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Crystal structure of hexakis(2,6-di-*O*-methyl)-α-cyclodextrin–acetonitrile dihydrate: a channel formed by methyl groups harbors a chain of five partially occupied water sites[☆,☆☆]

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Abstract

Hexakis(2,6-di-*O*-methyl)-α-cyclodextrin (DIMEA) crystallizes from 1:1 water–acetonitrile as DIMEA-acetonitrile-dihydrate in the orthorhombic space group $P2_12_12_1$, unit cell dimensions $a = 14.2775(5)$, $b = 15.7312(5)$, $c = 31.1494(11)$ Å. Refinement of the structure against 5540 X-ray diffraction data converged at an R factor of 0.083. The macrocycle exhibits a 'round' conformation and is stabilized by intramolecular, interglucose O-3–H(n)···O-2($n+1$) and C-6–H(n)···O-5($n+1$) hydrogen bonds. Acetonitrile is included in the central cavity of DIMEA and held in position by C-5–H···N interactions. The two water molecules in the asymmetric units are distributed over six sites. One is fully occupied due to hydrogen bonding to O-3 groups of two symmetry-related DIMEA molecules, whereas the five remaining sites show occupancies between 0.15 and 0.25. These sites are in hydrogen bonding contact with O···O distances between 2.59 and 3.50 Å and are located in infinite, hydrophobic channels parallel to the *a*-axis, which are coated with methyl groups of symmetry-related DIMEA. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: α-Cyclodextrin; Hexakis(2,6-di-*O*-methyl)-α-cyclodextrin; Acetonitrile inclusion complex; Hydrogen bonding; Water chain; Hydrophobic channel

1. Introduction

Cyclodextrins (CDs) are a family of cyclic oligosaccharides composed of 6, 7, and 8 α-(1→4)-linked D-glucose units which are known as α-, β-, and γ-CDs, respectively [1]. Since all glucoses are oriented *syn*, the CDs are torus-like macrocycles with hydrophobic central cavities coated by C-3–H, C-5–H, and O-4, and hydrophilic rims occupied by primary O-6–H hydroxyl groups on the narrow side and secondary O-2–H and O-3–H hydroxyl groups on the wide side. The latter form systematic intramolecular O-3(n)···O-2($n+1$) hydrogen bonds between neighboring glucose units, thereby contributing to the stability of the macrocyclic 'round' conformation. CDs are able to form inclusion complexes with various types of guest

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molecules fitting totally or partially into the host CD cavity [2]. If the O-2–H and O-6–H or O-2–H, O-3–H, and O-6–H hydroxyl groups of the CDs are methylated, the solubility coefficient in water becomes negative, i.e., they are only slightly soluble in hot water but are very soluble in cold water [3]. Methylation of the CD also affects the stability and water solubility of the inclusion complexes formed with some guest molecules; they are increased compared with analogous complexes of the native CDs [3,4]. The unique inclusion properties of native and methylated CDs have found application in several branches of the pharmaceutical industry [3].

In the present paper, we describe the inclusion complex of hexakis(2,6-di-*O*-methyl)-α-CD (DIMEA)–acetonitrile, which crystallized as a dihydrate. Its structure is compared with that obtained recently for the corresponding native CD, α-CD–acetonitrile hexahydrate [5].

Table 1
Summary of crystallographic data for DIMEA-$CH_3CN\cdot2\ H_2O$

Chemical formula	$C_{48}H_{84}O_{30}\cdot CH_3CN\cdot 2\ H_2O$
Formula weight	1214.21
Crystal habit, color	rod, colorless
Crystal size (mm^3)	$0.2\times0.4\times1.0$
Crystal system	orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	
a (Å)	14.2775(5)
b (Å)	15.7312(5)
c (Å)	31.1494(11)
Volume (Å^3)	6996.2(4)
Z	4
D_{calc} (g cm^{-3})	1.153
μ (mm^{-1})	0.097
F(000)	2600
Diffractometer	Bruker, CCD
Wavelength (Mo K_α, Å)	0.71073
Temperature (°C)	20
θ range for data collection (°)	1.45–23.29 (0.9 Å resolution)
Measured reflections	29,618
Unique reflections	5540
Index ranges	$0<h<15$, $0<k<17$, $0<l<34$
Structure solution	direct methods (SHELXS-97)
Refinement method	full-matrix least-squares on F^2
Data/parameters	5540/760
R (F^2)	$R=0.083$
Goodness of fit	1.142
Highest peak and deepest hole (e Å^{-3})	0.70 and −0.33

2. Experimental

Crystallization.—DIMEA was purchased from Cyclolab (Budapest, Hungary) and used without further purification. DIMEA (200 mg) was dissolved in 1 mL of a 1:1 water–MeCN mixture at 0 °C, and the solution was stored at 18 °C to reduce solubility. After about one week, rod-shaped crystals had formed.

