Molecular structures of the inclusion complexes β-cyclodextrin–1,2-bis(4-aminophenyl)ethane and β-cyclodextrin–4,4′-diaminobiphenyl; packing of dimeric β-cyclodextrin inclusion complexes

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The present investigation is part of an ongoing study on the influence of the long end-functonalized guest molecules DBA and BNZ in the crystal packing of β-cyclodextrin (βCD) dimeric complexes. The title compounds are 2:2 host:guest complexes showing limited host–guest hydrogen bonding at the primary faces of the βCD dimers. Within the βCD cavity the guests exhibit mutual $\pi\cdots\pi$ interactions and between βCD dimers perpendicular NH$\cdots\pi$ interactions. The DBA guest molecule exhibits one extended and two bent conformations in the complex. The BNZ guest molecule is not planar inside βCD, in contrast to the structure of BNZ itself, which indicates that the cavity isolates the molecules and forbids the $\pi\cdots\pi$ stacking of the aromatic rings. NMR spectroscopy studies show that in aqueous solution both DBA and BNZ form strong complexes that have 1:1 stoichiometry and structures similar to the solid state ones. The relative packing of the dimers is the same in both complexes. The axes of two adjacent dimers form an angle close to 20° and have a lateral displacement $\simeq$2.45 Å, both of which characterize the screw-channel mode of packing. Although the βCD/BNZ complex indeed crystallizes in a space group characterizing the latter mode, the βCD/DBA complex crystallizes in a space group with novel dimensions not resembling any of the packing modes reported so far. The new lattice is attributed to the three conformations exhibited by the guest in the crystals. However, this lattice can be transformed into another, which is isostructural to that of the βCD/BNZ inclusion complex, if the conformation of the guest is not taken into account.

1. Introduction

The common cyclodextrins (CDs), obtained by enzymatic degradation of starch, are macrocycles composed of six, seven and eight α-1,4-linked-D-glucopyranose residues (α-, β- and γCD, respectively),

(I)
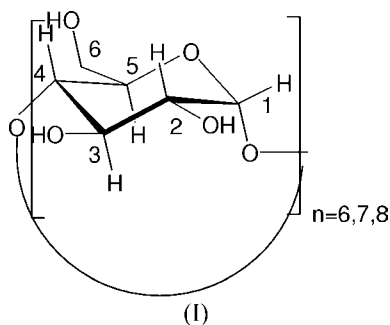
thus having the shape of truncated hollow cones (Szejtli, 1998). CDs are water soluble, since they are lined by a large number of hydroxy groups, three per glucose residue: one

primary, occupying the narrow end of the truncated cone, and two secondary, occupying its wider side. Along with their synthetic derivatives, CDs are used for micro encapsulation of organic molecules inside their relatively apolar cavity by forming inclusion compounds both in aqueous solutions and in the crystalline state (Harata, 1998). This property has been used extensively to solubilize and/or stabilize apolar/unstable molecules, especially drugs (Uekama *et al.*, 1998). One-dimensional and two-dimensional NMR studies of CD inclusion complexes in aqueous solutions give invaluable information on the kinds of species present, as well as of their molecular structures, stoichiometry and formation constants. Although very frequently the complexes exist in more than one molecular structure in solution (Eliadou *et al.*, 1999), the most stable form crystallizes. The factors contributing to the stabilization of CD host–guest complexes are van der Waals interactions and hydrogen bonding, depending on the nature of the guest molecules (Saenger, 1980). Therefore, it is very interesting to study and, if possible, to predict the molecular structure of the complexes and subsequently the molecular arrangement in the crystal.

βCD is the most common of the natural CDs and its inclusion complexes are abundant. The majority of them crystallize as dimers formed by self-association of two βCD monomers (Mavridis *et al.*, 1991) that enclose one, two and sometimes more molecules. The βCD dimer is a very symmetrical entity that has the shape of a cylinder or rather a barrel with an elongated hydrophobic cavity. As has been shown by a detailed analysis of the hydrogen bonding in the βCD dimer (Makedonopoulou & Mavridis, 2000), the secondary hydroxy groups are involved in hydrogen bonding intramolecularly within the βCD monomers, as well as intermolecularly between monomers in order to form the dimer (only the secondary hydroxyls O3H), and with numerous water molecules at the exterior of the βCD barrel, thus they do not form hydrogen bonds with guest molecules in the interior of the cavity. The intra-dimer ring of the secondary hydroxyls, where the two monomers meet, is hydrophobic and βCD dimers can host lipophilic guests that span the entire length of their cavity.

In the crystalline state there have been some attempts to analyze systematically available crystallographic data of αCD (Saenger, 1985) and βCD complexes (Mentzafos *et al.*, 1991). In βCDs the secondary hydroxyls are not influenced by the guest and form an invariant network of hydrogen bonds with neighboring dimers and water molecules in the outside (Le Bas & Tsoucaris, 1994). On the other hand, although the primary hydroxy groups at the top and bottom of the barrel form a number of hydrogen bonds with adjacent barrels commonly observed in various complexes, their mutual interactions are also influenced by the presence of the guest in that region. In the dimeric βCD complexes a semi-invariant network of hydrogen bonds is formed that connects each dimer to other dimers either directly or through water molecules co-crystallized around them. The result is the formation of infinite two-dimensional layers (Mentzafos *et al.*, 1991; Le Bas & Tsoucaris, 1994) of C-centered or pseudo C-centered

geometry, depending on the space group, with two orthogonal axes of dimensions close to 19 and 24 Å. Therefore, we can claim that the βCD dimer is an entity maintaining its integrity irrespective of the nature of the guest that forms practically invariant C-centered two-dimensional layers. The guest emerging from the primary faces plays a crucial role in the association of these two-dimensional layers to form the crystal. The layers have the primary faces of the βCD dimers, and consequently the parts of guests located there, exposed to the solvent. It is thus obvious that they associate through primary hydroxy groups, water and/or the guest molecule(s) to form the three-dimensional lattice. Limited packing patterns of dimeric βCD complexes have been observed, classified as

(i) channel (CH),
(ii) screw-channel (SC),
(iii) chessboard (CB) and
(iv) intermediate (IM) (Mentzafos *et al.*, 1991).

Complexes belonging to the same mode are isostructural, an important regularity that allows the determination of their crystal packing just by knowledge of their unit cell.

The present investigation is one in a series of articles involving systematic studies of the structure of cyclodextrin complexes with long end-functonalized guest molecules, *i.e.* amino acids (Eliadou *et al.*, 1999), dicarboxylic acids (Makedonopoulou *et al.*, 1999; Makedonopoulou & Mavridis, 2000) and diamines (Rontoyianni & Mavridis, 1999; Giastas *et al.*, 2003). The guests under study presently are 1,2-bis(4-aminophenyl)ethane (DBA) and 4,4′-diaminobiphenyl (BNZ).
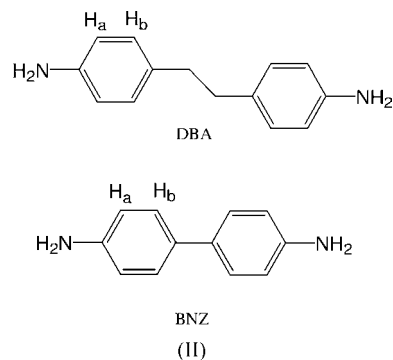
The guest's end-groups induce the same packing on the two-dimensional C-centered layers of the βCD dimers, but the compounds crystallize in different space groups. This behavior is due to the guest molecule of one complex being trapped in different conformations in two adjacent layers. This fact results in a space group and cell dimensions that are observed for the first time in dimeric βCD complexes [although it seems that an isostructural complex, βCD/diacetamate (Dodds, 1999) exists]. However, it is shown that the packing modes of the two complexes are equivalent.

2. Experimental

2.1. Materials

βCD was a product of Fluka. 1,2-Bis(4-aminophenyl)ethane (Aldrich) was purified using a short silica gel column and

Table 1
Experimental details.

