Table 1
Summary of crystallographic data for 2β-CD·2BA·0.7$C_2H_5OH$·20.65$H_2O$

| | |
|---|---|
| Chemical formula | $2(C_6H_{10}O_5)\cdot 2(C_7H_6O_2)\cdot 0.7(C_2H_6O)\cdot 20.65H_2O$ |
| Chemical formula weight | 2917.6 |
| Crystal habit, color | rod, colorless |
| Crystal size ($mm^3$) | 0.5 × 0.6 × 0.7 |
| Crystal system | triclinic |
| Space group | $P1$ |
| $a$ (Å) | 15.210(1) |
| $b$ (Å) | 15.678(1) |
| $c$ (Å) | 15.687(1) |
| $\alpha$ (°) | 89.13(1) |
| $\beta$ (°) | 74.64(1) |
| $\gamma$ (°) | 76.40(1) |
| $V$ ($Å^3$) | 3501.4(1) |
| $Z$ | 1 |
| $D_{calcd}$ (g $cm^{-3}$) | 1.364 |
| $\mu$ ($mm^{-1}$) | 0.12 |
| $F(000)$ | 1515 |
| Diffractometer | SMART CCD (Bruker) |
| Radiation type, wavelength (Å) | Mo $K_\alpha$, 0.71073 |
| Temperature (°C) | 20 |
| Data collection method | $\omega$ scans with 0.3° steps |
| $\theta$ Range (°) | 1.35–30.50 |
| Index ranges | $-21 \le h \le 0$, $-22 \le k \le 19$, $-21 \le l \le 22$ |
| Resolution (Å) | 0.7 |
| Reflections measured | 25,704 |
| Independent reflections | 16,201 [$R_{int} = 0.037$] |
| Reflections observed [$I > 2\sigma(I)$] | 10,022 |
| Structure solution | Molecular replacement (PATSEE) |
| Refinement method | blocked-matrix least-squares on $F^2$ |
| Weighting scheme | $w = [S^2(F_o^2) + (0.0963P)^2 + 2.2578P]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$ |
| Data/parameters | 16,201/1840 |
| $R$ [$F^2 > 2\sigma(F^2)$] | $R^a = 0.078$, $wR^b = 0.177$ |
| $R$ (all data) | $R^a = 0.134$, $wR^b = 0.216$ |
| Goodness-of-fit | 1.031 |
| Highest peak/deepest hole (e $Å^{-3}$) | 0.52/−0.30 |

[a] $R = \Sigma \| |F_o| - |F_c| \| / \Sigma |F_o|$.
[b] $wR = \Sigma \{ w(F_o^2 - F_c^2)^2 / \Sigma w(F_o^2)^2 \}^{1/2}$.

ring is parallel to the CD molecular axis and the COOH group points toward the narrower rim of the cone. A detailed structure of the inclusion complex is not yet reported so far. In this paper, we present insight into the three-dimensional structure of β-CD–BA inclusion complex by means of X-ray crystallography.

## 2. Experimental

### 2.1. Crystallization and X-ray diffraction

β-CD purchased from Cyclolab (Budapest/Hungary) BA and EtOH from Merck were used as received. β-CD (0.05 mol) and BA (0.10 mol) were dissolved in 2 mL of 50:50 (% v/v) water–EtOH at room temperature (rt). The solution was warmed to 60 °C for 1 h and cooled down slowly. Rodlike, colorless crystals formed in 1 week by slow solvent evaporation.

A single crystal of β-CD–BA complex with dimensions 0.4 × 0.5 × 0.7 $mm^3$ was mounted in a glass capillary sealed at both ends with a trace of mother liquor. X-ray data collection was performed at rt using a SMART CCD diffractometer (Bruker) with Mo $K_\alpha$ radiation ($\lambda = 0.71073$ Å) operating at 50 kV, 30 mA. A total of 25,704 reflections were measured in $\theta$ range of 1.35–30.50° (0.7 Å resolution). Data were corrected for Lorentz, polarization, and absorption effects and merged by SADABS[9] and SHELXTL[10] to yield 16,201 unique reflections. The crystal belongs to triclinic space group $P1$ (for more details, see Table 1).

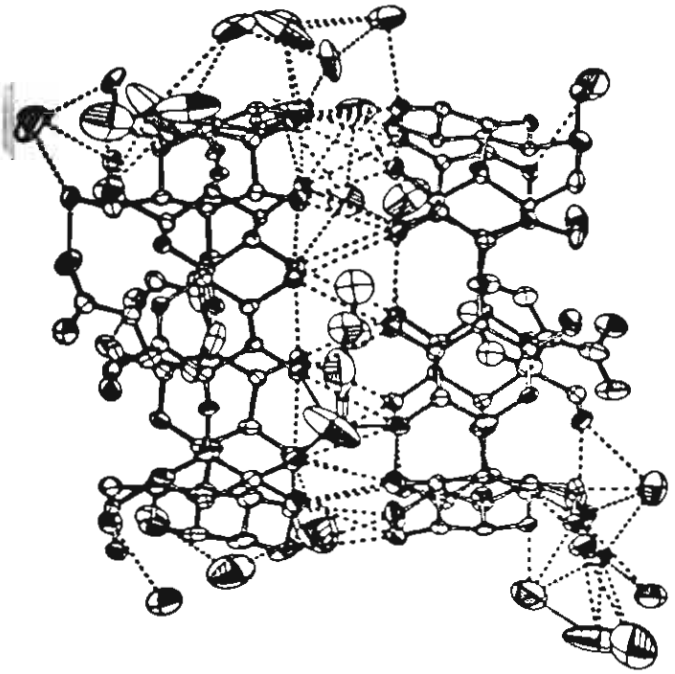
### 2.2. Structure determination and refinement

The crystal structure was determined by molecular replacement with program PATSEE[11] using the structure of β-CD–7-hydroxy-4-methylcoumarin complex[12] as a phasing model (only the β-CD backbone was used for the calculations, O-6 atoms were omitted). β-CD O-6 atoms, water oxygen atoms, BA, and EtOH molecules could be located by difference Fourier electron density maps aided by the graphic program XTALVIEW.[13] All O-6 atoms of the two β-CD molecules are fully occupied, except for O-66 of β-CD #1 that is doubly disordered. Two BA molecules are found fully occupied within the β-CD cavities. Ethanol (occupancy 0.7) was located in the channel of the β-CD dimer. Water molecules (20.65) were distributed over 30 sites, located preferentially in the interstices between β-CD molecules. All hydrogen atoms were placed at theoretical positions according to the 'riding model'.[14] The structure was refined by blocked-matrix least-squares on $F^2$ with program SHELXL-97.[14] Anisotropic refinement of 1840 atomic parameters against 16,201 data with $F^2 > 2\sigma(F^2)$ converged at $R = 0.078$ (except for EtOH that was refined isotropically). All atoms show normal thermal motion with $U_{eq}$ in the range 0.03–0.14 $Å^2$, except for EtOH and most water molecules that have higher $U_{eq}$, 0.10–0.31 $Å^2$ (see the thermal ellipsoid plots in Fig. 2).

A summary of crystallographic data and the geometrical parameters for the β-CD–BA inclusion complex are given in Tables 1 and 2, respectively. The final fractional atomic coordinates and equivalent isotropic

ermal displacement factors are given as supplementry material.

The atomic numbering scheme is that used conventionally for carbohydrates, i.e., the first number denotes the position in the glucose and the second number the glucose number in the CD macrocycle. Additionally, extra numbers 1 and 2 are used to indicate the β-CD molecules # 1 and 2, respectively. For example C-32_1 denotes C-3 of glucose unit # 2 of β-CD molecule # 1 (see Fig. 1). The letters A, B indicate disordered atoms. For the guest molecules, similar atomic numbering is adopted and the letter Z indicates the two BA molecules, e.g., C-4Z_2 stands for C-4 of BA molecule # 2 (see Fig. 1).



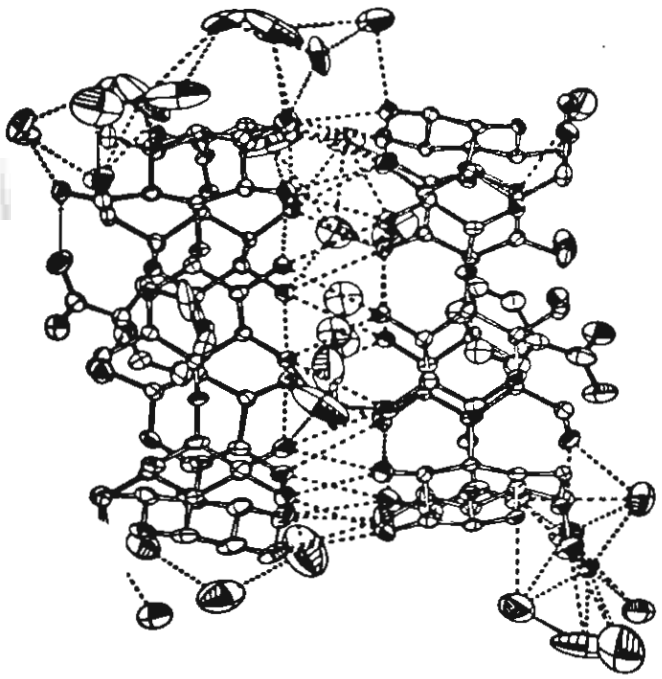


Fig. 2. ORTEP-III[22] stereo plot of the 2β-CD·2BA·0.7$C_2H_5OH$·20.65$H_2O$ inclusion complex drawn with thermal ellipsoid (30%) representation. Ellipsoids with and without octant shading are $O_{CD}$, $O_W$ and $C_{CD}$, respectively; β-CD bonds are represented by white sticks and BA bonds black sticks. Dashed lines indicate possible O–H···O hydrogen bonds with O···O separation within 3.5 Å.

