$/Å$^2$ |
|---|---|---|---|---|
| C(1,G1) | −1361(5) | 568(8) | 3589(4) | 3.39 |
| C(2,G1) | −2030(6) | 207(8) | 2879(4) | 3.64 |
| C(3,G1) | −1950(5) | 1162(8) | 2353(4) | 3.03 |
| C(4,G1) | −2049(5) | 2599(8) | 2564(4) | 2.89 |
| C(5,G1) | −1414(5) | 2873(8) | 3286(4) | 3.38 |
| C(6,G1) | −1602(7) | 4209(9) | 3560(5) | 4.87 |
| O(2,G1) | −1804(4) | −1116(6) | 2725(3) | 4.06 |
| O(3,G1) | −2665(4) | 934(6) | 1694(3) | 3.67 |
| O(4,G1) | −1807(3) | 3390(5) | 2099(3) | 3.12 |
| O(5,G1) | −1545(4) | 1910(6) | 3747(3) | 3.61 |
| O(6,G1) | −2597(5) | 4248(8) | 3445(4) | 6.72 |
| C(1,G2) | 2188(5) | −1119(9) | 4687(4) | 3.71 |
| C(2,G2) | 1352(5) | −2125(8) | 4469(4) | 3.59 |
| C(3,G2) | 488(5) | −1505(9) | 3947(4) | 3.52 |
| C(4,G2) | 282(5) | −138(8) | 4213(4) | 3.16 |
| C(5,G2) | 1134(5) | 719(9) | 4493(4) | 3.45 |
| C(6,G2) | 960(7) | 1901(10) | 4894(5) | 5.41 |
| O(2,G2) | 1601(4) | −3263(6) | 4157(3) | 4.23 |
| O(3,G2) | −299(4) | −2383(6) | 3812(3) | 4.28 |
| O(4,G2) | −414(3) | 485(6) | 3628(3) | 3.33 |
| O(5,G2) | 1925(4) | 3(6) | 4977(3) | 3.62 |
| O(6,G2) | 1824(7) | 2706(8) | 5189(5) | 8.30 |
| C(1,G3) | 4749(5) | −495(9) | 3632(4) | 3.63 |
| C(2,G3) | 4279(6) | −1885(9) | 3574(4) | 3.82 |

TABLE 1. (Continued)