X-ray diffraction experiment.—All relevant data are in Table 1. A crystal was sealed in a glass capillary with a drop of mother liquor. A total of 29,618 X-ray diffraction data were collected at room temperature (rt) to 0.9 Å resolution on a Bruker-AXS diffractometer equipped with a CCD area detector using graphite-monochromatized Mo K_α radiation ($\lambda=0.71073$ Å). Data were corrected for Lorentz, polarization, and absorption effects and merged by SAINT [6] and SHELXTL [7] to yield 5540 unique reflections. The crystal space group is orthorhombic $P2_12_12_1$; for further details, see Table 1.

Structure solution and refinement.—The crystal structure was solved by direct methods with SHELXS-97 [8]. Anisotropic refinement by full-matrix least-squares on F^2 [9] was carried out for all non-hydrogen atoms except for the partially occupied water sites W-2–W-6, which are located in the hydrophobic voids formed between DIMEA molecules; they were refined isotropically. Hydrogen atoms were placed at theoretical positions according to the 'riding model' [9], except for water molecules where hydrogen atoms could not be located. The refinement of 760 parameters converged at an *R* factor of 0.083 for all 5540 data.

The final fractional atomic coordinates and equivalent isotropic thermal displacement factors are listed in Table 2. The geometrical parameters collected in Table 3 were calculated by PARST-96 [10], and the thermal ellipsoid plots were drawn by ORTEP-III [11].

Table 2
Fractional atomic coordinates and equivalent isotropic thermal displacement factors of DIMEA-CH_3CN·2 H_2O, all atoms being fully occupied except for water sites W-2–W-6 [a]

Atom	x/a	y/b	z/c	U_{eq} (Å^2)
C-11	0.1951(4)	0.2906(3)	0.04264(14)	0.0827(13)
C-21	0.1332(5)	0.3698(3)	0.04106(15)	0.0892(15)
C-31	0.0409(4)	0.3524(3)	0.06196(15)	0.0824(14)
C-41	−0.0031(4)	0.2726(3)	0.04475(15)	0.0850(15)
C-51	0.0653(5)	0.1977(3)	0.04463(16)	0.0891(15)
C-61	0.0310(6)	0.1190(4)	0.0224(2)	0.115(2)
C-71	0.2168(7)	0.4995(5)	0.0336(3)	0.136(3)
C-81	−0.0263(8)	0.0618(6)	−0.0405(3)	0.166(4)
O-21	0.1797(3)	0.4393(2)	0.06232(12)	0.0985(11)
O-31	−0.0184(3)	0.4235(2)	0.05544(13)	0.1018(12)
O-41	−0.0808(3)	0.2536(2)	0.07277(9)	0.0846(9)
O-51	0.1513(3)	0.2224(2)	0.02342(10)	0.0957(11)
O-61	0.0057(5)	0.1349(3)	−0.01880(16)	0.1453(19)
C-12	−0.1710(4)	0.2457(3)	0.05556(16)	0.0877(15)
C-22	−0.2373(4)	0.2973(3)	0.08257(17)	0.0904(16)
C-32	−0.2410(4)	0.2626(3)	0.12763(16)	0.0785(12)
C-42	−0.2594(4)	0.1676(3)	0.12837(16)	0.0803(13)
C-52	−0.1944(5)	0.1195(3)	0.09679(15)	0.0874(15)
C-62	−0.2098(5)	0.0276(4)	0.0909(2)	0.119(2)
C-72	−0.2725(7)	0.4443(4)	0.0699(3)	0.138(3)
C-82	−0.3237(10)	−0.0727(4)	0.0762(4)	0.203(5)
O-22	−0.2070(3)	0.3838(2)	0.08322(13)	0.0986(11)
O-32	−0.3104(3)	0.3065(2)	0.15209(13)	0.0990(11)
O-42	−0.2399(2)	0.14052(18)	0.17100(10)	0.0718(8)
O-52	−0.1976(3)	0.1594(2)	0.05482(11)	0.0968(11)
O-62	−0.3025(4)	0.0133(3)	0.07943(19)	0.1409(17)
C-13	−0.3068(3)	0.0941(3)	0.19416(17)	0.0755(12)
C-23	−0.3170(3)	0.1319(3)	0.23799(17)	0.0726(11)
C-33	−0.2277(3)	0.1213(3)	0.26408(15)	0.0680(10)
C-43	−0.1932(3)	0.0297(3)	0.26246(15)	0.0653(10)
C-53	−0.1886(3)	−0.0053(3)	0.21757(16)	0.0686(11)
C-63	−0.1691(4)	−0.0982(3)	0.21516(18)	0.0811(13)
C-73	−0.3813(4)	0.2627(3)	0.2674(2)	0.0949(16)
C-83	−0.1422(6)	−0.2075(4)	0.1652(3)	0.125(2)
O-23	−0.3414(2)	0.2193(2)	0.23141(12)	0.0855(9)
O-33	−0.2438(2)	0.1459(2)	0.30732(11)	0.0896(10)
O-43	−0.09968(18)	0.03206(17)	0.28060(9)	0.0633(7)
O-53	−0.2798(2)	0.00719(18)	0.19750(12)	0.0789(9)
O-63	−0.1471(3)	−0.1194(2)	0.17215(13)	0.1007(11)
C-14	−0.0785(3)	−0.0204(3)	0.31631(14)	0.0692(11)
C-24	−0.0307(3)	0.0335(3)	0.35016(14)	0.0707(11)
C-34	0.0639(3)	0.0641(3)	0.33485(14)	0.0655(10)
C-44	0.1223(3)	−0.0075(2)	0.31459(14)	0.0650(10)
C-54	0.0658(3)	−0.0613(3)	0.28359(14)	0.0640(10)
C-64	0.1180(3)	−0.1415(3)	0.27069(18)	0.0823(13)
C-74	−0.0809(5)	0.1412(5)	0.4006(2)	0.121(2)
C-84	0.1035(5)	−0.1586(6)	0.1960(2)	0.123(2)
O-24	−0.0926(2)	0.1022(2)	0.35918(11)	0.0855(9)
O-34	0.1131(2)	0.1014(2)	0.36946(11)	0.0837(9)
O-44	0.19512(18)	0.03567(17)	0.29198(9)	0.0653(7)
O-54	−0.0198(2)	−0.08849(17)	0.30396(11)	0.0735(8)
O-64	0.0757(3)	−0.1858(2)	0.23652(15)	0.0967(11)
C-15	0.2896(3)	0.0124(3)	0.29874(15)	0.0685(11)
C-25	0.3436(3)	0.0930(3)	0.31081(16)	0.0756(12)
C-35	0.3359(3)	0.1571(3)	0.27479(16)	0.0700(11)
C-45	0.3683(3)	0.1177(3)	0.23305(15)	0.0678(11)
C-55	0.3214(3)	0.0327(3)	0.22351(14)	0.0662(10)
C-65	0.3628(3)	−0.0148(3)	0.18656(16)	0.0767(12)
C-75	0.3675(6)	0.1639(6)	0.3781(2)	0.138(3)
C-85	0.5046(5)	−0.0713(5)	0.1599(2)	0.122(2)
O-25	0.3047(2)	0.1238(2)	0.34973(11)	0.0858(9)