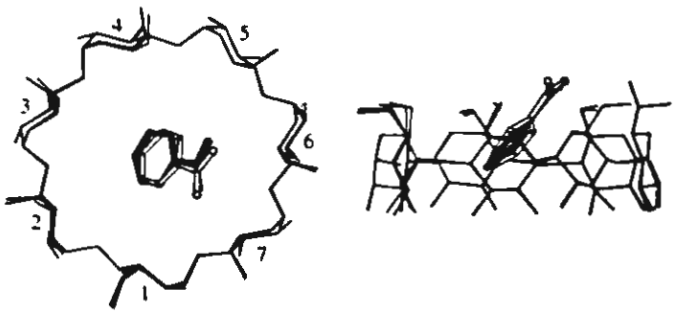



Fig. 3. Superposition of β-CD # 1 (thin line) on β-CD # 2 (thick line). BA # 1 and # 2 shown with white and black ball-and-stick, respectively (small balls are C and bigger O). Top view on the left and side view on the right.

## 3. Results and discussion

### 3.1. Structural description of β-CD macrocycles

The asymmetric unit consists of two β-CDs, two BAs, 0.7 ethanol, and 20.65 water molecules. The two β-CD molecules are almost identical as indicated by small rms deviation of superposition 0.13 Å (O-6 and H-atoms were excluded from the calculations), see Fig. 3. All glucose residues adopt a slightly distorted $^4C_1$ chair conformation as shown by the Cremer–Pople puckering parameters, $Q$ and $\theta$[15] in the range 0.54–0.58 Å, 3–10°, respectively, Table 2. The orientation of the glucose about the O-4 glycosidic bond is described by the torsion angles $\psi$, $\phi$ in the ranges 108.7–128.1°, 119.1–132.1°, showing that all glucoses are oriented *syn* (i.e., all O-2–H, O-3–H groups are on the same side of the cone), Table 2. This can be seen also by the narrow span of tilt angle 1.9–12.6°. The annular shape of β-CD is stabilized by intramolecular, interglucose O-3($n$)···O-2($n+1$) hydrogen bonds with O···O distances 2.69–2.85 Å. In addition, the O-4($n+1$)–O-4($n$)–O-4($n-1$) angles 124.8–132.2° and the small deviations of O-4 atoms from their common least-squares plane (< 0.11 Å) are evidences for the well defined heptagon formed by the lines connecting the O-4 atoms in the β-CD macrocycles.

The orientation of the C-6–O-6 bond is described by torsion angles C-4–C-5–C-6–O-6 and O-5–C-5–C-6–O-6

Table 2
Geometrical parameters of 2β-CD·2BA·0.7$C_2H_5OH$·20.65$H_2O$ (distances in Å and angles in °)

| Residue | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| $Q$ [a], $\theta$ [b] | 0.58, 10 | 0.56, 6 | 0.57, 4 | 0.57, 4 | 0.55, 3 | 0.57, 4 | 0.57, 5 |
| | **0.55, 4** [i] | **0.58, 7** | **0.57, 8** | **0.58, 3** | **0.54, 4** | **0.55, 8** | **0.57, 9** |
| $\phi$ [c], $\psi$ [c] | 112.4(7), 119.5(7) | 128.1(7), 126.1(8) | 112.2(7), 132.1(7) | 113.2(6), 128.3(6) | 108.7(6), 127.8(6) | 112.8(6), 127.6(6) | 115.6(6), 123.8(6) |
| | **115.8(6), 131.2(6)** | **116.0(6), 129.3(6)** | **113.4(6), 129.4(6)** | **113.2(6), 125.4(6)** | **115.2(7), 126.2(7)** | **116.7(6), 119.1(7)** | **122.6(6), 123.4(6)** |
| Tilt angle [d] | 3.7(2) | 5.8(5) | 10.9(5) | 12.6(3) | 10.0(1) | 9.9(2) | 6.4(2) |
| | **7.2(4)** | **10.1(3)** | **8.9(1)** | **6.7(2)** | **6.9(2)** | **1.9(1)** | **3.6(3)** |
| O-4 angle [e] | 124.8(2) | 128.5(2) | 132.2(1) | 126.3(1) | 126.6(1) | 130.9(1) | 130.2(1) |
| | **130.5(1)** | **126.3(1)** | **127.0(1)** | **132.4(1)** | **127.8(1)** | **125.6(1)** | **130.3(1)** |
| *Distances* | | | | | | | |
| O-4 deviation [f] | −0.11 | 0.06 | −0.01 | 0.01 | −0.03 | −0.01 | 0.09 |
| | **0.01** | **0.03** | **−0.01** | **−0.01** | **−0.01** | **0.06** | **−0.06** |
| O-3($n$)···O-2($n$+1) | 2.76(1) | 2.85(1) | 2.79(1) | 2.84(1) | 2.82(1) | 2.76(1) | 2.69(1) |
| | **2.77(1)** | **2.83(1)** | **2.79(1)** | **2.76(1)** | **2.73(1)** | **2.70(1)** | **2.82(1)** |
| O-3($n$)_1···O-2($m$)_2 [g] | 2.94(1) | 3.15(1) | 2.99(1) | 3.05(1) | 3.00(1) | 3.11(1) | 3.11(1) |
| O-3($n$)_1···O-3($m$)_2 [g] | 3.12(1) | 3.10(1) | 2.88(1) | 2.81(1) | 2.79(1) | 2.89(1) | 2.85(1) |
| O-2($n$)_1···O-2($m$)_2 [g] | 3.16(1) | 3.42(1) | 3.27(1) | 3.04(1) | 2.96(1) | 3.08(1) | 3.11(1) |
| O-2($n$)_1···O-3($m$)_2 [g] | 2.90(1) | 3.31(1) | 3.11(1) | 3.11(1) | 2.96(1) | 3.05(1) | 3.02(1) |
| *Torsion angle* | | | | | | | |
| C-4–C-5–C-6–O-6 | 61.0(9) | 50.3(9) | 50.5(10) | 54.0(8) | 56.5(8) | 179.0(8) [h], 50.3(12) [h] | 54.8(9) |
| | **57.6(8)** | **61.2(7)** | **55.3(10)** | **57.3(8)** | **61.7(10)** | **57.9(8)** | **56.1(8)** |
| O-5–C-5–C-6–O-6 | −61.9(8) | −71.3(9) | −69.4(8) | −67.7(8) | −65.2(7) | 59.0(10) [h], −69.8(11) [h] | −66.0(8) |
| | **−62.9(7)** | **−60.0(7)** | **−67.3(9)** | **−61.6(7)** | **−62.8(9)** | **−65.5(7)** | **−65.1(8)** |

[a] Cremer-Pople puckering amplitude.[19]
[b] Indicates the deviation from the theoretical chair conformation (ideal value: $\theta = 0$).
[c] Torsion angles $\phi$ and $\psi$ at glycosidic O-4, defined as O-5($n$)-C-1($n$)-O-4($n-1$)-C-4($n-1$) and C-1($n$)-O-4($n-1$)-C-4($n-1$)-C-3($n-1$), respectively.
[d] Tilt angles, defined as the angles between the O-4 plane and the planes through C-1($n$), C-4($n$), O-4($n$) and O-4($n-1$).
[e] Angle at each glycosidic O-4: O-4($n+1$)-O-4($n$)-O-4($n-1$).
[f] Deviation of O-4 atoms from the least-squares plane through the seven O-4 atoms.
[g] Intradimeric hydrogen bonds between O-2, O-3 of glucose unit $n$ (β-CD # 1) and of glucose unit $m$ (β-CD # 2).
[h] Values for twofold disordered O-66_1 with the occupancy factors 0.5 for both sites A and B.
[i] Bold numbers are the values of β-CD # 2.

Table 2. All C-6–O-6 bonds are directed 'away' from the β-CD cavities and are hydrogen bonded with neighboring water sites and O-6–H groups (Figs. 3, 5 and 6), as shown by torsion angles C-4–C-5–C-6–O-6 and O-4–C-5–C-6–O-6 in the ranges 50.3–61.7° and −60.0 to −71.3°, respectively (Table 2). Except for O-66A_1 that points 'toward' the cavity and hydrogen bonds to water sites W-9, W-21, W-23 and O-2Z_1, Fig. 6. The corresponding torsion angles are 179.0 and 59.0°, Table 2.

Two β-CD molecules form a dimer where their O-2–H, O-3–H groups are engaged in intermolecular O-2(*n*)_1/O-3(*n*)_1···O-2(*m*)_2/O-3(*m*)_2 hydrogen bonds with O···O distances 2.79–3.16 Å, except O22_1···O26_2 (3.42 Å), O-22_1···O-35_2 (3.31 Å), and O-23_1···O-25_2 (3.27 Å), Table 2. Such feature has been observed frequently in crystal structures of β-CD.[3] Since the X-ray data at room temperature of the present structure did not permit the H-atom positions to be determined, the detailed hydrogen bonding in the β-CD dimer could not be obtained. However, the recent study of β-CD–1,12-dodecanedioic acid inclusion complex using synchrotron high-resolution data (0.65 Å) at 100 K[16] allowed the accurate location of H-atoms of the β-CD O–H groups to be verified. The results showed that only O-3–H groups of a β-CD monomer are involved in the intermolecular hydrogen bonds at the O-2-, O-3-sides of the β-CD dimer.