| | x | y | z | $B_{eq}$/Å$^2$ |
|---|---|---|---|---|
| C(3,G3) | 3253(5) | −1705(8) | 3514(4) | 3.56 |
| C(4,G3) | 3317(5) | −916(8) | 4149(4) | 3.23 |
| C(5,G3) | 3748(6) | 442(9) | 4137(4) | 3.83 |
| C(6,G3) | 3837(7) | 1252(11) | 4747(5) | 5.12 |
| O(2,G3) | 4339(5) | −2602(6) | 3014(3) | 4.78 |
| O(3,G3) | 2851(4) | −2984(6) | 3504(3) | 4.50 |
| O(4,G3) | 2356(3) | −779(6) | 4105(3) | 3.22 |
| O(5,G3) | 4705(4) | 200(6) | 4179(3) | 4.29 |
| O(6,G3) | 4216(5) | 583(8) | 5368(3) | 5.62 |
| C(1,G4) | 5124(5) | 2168(8) | 1637(4) | 3.30 |
| C(2,G4) | 4919(5) | 686(8) | 1497(4) | 3.23 |
| C(3,G4) | 4361(5) | 224(8) | 1912(4) | 3.27 |
| C(4,G4) | 4876(5) | 520(8) | 2646(4) | 3.05 |
| C(5,G4) | 5091(5) | 2038(8) | 2745(4) | 3.32 |
| C(6,G4) | 5632(7) | 2465(10) | 3449(5) | 4.72 |
| O(2,G4) | 4442(4) | 467(6) | 791(3) | 3.72 |
| O(3,G4) | 4219(4) | −1198(6) | 1835(3) | 4.13 |
| O(4,G4) | 4304(3) | 137(6) | 3009(3) | 3.26 |
| O(5,G4) | 5591(3) | 2425(6) | 2330(3) | 3.22 |
| O(6,G4) | 6527(4) | 1839(7) | 3752(3) | 5.31 |
| C(1,G5) | 2758(5) | 5970(8) | 268(4) | 2.77 |
| C(2,G5) | 2942(5) | 4889(8) | −159(4) | 3.14 |
| C(3,G5) | 3265(5) | 3627(8) | 287(4) | 2.95 |
| C(4,G5) | 4096(5) | 3928(8) | 924(3) | 2.63 |
| C(5,G5) | 3951(5) | 5168(8) | 1308(4) | 2.83 |
| C(6,G5) | 4878(5) | 5678(9) | 1835(4) | 3.75 |
| O(2,G5) | 2133(4) | 4643(6) | −772(3) | 3.69 |
| O(3,G5) | 3508(4) | 2628(6) | −96(3) | 3.44 |
| O(4,G5) | 4216(3) | 2817(5) | 1360(3) | 2.95 |
| O(5,G5) | 3572(3) | 6245(5) | 839(3) | 3.04 |
| O(6,G5) | 5485(4) | 6126(6) | 1512(3) | 4.33 |
| C(1,G6) | −493(5) | 6951(8) | 515(4) | 3.07 |
| C(2,G6) | −493(5) | 6681(9) | −178(4) | 3.34 |
| C(3,G6) | 372(5) | 5862(8) | −133(4) | 3.25 |
| C(4,G6) | 1261(5) | 6453(8) | 382(4) | 3.13 |
| C(5,G6) | 1197(5) | 6641(8) | 1065(4) | 3.04 |
| C(6,G6) | 2028(5) | 7310(9) | 1605(4) | 3.95 |
| O(2,G6) | −1351(3) | 6063(7) | −608(3) | 4.04 |
| O(3,G6) | 483(4) | 5790(7) | −756(3) | 4.52 |
| O(4,G6) | 2016(3) | 5534(5) | 457(3) | 3.01 |
| O(5,G6) | 387(3) | 7494(6) | 967(3) | 3.36 |
| O(6,G6) | 2231(4) | 8557(7) | 1369(4) | 5.41 |
| C(1,G7) | −2346(5) | 4563(9) | 1833(4) | 3.60 |
| C(2,G7) | −2760(5) | 4484(8) | 1079(4) | 3.49 |
| C(3,G7) | −2018(5) | 4558(8) | 769(4) | 3.09 |
| C(4,G7) | −1386(5) | 5758(9) | 1070(4) | 3.19 |
| C(5,G7) | −960(5) | 5643(8) | 1829(4) | 3.11 |
| C(6,G7) | −259(5) | 6712(9) | 2221(4) | 3.94 |
| O(2,G7) | −3316(3) | 3275(6) | 861(3) | 3.75 |
| O(3,G7) | −2401(4) | 4563(7) | 45(3) | 4.25 |
| O(4,G7) | −670(3) | 5747(5) | 790(3) | 2.92 |
| O(5,G7) | −1732(4) | 5685(6) | 2069(3) | 3.35 |
| O(6,G7) | −610(4) | 8028(6) | 2005(3) | 4.38 |
| C(1,BA) | 1333(6) | 1878(10) | 2512(4) | 4.67 |
| C(2,BA) | 1908(8) | 2021(11) | 2144(6) | 6.21 |
| C(3,BA) | 2392(8) | 3212(2) | 2186(6) | 7.11 |
| C(4,BA) | 2336(10) | 4218(13) | 2612(7) | 8.62 |
| C(5,BA) | 1723(11) | 4092(13) | 2957(8) | 9.39 |
| C(6,BA) | 1197(9) | 2888(13) | 2900(6) | 7.43 |
| C(7,BA) | 829(9) | 528(12) | 2489(6) | 7.01 |
| O(1,BA) | 783(5) | −241(6) | 1949(3) | 4.98 |
| O(W1) | 6037(5) | −100(9) | 5702(4) | 7.56 |
| O(W2) | 7193(5) | 119(7) | 4837(4) | 6.50 |
| O(W3) | 3494(7) | 1487(10) | 6233(5) | 9.49 |
| O(W4) | 3286(7) | 2486(13) | 7379(5) | 11.84 |
| O(W5) | 5083(4) | 3107(6) | −413(3) | 4.31 |