Table 2 *(Continued)*

Atom	x/a	y/b	z/c	U_{eq} (Å^2)
O-35	0.3885(3)	0.2301(2)	0.28462(12)	0.0927(10)
O-45	0.3460(2)	0.17665(18)	0.19976(10)	0.0702(7)
O-55	0.3275(2)	−0.02213(18)	0.26073(10)	0.0745(8)
O-65	0.4599(2)	−0.0259(3)	0.19322(13)	0.0981(11)
C-16	0.4164(3)	0.2062(3)	0.17239(17)	0.0778(12)
C-26	0.4022(3)	0.3013(3)	0.16625(17)	0.0795(13)
C-36	0.3118(4)	0.3169(3)	0.14241(15)	0.0728(11)
C-46	0.3078(4)	0.2648(3)	0.10168(15)	0.0778(12)
C-56	0.3291(5)	0.1720(3)	0.11008(16)	0.0879(15)
C-66	0.3433(8)	0.1219(4)	0.0662(3)	0.165(4)
C-76	0.4503(5)	0.4184(4)	0.2107(3)	0.115(2)
C-86	0.367(3)	−0.0125(13)	0.0415(6)	0.44(3)
O-26	0.4024(3)	0.3397(2)	0.20762(12)	0.0931(10)
O-36	0.3041(3)	0.40563(19)	0.13238(12)	0.0890(9)
O-46	0.2128(3)	0.2737(2)	0.08703(9)	0.0800(9)
O-56	0.4162(3)	0.1652(2)	0.13292(13)	0.0941(10)
O-66	0.3464(6)	0.0378(4)	0.0746(2)	0.177(3)
N-1	0.0803(12)	0.0775(9)	0.1553(4)	0.235(6)
C-2	0.0663(7)	0.1273(6)	0.1761(4)	0.134(3)
C-3	0.0666(12)	0.1895(9)	0.2081(5)	0.216(6)
O-1–W-1	0.3826(8)	0.5785(7)	0.1319(4)	0.240(4)
O-1–W-2 [a]	0.037(5)	−0.099(5)	0.086(2)	0.29(3)
O-1–W-3 [a]	0.033(7)	−0.248(7)	0.012(3)	0.31(4)
O-1–W-4 [a]	−0.101(5)	−0.182(5)	−0.049(2)	0.24(3)
O-1–W-5 [a]	0.286(5)	−0.212(4)	0.0984(19)	0.31(2)
O-1–W-6 [a]	0.209(4)	−0.218(4)	0.000(2)	0.31(2)

[a] Occupancy factors of water sites W-2–W-6 are 0.20, 0.15, 0.15, 0.25, and 0.25, respectively.