	DBA	BNZ
Crystal data		
Chemical formula	$C_{112}H_{127.17}N_4O_{88.08}$	$C_{108}H_{112}N_4O_{94.72}$
M_r	2938.71	2981.62
Cell setting, space group	Monoclinic, $C2$	Monoclinic, $P2_1$
a, b, c (Å)	19.319 (2), 24.19 (6), 33.315 (7)	15.394 (7), 31.995 (12), 15.621 (7)
β (°)	103.924 (14)	103.738 (15)
V (Å^3)	15111 (5)	7473 (5)
Z	4	2
D_x (Mg m^{-3})	1.292	1.325
Radiation type	Cu $K\alpha$	Cu $K\alpha$
No. of reflections for cell parameters	20	30
θ range (°)	9.7–17.2	10.0–20.3
μ (mm^{-1})	1.00	1.05
Temperature (K)	293 (2)	293 (2)
Crystal form, color	Prismatic, colorless	Prism, colourless
Crystal size (mm)	$0.6 \times 0.4 \times 0.3$	$0.4 \times 0.4 \times 0.4$
Data collection		
Diffractometer	SYNTEX P21	SYNTEX P21
Data collection method	$\theta/2\theta$	$\theta/2\theta$
Absorption correction	None	None
No. of measured, independent and observed parameters	10 112, 10 105, 6985	9299, 9160, 6482
Criterion for observed reflections	$I > 2\sigma(I)$	$I > 2\sigma(I)$
R_{int}	0.041	0.038
θ_{max} (°)	55.1	55.0
Range of h, k, l	$0 \Rightarrow h \Rightarrow 20$	$0 \Rightarrow h \Rightarrow 15$
	$0 \Rightarrow k \Rightarrow 25$	$0 \Rightarrow k \Rightarrow 32$
	$-35 \Rightarrow l \Rightarrow 35$	$-16 \Rightarrow l \Rightarrow 16$
No. and frequency of standard reflections	3 every 97 reflections	3 every 97 reflections
Refinement		
Refinement on	F^2	F^2
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.083, 0.257, 1.06	0.087, 0.259, 1.02
No. of relections	10 105 reflections	9160 reflections
No. of parameters	1383	1111
H-atom treatment	Mixture of independent and constrained refinement	Mixture of independent and constrained refinement
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.1564P)^2 + 26.9454P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.1439P)^2 + 15.5108P]$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	0.188	0.016
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.52, -0.44	0.41, -0.33
Absolute structure	Flack (1983)	Flack (1983)
Flack parameter	0.9 (4)	0.5 (4)

Computer programs: *Crystal logic* (Strouse, 2002); *DIRDIF*94 (Beurskens *et al.*, 1994; Hamilton & Chen (1988*a*); *SHELXL*97 (Sheldrick, 1997); Jones & Kjeldgaad (1993); *Molscript* (Kraulis, 1991); *ORTEP*II (Johnson, 1976).

chloroform as eluent. 4,4′-Diaminobiphenyl (Panreac) was used without further treatment. Deuterated solvents were purchased from Aldrich.

2.2. Measurements of binding constants by NMR in aqueous solution

NMR spectra were recorded on an Avance DRX 500 MHz spectrometer using standard pulse programs. Two-dimensional ROESY spectra were acquired with presaturation of the residual water signal using the TPPI method, and mixing (spin-lock) time 350 ms at a field of $\simeq 2$ kHz. In all spectra the internal water peak at 300 K was the reference frequency. Titration (mole-ratio method) of a 1.9 m*M* solution of βCD in D$_2$O with DBA, and of a 2.7 m*M* solution of βCD in D$_2$O with BNZ, resulted in measurable chemical shift displacements of the βCD cavity protons H3 or H5 at each concentration of added guest. Fitting of the data to the equation that describes 1:1 host–guest association in fast exchange (Eliadou *et al.*, 1999), using the *GraphPad Prism* software, provided the values of the binding constants for the two host–guest systems. In the βCD/DBA complex there were considerable solubility problems; therefore, good curve fitting was obtained only with a reduced actual concentration of the added guest. The corresponding K value obtained is, therefore, only indicative.

2.3. Crystallization of βCD/1,2-bis(4-aminophenyl)ethane (DBA) inclusion complex

The complex was prepared by adding 1,2-bis(4-aminophenyl)ethane (0.0126 mmol) to an aqueous solution of βCD (0.0126 mmol). The precipitant was redissolved in water at 343 K and the solution was allowed to return to room temperature over a period of 6 d, at the end of which prismatic colorless crystals were formed.

2.4. Crystallization of βCD/4,4′-diaminobiphenyl (BNZ) inclusion complex

The crystals were prepared by adding 0.0641 mmol of 4,4′-diamino-biphenyl and 0.0618 mmol of βCD to 1.6 ml of water, where the guest existed as a suspension along with undissolved βCD. Upon storing the reaction mixture in a closed vessel for 5 d at 355 K colorless crystals were formed.

2.5. X-ray crystallography

The chosen single crystals of both inclusion complexes were sealed into glass capillaries with mother liquor. Diffraction data were collected on a SYNTEX diffractometer equipped with a Rigaku rotating anode and a graphite monochromator. The data were corrected for Lorentz and polarization effects.

X-ray data and refinement details are summarized in Table 1.[1] Least-squares refinement on F^2 was carried out using the program SHELXL97 (Sheldrick, 1997).

2.5.1. βCD/DBA inclusion complex. The structure was solved by the molecular replacement method (Beurskens et al., 1994) using the βCD skeleton coordinates in the complex βCD/Z-7-tetradecenal (Yannakopoulou et al., 2002). The remaining host atoms, as well as the guest and co-crystallized water molecules, were found in subsequent difference-Fourier maps. The structure was refined by full-matrix least-squares refinement based on F^2 (Table 1). Anisotropic refinement was applied only to non-disordered O atoms, the C6 atoms of the βCD host and most water O atoms. During the refinement four hydroxy O atoms of the primary side (two on each host monomer) were found to be disordered. H atoms added at calculated positions to the C and O atoms, except for the disordered ones, were assigned $U_{eq} = 1.3U'_{eq}$ of the corresponding atom to which they are bonded and were refined by the riding model.

2.5.2. βCD/BNZ inclusion complex. The structure was solved with the isomorphous replacement method using the skeleton coordinates of a βCD molecule of the complex βCD/(R)-(−)-fenoprofen clathrate hydrate (Hamilton et al., 1988a). The remaining atoms as well as the guest and the co-crystallized water molecules were found in subsequent difference-Fourier maps. During refinement five primary hydroxy O atoms were found to be disordered (three on monomer A and two on monomer B). The structure was refined anisotropically for all the non-H atoms by full-matrix least-squares refinement based on F^2 (Table 1). By the end of the refinement some H atoms were located by difference-Fourier maps and the remainder were added at calculated positions to the C and O atoms, except for the disordered ones. H atoms were assigned $U_{eq} = 1.3U'_{eq}$ of the corresponding atom to which they are bonded and were refined by the riding model.

3. Results and discussion

3.1. βCD/1,2-bis(4-aminophenyl)ethane (DBA) inclusion complex

3.1.1. Stoichiometry, binding and structure in aqueous solution. DBA readily complexes with βCD in aqueous solution, as indicated by the observation of large chemical shifts of the cavity protons in the ^{1}H NMR spectra and the detection of intermolecular interactions in the ROESY spectrum (Giastas et al., 2003). The stoichiometry of the crystalline complex was found to be 1:1 (dissolution in DMSO and integration of the host–guest signals in the ^{1}H NMR spectra). The same result was obtained using the mole-ratio (titration) method for the complex formed in solution. The aqueous solubility of the adduct formed was limited and the titration ended before reaching the 1:1 ratio; however, it is obvious from the data points obtained (Fig. 1) that the chemical shift changes

increase past the 0.5 mole-ratio value and curve down as the ratio approaches 1:1. Fitting of the data to the equation for 1:1 stoichiometry based on fast exchange of the host between free and complexed states in the NMR timescale, as described previously (Botsi et al., 1995; Eliadou et al., 1999), affords an estimated binding constant of 2700 (500) M^{-1} (R^2 = 0.9744). The two-dimensional ROESY spectra of βCD/DBA have
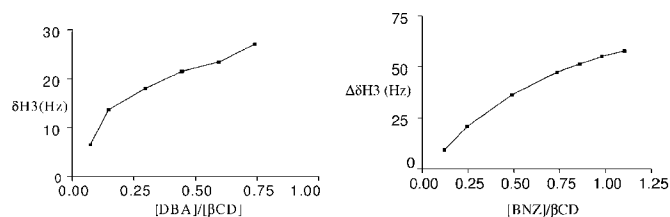

Figure 1
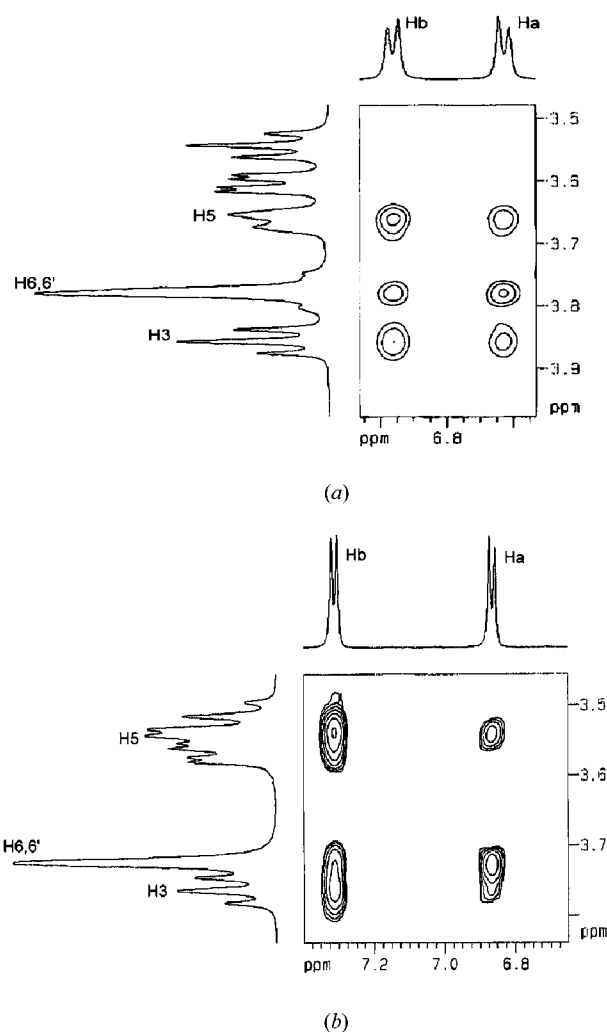Mole-ratio plots versus chemical shift changes of the cavity proton H3 (300 K, D$_2$O).