### 3.2. Inclusion geometry of BA molecules

Fig. 4 shows that both BA molecules are placed in the central cavities of β-CD molecules. The two aromatic ring centers of BA are shifted from the O-4-plane centers to the O-6-sides of β-CD by approx 1.0 Å (distance *d*), see Figs. 2 and 3. The two aromatic ring planes are inclined 52° with respect to the O-4 plane (angle τ) and make an angle of 13° with respect to each other. The BA molecules protrude with their COOH groups at the β-CD O-6-sides and are maintained in positions by hydrogen bonding to the surrounding O-6–H groups and water molecules, Figs. 2–4. They are almost in the same environment as their COOH groups are coordinated via six O–H···O hydrogen bonds (O···O distances 2.58–3.35 Å), except for O-2Z_1 that is additionally hydrogen bonded to O-66A_1, Fig. 4. The inclusion geometry of BA in the present structure agrees with those proposed by previous studies[5,8] as the

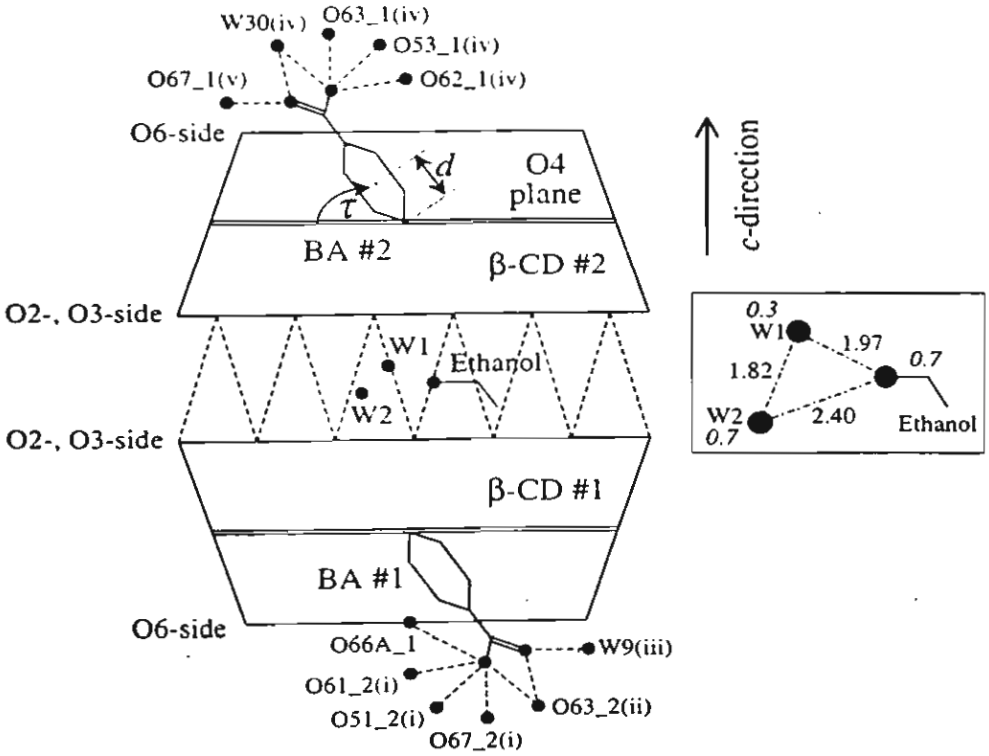



Fig. 4. Schematic presentation of the inclusion geometry of the BA molecules in the β-CD cavities. Aromatic rings of the two BA molecules are represented with gray hexagons. *d* defined as the center-to-center distance of the BA aromatic ring to β-CD O-4 plane. Angle τ showing inclination of the BA molecular axis (dotted line) with respect to the glycosidic O-4 plane (double line). Filled circles indicate oxygen atoms and dashed lines intermolecular O–H···O hydrogen bonds. Dashed lines linked between the β-CD monomer show O-2(*m*)_1/O-3(*m*)_1···O-2(*n*)_2/O-3(*n*)_2 hydrogen bonds in the β-CD dimer. Connection of water sites W-1, W-2, and ethanol molecule is depicted in the framed area. Symmetry operations: (i) $x, y, z-1$; (ii) $x+1, y, z-1$; (iii) $x+1, y-1, z-1$; (iv) $x, y, z+1$; (v) $x-1, y, z+1$.

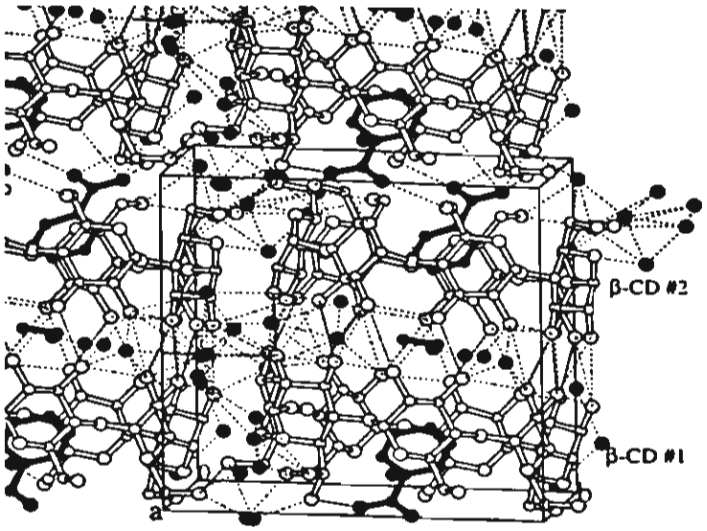



Fig. 5. Crystal packing of the 2β-CD·2BA·0.7$C_2H_5OH$·20.65$H_2O$ inclusion complex in channel mode that is stabilized by O-2($m$)_1/O-3($m$)_1···O-2($n$)_2/O-3($n$)_2 (tail-to-tail), O-6($m$)_1···$O_W$···O-6($n$)_2 (head-to-head) hydrogen bonds (dashed lines) between β-CD # 1 and # 2. $O\text{-}2_{CD}$, $O\text{-}3_{CD}$, $O\text{-}6_{CD}$ and $O_W$ are represented with gray and black spheres, respectively. The BA molecules are black and H-atoms not shown. Drawn with program MOLSCRIPT.[23]

BA COOH group is directed to the narrower rim of the cone.

It is worth comparing the present structure with the β-CD complexes with BA derivatives crystallized in the triclinic space group $P1$.[17–19] Although the host β-CD molecules have the same dimeric structures as found in the present structure, the inclusion geometries are different. In the complex of 4-*t*-butylbenzoic acid,[17] the host–guest ratio is 2:2 and the two guest molecules are in different environments in the β-CD cavities. The aromatic ring of one guest molecule is included in the β-CD cavity while that of the other one is in the channel of the β-CD dimer. In the complex of 3,5-dimethylbenzoic acid,[18] the guest molecules are extensively disordered. For the guest sites in the β-CD cavities, their COOH groups point to the O-2-, O-3-side while some are in the channel of the β-CD dimer. In the complex of acetylsalicylic acid–salicylic acid,[19] the aromatic rings of two acetylsalicylic acid molecules are embedded in each β-CD cavity and the salicylic acid is in the channel of the β-CD dimer.

### 3.3. Disordered water molecules

Water molecules (20.65) are distributed over 30 positions (W-3–W-7, W-12, W-18–W-20, W-22, W-23, W-30 are fully occupied while the others have occupancies in the ranges 0.25–0.75) in the interstices between β-CD macrocycles, except for the water sites W-1, W-2 that are in the channel of the β-CD dimer, Figs. 2, 4 and 5. Water site W-1 is too close to the ethanol OH group (1.97 Å) and water site W-2 (1.82 Å), i.e., they are not in hydrogen bonding distance indicating that water site W-1 cannot be occupied simultaneously with water site W-2 and ethanol (their occupancies sum up to one). The W-2–ethanol distance 2.40 Å accounts for hydrogen bond interaction showing that water site W-2 and ethanol may coexist (Fig. 4). In addition, short interatomic distances among water sites W-9–W-10 (1.22 Å), W-14–W-15 (1.63 Å), W-24–W-26 (1.57–1.74 Å), and W-27–W-29 (1.07–1.64 Å) suggest that the water sites in each cluster are not coexistent. Water sites play an important role in stabilizing the crystal structure as they contribute to hydrogen bonding as bridges, e.g., at O-2-, O-3-side: O-21_1···W-19···O-36_2, O-22_1···W-16···O-35_2, O-32_1···W-26···O-25_2, O-23_1···W-3···O-25_2; at O-6-side: O-61_1···W-18···O66_2, O-61_1···W-7···O-64_2, O-62_1···W-11···W-23···O-62_2, O-65_1···W-21···O-65_2, O-66A_1···W-9···O-65_2 (Fig. 6). The hydrogen-bonding network in the present structure is complicated since there are many partially occupied water sites (Fig. 6).

### 3.4. Crystal packing

The β-CD molecules are stacked along the crystallographic *c*-axis, in the alternative head-to-head and tail-to-tail channel mode[20] as frequently observed in the β-CD crystal structures[3] (Fig. 5). The glycosidic O-4 planes of the β-CD # 1, 2 are almost parallel. They are slightly inclined approx 11.1, 9.8° to the *ab*-plane, and make an angle of 2.8° with respect to each other. The distance from O-4-plane center of β-CD # 1 to # 2 is 7.17 Å. Both O-4-plane centers are not lined vertically but are shifted 2.89 and 1.33 Å in *a*- and *b*-directions, respectively. The molecular arrangement is stabilized at one end of β-CD (in the same column) by intermolecular O-2($m$)_1/O-3($m$)_1···O-2($n$)_2 O-3($n$)_2 hydrogen bonds (O···O distances 2.79–3.42 Å), Figs. 2 and 5, Table 2. At the other end, the O-6–H groups are not directly hydrogen bonded to the O-6–H groups of adjacent β-CD but linked by one or two bridging water molecules, e.g., O-61_1···W-18···O-66_2, O-62_1···W-11···W-23···O-62_2, O-65_1···W-21···W-7···O-64_2. In addition, a number of $O_{CD}$···$O_{CD}$, $O_{CD}$···$O_W$···$O_{CD}$, $O_{CD}$···$O_W$···$O_W$···$O_{CD}$ hydrogen bonds found between neighboring β-CD columns contribute to the stability of the crystal structure (Figs. 5 and 6).

