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Carbohydrate Research 324 (2000) 141–146

CARBOHYDRATE RESEARCH

Note

# Topography of the 1:1 α-cyclodextrin–nitromethane inclusion complex☆

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Received 23 August 1999; accepted 12 October 1999

**Abstract**

Dissolution of α-cyclodextrin (α-CD) in 9:1 water–nitromethane smoothly generates the title compound, which crystallizes as the pentahydrate in the orthorhombic space group $P2_12_12_1$ with $a = 9.452(4)$, $b = 14.299(3)$, $c = 37.380(10)$ Å, and $Z = 4$. Its crystal structure analysis revealed the α-CD macrocycle in an unstrained conformation stabilized through a ring of O-2···O-3′ hydrogen bonds between five of the six adjacent glucose residues. The nitromethane is located in the α-CD cavity in an orientation parallel to the plane of the macrocycle, and assumes two sites of equal population with the nitro group in excessive thermal motion; the guest is held by van der Waals contacts and C-H···O-type hydrogen bonds to the pyranose H-3 and H-5 protons. The packing of the macrocycles in the crystal lattice is of cage herringbone-type with an extensive intra- and intermolecular hydrogen bonding network. The ready formation of a nitromethane inclusion complex in aqueous nitromethane, and the subtleties of its molecular structure amply demonstrate the ease with which water is expelled from the α-CD cavity by a more hydrophobic co-solvent. 

*Keywords:* α-Cyclodextrin; Nitromethane inclusion complex

## 1. Introduction

Various small organic molecules have been shown to be readily included into the apolar cavity of α-cyclodextrin (α-CD, Scheme 1), such as methanol [2], dimethylformamide [3], and dimethyl sulfoxide [4], and their topographies have been thoroughly characterized by solid-state structures. Surprisingly, nitromethane, a standard solvent as well as a reagent, has not been reported to complex with α-CD or any of the other cyclodextrins [5,6]. Here we report on the ready preparation of a 1:1 α-CD–$CH_3NO_2$ inclusion complex (**1**) and its topography on its X-ray based structure.

## 2. Results and discussion

The atomic numbering scheme and the molecular structure of the α-CD–nitromethane inclusion complex (**1**) are shown in Scheme 1 and Fig. 1; some averaged geometric parameters are listed in Table 1. The nitromethane is incorporated into the central cavity of the torus-shaped α-CD, and five

☆ Molecular modeling of saccharides, Part 23. For Part 22, see Ref. [1].

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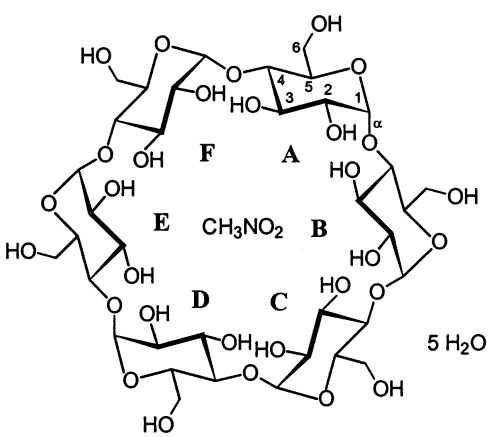
0008-6215/00/$ - see front matter 
PII: S0008-6215(99)00285-2

water molecules occupy interstitial positions between the CD macrocycles in the crystal lattice. The CD macrocycles are arranged in a typical herringbone-type pattern in the crystal environment (space group $P2_12_12_1$, views along the *a* and *b* axis are given in Fig. 2), as is, for example, also found in the three α-CD hydrate solid-state structures [7–9].