(a)

(b)

Figure 2
Two-dimensional ROESY spectra in D$_2$O of (a) βCD/DBA, 298 K; (b) βCD/BNZ, 300 K.

shown strong interactions of the $-CH_2-CH_2-$ group of DBA with all cavity protons, indicating

(i) threading of DBA inside the cavity, and

(ii) possible *bending* of the ethylene part (Giastas *et al.*, 2003).

Fig. 2(*a*) shows slightly weaker interactions of *Ha* with the cavity protons H3 and H5 and stronger interactions with H6,6′ than the corresponding interactions of *Hb*, indicating that the *Ha* H atoms are located at the rims of the βCD cup. This information, combined with the 1:1 stoichiometry, suggests a structure in solution in which the guest in its entire length hides inside the host and, despite the flexibility of the ethylene part, forms a strong complex.

3.1.2. Structure in the crystalline state. X-ray analysis of the crystalline complex provided the supramolecular structure of the adduct. The βCD host, forming head-to-head dimers, encloses two guest molecules. There are two independent monomeric hosts (*A* and *B*) in the asymmetric unit. Two crystallographically independent βCD dimers arise by the twofold crystallographic axis. The numbering scheme for the βCD molecules is given in Fig. 3(*a*) (Johnson, 1976). C(*A* or *B*)*mn* and O(*A* or *B*)*mn* denote the *m*th atom within the *n*th glucosidic residue (G*n*) of the crystallographically independent βCD molecules *A* and *B*. Moreover, depending on the conformation of the guest molecules (guest **a**, **b** and **c**, Fig. 3*b*), three types of complexes are observed in the crystal structure. The following explain the reason for such a variation: The present structure belongs to the *C*2 space group, but unlike the other βCD dimeric complexes crystallizing in the same space
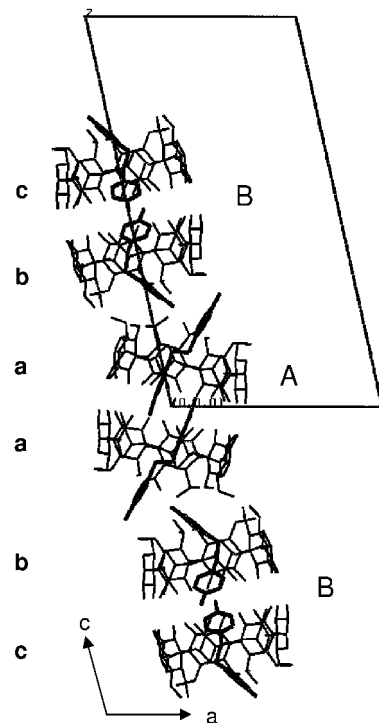
Figure 3
Conformation and numbering scheme of the βCD/DBA complex: (*a*) βCD; (*b*) the three conformations of DBA observed.

Figure 4
Packing of the βCD/DBA complex.

Table 2
Cell dimensions of the packing modes of dimeric βCD complexes.

Packing mode	Space group	a (Å)	b (Å)	c (Å)	α (°)	β (°)	γ (°)	V/βCD (Å^3)
CH	$P1$	15.5	15.6	15.7	100.0	101.0	103.7	1756
CH	$C2$	19.2	24.6	15.8		109.5		1760
IM	$P1$	18.0	15.4	15.5	103.1	117.1	104.3	1860
CB	$C222_1$	19.2	24.4	32.7				1910
SC	$P2_1$	15.3	32.5	15.4		102.1		1870
βCD/DBA (SC)	$C2$ ($P2_1$)	19.319	24.190	33.315		103.92		1889

Table 3
Conformations of the macrocycles.

$D = $ O4$n\cdots$O4$(n + 1)$ distances; $\varphi = $ O4$(n - 1)\cdots$O4$\cdots$O4$(n + 1)$ angles; $d = $ deviations (Å) from the least-squares optimum plane of the seven O4n atoms; $\alpha = $ tilt angles between the optimum O4n plane and the mean planes through atoms O4$(n - 1)$, C1n, C4n, O4n (with s.u. values in parentheses). $D_3 = $ intramolecular hydrogen-bond distances between atoms O2$n\cdots$O3$(n - 1)$.

(*a*) β-CD/DBA inclusion complex.

Residue	D (Å)	φ (°)	d (Å)	α (°)	D_3 (Å)	Torsion angle (°) O5n−C5n−C6n−O6n
Molecule *A*						
G1	4.38 (5)	130.3 (1)	0.008 (7)	5.5 (3)	2.72 (2)	−67 (1)
						77 (1)
G2	4.30 (0)	124.2 (9)	0.000 (8)	10.0 (4)	2.79 (9)	−66 (1)
G3	4.45 (2)	130.8 (4)	−0.012 (9)	10.4 (2)	2.84 (0)	−68 (1)
G4	4.34 (0)	129.9 (2)	0.000 (4)	7.9 (0)	2.87 (4)	−67 (1)
						47 (3)
G5	4.36 (7)	127.0 (1)	0.024 (6)	12.7 (5)	2.80 (5)	−64 (1)
G6	4.31 (7)	128.0 (2)	−0.028 (8)	10.2 (6)	2.80 (2)	−67 (1)
G7	4.45 (6)	129.6 (1)	0.007 (4)	10.2 (4)	2.79 (4)	−64 (1)
Molecule *B*						
G1	4.37 (1)	128.1 (1)	0.026 (7)	9.9 (1)	2.75 (5)	−63 (1)
G2	4.44 (6)	130.1 (9)	0.022 (8)	8.7 (7)	2.85 (3)	66 (1)
G3	4.34 (6)	128.2 (4)	0.003 (4)	10.2 (9)	2.77 (2)	−62 (1)
						67 (1)
G4	4.34 (4)	126.9 (3)	0.008 (4)	6.8 (0)	2.84 (1)	−72 (1)
G5	4.42 (4)	129.5 (5)	−0.004 (0)	3.8 (9)	2.80 (9)	−64 (1)
G6	4.36 (5)	129.9 (5)	0.000 (5)	8.4 (2)	2.84 (5)	−67 (1)
G7	4.34 (7)	127.0 (1)	−0.012 (1)	5.9 (8)	2.74 (9)	−62 (1)
						48 (1)

(*b*) βCD/BNZ inclusion complex.

Residue	D (Å)	φ (°)	d (Å)	α (°)	D_3 (Å)	Torsion angle (°) O5n−C5n−C6n−O6n
Molecule *A*						
G1	4.34 (4)	127.4 (0)	−0.006 (7)	7.4 (3)	2.85 (1)	−70 (1)
G2	4.47 (3)	130.6 (6)	0.019 (8)	8.7 (6)	2.79 (7)	−66 (1)
						56 (6)
G3	4.26 (7)	128.2 (4)	0.002 (7)	12.2 (7)	2.77 (3)	−61 (1)
G4	4.38 (8)	127.2 (0)	−0.015 (8)	5.2 (3)	2.78 (8)	−63 (1)
						67 (3)
G5	4.39 (8)	129.0 (8)	−0.009 (7)	5.2 (9)	2.76 (9)	−61 (1)
G6	4.37 (9)	129.7 (7)	0.040 (0)	11.6 (1)	2.83 (4)	65 (1)
G7	4.32 (6)	127.6 (1)	−0.030 (4)	8.8 (0)	2.76 (9)	−66 (1)
						69 (2)
Molecule *B*						
G1	4.40 (0)	126.8 (4)	0.015 (6)	8.9 (6)	2.80 (4)	−55 (1)
						51 (4)
G2	4.31 (1)	128.9 (3)	0.042 (9)	10.1 (7)	2.84 (1)	−62 (1)
						56 (3)
G3	4.47 (2)	129.5 (4)	−0.065 (3)	5.5 (8)	2.79 (0)	−66 (1)
G4	4.30 (2)	128.9 (8)	0.017 (7)	11.6 (7)	2.75 (3)	69 (1)
G5	4.37 (6)	125.5 (5)	0.031 (3)	9.6 (1)	2.82 (3)	−68 (1)
G6	4.43 (1)	131.1 (1)	−0.017 (9)	7.8 (7)	2.81 (9)	−69 (1)
G7	4.30 (6)	128.9 (6)	−0.024 (4)	13.2 (3)	2.83 (7)	−63 (1)

group (Table 2) it exhibits a **c** crystallographic axis of double length ($\simeq$33 Å). This is because, unlike all βCD dimeric complexes reported so far, there are two types of βCD C-centered layers of dimers (corresponding to monomers *A* and *B*) packed on top of each other. These layers of dimers differ in the guest conformation (Fig. 4). In the middle layer the guest is found in an extended conformation (guest **a**), whereas in the top and bottom the guest is in a puckered conformation, disordered over two positions (guest **b** and **c**). The sevenfold axis of dimer *A* forms an angle of 23° with the **c** axis (Fig. 4, Jones & Kjeldgaad, 1993), whereas the axis of dimer *B* forms an angle of 3°. The relative angle between dimers *A* and *B* is 20° and their lateral displacement $\simeq$2.45 Å. As a result of the described stacking, the βCD dimers do not pack in the channel mode (CH) as in the corresponding complexes of space group $C2$, their packing resembling rather the screw-channel mode (SC).