factors, anisotropic temperature factors of non-hydrogen atoms, atomic parameters of hydrogen atoms, bond distances, angles, conformation angles, and plane equations with atomic deviations from the plane are kept at The Chemical Society of Japan (Document No. 8520). The computation was carried out on a FACOM M-380 computer at the Center of the Research Information Processing System (RIPS), Agency of Industrial Science and Technology, Tsukuba.

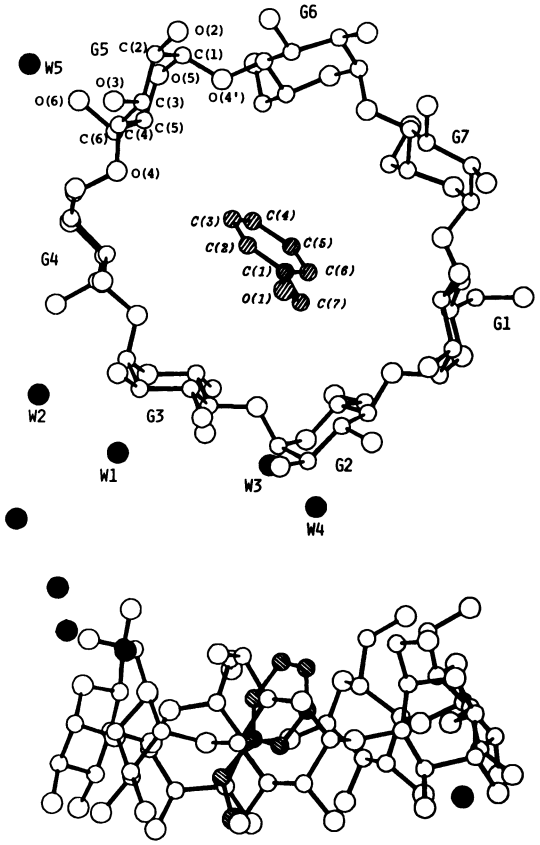


Fig. 1. The structure of the β-cyclodextrin–benzyl alcohol complex. Benzyl alcohol is shown by shaded circles. Water molecules are shown by full circles.

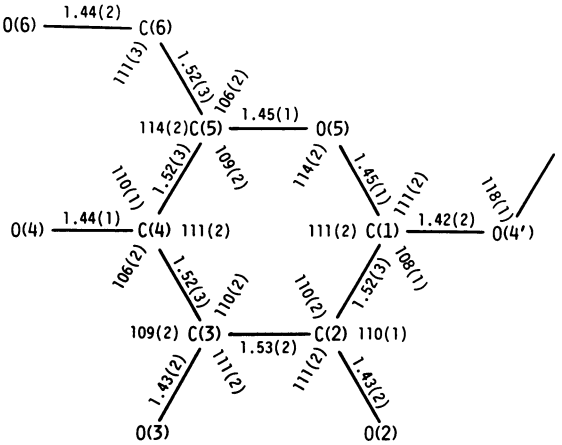


Fig. 2. Average bond distances and angles over seven glucose residues in β-cyclodextrin. Standard deviations in parentheses were estimated according to the equation:

$$\sigma = [\sum_{i=1}^{7} (x_i - \bar{x})^2/6]^{1/2}$$

where $x_i$ refers to the bond distance or angle of the $i$-th residue and $\bar{x}$ is the average value.