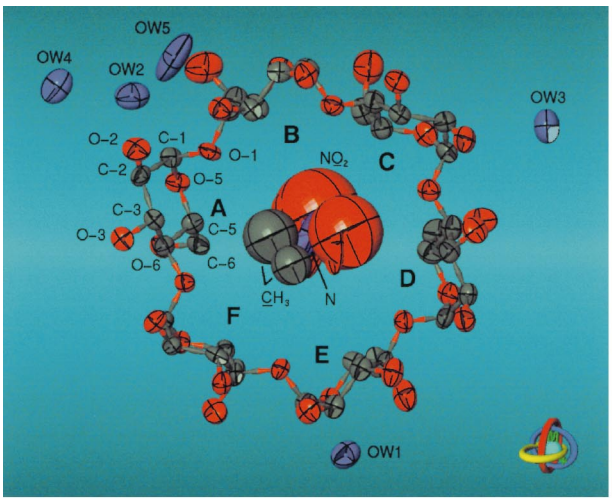
*Conformation of the macrocycle.*—As indicated by the intersaccharidic $\Phi/\Psi$ torsion angles (cf. Table 1) and their rather small fluctuations, the α-CD macrocycle in **1** adopts its usual conical shape similar to the one realized in a large variety of related complexes [6,10,11]. The mean tilt angle $\tau$ [11,12] of the glucose units in relation to the macroring displays a slight rotation of the pyranoses with their 6-OH sides towards the center of the molecule (i.e., $\tau > 90°$), leaving the opposite 2-OH/3-OH face as the wider opening of the torus. All the 6-$CH_2OH$ groups point away from the central axis of **1** (*gg* arrangements, $\omega \approx -70°$). The glucose units are in the rather rigid $^4C_1$ conformation with standard ring torsion angles $\Theta_1 - \Theta_6$ around $\pm 55°$, and with typical Cremer–Pople ring puckering parameters [13,14]. The intersaccharidic O-1 atoms are fairly coplanar (RMS deviation of only 0.06 Å from the common least-squares plane) and form a symmetrical hexagon with nearly identical diagonal distances of $8.45 \pm 0.2$ Å.

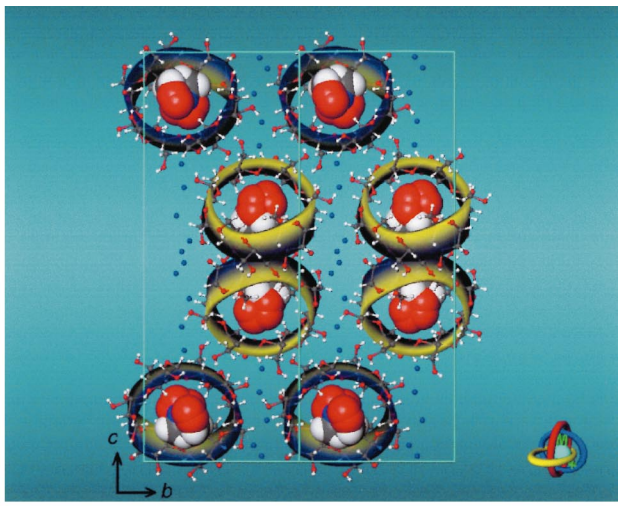
*Hydrogen bonding.*—The comparatively unrestrained overall geometry of the α-CD host is stabilized through an almost complete ring of O-2···O-3′ hydrogen bonds between five out of six adjacent glucose residues (cf. Fig. 3 and Table 2, hydrogen bonds labeled 1–5); and no other intramolecular hydrogen bonds are formed. However, the solid-state geometry displays an extensive three-dimensional hydrogen-bonding network between the α-CD, the five water molecules of crystallization (Table 2, entries 6–11), and the symmetry-related molecules in the crystal lattice (entries 12–30) as is usually observed for carbohydrate crystal structures [15]. All hydroxyl groups satisfy their hydrogen-bonding requirements through formation of two to three H-bonds, and all water molecules are involved in three to four H-bonds.

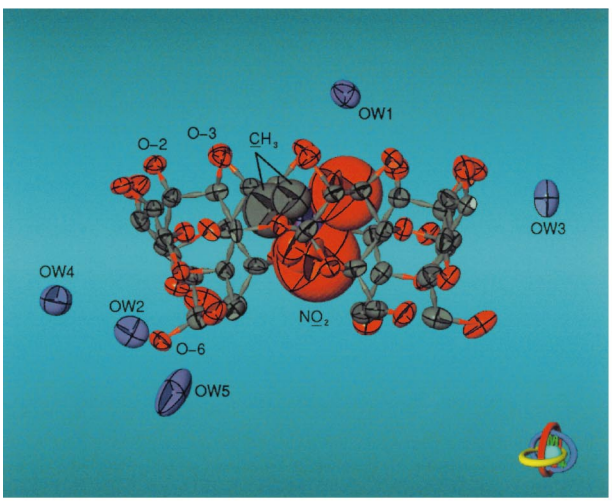



Scheme 1. α-Cyclodextrin–nitromethane inclusion complex (**1**); the α-(1→4)-linked glucose units are labeled A–F.