In comparison with the complexes of BA derivatives, the complex of 4-*t*-butylbenzoic acid[17] and of 3,5-dimethylbenzoic acid[18] show similar packing patterns as the present crystal structure. This contrasts with the complex of acetylsalicylic acid–salicylic acid[19] in which β-CD dimers are stacked in layers like bricks in a wall.

After the β-CD–BA inclusion complex has been characterized both in solution and gas phase by various

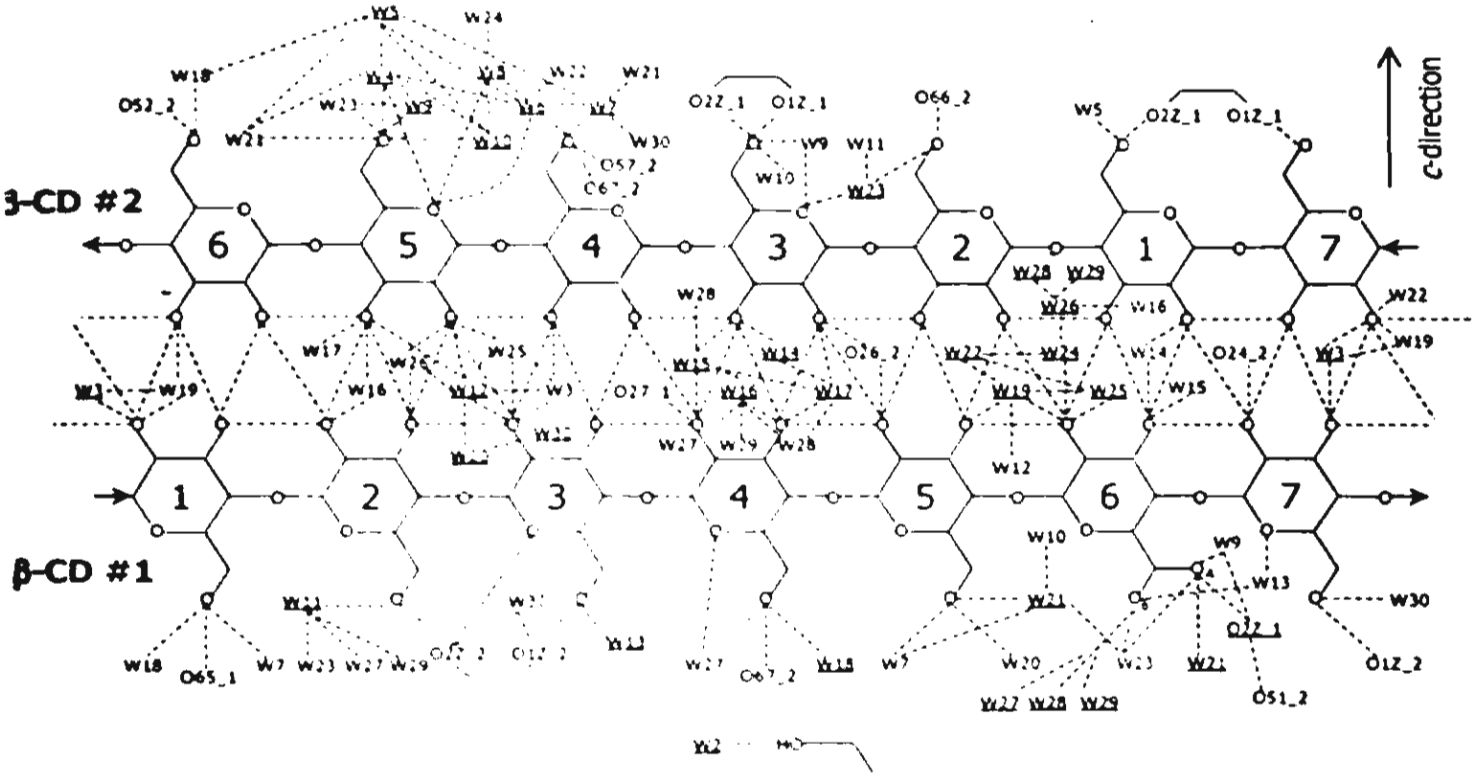



Fig. 6. O–H···O hydrogen bonds (dashed lines) in the 2β-CD·2BA·0.7C$_2$H$_5$OH·20.65H$_2$O inclusion complex with O···O distance within 3.5 Å. Underlined atomic names indicate atoms in the general position $x, y, z$, the others are in symmetry related positions. Arrows show connection of glucose units in β-CD.

techniques since 25 years ago,[2] its structural evidence in crystalline state is finally reported in the present paper. The previous results forecasted a 1:1 host–guest stoichiometry and orientation of BA with its aromatic ring parallel to the CD molecular axis and the COOH group points to the CD O-6-side. This agrees well with the crystallographic results. However, X-ray analysis reveals deeper details of BA inclusion geometry. The stoichiometry is 2:2 and the BA aromatic ring is in fact, not parallel but slanted to the β-CD molecular axis. BA is maintained in position by hydrogen bonds to the surrounding O-6–H groups and water molecules.

The present finding is not consistent with the inclusion complexes of β-CD with other BA derivatives both in terms of stoichiometry and inclusion geometry as mentioned above. Since the functional groups attached to the aromatic ring have different hydrogen bonding donor/acceptor functionality and bulkiness, they are oriented differently in the β-CD cavity to be energetically stable. Therefore, a general direction for predicting the authentic CD inclusion complexes is not possible and these complexes needed to be investigated case by case.

## Supplementary material

stallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Center as supplementary publication No. CSD-191347. These data can be obtained free of charge via www.ccdc.cam.ac.uk conts/retrieving.html or from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Tel.: +44-1223-336-408; fax: +44-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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# Crystal Structures of β-Cyclodextrin Complexes with Formic Acid and Acetic Acid

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**Abstract**

β-cyclodextrin (β-CD)–formic acid (**1**) and β-CD–acetic acid (**2**) inclusion complexes crystallize as β-CD·0.3HCOOH·7.7$H_2O$ and β-CD·0.4$CH_3COOH$·7.7$H_2O$ in the monoclinic space group $P2_1$ with comparable unit cell constants. Anisotropic refinement of atomic parameters against X-ray diffraction data with $F_o^2 > 2\sigma(F_o^2)$ (986/8563 and 991/8358) converged at *R*-factors of 0.051 and 0.054 for **1** and **2**, respectively. In both complexes, the β-CD molecular conformation, hydration pattern and crystal packing are similar, but the inclusion geometries of the guest molecules are different. The β-CD macrocycles adopt a "round" conformation stabilized by intramolecular, interglucose O3($n$)···O2($n$ + 1) hydrogen bonds and their O6–H groups are systematically hydrated by water molecules. In the asymmetric unit, each complex contains one β-CD, 0.3 formic acid (or 0.4 acetic acid), and 7.7 water molecules that are distributed over 9 positions. Water sites located in the β-CD cavity hydrogen bond to the guest molecule. In the crystal lattice, β-CD molecules are packed in a typical "herringbone" fashion. In **1**, the formic acid (occupancy 0.3) is entirely included in the β-CD cavity such that its C atom is shifted from the O4-plane center to the β-CD O6-side by 2.90 Å and C=O, C–O bonds point to this side. In **2**, the acetic acid (occupancy 0.4) is completely embedded in the β-CD cavity, in which the carboxylic C atom displaces from the O4-plane center to the β-CD O6-side by 0.87 Å; the C=O bond directs to the β-CD O6-side and makes an angle of 15° to the β-CD molecular axis.

*Key words*: acetic acid, crystal structure, β-cyclodextrin, formic acid, hydrogen bond, inclusion complex, X-ray analysis

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## Introduction

α-, β-, γ-Cyclodextrins (CDs) are cyclic oligosaccharides consisting of 6, 7, 8 D-glucose units linked by α-(1→4) glycosidic bonds [1]. They have the shape of a truncated cone and are amphiphilic with an apolar cavity coated by C–H groups and O4, O5 atoms, and hydrophilic rims lined by O6–H groups on the narrower side, and O2–H, O3–H groups on the wider side (Figure 1).

CDs are well known for their ability to form inclusion complexes [2] with a variety of guest molecules fitting partially or completely into the host CD cavity as shown by many CD crystal structures [3]. In the crystal lattice, CDs arrange in two different types according to the feature of the formed cavity: (i) cage (herringbone or brick motifs) and (ii) channel depending on the size and shape of the guest molecule [4].

Inclusion complexes of α-CD with a series of aliphatic carboxylic acids with 2–5 C atoms have been investigated by Saenger et al. since 30 years ago [5]. Although the crystal structures were not determined, the crystallographic data gave information on crystal packing. Clearly, the complexes with small guest-molecules like acetic acid, propionic acid, butyric acid, crystallize in the orthorhombic space group $P2_12_12_1$ and have a cage structure, whereas the complex with the longer molecule, valeric acid, crystallizes in a hexagonal space group and forms a channel structure. In past years, Mavridis et al. studied the inclusion complexes of β-CD with long aliphatic monocarboxylic and α,ω-dicarboxylic acids [6–12]. Both complexes with aliphatic monoacids and with aliphatic diacids likely crystallize in the triclinic space group $P1$ and β-CDs form dimer enclosing the guest molecules. In the monoacids with 12–16 C atoms the packing pattern is a channel structure [6–9], whereas in the diacids with 10–16 C atoms the packing style is an intermediate between cage (brick motif) and channel [10–12]. In addition, an inclusion complex of dimethyl-β-CD with acetic acid has been reported [13]. The complex crystallizes in the monoclinic space group $P2_1$ and the CD molecules are stacked in a herringbone cage-type.