3.2. Geometry of the host molecules

The host molecules possess near sevenfold symmetry, the pyranose rings having the $^4C_1$ conformation: As shown in Table 3(*a*), the values of the angles between the glucosidic O atoms O4n do not differ significantly from 128.5°, the angle of the regular heptagon, while the glucose units tilt slightly towards the sevenfold axis. The deviations (*d*) of the O4n atoms from their optimum plane are close to zero. The conformation of each βCD macrocycle is stabilized through intramolecular hydrogen bonds connecting the O3n and O2$(n + 1)$ atoms of neighboring glucosidic units [average O3$n\cdots$O2$(n + 1)$ distances 2.80 (5) Å]. Their angles, C3n−O3$n\cdots$O2$(n + 1)$ [average 116.4 (2)°] and O3$n\cdots$O2$(n + 1)$−C2$(n + 1)$ [average 117.3 (3)°], lie within the normal values for hydrogen bonds. The βCD dimer is formed *via* OA3$n\cdots$OA'3$(8 - n)$ hydrogen bonds (Makedonopoulou & Mavridis, 2000) with an average distance of

Table 4
Hydrogen bonds of the guests' amine groups (bold indicates hydroxy groups pointing inwards).

| Molecule a	Distance (Å)	C—N···O (°)	N···O—C (°)
(a) βCD/DBA inclusion complex			
N1A···O66B2	2.4 (1)	133 (2)	
N1A···O65B	2.79 (3)	141 (1)	
N1A···O66B4	3.2 (1)	140 (1)	
N1C···O**B**67b	3.24 (4)	115 (1)	122 (1)
(b) βCD/BNZ inclusion complex			
N1A···O**B**64	3.23 (3)	112 (1)	107 (1)
N1B···O63A3	2.6 (1)	146 (3)	
N1B···O**B**62b	3.15 (7)	83 (2)	126 (4)

2.82 (6) and 2.84 (9) Å for host monomers A and B, respectively. The angles $CA3n-OA3n\cdots OB3(8-n)$ and $OA3n\cdots OB3(8-n)-CB3(8-n)$ have mean values of 118.5 (6) and 118.4 (3)°, respectively.

The primary hydroxy groups show a variety of conformations (Table 3a): residue G2 of monomer B exhibits (+)-*gauche* conformation and points inwards. Monomer A has two disordered hydroxy groups, one in residue G1 with a major (−)-*gauche* conformation (83%) and a minor (+)-*gauche* pointing inwards, another in residue G4, where the conformation pointing inwards is the major one (57%). Monomer B also has two disordered hydroxy groups on residues G3 and G7, their major conformations (57 and 69% respectively) pointing outwards. The remaining hydroxy groups have the (−)-*gauche* conformation and point outwards. Inward pointing hydroxyls form hydrogen bonds mainly with adjacent dimers, thus stabilizing the lattice (*see below*).

3.2.1. Guest geometry and interactions with its environment. Two guest molecules are enclosed within each βCD dimer, but as mentioned above, there are two types of dimers, aligned in layers, differing in the guests' conformations (Fig. 4): guest a in the middle layer, and the disordered guest, b and c, above and below. One of guest c's N atoms resides on the twofold axis; therefore, it can exist only in one monomer of the dimer. Thus, in this dimeric layer the two βCD monomers have the guests in different conformations b and c. One phenyl ring of guest b is related by the twofold axis to a phenyl ring of c, whereas the others are different. The dihedral angles between the phenyl rings are 12 (1), 56.0 (9) and 57 (1)° for guests a, b and c, respectively. Guest a's phenyl rings form angles of 75.4 (7) and 66.7 (5)° with the planes of the glucosidic O4 atoms of the dimer. The corresponding angles for guest b are 47.7 (4) and 36.8 (7)° and for guest c 47.7 (4) and 38.2 (8)°. The *trans* conformation of guest a compares well with the determined conformations of 1,2-diarylethanes that compose the skeleton of the present guest molecule (Ross & Wardell, 1994; Kahr *et al.*, 1995): The planar phenyl rings occupy almost parallel planes that are approximately at right angles to the connecting aliphatic moiety. The value of the central CH_2-CH_2 bond is 1.56 Å and the mean value of the $C(Ar)-(CH_2)$ bonds is 1.50 Å. The puckered conformation observed in the complex is a less stable *gauche* conformation.

The corresponding lengths for the central and flanking bonds are 1.61 and 1.47 Å, respectively. The central bond lengths are probably overestimated because no H atoms were included in the refinement (Kahr *et al.*, 1995), more so in the case of the bent guest which is disordered.

Within the βCD dimer cavities the guest molecules exhibit $\pi\cdots\pi$ interactions (Fig. 4), which are weaker (mean distance 3.69 Å) for guest a than for guests b and c (mean distance 3.53 Å). Between βCD dimers the guests approach each other almost vertically. The number of interactions of the guests with their environment is rather limited: The close contacts of the guests' amino groups are shown in Table 4(a). The amino nitrogen N1A of guest a (emerging from the primary side and pointing towards the solvent) forms one strong and two weak hydrogen bonds with water molecules, whereas the corresponding N atom of guest c interacts weakly with primary hydroxy groups, two of them pointing inwards (Fig. 5; Kraulis, 1991). Finally, the amino group of guest b, emerging from the other primary side of βCD dimer B, points towards the cavity of adjacent dimer A almost vertically to guest a's phenyl ring (smallest distance N1B···C5A = 2.96 Å). Thus, along the

(a)

(b)
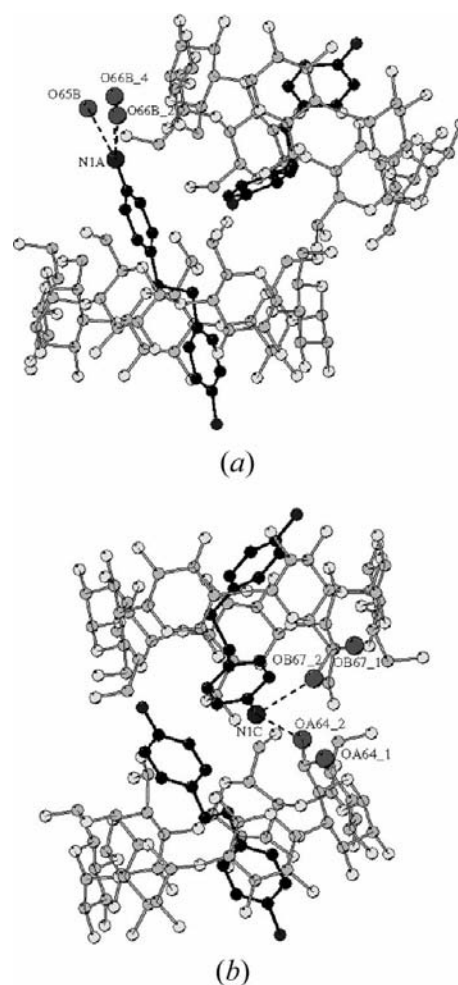
Figure 5
Details of the interdimer region between dimers A and B of CD/DBA. (a) The interaction involving the amino N1A atom of guest a, and (b) the interaction involving the corresponding N atom of guest c.

Table 5
Direct hydrogen bonds of primary hydroxy groups between βCD dimers (bold indicates hydroxy groups pointing inwards).

$Omn\cdots Om'n'$	Distance (Å) $Omn\cdots Om'n'$	Angle (°) $Cmn-Omn\cdots Om'n'$	Angle (°) $Omn\cdots Om'n'-Cm'n'$
(a) βCD/DBA inclusion complex			
$OA25\cdots OA27^{i}$	2.75 (1)	112.4 (6)	106.5 (6)
$OA67\cdots OA63^{ii}$	2.80 (1)	106.9 (7)	123.1 (7)
$OA65\cdots \mathbf{OA61b}^{iii}$	3.17 (3)	115 (1)	142 (1)
$OB25\cdots OB27^{iv}$	2.76 (1)	109.8 (7)	107.9 (6)
$OB67a\cdots OB63a^{v}$	3.0 (1)	113 (1)	131 (1)
$OB65\cdots OB61^{ii}$	2.86 (1)	109.1 (8)	130.6 (7)
$OA62\cdots \mathbf{OB63b}^{iii}$	2.61(2)	111 (1)	146 (1)
$OA62\cdots \mathbf{OB62}^{i}$	2.68(1)	130(1)	102.3(7)
(b) βCD/BNZ inclusion complex			
$\mathbf{OA66}\cdots OB65^{vi}$	2.66 (1)	100.6 (9)	125 (1)
$\mathbf{OA67b}\cdots OB65^{vi}$	2.47 (4)	147 (2)	107 (1)
$OA65\cdots OA62a^{vii}$	2.86 (1)	131.4 (8)	108.7 (8)
$OB63\cdots OB66^{vii}$	2.77 (1)	107.5 (8)	124.9 (9)
$OB23\cdots OA22^{vii}$	2.76 (1)	109.1 (6)	112.2 (7)
$OA24\cdots OB21^{viii}$	2.80 (1)	104.5 (6)	112.8 (7)
$OA64a\cdots OA67a^{viii}$	2.92 (2)	111.5 (9)	129 (1)

(i) $\frac{3}{2}-x, -\frac{1}{2}+y, 2-z$; (ii) $-\frac{1}{2}+x, \frac{1}{2}+y, z$; (iii) x, y, z; (iv) $\frac{3}{2}-x, \frac{1}{2}+y, 1-z$; (v) $-\frac{1}{2}+x, -\frac{1}{2}+y, z$; (vi) $-x, \frac{1}{2}+y, -z$; (vii) $-1+x, y, z$; (viii) $x, y, 1+z$.

channel the guests exhibit alternate parallel $\pi\cdots\pi$ and vertical NH$\cdots\pi$ interactions (Fig. 4).