## Description and Discussion of the Structure

The structure of the β-cyclodextrin–benzyl alcohol complex is shown in Fig. 1. Average bond distances and angles of β-cyclodextrin are given in Fig. 2. Except for the orientation of C(6)–O(6) bonds, no significant structural difference was found among the seven glucose residues. The C(6)–O(6) bond in the G2 residue showed a *gauche-trans* conformation, while the other C(6)–O(6) bonds were in a *gauche-gauche* conformation. The average value of the glycosidic oxygen angles, 118 (1)°, is in good agreement with those of other β-cyclodextrin complexes.[6-8] The torsion-angle indices (Table 2), being in the range 109—140°, show a strong linear correlation with O(4)···O(4′) distances between adjacent glucose residues. Such a linear correlation is commonly observed in α- and β-cyclodextrin complexes.[7,9]

The β-cyclodextrin ring is somewhat elliptically distorted from the regular heptagonal symmetry. The radius and side length of the heptagon composed of seven O(4) atoms are in the range 4.71—5.28 Å and 4.17—4.55 Å, respectively. The radius (5.28 Å) measured from the O(4,G2) atom is 0.57 Å longer than the radius measured from the O(4,G4) atom. The largest values of radius and side length are found in a direction parallel to the plane of the guest molecule; O(4,G2)···center of the O(4) heptagon and O(4,G3)···O(4,G4), respectively. In spite of such elliptical distortion of the β-cyclodextrin ring, the average value of the radius (5.02 Å) and the side length (4.36 Å) of the O(4) heptagon are in good agreement with the corresponding values (5.05 and 4.38 Å, respectively) of the β-cyclodextrin complex with hexamethylenetetramine,[8] in which β-cyclodextrin shows a round structure owing to the inclusion of a spherically-shaped molecule. The

TABLE 2. GEOMETRICAL DATA FOR β-CYCLODEXTRIN

I. Radius of the O(4) heptagon[a]

| Residue | Radius *l*/Å | Residue | Radius *l*/Å |
|---|---|---|---|
| G1 | 4.97 | G5 | 5.26 |
| G2 | 5.28 | G6 | 5.18 |
| G3 | 4.97 | G7 | 4.78 |
| G4 | 4.71 | Average | 5.02 |

a) The radius is measured from the center of gravity of seven O(4) atoms to each O(4) atom.

II. O(4)···O(4) distance between adjacent glucose residues

| Distance *l*/Å | | Distance *l*/Å | |
|---|---|---|---|
| O(4,G1)···O(4,G2) | 4.29 | O(4,G5)···O(4,G6) | 4.20 |
| O(4,G2)···O(4,G3) | 4.17 | O(4,G6)···O(4,G7) | 4.45 |
| O(4,G3)···O(4,G4) | 4.55 | O(4,G7)···O(4,G1) | 4.50 |
| O(4,G4)···O(4,G5) | 4.39 | Average | 4.36 |

III. Tilt-angle[a] and torsion-angle index[b]

| Residue | Tilt-angle φ/° | Torsion-angle index φ/° |
|---|---|---|
| G1 | 6.6 | 126 |
| G2 | 20.5 | 140 |
| G3 | 17.4 | 116 |
| G4 | −2.2 | 118 |
| G5 | 11.4 | 132 |
| G6 | 25.2 | 109 |
| G7 | 17.0 | 105 |
| Average | 13.7 | 121 |

a) The tilt-angle is defined as the angle made by the O(4) plane and the plane through C(1), C(4), O(4), and O(4′) of each glucose residue. b) The torsion-angle index is defined as follows: $\phi=|\phi(C(1)\text{-}C(2))|+|\phi(C(2)\text{-}C(3))|-|\phi(C(3)\text{-}C(4))|-|\phi(C(4)\text{-}C(5))|+|\phi(C(5)\text{-}O(5))|+|\phi(O(5)\text{-}C(1))|$, where $\phi(C(1)\text{-}C(2))$ is the conformation angle of O(5)–C(1)–C(2)–C(3).