Because the inclusion complexes of β-CD with formic acid and acetic acid have not yet been evidenced crystallographically so far. Therefore, it is of interest to determine the crystal structures of the β-CD complexes with small aliphatic carboxylic acids and to compare them to the corresponding complex of α-CD and other relevant complexes.

## Experimental

### *Crystallization and X-ray diffraction*

β-CD purchased from Cyclolab (Budapest, Hungary), formic acid and acetic acid from Fluka were used without further purification. Each 0.05 mmol of β-CD was dissolved in 2 mL of 5% formic acid and 10% acetic acid at RT. The rodlike, colorless single crystals grew in two weeks by slow solvent evaporation.

A single crystal of each complex was mounted in a glass capillary sealed at both ends by a drop of mother liquor. X-ray diffraction experiments were carried out at RT using a SMART CCD (Bruker) with MoKα radiation (λ = 0.71073 Å) operating at 50 kV, 30 mA. A total of 15,883 (β-CD–formic acid complex) and 16,086 (β-CD–acetic acid complex) reflections were measured in the $\theta$-range 1.0–30.5° (0.7 Å resolution). Data were corrected for Lorentz, polarization, and absorption effects and merged by SADABS [14] and SHELXTL [15] to yield 10,384 and 10,886 unique reflections for the formic acid and acetic acid complexes, respectively. The crystals of both complexes belong to monoclinic space group $P2_1$ (further details, see Table 1).

### *Structure determination and refinement*

The crystal structures were determined by molecular replacement with program PATSEE [16] using the structure of β-CD–ethylene glycol complex [17] as a phasing model (only the β-CD skeleton was used for the calculations, O6 atoms were omitted). β-CD O6 atoms, guest molecules, water oxygen atoms, and most of CH, $CH_2$ H-atoms of β-CD could be located by difference Fourier electron density maps aided by the graphic program XTALVIEW [18]. The remaining H atom positions were placed according to the "riding model" [19]. The structures were refined by full-matrix least-squares on $F^2$ with program SHELXL-97 [19]. Anisotropic refinement of atomic parameters against X-ray diffraction data with $F_o^2 > 2\sigma(F_o^2)$ (986/8563 and 991/8358) converged at $R$-factors of 0.051 and 0.054 for the formic acid and acetic acid complexes, respectively (except for the guest molecules that were refined isotropically). The O6 atoms of glucose residues 1, 7 are twofold disordered with occupancies for sites A, B are 0.6, 0.4; 0.7, 0.3 (formic acid); 0.45, 0.55; 0.85, 0.15 (acetic acid). Besides the disordered guest molecules, some water sites were found in the β-CD cavity (e.g., W8, W9 (formic acid); W1, W2, W3 (acetic acid)). The 7.7 water molecules are distributed over 9 sites with average

occupancy 0.86. Both β-CD structures show normal thermal motion with $U_{eq}$ in the ranges 0.042–0.095 Å$^2$ (β-CD skeleton), 0.069–0.142 Å$^2$ (β-CD O6), whereas some water sites and guest molecules exhibit higher thermal motion with $U_{eq}$ 2–3 times more.

A summary of crystallographic data and the geometrical parameters for both the inclusion complexes are given in Tables 1 and 2, respectively. The final fractional atomic coordinates and equivalent isotropic thermal displacement factors are deposited at the Cambridge Crystallographic Data Center [20].

The atomic numbering scheme is that used conventionally for carbohydrates (i.e., the first number denotes the position in the glucose and the second number the glucose number in the CD macrocycle), Figure 1. Letters A, B indicate disordered atoms. For example, O61A stands for site A of the disordered O6 of glucose unit 1. In addition, letters M and T show the formic acid and acetic acid, respectively; the β-CD–formic acid complex is given as **1** and β-CD–acetic acid **2**.

## Results and discussion

### *Isomorphous β-CD macrocycle*

In both complexes, the structures of host β-CD molecules are identical as shown by very small rms deviation of superposition 0.05 Å (all C, O atoms were used for the calculations). The 14 glucose units adopt a regular $^4C_1$ chair conformation as indicated by the Cremer-Pople puckering parameters $Q$, $\theta$ [21] and torsion angles $\phi$, $\psi$, in the ranges 0.54–0.59 Å, 1–9° and 102.2–117.3°, 113.9–140.8°, respectively (Table 2, Figures 2(a,b)). The annular geometry of the β-CD macrocycles is stabilized by intramolecular, interglucose O3($n$)···O2($n$ + 1) hydrogen bonds with O···O distances 2.78–3.00 Å (Table 2, Figures 2(a,b)). Tilt angles showing inclination of glucose to the β-CD central cavity are in the range 4.0–13.3°, except for those of glucose residues 1, 5, 7 that are 17.4–26.5° (Table 2, Figures 2(a,b)). In addition, the lines connecting the seven O4-atoms give a well-defined heptagon as indicated by the O4 ($n$ – 1)···O4($n$)···O4($n$ + 1) angles 123.9–133.9° and the deviations of O4 atoms from their common least-squares plane < 0.28 Å (Table 2, Figures 2(a,b)).

The orientation of C6–O6 groups is generally described by the torsion angle O5–C5–C6–O6. All C6–O6 groups point "away" from the β-CD cavity (–*gauche* orientation) as shown by the torsion angle O5–C5–C6–O6 in the range –59.1° to –72.0° (Table 2, Figures 2

(a,b)). Exceptions are C61–O61B, C65–O65, C67–O67B groups that point "toward" the β-CD cavity (+*gauche* orientation) as shown by the corresponding angles of 58.9–77.6° (Table 2, Figures 2(a,b)). This is because these O6–H groups hydrogen bond to the guest molecules and to water molecules embedded in the β-CD cavity (Figures 2(a,b)).

*Different inclusion geometries of the guest molecules*

Although the structures of formic acid and acetic acid are similar, each small acid orients differently in the large β-CD cavity to yield a stable complex with sufficient host-guest interactions. In **1**, the formic acid (occupancy 0.3) is located at the β-CD O6-side such that its C-atom shifts from the O4-plane center by 2.90 Å and C=O, C–O bonds point to this side (Figure 2(a)). It is maintained in position by hydrogen bonding to the surrounding water sites and β-CD OH groups. For example, O25···O1M($x$, $y-1$, $z$), O65···O1M, O67B···O1M, W3···O1M, O34···O2M($x$, $y-1$, $z$), O25···O2M($x$, $y-1$, $z$), O67B···O2M, W1···O2M, W3···O2M (O···O separation 2.66–3.49 Å, Figures 2(a), 4(a)). In **2**, the acetic acid (occupancy 0.4) is almost placed at the center of β-CD cavity, in which the carboxylic C-atom displaces from the O4-plane center to the O6-side by 0.87 Å and the C=O bond points to the O6-side and makes an angle of 15° to the β-CD molecular axis (Figures 2(b), 3). It is maintained in position by hydrogen bonding in similar way, as is the formic acid, but has fewer number of O–H···O interactions. For example, W8···O1T, W7···O1T($x$, $y-1$, $z$), O67B···O1T, W9···O2T, W8···O2T (O···O separation 2.71–3.30 Å, Figures 2(b), 4(b)).

In comparison to the inclusion complex of dimethyl-β-CD with acetic acid [13], methylation has little effect on the β-CD.macrocycle, but much on the inclusion geometry of acetic acid in the β-CD cavity. Figure 3 shows the similarity between the structures of β-CD–acetic acid and dimethyl-β-CD–acetic acid [13] complexes which is indicated by the small rms deviation of superposition 0.27 Å (only C1–C6, O2–O5 atoms of CD macrocycles were used for the calculations). The acetic acid (occupancy 0.5) is located below the O4-plane such that its carboxylic C-atom shifts from the O4-plane center by 0.82 Å and the C–C bond inclines 50° to the β-CD molecular axis (Figure 3). It is in van der Waals contacts to the CD macrocycle and has no hydrogen bond interactions to the water molecules. This suggests that the acetic acid is less energetically favored in the cavity of methylated derivative than in that of native β-CD.

*Water molecules as hydrogen bonding mediator*

Each inclusion complex contains 7.7 water molecules that are distributed over 9 positions (average occupancy 0.86). In **1**, the water sites W1, W3, W4 are disordered with occupancies 0.6, 0.3, 0.8 and the rest is fully occupied. Water sites W1, W2, W3 located in the β-CD cavity hydrogen bond to the formic acid (Figure 2(a)). In **2**, the disordered water sites W3, W4, W7 (occupancies 0.8, 0.2, 0.7) are located outside the β-CD cavity and the others are fully occupied. Water sites W8 and W9 located at the O6-side and O2-, O3-side of the β-CD cavity hydrogen bond to the acetic acid (Figure 2(b)). Similar hydration patterns are observed in both complexes (Figures 4(a,b)). The β-CD O6–H groups are systematically hydrated by water sites (e.g., W4, W6, W9, W8, W9, W7, W4 (**1**); W9, W2, W5, W6, W4, W3, W8 (**2**)). Some water sites bridge O5 to O6–H of the glucose units 1, 2, 4, 5 (e.g., W4, W5, W8, W7 (**1**); W9, W1, W5, W4 (**2**)). Some water sites link O3($n$)–H to O2($n$ + 1)–H (e.g., O32···W5··· O23, O34···W1···W8···W9···O25 (**1**); O32···W1···O23, O34···W7···W6···W5···O25 (**2**)). Water molecules play a crucial role as hydrogen bonding mediator in stabilizing the crystal structure.