3.3. Hydrogen-bonding network and solvent molecules

There are eight direct hydrogen bonds among hydroxy groups of adjacent host dimers (Table 5a), of which two bind dimers A and B along the c axis and six bind hydroxy groups in the two-dimensional layers, three along the $\mathbf{a}+\mathbf{b}$ direction ($OA25\cdots OA27$, $OA67\cdots OA63$ and $OA65\cdots OA61b$) and three along the $\mathbf{a}-\mathbf{b}$ direction ($OB25\cdots OB27$, $OB67a\cdots OB63a$ and $OB65\cdots OB61$). Four of the above bonds, $OA25\cdots OA27$, $OA67\cdots OA63$, $OB25\cdots OB27$ and $OB67a\cdots OB63a$, are observed in all dimeric CD complexes irrespective of the crystal packing.

There are 18.08 (6) water molecules in the asymmetric unit distributed over 53 sites around the βCD dimers and 45 of them are within hydrogen-bonding distance of O atoms of the hydroxy groups, as shown in Table 6. The water sites have been labeled from the number of the closest O atom to which they are hydrogen bonded. Hydrogen-bonding distances up to 3.25 Å and angles C—O(H)$\cdots$O(water) up to 145° are assumed in order to compare with other published structures with related guest molecules. The angle range, although quite wide, is justifiable because of the usual disorder accompanying water molecules and the inability to locate their H atoms. Water molecules at eight positions interact only among themselves.

3.4. βCD/4,4'-diaminobiphenyl (BNZ) inclusion complex

3.4.1. Stoichiometry, binding and structure in aqueous solution. In a way analogous to DBA, benzidine (BNZ) enters inside the βCD host and forms a water-soluble complex that allows a complete set of titration data to be collected (Fig. 1b).

The chemical shift changes of the cavity proton H3 upon increasing (BNZ) observed here are nearly twice those for βCD/DBA without the formation of a precipitate. A binding curve is obtained which becomes level near the 1:1 mole ratio, also suggesting a 1:1 complex. Fitting this data set to the corresponding equation provides a value for the binding constant of 3000 (700) M^{-1} (R^2 = 0.9986), somewhat larger than that of βCD/DBA, a result of better solubility of the complex and probably a better localization of BNZ, compared with DBA, inside the βCD cavity. The corresponding ROESY spectrum (Fig. 2b) shows that the cavity proton H5 has become extensively deshielded and overlaps H2, and that benzidine's protons Ha interact stronger with H6,6' than H3, indicating that here also the amino groups are located at the edges of the host and all of the BNZ molecule is included.

3.4.2. Structure in the crystalline state. There are two independent host molecules (A and B) in the asymmetric unit forming head-to-head dimers.
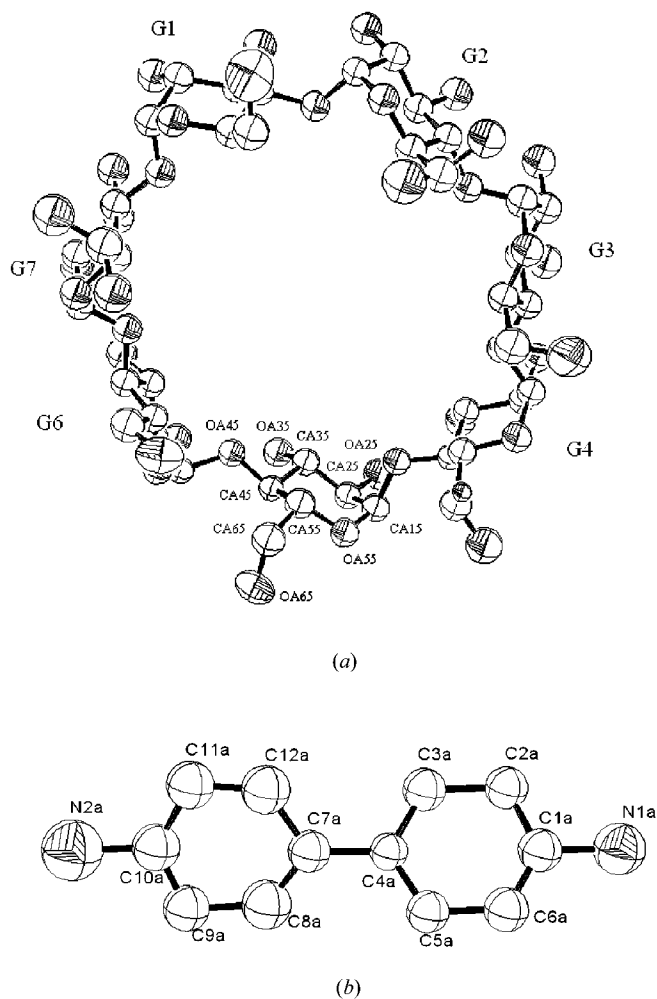

(a)

(b)

Figure 6
Conformation and numbering scheme of the βCD/BNZ complex: (a) βCD; (b) BNZ.

Table 6
Hydrogen bonds between βCD hydroxyls, O$A(B)nm$, and water molecules, O$nmA(B)$, in the βCD/DBA inclusion complex.

Molecule A	O···O distance (Å)	C—O···O angle (°)	Molecule B	O···O distance (Å)	C—O···O angle (°)
OA21···O21A	2.66 (8)	112 (1)	OB21···O21B1	2.64 (2)	109.1 (8)
OA21···O35A	2.80 (4)	113 (1)	OB21···O21B2	2.82 (5)	99 (1)
			OB21···O35B	2.88 (7)	110 (1)
OA22···O22A	2.61 (3)	102 (1)	OB22···O22B	2.78 (2)	105 (1)
OA23···O23A	2.81 (2)	105.4 (8)	OB23···O23B1	2.56 (5)	107 (1)
			OB23···O23B2	2.63 (4)	101 (1)
OA24···O36A	2.75 (7)	100 (1)	OB24···O24B	2.71 (2)	97 (1)
OA24···O24A	2.81 (4)	92 (1)			
OA24···O34A1	2.9 (1)	108 (2)			
OA26···O26A1	2.73 (4)	105 (3)	OB26···O26B1	2.65 (4)	102 (1)
OA26···O26A2	2.79 (4)	101.3 (9)	OB26···O26B2	2.95 (6)	102 (1)
			OB26···O26B3	2.96 (5)	105 (1)
			OB26···O21B1	3.17 (2)	114.7 (8)
OA32···O32A	2.82 (4)	129 (1)	OB32···O26B3	3.01 (5)	142 (1)
			OB32···O32B	3.1 (1)	118 (1)
OA34···O34A1	2.6 (1)	140 (2)	OB34···O22B	2.86 (2)	113 (1)
OB34···O22A	2.75 (3)	110 (1)			
OB34···O34A2	3.06 (7)	99 (1)			
OA35···O35A	2.75 (3)	121 (1)	OB35···O35B	2.62 (5)	121 (1)
OA35···O21A	2.95 (7)	117 (1)	OB35···O21B1	3.04 (2)	114.7 (8)
OA36···O36A	2.60 (7)	111 (1)	OB36···O24B	2.90 (2)	108 (1)
OA36···O24A	3.01 (3)	109 (1)	OB36···O22B	3.06 (3)	143.3 (9)
OA36···O34A1	2.9 (1)	127 (2)			
OA37···O35A	3.07 (5)	138 (1)	OB37···O35B	2.84 (5)	138 (1)
			OB37···O23B1	3.00 (5)	113 (1)
OA61a···O61B1	2.83 (1)	99 (1)	OB61···O61B1	2.70 (1)	110.3 (7)
			OB61···O61B2	2.96 (3)	94.5 (9)
OA61b···O61A	2.24 (8)	145 (2)			
OA61b···O64Aa2	2.77 (3)	118 (1)			
OA62···O63Bb2	2.99 (3)	134 (1)	OB62···O67A	2.76 (1)	112.9 (7)
OA63···O63A	2.70 (1)	120.3 (7)	OB63a···O63Ba	2.61 (3)	125 (1)
			OB63a···O64Aa1	2.72 (3)	108 (1)
			OB63a···O66B3	2.83 (3)	120 (1)
			OB63b···O63Bb1	2.68 (5)	115 (2)
			OB63b···O63Bb2	2.78 (4)	132 (2)
OA64a···O64Aa1	2.60 (3)	118 (1)	OB64···O64B	2.58 (8)	134 (2)
OA64a···O64Aa2	2.74 (2)	120 (1)	OB64···O61B1	2.85 (1)	105.9 (9)
OA64a···O63Ba	2.88 (2)	102 (1)	OB64···O61A	2.93 (8)	94 (1)
OA64b···O66B3	2.93 (6)	108 (3)			
OA64b···O63Ba	3.00 (6)	101 (3)			
OA65···O65A1	2.48 (7)	132 (2)	OB65···O65B	2.80 (2)	130.0 (9)
OA65···O65A2	2.86 (2)	126 (2)			
OA66···O63A	2.75 (1)	109.4 (9)	OB66···O66B1	2.70 (7)	138 (1)
OA66···O66A_1	2.98 (6)	109 (1)	OB66···O66B2	2.73 (9)	114 (2)
OA66···O66A2	3.06 (5)	93 (1)	OB66···O66B3	2.77 (2)	109 (1)
OA66···O66A3	3.17 (7)	114 (1)	OB66···O66B4	3.04 (8)	121 (1)
OA67···O67A	2.72 (1)	118.9 (7)	OB67a···O67Ba1	2.75 (4)	123 (1)
			OB67a···O67Ba2	2.76 (9)	131 (2)
			OB67a···O63Ba	2.91 (2)	104 (1)
			OB67b···O63Ba	2.96 (4)	98 (1)
			OB67b···O66B3	3.13 (4)	135 (1)