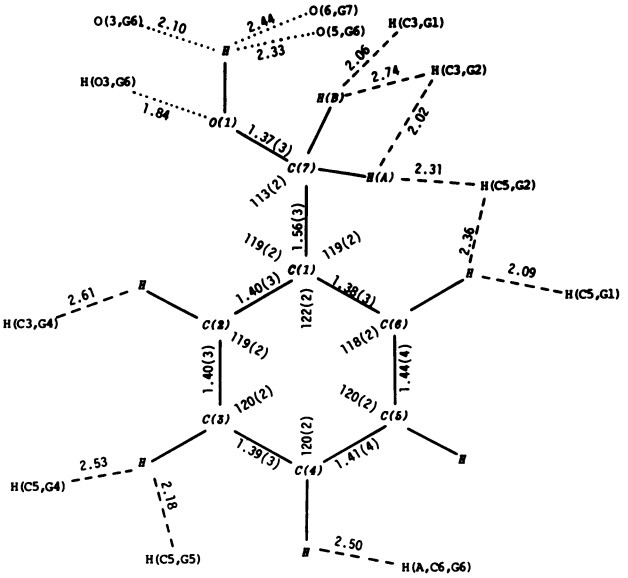


Fig. 3. Bond distances and angles in benzyl alcohol and host-guest distances less than 2.8 Å. Intermolecular contacts with adjacent β-cyclodextrin molecules are shown by dotted lines.

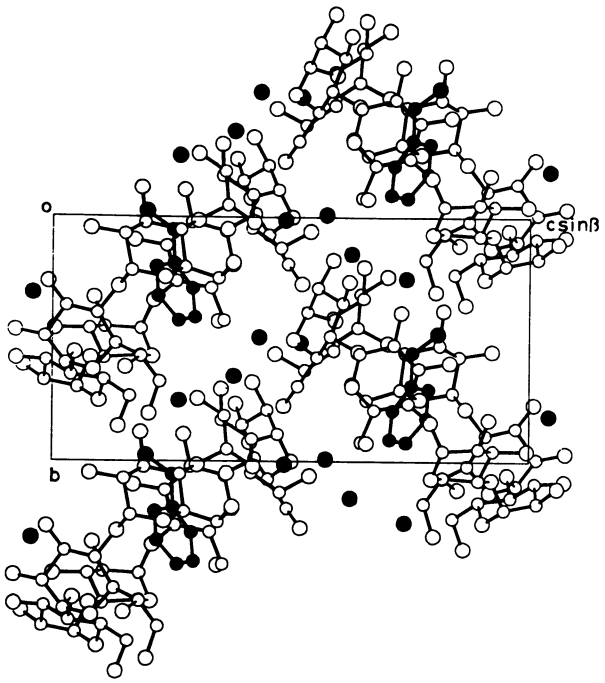


Fig. 4. The crystal structure viewed along the a axis. Benzyl alcohol and water molecules are shown by full circles.