4(a,b)

*Crystal packing*

In **1** and **2**, the β-CD molecules are packed in a herringbone cage-type [4] as observed in the β-CD hydrates [22,23] and in the β-CD inclusion complexes with small guest molecules like methanol [24], ethanol [25], DMSO [26]. The unit cell volumes of the above-mentioned β-CD inclusion complexes (this work and refs. 24–26) are so comparable to those of β-CD hydrates [22,23] with only 1% difference. This shows that when the small guest molecules are entirely included in the β-CD cavity, the herringbone packing structure of CD host molecules is intact. The inclusion complexes of α-CD and β-CD with acetic acid have different packing styles. The former [5] crystallizes in the orthorhombic space group $P2_12_12_1$ and arranges in a brick cage-type, whereas the latter crystallizes in the monoclinic space group $P2_1$ and prefers a herringbone cage-type. However, albeit the complexes of α-CD with long aliphatic carboxylic acids have not yet been determined, it is expected that they should have a channel structure as observed in the complexes with long molecules (e.g., α-CD–12-aminododecanoic acid [27] and, α-CD–4,4'-biphenyldicarboxylic acid [28]). This will be similar to the corresponding complexes of β-CD [6–9]. Furthermore, both dimethyl-β-CD–acetic acid [13] and β-CD–acetic acid complexes form a cage structure, showing that for the guest acetic acid that is

completely embedded in the host cavity, methylation does not affect the β-CD crystal packing.

## Conclusions

The β-CD–formic and β-CD–acetic acid inclusion complexes show similarity both in terms of molecular structure (β-CD macrocycle, hydration pattern) and crystal packing. A striking difference is observed only in the orientation of guest molecules in the β-CD cavity. When each small aliphatic acid (e.g., formic acid, acetic acid) can be totally included in an individual β-CD cavity, the β-CD arranges in a herringbone cage-structure. As the number of C atoms in the aliphatic acids increases, each long acid occupies more than one β-CD cavity; the β-CD prefers to form dimer and exhibits a channel structure [6–9]. The results are consistent with the previous structure elucidations of CD inclusion complexes [29].

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**Figure captions**

*Figure 1*. Chemical structures and atomic numbering of CD, formic acid, and acetic acid.

*Figure 2*. Ball-and-stick representation of (a) β-CD–formic acid and (b) β-CD–acetic acid inclusion complexes; top views on the left and side views on the right. Annular geometry of β-CD is stabilized by intramolecular, interglucose O3($n$)···O2($n$ + 1) hydrogen bonds (solid lines). For clarity, β-CDs is shown in white ball-and-stick and acids in black. water sites in grey balls, and hydrogen atoms are not shown. O–H···O hydrogen bonds are represented with dashed lines. Drawn with MOLSCRIPT [30].

*Figure 3*. Superposition of β-CD–acetic acid (thick line–black ball-and-stick) on dimethyl-β-CD–acetic acid[13] (thin line–white ball-and-stick); small balls are C and bigger O. For clarity, water molecules and hydrogen atoms not shown. Top view on the left and side view on the right. Drawn with MOLSCRIPT [30].

*Figure 4*. O–H···O hydrogen bonds (dashed lines) in the (a) β-CD·0.3HCOOH·7.7$H_2O$ and (b) β-CD·0.4$CH_3COOH$·7.7$H_2O$ inclusion complexes with O···O distances within 3.5 Å. Underlined atomic names indicate atoms in the general position $x$, $y$, $z$; the others are in symmetry related positions. Arrows show connection of glucose units in β-CD. Atomic numbering of the β-CD and acids is also given.

*Table 1.* Crystallographic data of β-CD·0.3HCOOH·7.7$H_2O$ and β-CD·0.4$CH_3COOH$·7.7$H_2O$

| | | |
|---|---|---|
| Chemical formula | $(C_6H_{10}O_5)_7 \cdot 0.3CH_2O_2 \cdot 7.7H_2O$ | $(C_6H_{10}O_5)_7 \cdot 0.4C_2H_4O_2 \cdot 7.7H_2O$ |
| Formula weight | 1287.51 | 1297.72 |
| Crystal habit, color | Rod, colorless | Rod, colorless |
| Crystal size ($mm^3$) | 0.4×0.6×1.0 | 0.5×0.6×0.9 |
| Crystal system | Monoclinic | Monoclinic |
| Space group | $P2_1$ | $P2_1$ |
| Unit cell dimensions | | |
| $a$ (Å) | 15.171(1) | 15.263(4) |
| $b$ (Å) | 10.169(1) | 10.157(2) |
| $c$ (Å) | 20.986(1) | 21.044(5) |
| $\beta$ (°) | 110.92(1) | 110.67(1) |
| Volume ($Å^3$) | 3024.2(1) | 3051.8(1) |
| $Z$ | 2 | 2 |
| $D_x$ (g $cm^{-3}$) | 1.400 | 1.397 |
| $\mu$ ($mm^{-1}$) | 0.13 | 0.13 |
| $F$(000) | 1348 | 1356 |
| Diffractometer | SMART CCD (Bruker) | |
| Wavelength, MoKα (Å) | 0.71073 | |
| Temperature (°C) | 20 | 20 |
| $\theta$ range for data collection (°) | 1.04 to 30.54 | 1.03 to 30.52 |
| Resolution (Å) | 0.70 | 0.70 |
| Measured reflections | 15883 | 16086 |
| Unique reflections | 10384 | 10886 |
| $R_{int}$ | 0.026 | 0.032 |
| Index ranges | $0 \le h \le 20, -14 \le k \le 12, 0 \le l \le 27$ | $0 \le h \le 19, -14 \le k \le 12, 0 \le l \le 30$ |
| Unique reflections $[F^2 > 2\sigma(F^2)]$ | 8563 | 8358 |
| Structure solution | Molecular replacement (PATSEE) | |
| Refinement method | Full-matrix least-squares on $F^2$ | |
| Weighting scheme | $w = [S^2(F_o^2) + (0.1085P)^2 + 0.0350P]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$ | $w = [S^2(F_o^2) + (0.1000P)^2 + 0.0218P]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$ |
| Data/parameters | 10384/986 | 10886/991 |
| $R$ $[F^2 > 2\sigma(F^2)]$ | $R^a = 0.051$, $wR^b = 0.140$ | $R^a = 0.054$, $wR^b = 0.139$ |
| $R$ (all data) | $R^a = 0.060$, $wR^b = 0.145$ | $R^a = 0.067$, $wR^b = 0.146$ |
| Goodness of fit | 1.006 | 0.995 |
| Highest peak/ Deepest hole (e $Å^{-3}$) | 0.25/–0.19 | 0.30/–0.19 |

[a] $R = \sum||F_o| - |F_c||/\sum|F_o|$.
[b] $wR = \sum\{w(F_o^2 - F_c^2)^2/\sum w(F_o^2)^2\}^{1/2}$.

*Table 2.* Geometrical parameters of β-CD macrocycles in the formic acid and acetic acid inclusion complexes (distances in Å and angles in °)

| Residue | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| $Q^a$, $\theta^b$ | 0.58, 2 | 0.54, 5 | 0.57, 2 | 0.58, 5 | 0.55, 6 | 0.56, 2 | 0.58, 9 |
| | **0.57, 3'** | **0.54, 5** | **0.57, 1** | **0.59, 5** | **0.55, 6** | **0.56, 3** | **0.58, 9** |
| $\phi^c$, $\psi^c$ | 106.6(3) | 102.6(3) | 108.2(3) | 113.2(3) | 117.2(3) | 103.0(3) | 115.8(3) |
| | 135.3(3) | 118.7(3) | 128.3(3) | 129.9(3) | 130.8(3) | 113.9(3) | 140.9(3) |
| | **107.3(3)** | **102.4(3)** | **106.8(3)** | **113.6(3)** | **117.3(3)** | **102.2(3)** | **115.5(3)** |
| | **133.9(3)** | **117.9(3)** | **128.1(3)** | **130.1(3)** | **130.2(3)** | **115.0(3)** | **140.8(3)** |
| Tilt angle [d] | 26.5(2) | 10.9(2) | 5.4(1) | 12.4(2) | 20.2(2) | 4.1(2) | 17.4(2) |
| | **26.3(2)** | **10.6(2)** | **5.6(1)** | **13.3(2)** | **20.3(2)** | **4.0(2)** | **17.7(2)** |
| O4 angle [e] | 127.5(1) | 124.4(1) | 133.8(1) | 128.0(1) | 124.0(1) | 131.6(1) | 129.0(1) |
| | **127.4(1)** | **124.0(1)** | **133.9(1)** | **128.4(1)** | **123.9(1)** | **130.8(1)** | **129.9(1)** |
| *Distance* | | | | | | | |
| O4 deviation [f] | −0.12 | 0.20 | 0.05 | −0.26 | 0.11 | 0.17 | −0.15 |
| | **−0.12** | **0.22** | **0.04** | **−0.28** | **0.14** | **0.17** | **−0.17** |
| O3($n$)···O2($n$ + 1) | 2.88(1) | 2.87(1) | 2.82(1) | 2.78(1) | 2.89(1) | 2.88(1) | 3.00(1) |
| | **2.87(1)** | **2.89(1)** | **2.80(1)** | **2.78(1)** | **2.94(1)** | **2.90(1)** | **2.97(1)** |

| Residue | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| *Torsion angle* | | | | | | | |
| O5–C5–C6–O6 | 58.9(6) [g] | −61.0(3) | −63.0(4) | −70.7(4) | 64.0(4) | −63.9(4) | −67.5(4) [g] |
| | −59.9(6) [g] | | | | | | 77.6(14) [g] |
| | **−60.7(5)** [h] | **−59.2(3)** | **−62.6(4)** | **−72.0(4)** | **62.5(4)** | **−63.4(3)** | **−66.4(5)** [h] |
| | **59.1(7)** [h] | | | | | | **69.5(7)** [h] |

[a] Cremer-Pople puckering amplitude [21].