As in the DBA complex two βCD hosts enclose two guest molecules (a and b). The numbering scheme for βCD (conventions as in the βCD/DBA complex) and the guest molecules is given in Fig. 6 (Johnson, 1976). The present structure belongs to space group $P2_1$ and exhibits the screw-channel (SC) packing mode (Fig. 7; Jones & Kjeldgaad, 1993). The dimer's sevenfold axis forms an angle of approximately 10° with the stacking axis and the lateral displacement between two consecutive βCD dimers along the channel is 2.7 Å.

3.5. Geometry of the host molecules

The host molecules possess near sevenfold symmetry, the pyranose rings having the $^4C_1$ conformation as in the βCD/DBA complex (Table 3b). The same also holds for the intramonomer hydrogen bonds, O3n···O2$(n+1)$, stabilizing the βCD macrocycle [average O3n···O2$(n+1)$ distances 2.80 (3) Å; angles C3n—O3n···O2$(n+1)$ [average 116.4 (2)°] and O3n···O2$(n+1)$—C2$(n+1)$ [average 118.5 (5)°]. The βCD dimer is formed via OA3n···OB3$(8-n)$ hydrogen bonds with an average distance 2.80 (6) Å. Angles CA3n—OA3n···OB3$(8-n)$ and OA3n···OB3$(8-n)$—CB3$(8-n)$ have mean values 117.7 (4) and 117.5 (4)°, respectively.

The conformations of the primary hydroxy groups are shown in Table 3(b): residues G6 of monomer A and G4 of monomer B exhibit the (+)-gauche conformation and point inwards. Monomer A has three disordered hydroxy groups with major (−)-gauche and minor (+)-gauche conformations, those of residues G2, G4 and G7 [occupancies for the (−)-gauche conformer 89, 90 and 75%, respectively], and monomer B has two, on G1 and G2 [occupancies for the (−)-gauche conformer 86 and 91%, respectively]. The remaining hydroxy groups have the (−)-gauche conformation.

3.6. Guest geometry and interactions with its environment

The two guest molecules a and b enclosed within each βCD dimer exhibit dihedral angles between the phenyl rings 52.7 (7) and 40 (1)°, respectively. The number of interactions of the guests with their environment is very limited (Table 4b): The only close contact of the guests' amino groups is between N1B (which is pointing towards the solvent) and the water molecule O63A3 (2.6 Å). This same group has a weak interaction (3.15 Å) with the disordered hydroxy group OB62b of the hosting macrocycle pointing inwards. The amino group, emerging from the other primary side of the βCD dimer, points towards the guest phenyl ring of a consecutive dimer almost perpendicularly (smallest distance N1A···C3B = 3.42 Å) and interacts weakly with the hydroxy group OB64 of the non-hosting macrocycle.

At the βCD secondary interface the remaining end-amino groups approach in a parallel fashion and exhibit $\pi\cdots\pi$ overlap (minimum distance 3.62 Å). Therefore, in a way quite analogous to the DBA complex the interactions among the guests in the deformed channel are alternately weak $\pi\cdots\pi$ and vertical NH$\cdots\pi$.

The twisted conformation of the biphenyl group is in contrast to that observed for crystals of neat biphenyl (Charbonneau & Delugeard, 1977) or biphenyl derivatives (Graham *et al.*, 1989) that exhibit almost planar conformation. However, the dihedral angles between the phenyl rings are similar to that of 4-amino-4′-nitrobiphenyl both in its inclusion complex with βCD and as an isolated molecule as determined by *ab initio* quantum mechanical calculations (Brett *et al.*, 1999). Apparently the βCD cavity isolates the molecules and forbids the $\pi\cdots\pi$ stacking that results in the biphenyl planarity observed in crystals of the neat compound.

3.7. Hydrogen-bonding network and solvent molecules

There are seven direct hydrogen bonds among hydroxy groups of adjacent host dimers (Table 5*b*), of which five bind hydroxy groups in the two-dimensional layers: three along the *a* axis, OA65$\cdots$OA62*a*, OB66$\cdots$OB63 and OA22$\cdots$OB23, and two along the *c* axis, OA24$\cdots$OB21 and OA67*a*$\cdots$OA64*a*.

There are 24.70 (6) water molecules in the asymmetric unit distributed over 55 sites around the βCD dimer and 49 of them

Figure 7
Packing of the βCD/BNZ complex.

are within hydrogen-bonding distance of O atoms of the hydroxy groups, as shown in Table 7. The water sites have been labeled as in the previous complex and hydrogen-bonding distances of up to 3.25 Å and C—O(H)$\cdots$O(water) angles of up to 145° are assumed. Water molecules at six positions interact only among themselves.

4. Concluding remarks on the crystal packing of the complexes

As mentioned in §1, βCD dimers crystallize in four different packing modes, as shown in Fig. 8. All have the common feature that they consist of close-packed layers of βCD dimers and are generated by the two-dimensional invariable layers' different relative positioning. In the CH mode the dimer's sevenfold axis forms an angle of approximately 10° with the stacking axis. The two-dimensional layers stack in parallel so that the dimers align almost on top of each other to form channels, slightly deformed in the interface between dimers (interdimer interface). The channels are hydrophobic and the guests inside them are shielded from the water environment. The lateral displacement between two consecutive βCD dimers along the channel is 2.7 Å. On the contrary, in CB mode the lateral distance between two dimers of successive layers is 8.9 Å, every dimer being surrounded by solvent molecules. The primary faces and therefore the guest are exposed to the polar environment of water molecules and neighboring hydroxy groups. The dimer's sevenfold axis forms an angle of approximately 10° with the stacking axis, but the two-dimensional layers are related by a twofold screw axis and they are not parallel (dihedral angle of 20°). In the IM mode, a case between the CH and CB modes, adjacent layers are parallel, but the dimer's sevenfold axis forms an angle of $\simeq$20° with the stacking axis. Consequently, dimers are far from exactly aligned, their lateral displacement being 6 Å (the inner diameter of the primary face of βCD). Thus, a breaking of the channel is observed that leaves parts of the guests free to interact with hydroxy groups of adjacent hosts, as well as with water molecules. Finally, in the SC mode, although the lateral displacement between two consecutive βCD dimers along the channel is only 2.7 Å as in the CH mode, the dimer's sevenfold axis forms an approximate angle of 10° with the stacking axis but the two-dimensional layers are related by a twofold screw axis and they are not parallel, therefore, the guests interact with water molecules and hydroxy groups of adjacent hosts channels.