3. Results and discussion

General.—The atomic labeling is used as in Ref. [5], i.e., C-32 means carbon atom 3 (C-3) of glucose residue 2, and the C atoms of methyl groups attached to O-2 and O-6 of each glucose are C-7 and C-8, respectively.

Molecular geometry and conformation of DIMEA.—The annular geometry of DIMEA is stabilized by systematic O-3–H(n)···O-2($n+1$) hydrogen bonds (Figs. 1(a,b) and 2, and Table 3). The narrow ranges of O-4(n)···O-4($n-1$) distances (4.21–4.31 Å), O-4($n+1$)···O-4(n)···O-4($n-1$) angles (119.4–121.6°), and the slight deviation of O-4 atoms from their common least-squares plane ($<$ 0.16 Å, Table 3), show that the O-4 atoms form a well-defined hexagon that also determines the 'round' shape of the DIMEA macrocycle. The six glucose units are in normal $^4C_1$ conformation as indicated by their puckering parameters Q and θ [12], which are in ranges 0.54–0.56 Å and 4–9°, respectively (Table 3). The orientations of the glucoses described by torsion angles ϕ, O-5(n)–C-1(n)–O-4($n-1$)–C-4($n-1$) and ψ, C-1(n)–O-4($n-1$)–C-4($n-1$)–C-3($n-1$) [13], are in narrowly defined ranges 101–115 and 123–135°, respectively. As frequently observed in the CDs [14], intramolecular, interglucose C-6–H(n)···O-5($n+1$) hydrogen bonds (Fig. 2) contribute to the stabilization of the DIMEA macrocycle with C-6(n)···O-5($n+1$) and H-6(n)···O-5($n+1$) distances within 3.38–3.55 and 2.55–2.77 Å, respectively (Table 3).

All O-2–CH_3 methoxy groups are directed 'away' from the cavity with torsion angles C-1–C-2–O-2–C-7 in + gauche to trans (105–162°, Table 3). The O-5–C-5–C-6–O-6 torsion angles of glucose units 3, 4, and 6 are + gauche, while the others are − gauche, and all C-5–C-6–O-6–C-8 torsion angles are trans except for glucose residue 4, which is + gauche (87.3°). The O-6–CH_3 group of this glucose points 'toward' the DIMEA cavity, all others point 'away', so that the overall shape of DIMEA resembles an open torus (Figs. 1(a,b) and 2). This agrees with crystals of

Table 3
Selected geometrical parameters of DIMEA-CH_3CN·2 H_2O (distances in Å and angles in °)

Residue	1	2	3	4	5	6
Q [a]	0.54	0.55	0.55	0.54	0.56	0.56
θ [b]	5	6	6	9	6	4
ϕ [c]	112.7(5)	106.3(5)	106.5(4)	107.7(4)	114.7(4)	100.9(5)
ψ [c]	134.8(4)	123.2(4)	127.0(4)	123.6(4)	128.5(4)	124.0(4)
Tilt angle [d]	17.1(2)	11.3(2)	8.8(2)	9.5(3)	16.4(2)	5.0(2)
O-4 deviation [e]	−0.09	0.08	0.05	−0.16	0.15	−0.03
O-4 angle [f]	119.4(1)	119.5(1)	121.6(1)	117.3(1)	121.3(1)	120.0(1)
Distances						
O-4(n)···O-4($n-1$)	4.23(1)	4.21(1)	4.31(1)	4.22(1)	4.22(1)	4.28(1)
O-3(n)···O-2($n+1$)	2.90(1)	2.86(1)	2.78(1)	2.83(1)	2.96(1)	2.86(1)
C-6(n)···O-5($n+1$)	3.47(1)	3.48(1)	3.50(1)	3.55(1)	3.38(1)	3.43(1)
H-6(n)···O-5($n+1$)	2.74(1)	2.77(1)	2.62(1)	2.65(1)	2.65(1)	2.55(1)
C-5–H(n)···N-1 [g]	3.02	3.44	3.56	3.62	3.20	3.16
Torsion angles						
C-1–C-2–O-2–C-7	104.7(6)	124.3(6)	162.4(4)	156.5(5)	146.5(5)	139.6(5)
O-5–C-5–C-6–O-6	−66.0(8)	−70.9(7)	73.1(5)	70.5(5)	−67.1(5)	71.6(10)
C-5–C-6–O-6–C-8	179.6(7)	−175.9(7)	−170.4(5)	87.3(6)	179.3(5)	−173.6(20)

[a] Puckering amplitude [12].