TABLE 3. HYDROGEN-BOND DISTANCES AND ANGLES

| | | Distance ($l$/Å) | | Angle ($\phi$/°) | |
|---|---|---|---|---|---|
| | | O-H | H···O | O···O | O-H···O |
| O(2,G1)·····H-O(3,G2) | | 1.09 | 1.82 | 2.86 | 158 |
| O(2,G1)·····H-O(6,G7) | (c) | 0.83 | 2.12 | 2.94 | 170 |
| O(2,G1)-H·····O(W4) | (i) | 0.98 | 2.20 | 2.61 | 104 |
| O(3,G1)·····H-O(2,G7) | | 0.95 | 2.04 | 2.89 | 148 |
| O(3,G1)-H·····O(2,G5) | (h) | 1.04 | 1.80 | 2.72 | 145 |
| O(5,G1)·····O(6,G4) | (b) | | | 2.97 | |
| O(6,G1)·····O(6,G4) | (b) | | | 2.97 | |
| O(6,G1)-H·····O(W3) | (f) | 1.40 | 1.99 | 2.87 | 115 |
| O(6,G1)-H·····O(5,G2) | (f) | 1.40 | 2.02 | 3.02 | 123 |
| O(2,G2)·····H-O(3,G3) | | 1.04 | 1.80 | 2.79 | 158 |
| O(6,G2)·····H(B)-O(W3) | | 1.29 | 2.15 | 2.93 | 114 |
| O(6,G2)·····O(W2) | (g) | | | 2.88 | |
| O(2,G3)-H·····O(3,G4) | | 1.02 | 1.89 | 2.83 | 152 |
| O(3,G3)·····H(B)-O(W1) | (k) | 0.97 | 2.33 | 2.85 | 113 |
| O(6,G3)·····O(W1) | | | | 2.69 | |
| O(6,G3)-H·····O(W3) | | 1.22 | 1.53 | 2.65 | 149 |
| O(2,G4)·····H-O(3,G5) | | 1.07 | 1.92 | 2.88 | 147 |
| O(2,G4)·····O(W5) | (j) | | | 2.71 | |
| O(2,G4)·····H-O(3,G7) | (h) | 0.79 | 2.68 | 3.08 | 113 |
| O(3,G4)-H·····O(6,G6) | (c) | 0.90 | 2.08 | 2.83 | 140 |
| O(6,G4)·····O(W2) | | | | 2.75 | |
| O(2,G5)-H·····O(3,G6) | | 0.76 | 2.12 | 2.81 | 151 |
| O(3,G5)·····H(A)-O(W5) | | 0.82 | 2.07 | 2.80 | 148 |
| O(6,G5)-H·····O(W5) | (e) | 1.00 | 2.08 | 2.94 | 143 |
| O(6,G5)·····H(B)-O(W4) | (g) | 0.96 | 1.82 | 2.75 | 162 |
| O(2,G6)-H·····O(3,G7) | | 0.99 | 2.01 | 2.93 | 154 |
| O(3,G6)-H·····O(1,BA) | (d) | 0.98 | 1.84 | 2.74 | 151 |
| O(3,G6)·····H-O(1,BA) | (d) | 1.00 | 2.10 | 2.74 | 121 |
| O(5,G6)·····H-O(1,BA) | (a) | 1.00 | 2.33 | 3.00 | 123 |
| O(2,G7)·····H(B)-O(W5) | | 1.07 | 1.85 | 2.87 | 158 |
| O(W1)-H(A)·····O(W2) | | 1.00 | 2.11 | 3.02 | 150 |
| O(W3)-H(A)·····O(W4) | | 1.18 | 1.86 | 2.77 | 130 |

Symmetry Code

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| None | $x$, | $y$, | $z$ | f | $-x$, | $1/2+y$, | $1-z$ |
| a | $x$, | $1+y$, | $z$ | g | $1-x$, | $1/2+y$, | $1-z$ |
| b | $-1+x$, | $y$, | $z$ | h | $-x$, | $-1/2+y$, | $-z$ |
| c | $x$, | $-1+y$, | $z$ | i | $-x$, | $-1/2+y$, | $1-z$ |
| d | $-x$, | $1/2+y$, | $-z$ | j | $1-x$, | $-1/2+y$, | $-z$ |
| e | $1-x$, | $1/2+y$, | $-z$ | k | $1-x$, | $-1/2+y$, | $1-z$ |

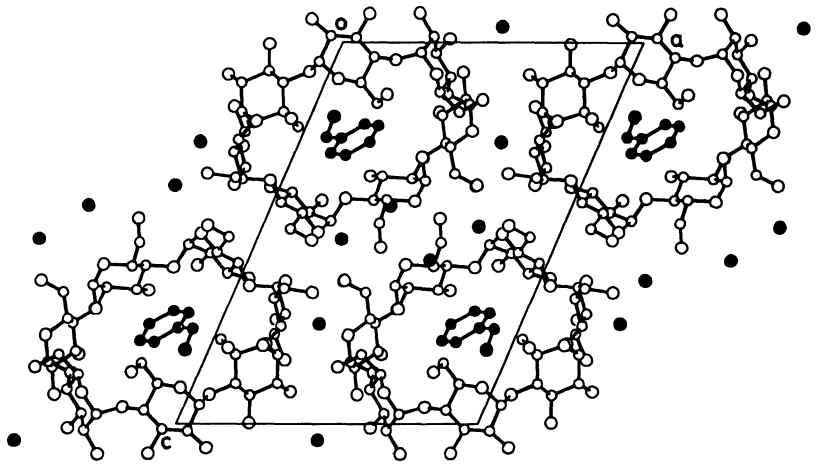


Fig. 5. The crystal structure viewed along the b axis. Benzyl alcohol and water molecules are shown by full circles.

seven O(4) atoms are coplanar within the maximum deviation of 0.228 Å.