The guest(s), emerging from the two primary faces of the dimer, is(are) situated between the previously mentioned, practically invariant layers and therefore plays a crucial role in the packing. Guests with hydrophilic, hydrogen-bond forming group(s) like hydroxy groups seem to favor extensive hydration of the primary faces and induce CB packing. On the contrary, hydrophobic groups at the primary faces favor channel formation in order to be isolated from the aqueous environment in the periphery of the βCD barrel. Our experience is that polar groups with a self-association tendency, such as the carboxylic group (Rontoyianni *et al.*,
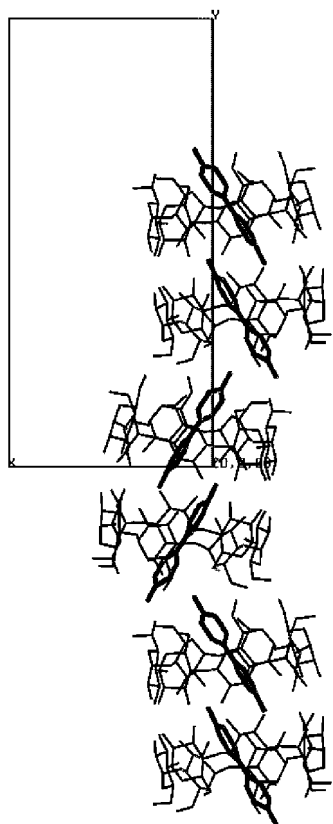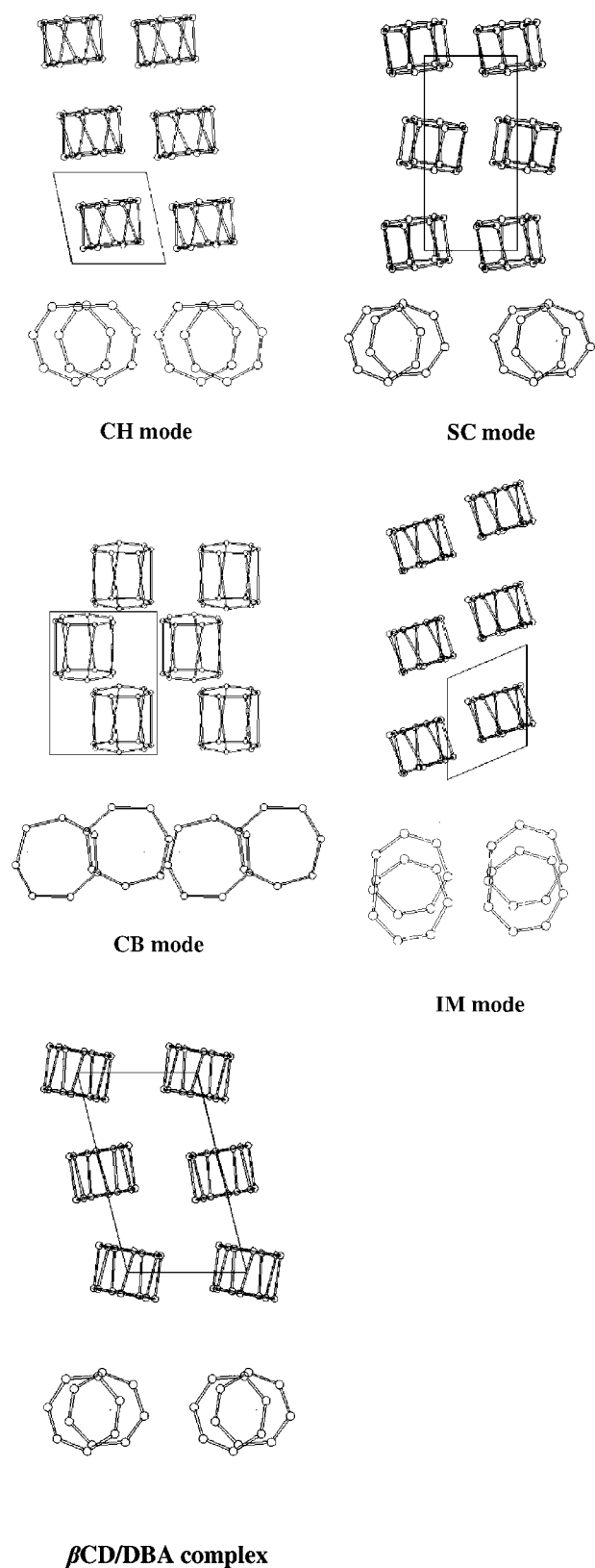
Figure 8
Schematic view of the packing modes of βCD dimers. In the upper part of the various modes each βCD monomer is represented by the heptagon of the O4 atoms. In the lower part the lateral displacement between two consecutive βCD dimers is shown and each heptagon represents a βCD dimer.

1994; Rontoyianni & Mavridis, 1996; Makedonopoulou et al., 1998, 1999; Makedonopoulou & Mavridis, 2000, 2001), or polar groups with an intermediate tendency to be hydrated favor IM packing. It seems that the latter is true for the SC mode, as shown from the complexes crystallized in SC (Hamilton & Chen, 1988a,b; Caira et al., 1996, 2002; Brett et al., 1999; Sanchez-Ruiz et al., 1999). However, it is difficult to deduce some clear relation between guest nature and the IM and SC packing modes.

The present guest molecules are end-substituted aromatic diamines differing in their length and flexibility. Summarizing their similarities we observe:

(i) They both form host:guest (2/2) complexes exhibiting limited host–guest close interactions.

(ii) Two parallel aryls of guests in the elongated cavity are stabilized by $\pi \cdots \pi$ interactions, whereas between βCD dimers there are vertical NH$\cdots \pi$ contacts.

(iii) The axes of two consecutive dimeric complexes (Figs. 7 and 4) form an angle close to $20°$ and have a lateral displacement $\simeq 2.45$ Å, both of which characterize the SC mode.

Indeed, the βCD/BNZ complex crystallizes in $P2_1$, in the SC mode, but βCD/DBA crystallizes in $C2$ with dimensions not resembling any of the packing modes described so far (Table 2). However, if we perform the transformation $\mathbf{a}' = (\mathbf{a} - \mathbf{b})/2$, $\mathbf{b}' = -\mathbf{c}$ and $\mathbf{c}' = (\mathbf{a} + \mathbf{b})/2$ we obtain the unit cell $\mathbf{a}' = 15.48$, $\mathbf{b}' = 33.31$, $\mathbf{c}' = 15.48$ Å, $\beta = 102.77°$, which is isostructural to the SC mode unit cell. Therefore, we suggest that although the packing of the βCD dimers in βCD/DBA is the same as in the βCD/BNZ and other SC mode complexes, the presence of the guest molecule in more than one conformation differentiates the lattice and the space group (Fig. 8).

It has been mentioned above that complexes belonging to the same mode are isostructural, a fact that permits us to determine the crystal packing of unknown complexes just by knowledge of their space group and unit-cell dimensions. Recently, however, there have been reports that close correspondence of unit-cell dimensions is a necessary, but not sufficient, condition for isostructurality. There are two cases of complexes in $P2_1$ and cell dimensions very close to those of the SC mode (Table 2) with dimers displaced laterally more than in the SC mode:

(i) In the βCD/paroxetin complex (Caira et al., 2002) the lateral displacement between dimers in adjacent layers is more than 6 Å

(ii) In the βCD/adamantanone complex (Sanchez-Ruiz et al., 1999) the corresponding displacement is even larger, close to that of the CB mode.

In both cases this difference is due to the location of the dimers with respect to the 2_1 axis parallel to the unique axis $\mathbf{b}$ and it has been attributed to the host/guest ratio (Caira et al., 2002). In the βCD/paroxetin complex the host/guest ratio is 2:1 and in βCD/adamantanone it is 2:2 nominally, but the guest is disordered, distributed over three positions. It is interesting to note that the unit-cell transformation $\mathbf{a}' = \mathbf{a} - \mathbf{c}$, $\mathbf{b}' = \mathbf{c} - \mathbf{a}$ and $\mathbf{c}' = \mathbf{b}$ leads to $\mathbf{a}' \simeq 19$, $\mathbf{b}' = 24$, $\mathbf{c}' = 32$ Å and α, β and γ nearly $90°$, which is the unit cell characterizing the CB struc-

Table 7
Hydrogen bonds between βCD hydroxyls, OA(B)nm, and water molecules, OnmA(B), in the βCD/BNZ inclusion complex.