[b] Indicates the deviation from theoretical chair conformation (ideal value: $\theta = 0$; [12]).

[c] Torsion angles ϕ and ψ 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 [13].

[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] Deviation of O-4 atoms from the least-squares plane through the six O-4 atoms.

[f] Angle between neighboring O-4 atoms, O-4($n+1$)···O-4(n)···O-4($n-1$).

[g] Interaction distances between the H-5 hydrogen atoms of DIMEA and the N-1 nitrogen atom of acetonitrile.

methylated CDs grown from cold water, DIMEA·H_2O [15] and heptakis(2,6-di-*O*-methyl)-β-cyclodextrin dihydrate (DIMEB·2 H_2O) [16]. By contrast, in most of the methylated CDs crystallized from hot water [15,17–21], two or three O-6–CH_3 groups are rotated 'inward' and close the cavity from this side, yielding bowl-shaped molecular structures.

Ternary complex of DIMEA-CH_3CN·2 H_2O.—The position of the acetonitrile molecule is fully occupied and stabilized in the central cavity of DIMEA by C-5–H···N hydrogen bonds with H···N distances 3.02–3.62 Å (Figs. 1(a,b), 2, 3, and 4, and Table 3). For the position of acetonitrile, two alternate orientations differing by 180° rotation are possible, CH_3–C≡N and N≡C–CH_3. The orientation is, in fact, as shown in Figs. 1–3, because the N≡C distance (1.04 Å) is much shorter than C–CH_3 (1.40 Å) so that a clear discrimination of the alternative orientations of acetonitrile is possible. In addition, alternate C-5–H···CH_3 interactions would be unfavorable and W-2 (albeit only at occupation of 0.2) could not hydrogen bond to the methyl group.

Two water molecules are located in the hydrophobic interstices between DIMEA molecules. They are distributed over six positions; W-1 is fully occupied, which associated with its hydrogen bonding to hydroxyl groups O-33 and O-36 of two symmetry-related DIMEA. W-2–W-6 are partially occupied with occupation parameters from 0.15 to 0.25, although their O···O distances of 2.59–3.50 Å would permit full occupation (see Figs. 1(a,b), 3, and 4, and footnote of Table 2). A possible hydrogen bonding network connecting the water sites, DIMEA, and acetonitrile is depicted in Figs. 3 and 4. The water molecules form an infinite hydrogen bonding chain parallel to the *a*-axis and located in a channel-like void formed between DIMEA molecules. The channel is coated by methyl groups so that the water molecules are only held by van der Waals forces, as indicated by their closest contacts to methoxy C and O atoms given in Table 4. These distances are all longer than