*Geometry of the nitromethane inclusion.*—The nitromethane molecule is located in the void of the α-CD macrocycle, with the methyl group being disordered over two sites with equal (50%) occupancy (Fig. 1), whereas the corresponding two nitrogen positions coincide in one fully occupied site. The oxygen atoms of the guest display excessive thermal motions (Fig. 1), indicating that the $NO_2$ group is statistically disordered; refinement of the structure was approximated by six positions over which the two oxygens are distributed (33% occupancy of each site). Only four 'reasonable' (in terms of bond angles) oxygen sites are retained in the ball-and-stick type representation of the complex, given in Fig. 4, with the superimposed molecular contact surfaces [16] visualizing the steric fit between the host and guest molecule. Side-view cross-sectional cuts through these surfaces (Fig. 4, bottom) show both nitromethane sites to be shifted away from the center of the α-CD torus towards the wider opening (i.e., the 2-OH/3-OH face). In either geometry, the nitromethane C–N bond points almost perpendicular away from the central axis of the complex. Obviously, the guest is held in the cavity by van der Waals contacts to a circular array of the pyranose hydrogens at C-3 and C-5. Although the $NO_2$ group is not involved in hydrogen bonds with the hydroxyl groups of the host, it does form hydrogen bonds of the O···H–C type to the C-3 and C-5 protons, respectively;



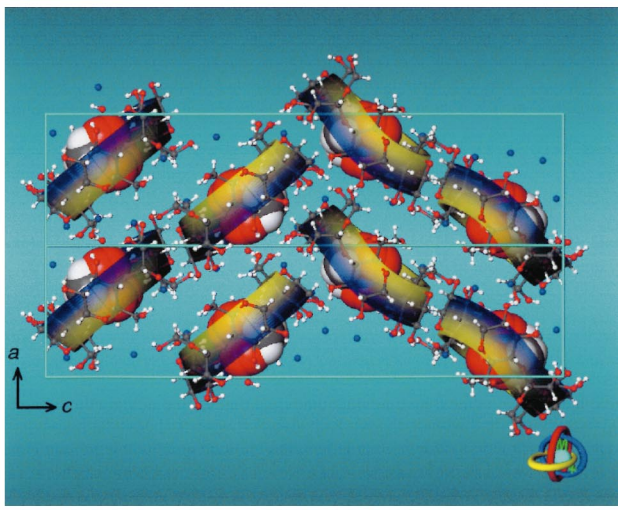




Fig. 1 Fig. 2

Fig. 1. Molecular structure of the asymmetric unit of the α-CD–nitromethane inclusion complex (**1**) showing the heavy-atom 50% probability ellipsoids; hydrogens are omitted for clarity (gray, C; red, O; blue, nitrogen and water-oxygens). The glucose units of α-CD are labeled A–F (cf. Scheme 1), and the water molecules located at interstitial positions outside the macrocycle are termed OW1–OW5. The nitromethane guest molecule shows excessive thermal motions and is disordered over two sites with equal occupancies; the statistical disordering of the $NO_2$ oxygen atoms is approximated by six atomic positions.

Fig. 2. Ball-and-stick models of the herringbone-type molecular packing in the crystal structure of **1**, as viewed down the *a* (top, $1 \times 2 \times 1$ unit cells) and *b* axis (bottom, $2 \times 1 \times 1$ cells). The α-CD molecules are represented as solid colored ribbon models, whereby blue colors correspond to the 2-OH/3-OH side of the macrocycles, yellow colors to the 6-OH face. The disordered nitromethane molecules are visualized as CPK-models, and the unit cell boundaries are indicated by solid cyan lines.

for each $NO_2$-oxygen position the shortest O···H-3 and O···H-5 distances are in the range of 2.48–2.82 Å.