[b] indicates the deviation from the theoretical chair conformation (ideal value: $\theta = 0$).

[c] Torsion angles $\phi$ and $\psi$ at glycosidic O4, defined as O5($n$)–C1($n$)–O4($n-1$)–C4($n-1$) and C1($n$)–O4($n-1$)–C4($n-1$)–C3($n-1$), respectively.

[d] Tilt angles, defined as the angles between the O4 plane and the planes through C1($n$), C4($n$), O4($n$) and O4($n-1$).

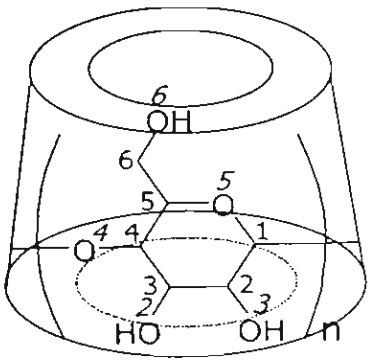
[e] Angle at each glycosidic O4: O4($n+1$)–O4($n$)–O4($n-1$).

[f] Deviation of O4 atoms from the least-squares plane through the seven O4 atoms.

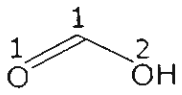
[g] Values for sites A, B of the twofold disordered O61, O67 with the occupancy factors 0.6, 0.4; 0.7, 0.3, respectively (formic acid).

[h] Values for sites A, B of the twofold disordered O61, O67 with the occupancy factors 0.45, 0.55; 0.85, 0.15, respectively (acetic acid).

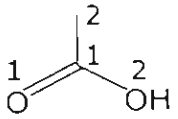
[i] Bold numbers are the values of the acetic acid inclusion complex.




n = 6; α-CD
n = 7; β-CD
n = 8; γ-CD

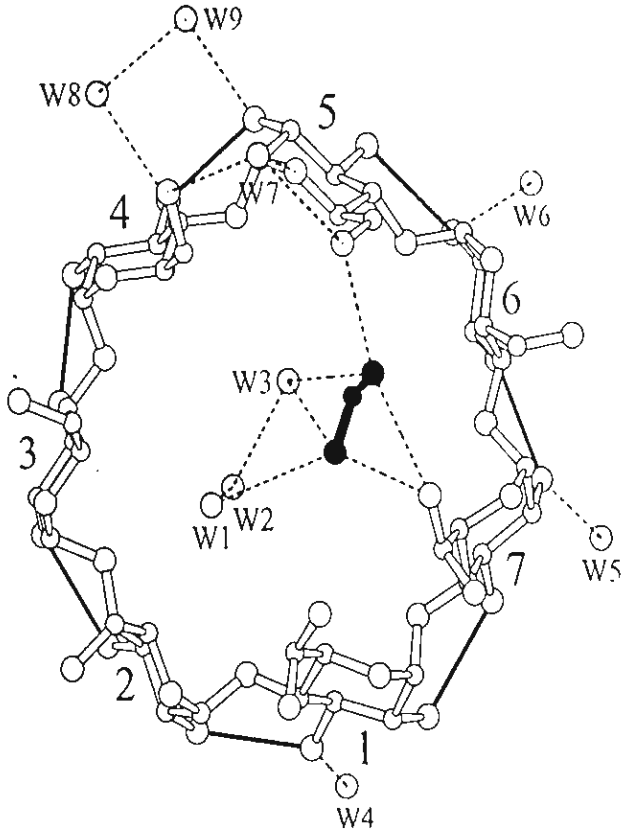



Formic acid




Acetic acid

Fig. 1



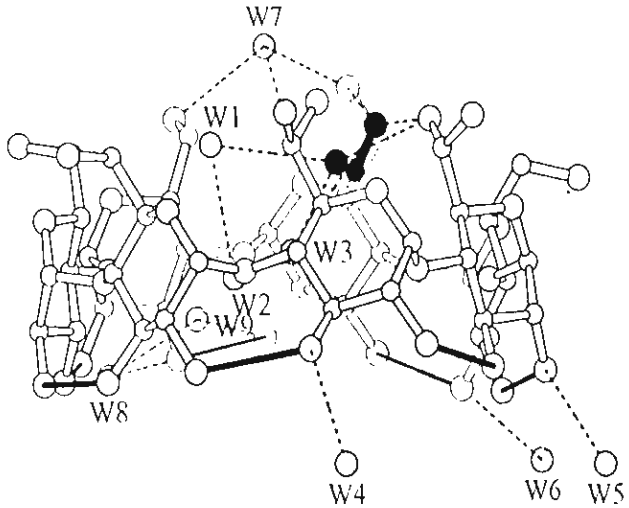




Fig. 2(a)

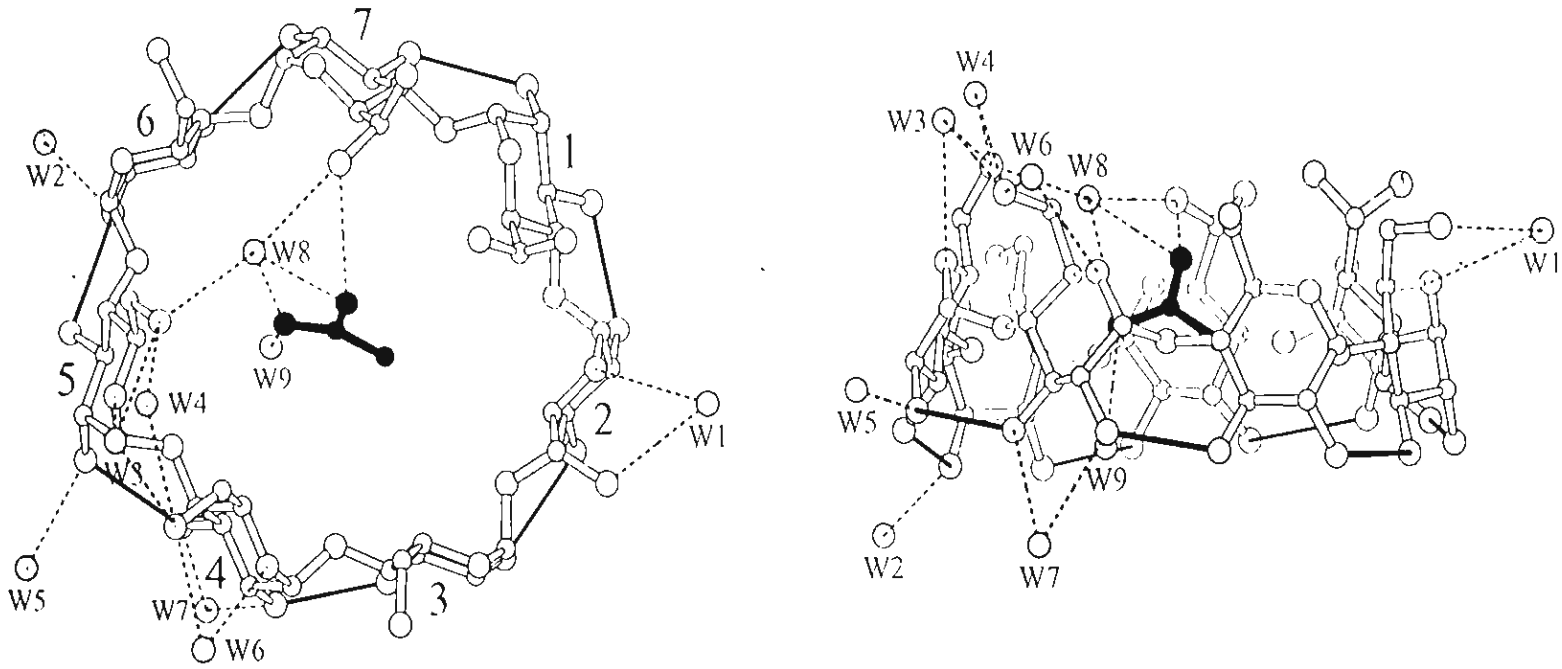



Fig. 2(b)