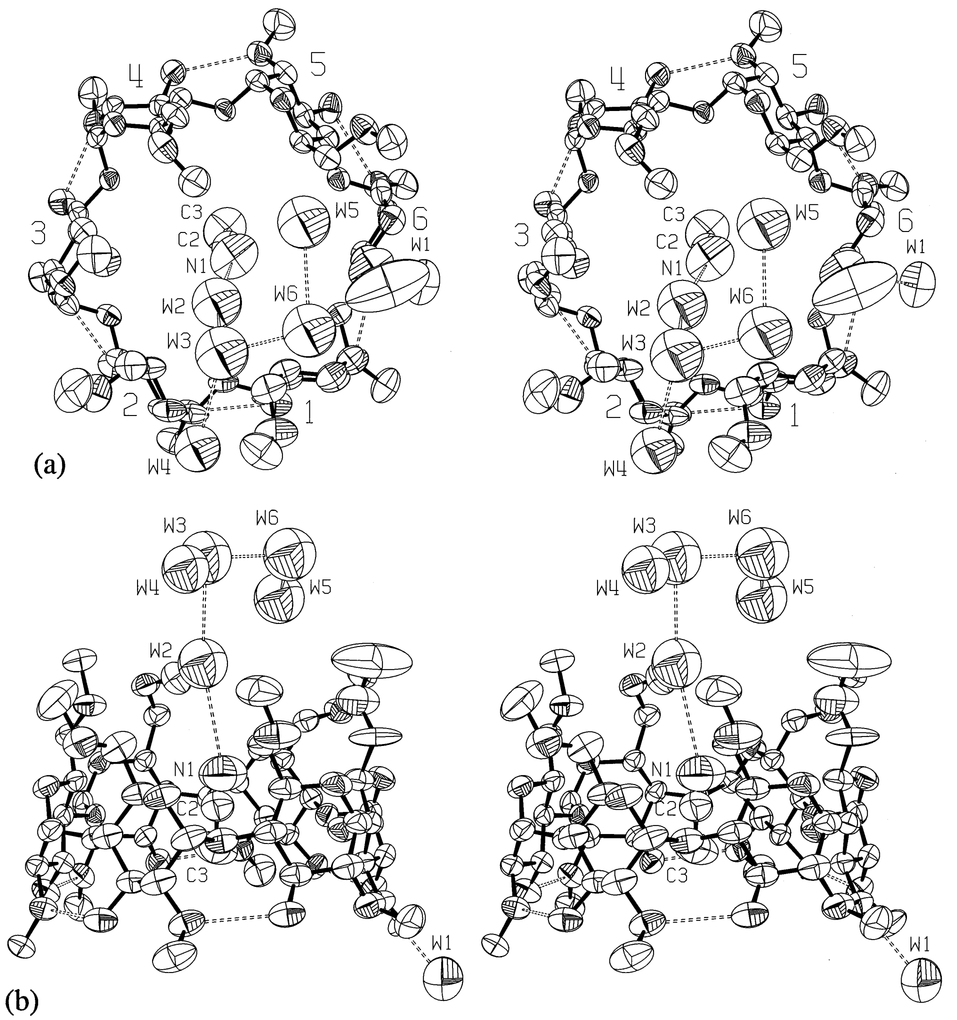

Fig. 1. ORTEP-III [11] stereo plot of the inclusion complex DIMEA-$CH_3CN \cdot 2\ H_2O$ drawn with displacement ellipsoids at the 40% probability level: (a) top view, and (b) side view. Dashed lines indicate possible hydrogen bonds within a distance of 3.6 Å between O···O and O···N. Water W-1 is fully occupied; all others are in the range 0.15–0.25.

3.6 Å, except for C-74···W-3, (3.31 Å) involving the low-occupancy (0.15) W-3, and the shortest O···W distance, O-33···W-5 (3.74 Å) is too long to be identified as a hydrogen bond. We assume that water molecules W-2–W-6 evaporated from the crystal before or during data collection because they are located in the hydrophobic channels formed by DIMEA packing and not directly hydrogen bonded to DIMEA (Figs. 3 and 4). This is supported by the observation that the crystal showed cracks after the data collection had been finished.

Crystal packing.—Fig. 3 shows the crystal structure of DIMEA-$CH_3CN \cdot 2\ H_2O$. DIMEA molecules are stacked along and slanted about 60° against the *b*-axis. The DIMEA cavity is blocked at the O-2-, O-3-side by a neighboring DIMEA related by the twofold screw operation along the *b*-axis. By contrast, the O-6-side is open to the hydrophobic intermolecular space where all partially occupied water sites are found. This molecular arrangement is different from the typical cage crystal packing where both sides of the CD cavity are blocked by symmetry-related CDs [22].

Structural comparison between DIMEA-$CH_3CN \cdot 2\ H_2O$ and α-CD-$CH_3CN \cdot 6\ H_2O$.—The molecular structures of both complexes are similar and superimpose with an rms deviation of 0.26 Å (only atoms C-1–C-6 and O-2–O-5 of each glucose residue are used for this calculation, see Fig. 5). The glucose units of DIMEA are slightly more tilted toward the molecular cavity (tilt-angle range 5.0–17.1°,

Table 3) than those of α-CD (2.5–12.5°) [5]. This shortens the H···N distances across the macrocycle (3.02–3.62 Å in DIMEA and 2.99–4.01 Å in α-CD) and leads to a better fit of the acetonitrile (fully occupied) to the DIMEA cavity when compared with the corresponding α-CD complex (occupancy of acetonitrile = 0.8) [5] (Fig. 2 and Table 3). The position of acetonitrile is in the center of the macrocycle cavity for the present structure, while it is shifted by 0.4 Å to the 'left' in α-CD-CH_3CN·6 H_2O [5] (Fig. 5). In both complexes, the structure of acetonitrile is not

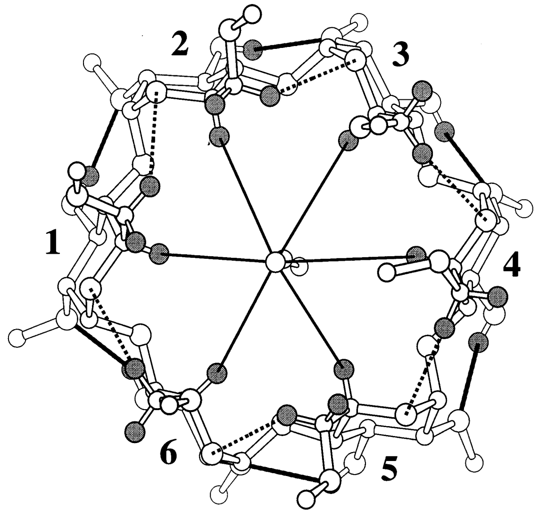

Fig. 2. 'Round' macrocyclic conformation of DIMEA is stabilized by intramolecular, interglucose O-3–H(n)···O-2(n + 1) and C-6–H(n)···O-5(n + 1) hydrogen bonds as shown with thick solid and dashed lines, respectively. The acetonitrile is held in position at the central cavity of DIMEA by C-5–H···N interactions (thin solid lines). For clarity, hydrogen atoms C-5–H, C-6–H_2, and O-3–H are shown as small spheres; C atoms are medium-sized spheres; and O and N atoms are large spheres.