The secondary hydroxyl groups form intramolecular hydrogen bonds, which may maintain the round shape of the β-cyclodextrin ring: four O(2)-H···O(3′) and three O(2)···H-O(3′) hydrogen bonds are found, as shown in Table 3. The O(2)···O(3′) distances are in the range 2.79—2.93 Å with the average value of 2.87

Å. The glucose residues are not perpendicular to the O(4) plane, but are inclined with their primary hydroxyl sides nearer to each other. The tilt-angles of glucose residues are in the range from −2.2 to 25.2°. The average value of 13.7° is greater than those found in the β-cyclodextrin dodecahydrate[6] and the β-cyclodextrin–hexamethylenetetramine complex[8] (12.5° and 11.4°, respectively). These larger tilt angles suggest that the glucose residues incline so as to make the shape and size of the host cavity more suitable for the accommodation of the guest molecule.

The guest benzyl alcohol molecule is fully enclosed within the β-cyclodextrin cavity. The phenyl group is located at the primary hydroxyl side of the cavity, and occupies the same position as that which the pyridyl group occupies in the β-cyclodextrin complex with nicotinamide.[10] Although in the nicotinamide complex the carbamoyl group protrudes outward from the primary hydroxyl side of the cavity, the hydroxyl group of benzyl alcohol is include within the cavity. The phenyl group has short contacts with C(5)–H methine groups of β-cyclodextrin: the C(3,BA)–H···H–C(5,G5) contact of 2.18 Å and the C(6,BA)–H···H–C(5,G1) contact of 2.09 Å, as shown in Fig. 3. The phenyl plane is not perpendicular to the O(4) plane, but makes an angle of 69.6°. As a result, the methylene group of benzyl alcohol has short contact with C(3)–H methine groups of the G1 and G2 residue: the C(7,BA)–H(A)···H–C(3,G2) contact of 2.02 Å and the C(7,BA)–H(B)···H–C(3,G1) contact of 2.06 Å. The hydroxyl group of benzyl alcohol forms hydrogen bonds with adjacent β-cyclodextrin molecules, as shown by dotted lines in Fig. 3.

β-Cyclodextrin molecules are stacked along the b axis (Figs. 4 and 5). As the O(4) plane of β-cyclodextrin makes an angle of 44.9° with the b axis, β-cyclodextrin molecules make a herringbone-like pattern along the bc plane. Adjacent β-cyclodextrin molecules block both ends of the β-cyclodextrin cavity. The isolated "cage", thus created, accommodates the guest molecule. Water molecules are not included within the host cavity, but fill intermolecular spaces between β-cyclodextrin molecules. As shown in Table 3, water molecules are involved in the formation of many hydrogen bonds. The W1 and W2 water molecules are linked to each other by the O(W1)–H···O(W2) hydrogen bond. The W3 water molecule forms the O(W3)–H···O(W4) hydrogen bond with the W4 water molecule. The W5 water molecule is isolated and forms hydrogen bonds with β-cyclodextrin molecules.

In many β-cyclodextrin complexes,[11–15] two β-cyclodextrin molecules are coupled to form a head-to-head dimer with the secondary hydroxyl sides facing each other. The cylindrical cavity formed by the dimerization can include a guest molecule with its size larger than the depth of a single β-cyclodextrin cavity. On the other hand, the shape and size of the guest molecule are quite restricted in the typical cage-type structure because of the limited space of the host cavity. In α-cyclodextrin complexes with the cage-type structure, for example, the host molecule includes only small molecules such as water,[16] iodine,[17] and alcohols,[18] *etc.* However, the present crystal structure demonstrates that the cage of β-cyclodextrin is sufficiently large to accommodate benzene derivatives. This is a first observation of the cage-structure in the β-cyclodextrin complex with benzene derivatives, although a similar structure was observed in the complex with nicotinamide having a pyridine ring.[10]

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