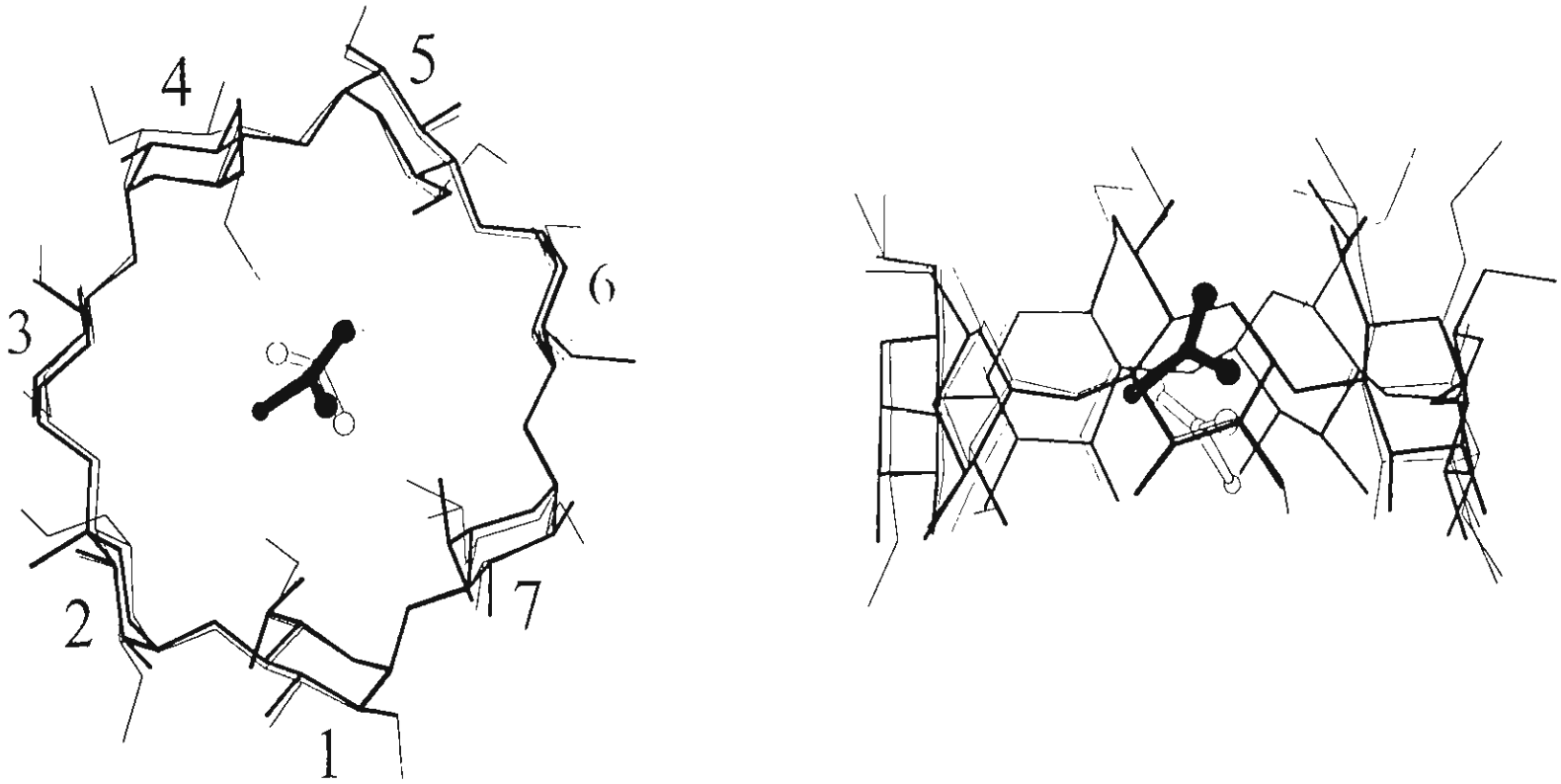



Fig. 3

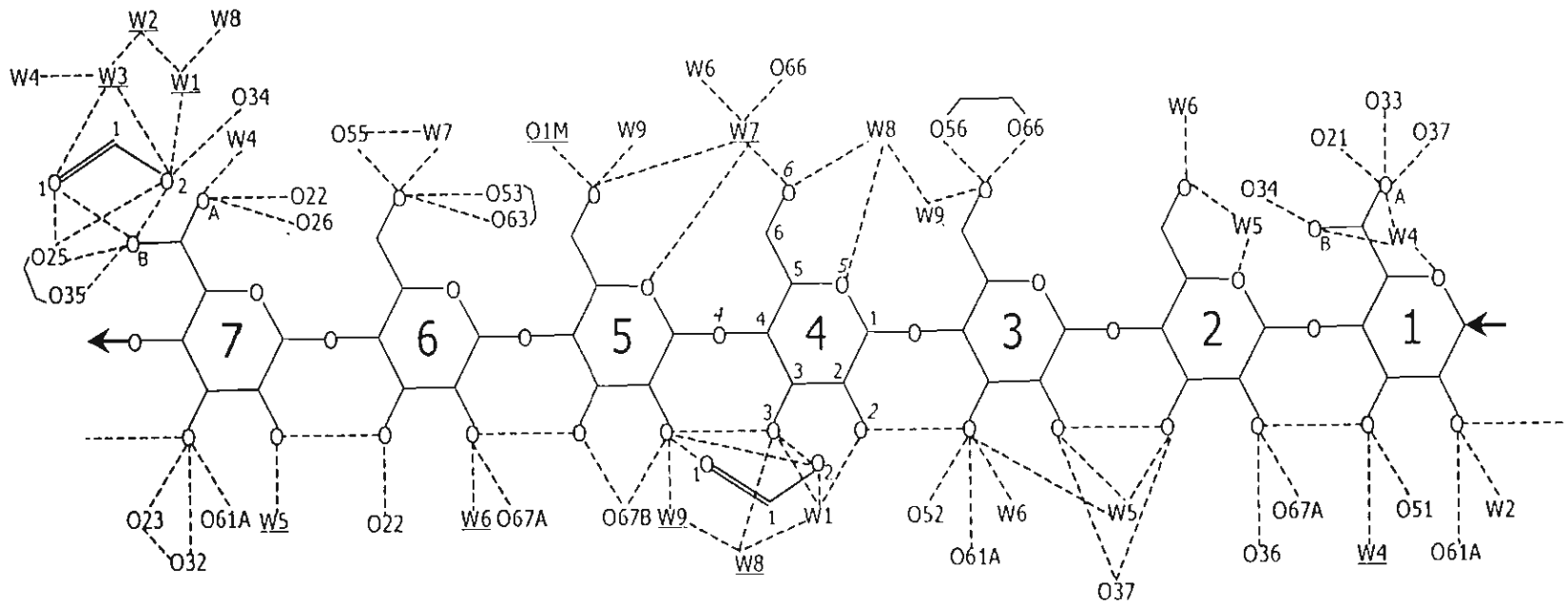

W2
W8
W4
W3
W1
O34
W4
O55
W7
O1M
W9
W6
O66
W7
W8
O56
O66
W6
O33
O21
O37
O22
O26
O53
O63
O25
O35
W9
O34
W5
W4
7
6
5
4
3
2
1
O23
O61A
W5
O32
O22
W6
O67A
O67B
W9
W8
W1
O52
W6
O61A
W5
O37
O67A
O36
O51
W4
W2
O61A

Fig. 4(a)

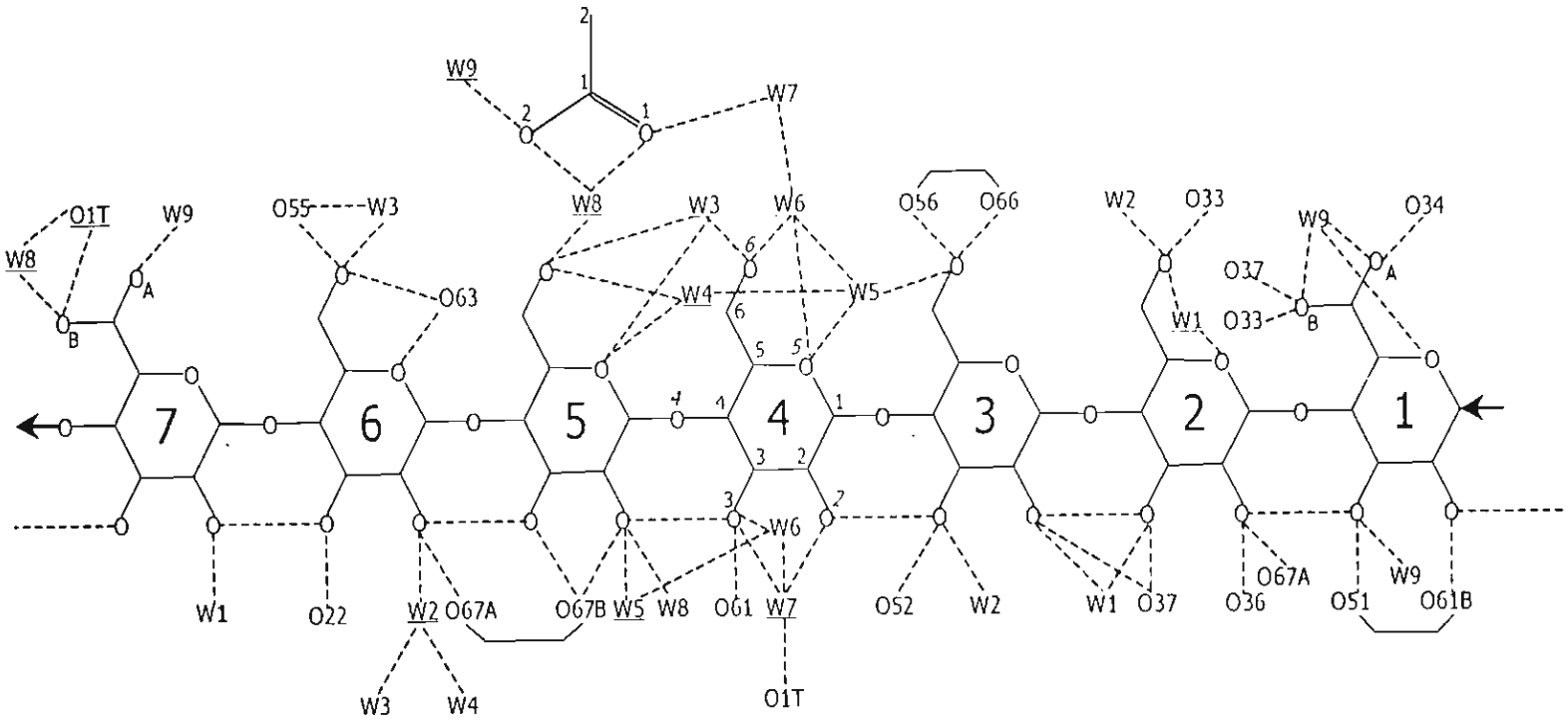

W9
W7
W8
W3
W6
O56
O66
W2
O33
O34
O1T
W9
O55
W3
W8
O63
W4
W5
O37
W1
O33
7
6
5
4
3
2
1
W1
O22
W2
O67A
O67B
W5
W8
O61
W7
O52
W2
W1
O37
O36
O67A
O51
W9
O61B
W3
W4
O1T

Fig. 4(b)