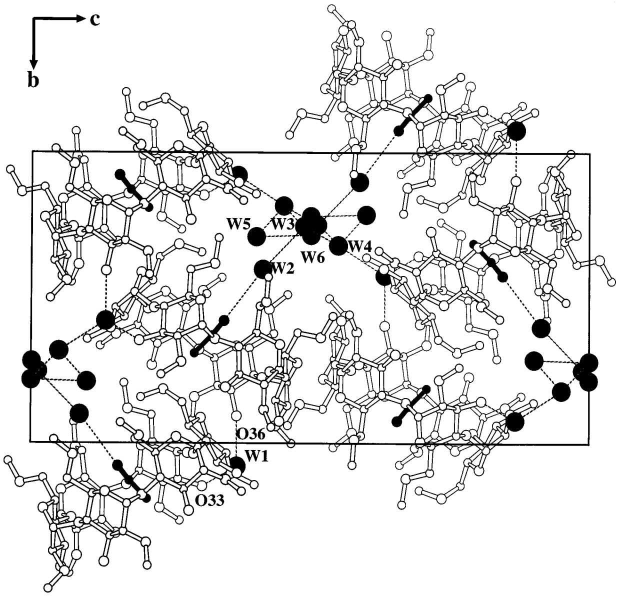

Fig. 3. Crystal packing of the inclusion complex DIMEA-CH_3CN·2 H_2O. Acetonitrile and water molecules are drawn with filled bonds and circles. Dashed lines indicate possible hydrogen bonds within a distance of 3.6 Å of O and N atoms, respectively. W-1 is fully and W-2–W-6 are partially (0.15–0.25) occupied. The latter are located in an infinite channel formed by methyl groups (see Fig. 4).

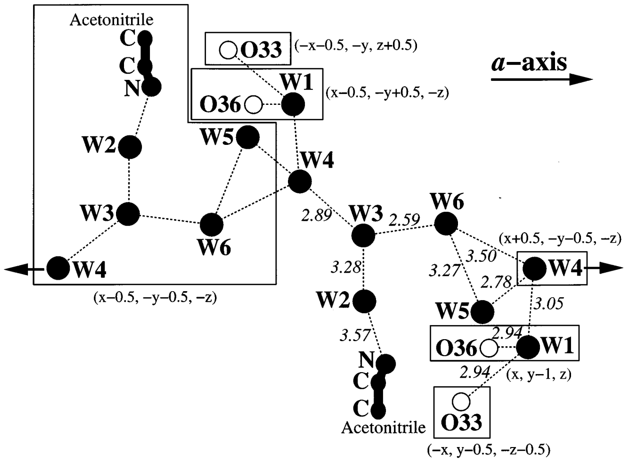

Fig. 4. Infinite hydrogen bonding network in the hydrophobic intermolecular space between DIMEA molecules. There are two chains of hydrogen bonds with W-3 and W-4 as linkages, one running infinitely in a horizontal direction, the other running finitely in a vertical direction between O-33, O-36 and N (acetonitrile). Arrows at W-4 show the continuation of the infinite chain. Acetonitrile and water molecules are drawn with filled bonds and circles. Open circles indicate oxygen atoms of DIMEA. Atoms from symmetry-related molecules are given with their symmetry operators. Dashed lines indicate possible hydrogen bonds within a distance of 3.6 Å; O···O and O···N distances are in Å.

Table 4
Contacts of water sites W-2–W-6 to DIMEA within a distance of 4.0 Å [a]

Contact	Distance	Symmetry
C-61···W-2	3.97	x, y, z
C-83···W-2	3.93	x, y, z
O-63···W-2	3.76	x, y, z
C-84···W-2	3.67	x, y, z
C-74···W-3	3.31	$-x, y+0.5, -z+0.5$
C-71···W-4	3.90	$x+0.5, -y+0.5, -z$
C-81···W-4	3.99	x, y, z
O-33···W-5	3.74	$-x, y+0.5, -z+0.5$
C-74···W-5	3.73	$-x, y+0.5, -z+0.5$
C-86···W-5	3.78	x, y, z

[a] These five water sites are located in the hydrophobic channel formed by DIMEA methyl groups (see Fig. 3).