Molecule A	O···O distance (Å)	C—O···O angle (°)	Molecule B	O···O distance (Å)	C—O···O angle (°)
OA21···O21A	2.76 (3)	95 (4)			
			OB22···O22B1	2.65 (6)	101 (1)
			OB22···O22B2	2.99 (6)	106 (1)
			OB22···O23A2	3.07 (4)	94 (1)
OA23···O23A1	2.84 (5)	102 (1)			
OA23···O23A2	2.95 (3)	94 (1)			
OA23···O25A1	3.10 (2)	121.9 (9)			
			OB24···O24B	2.71 (1)	113.1 (7)
			OB24···O33B	3.16 (4)	139 (1)
			OB24···O26B	3.19 (4)	95 (1)
OA25···O25A1	2.65 (2)	108.4 (8)	OB25···O25B	2.67 (3)	98 (1)
OA25···O33B	2.90 (4)	114 (1)	OB25···O37B	2.9 (1)	112 (2)
OA25···O25A2	3.02 (7)	96 (1)			
OA26···O26A1	2.72 (6)	91 (1)	OB26···O26B1	2.77 (4)	99 (1)
OA26···O26A2	2.73 (4)	110 (1)	OB26···O33B	3.11 (4)	111 (1)
OA27···O27A1	2.60 (5)	103 (1)	OB27···O27B	2.77 (4)	93 (1)
OA27···O27A2	2.70 (2)	105.9 (9)	OB27···O32B	2.87 (5)	108 (1)
OA31···O26A2	2.74 (9)	116 (1)	OB31···O24B	2.85 (2)	115.1 (8)
OA31···O32B	2.91 (5)	140 (1)			
OA31···O26A1	3.11 (7)	99 (1)			
OA32···O33B	2.74 (4)	129 (1)	OB32···O32B	2.72 (5)	121 (1)
OA32···O25A1	2.88 (2)	121.0 (8)	OB32···O26A2	2.92 (4)	145 (1)
			OB32···O27B	2.93 (4)	104 (1)
OA33···O21A	2.84 (2)	116 (1)	OB33···O33B	2.65 (4)	129 (1)
OA33···O37B	2.9 (1)	143 (2)			
OA34···O27A1		112 (1)			
			OB35···O35B1	2.77 (5)	128 (1)
				2.97 (6)	
OA36···O36A	2.86 (7)	120 (1)			
OA36···O22B2	3.01 (5)	143 (1)			
			OB37···O37B	2.8 (1)	127 (2)
			OB37···O25B	2.84 (4)	109 (1)
OA61···O61A1	2.4 (1)	128 (3)	OB61a···O61Ba	2.78 (2)	126 (1)
			OB61a···O61Bb1	2.87 (9)	98 (2)
OA61···O61Bb2	2.71 (6)	112 (1)			
OA61···O65A2	2.80 (1)	104.9 (9)			
OA61···O61A2	2.82 (8)	114 (2)			
OA61···O65A1	2.93 (7)	113 (3)			
OA61···O61Bb1	3.1 (1)	88 (2)			
			OB61b···O61Bb1	2.5 (1)	119 (5)
			OB61b···O61Bb2	2.5 (1)	131 (5)
			OB61b···O61Bb3	2.6 (1)	116 (5)
			OB61b···O67B2	2.9 (1)	133 (5)
			OB61b···O61Bb4	3.0 (1)	99 (4)
OA62···O62A	2.73 (2)	130.5 (9)	OB62···O62Ba1	2.78 (5)	141 (1)
OA62···O65A3	3.19 (2)	128 (1)	OB62···O66B	2.79 (2)	110 (1)
			OB62···O62Bb3	3.15 (4)	94 (1)
			OB62···O62Ba2	3.18 (7)	109 (1)
			OB62b···O62Bb1	2.99 (9)	137 (4)
			OB62b···O62Bb2	3.07 (8)	117 (4)
			OB62b···O62Bb3	3.13 (7)	98 (3)
OA63···O63A1	2.74 (2)	112 (1)	OB63···O63B	2.72 (1)	117.4 (8)
OA63···O63A2	2.88 (8)	135 (1)			
OA63···O63A3	2.8 (1)	112 (2)			
OA63···O63A4	2.94 (5)	118 (1)			
OA64···O64A	2.73 (2)	124 (1)	OB64···O65A2	2.79 (1)	103 (1)
OA64···O67A2	2.96 (6)	100 (1)			
OA65···O65A1	2.30 (1)	101 (4)	OB65···O67Ab	3.04 (3)	136 (1)
OA65···O65A2	2.73 (1)	111.7 (9)			
OA65···O65A3	2.99 (2)	101 (1)			
OA66···O63B	2.74 (1)	110.6 (9)	OB66···O66B	2.73 (2)	122.4 (1)
OA67a···O67Aa1	2.67 (3)	106 (1)	OB67···O67Aa1	2.69 (3)	121 (1)
OA67a···O67Aa2	2.78 (6)	122 (1)	OB67···O67B1	2.70 (4)	126 (1)
OA67a···O63A1	2.81 (3)	120 (1)	OB67···O67B2	2.81 (7)	104 (2)
			OB67···O67Aa2	2.98 (6)	105 (1)
			OB67···O61Bb3	3.00 (7)	104 (1)
OA67b···O67Ab	2.74 (5)	125 (2)			

tures and it has the same symmetry, if the guest is not taken into account. Therefore, we can suggest that both structures are pseudo-CB having packing arrangements and symmetry similar to CB. Because of the guest molecule, the lattice cannot have the exact symmetry of space group $C222_1$ and acquires a lower symmetry, $P2_1$, that does not require the two halves of the dimer complex to be related by a twofold axis.

The above discussion shows that the guest molecule not only influences changes of one packing mode to the other, but dictates sometimes subtler variations as in the case of the present βCD/DBA complex. However, the crystal packing of βCD dimers is determined by the dimer's structure and properties, especially the fact that dimers form C-centered or pseudo C-centered two-dimensional layers with two orthogonal axes of specific dimensions. This explains the fact that the lattices observed up to now, including the present, can be transformed one into another, if the symmetry of the guest is ignored. Thus, the isostructurality of βCD dimeric complexes is not always a sufficient condition in order to predict their crystal packing.

References

Beurskens, P. T., Admiraal, G., Beurskens, G., Bosman, W. P., de Gelder, R., Israel, R. & Smits, J. M. M. (1994). *The DIRDIF94 Program System.* Crystallography Laboratory, University of Nijmegen, The Netherlands.

Botsi, A., Yannakopoulou, K., Perly, B. & Hadjoudis, E. (1995). *J. Org. Chem.* **60**, 4017–4023.

Brett, T. J., Shuncheng, L., Coppens, P. & Stezowski, J. J. (1999). *Chem. Commun.* pp. 551–552.

Caira, M. R., De Vries, E., Nassimbeni, L. R. & Jacewicz, V. W. (2002). *J. Inclus. Phenom. Macromol. Chem.* In the press.

Caira, M. R., Griffith, V. J., Nassimbeni, L. R. & Van Oudtshoorn, B. (1996). *Supramol. Chem.* **7**, 119–124.

Charbonneau, G.-P. & Delugeard, Y. (1977). *Acta Cryst.* B**33**, 1586–1588.

Dodds, D. R. (1999). PhD thesis, University of Cape Town, South Africa.

Eliadou, K., Yannakopoulou, K., Rontoyianni, A. & Mavridis, I. M. (1999). *J. Org. Chem.* **64**, 6217–6226.

Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.

Giastas, P., Mourtzis, N., Yannakopoulou, K. & Mavridis, I. M. (2003). *J. Inclus. Phenom. Macromol. Chem.* In the press.

Graham, E. M., Miskowski, V. M., Perry, J. W., Coulter, D. R., Stiegman, W. P., Schaeffer, W. P. & Marsh, R. E. (1989). *J. Am. Chem. Soc.* **111**, 8771–8779.

Hamilton, J. A. & Chen, L. (1988a). *J. Am. Chem. Soc.* **110**, 4379–4391.

Hamilton, J. A. & Chen, L. (1988b). *J. Am. Chem. Soc.* **110**, 5933–5841.

Harata, K. (1998). *Chem. Rev.* **98**, 1803–1827.

Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

Jones, T. A. & Kjeldgaad, M. (1993). *'O' Molecular Modelling Program.* Version 5.9. Upsala, Sweden.

Kahr, B., Mitchel, C. A., Chance, J. M., VernonClark, R., Gantzel, P., Baldridge, K. K. & Siegel, J. S. (1995). *J. Am. Chem. Soc.* **117**, 4479–4482.

Kraulis, P. (1991). *J. Appl. Cryst.* **24**, 946–950.

Le Bas, G. & Tsoucaris, G. (1994). *Supramol. Chem.* **4**, 13–16.

Makedonopoulou, S. & Mavridis, I. M. (2000). *Acta Cryst.* B**56**, 322–331.

Makedonopoulou, S. & Mavridis, I. M. (2001). *Carbohydr. Res.* **335**, 213–220.

Makedonopoulou, S., Mavridis, I. M., Yannakopoulou, K. & Papaioannou, J. (1998). *J. Chem. Soc. Chem. Commun.* pp. 2133–2134.

Makedonopoulou, S., Tulinsky, A. & Mavridis, I. M. (1999). *Supramol. Chem.* **11**, 73–81.

Mavridis, I. M., Hadjoudis, E. & Tsoucaris, G. (1991). *Carbohydr. Res.* **220**, 11–21.

Mentzafos, D., Mavridis, I. M., Le Bas, G. & Tsoucaris, G. (1991). *Acta Cryst.* B**47**, 746–757.

Rontoyianni, A. & Mavridis, I. M. (1996). *Acta Cryst.* C**52**, 2277–2281.

Rontoyianni, A. & Mavridis, I. M. (1999). *Supramol. Chem.* **10**, 213–218.

Rontoyianni, A., Mavridis, I. M., Hadjoudis, E. & Duisenberg, A. J. M. (1994). *Carbohydr. Res.* **252**, 19–32.

Ross, J.-N. & Wardell, J. (1994). *Acta Cryst.* C**50**, 976–977.

Saenger, W. (1980). *Angew. Chem. Int. Ed. Engl.* **19**, 344–362.

Saenger, W. (1985). *Israel J. Chem.* **25**, 43–50.

Sanchez-Ruiz, X., Alvarez-Larena, A., Jaime, C., Piniella, J. F., Redondo, J., Virgili, A., Sanchez-Ferrando, F., Germain, G. & Baert, F. (1999). *Supramol. Chem.* **10**, 219–223.

Sheldrick, G. M. (1997). *SHELX*97. University of Göttingen, Germany.

Strouse, C. (2002). Unpublished.

Szejtli, J. (1998). *Chem. Rev.* **98**, 1743–1753.

Uekama, K., Hirayama, F. & Irie, T. (1998). *Chem. Rev.* **98**, 2045–2076.

Yannakopoulou, K., Ripeester, J. A. & Mavridis, I. M. (2002). *J. Chem. Soc. Perkin Trans.* 2, pp. 1639–1644.