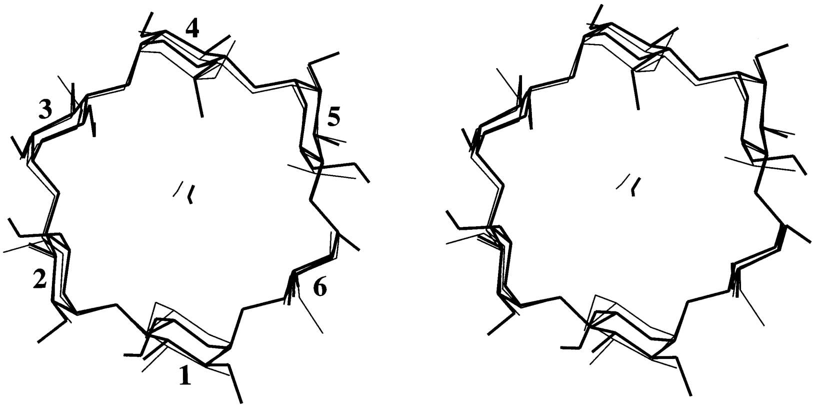

Fig. 5. Stereo plot of superposition of DIMEA-CH_3CN·2 H_2O and α-CD-CH_3CN·6 H_2O [5] (all water molecules omitted). The thick and thin lines represent DIMEA–CH_3CN and α-CD-CH_3CN, respectively. Note that CH_3CN is in the center of the cavity in DIMEA but shifted 0.4 Å to the 'left' in α-CD.

linear (C–C–N angle is 167° for the present structure).

4. Supplementary material

Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication No. CSD-117000. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 IEZ, UK (fax: +44-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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References

[1] (a) M.L. Bender, M. Komiyama, *Cyclodextrin Chemistry*, Springer, Berlin, 1978. (b) W. Saenger, *Angew. Chem., Int. Ed. Engl.*, 19 (1980) 344–362. (c) W. Saenger, in J.L. Atwood, J.E.D. Davies, D.D. MacNicol (Eds.), *Inclusion Compounds*, Vol. 2, Academic Press, London, 1984, pp. 231–259.

[2] J. Szejtli, *Cyclodextrins and Their Inclusion Complexes*, Akademiai Kiado, Budapest, 1982.

[3] K. Uekama, T. Irie, in D. Duchêne (Ed.), *Cyclodextrins and Their Industrial Uses*, Editions de Santé, Paris, 1987, pp. 395–439.

[4] M.V. Rekharsky, Y. Inoue, *Chem. Rev.*, 98 (1998) 1875–1917.

[5] T. Aree, J. Jacob, W. Saenger, H. Hoier, *Carbohydr. Res.*, 307 (1998) 191–197.

[6] Siemens, SAINT, Data Integration Software, Siemens Analytical X-ray Instruments Inc., Madison, WI, USA, 1996.

[7] Siemens, SHELXTL, Version 5.0, Siemens Analytical X-ray Instruments Inc., Madison, WI, USA, 1996.

[8] G.M. Sheldrick, SHELXS-97, Program for Crystal Structure Solution, University of Göttingen, Germany, 1997.

[9] G.M. Sheldrick, SHELXL-97, Program for Crystal Structure Refinement, University of Göttingen, Germany, 1997.

[10] M. Nardelli, *J. Appl. Crystallogr.*, 28 (1995) 659.

[11] M.N. Burnett, C.K. Johnson, ORTEP-III, Thermal-Ellipsoid Plot Program for Crystal Structure Illustrations, Oak Ridge Natl. Lab., 1996.

[12] D. Cremer, J.A. Pople, *J. Am. Chem. Soc.*, 97 (1975) 1354–1358.

[13] IUPAC–IUB Joint Commission on Biochemical Nomenclature (JCBN), Symbols for specifying the conformation of polysaccharide chains, Recommendations 1981, *Eur. J. Biochem.*, 131 (1983) 5–7.

[14] T. Steiner, W. Saenger, *J. Am. Chem. Soc.*, 114 (1992) 10146–10154.

[15] K. Harata, *Supramol. Chem.*, 5 (1995) 231–236.

[16] T. Aree, W. Saenger, P. Leibnitz, H. Hoier, *Carbohydr. Res.*, 315 (1999) 199–205.

[17] T. Steiner, W. Saenger, *Carbohydr. Res.*, 282 (1996) 53–63.

[18] T. Steiner, K. Hirayama, W. Saenger, *Carbohydr. Res.*, 296 (1996) 69–82.

[19] T. Steiner, W. Saenger, *Carbohydr. Res.*, 275 (1995) 73–82.
[20] M.R. Caira, V.J. Griffith, L.R. Nassimbeni, B. van Oudtshoorn, *J. Chem. Soc.*, *Perkin Trans. 2*, (1994) 2071–2072.
[21] T. Steiner, W. Saenger, *Angew. Chem.*, *Int. Ed. Engl.*, 37 (1998) 3404–3407.
[22] W. Saenger, *Isr. J. Chem.*, 25 (1985) 43–50.