## 3. Conclusions

The solid-state structure of the α-CD–nitromethane pentahydrate complex shows that the mode with which the guest molecule is incorporated into the cavity results from a balance of at least two effects contributing to the stability of such assemblies; hydrophobic effects conceivably favor the hydrophobic methyl group pointing into the cavity, thereby leaving the nitro group to stick out of the α-CD torus at the opposite, hydrophilic rim, whereas the antiparallel arrangement of dipoles of host and guest would lead to the opposite regioselectivity. The inclusion of nitromethane almost perpendicular to the molecular axis displays a counterbalance of these effects, while the α-CD cavity itself is large enough to allow for excessive thermal

Table 1
Selected geometric parameters (mean values averaged over all glucose units and root mean-square deviations) for the α-CD macrocycle in **1**

| | |
|---|---|
| *Intersaccharidic torsion angles* (°) | |
| $\Phi$ (O-5–C-1–O-1–C-4′) | 107.4 ± 4.8 |
| $\Psi$ (C-l–O-1–C-4′–C-3′) | 129.4 ± 11.3 |
| *Tilt angles* | |
| $\tau$ (°) | 101.6 ± 9.3 |
| *Pyranose torsion angles* (°) | |
| $\omega$ (O-5–C-5–C-6–O-6) | −68.8 ± 7.3 |
| $\Theta_1$ (O-5–C-1–C-2–C-3) | 57.6 ± 2.3 |
| $\Theta_2$ (C-l–C-2–C-3–C-4) | −51.8 ± 2.7 |
| $\Theta_3$ (C-2–C-3–C-4–C-5) | 49.7 ± 3.4 |
| $\Theta_4$ (C-3–C-4–C-5–O-5) | −50.8 ± 3.3 |
| $\Theta_5$ (C-4–C-5–O-5–C-1) | 58.2 ± 1.6 |
| $\Theta_6$ (C-5–O-5–C-1–C-2) | −62.0 ± 2.2 |
| *Cremer–Pople parameters* | |
| $Q$ (Å) | 0.550 ± 0.023 |
| $\theta$ (°) | 5.5 ± 3.5 |
| $\phi$ (°) | 50.4 ± 29.7 |
| *Distances* (Å) | |
| O-1(A)–O-1(D) | 8.32 |
| O-1(B)–O-1(E) | 8.62 |
| O-1(C)–O-1(F) | 8.44 |

motions of the guest and rotation of the nitro group. The ready preparation of the complex, and the subtleties of its molecular structure presented here, amply demonstrate the ease with which water is expelled from the α-CD cavity by a co-solvent.

## 4. Experimental

*Preparation of the α-cyclodextrin – nitromethane complex.*—To a stirred solution of α-CD (2.49 g, 2.56 mmol) in water (25 mL) was added dropwise nitromethane (3 mL), and the reaction mixture was kept overnight in a refrigerator. The colorless crystals formed were collected by filtration and dried in a desiccator over silica gel: 1.79 g (62%). A second crop (0.70 g, 24%) was obtained from the mother liquor on evaporation to about one third of its volume, followed by saturation with nitromethane. The crystals became opaque at 90–100 °C and started browning at ~265 °C. $[\alpha]_D^{22}$ +130° (*c* 0.91, water); $[\alpha]_D^{22}$ +120° (*c* 0.90, water saturated with $CH_3NO_2$); IR (KBr): $NO_2$ asymmetric stretching vibration band at 1561 $cm^{-1}$ and symmetric band at 1381 $cm^{-1}$; $^1H$ and $^{13}C$ NMR spectra of the complex in $[D_6]Me_2SO$ are of little significance, as they showed only minor chemical shift differences in comparison to those of pure α-CD as well as nitromethane in $[D_6]Me_2SO$, conceivably due to formation — in part at least — of an α-CD–$[D_6]Me_2SO$ complex by displacement of the nitromethane from the cavity. Anal. Calcd for $C_{36}H_{60}O_{30}\cdot CH_3NO_2\cdot 5\ H_2O$ (1123.96): C, 39.54; H, 6.55; N, 1.25. Found: C, 39.61; H, 6.41; N, 1.10.

The complex is stable at room temperature, yet loses nitromethane on heating to 110 °C in vacuum (90% after 12 h).

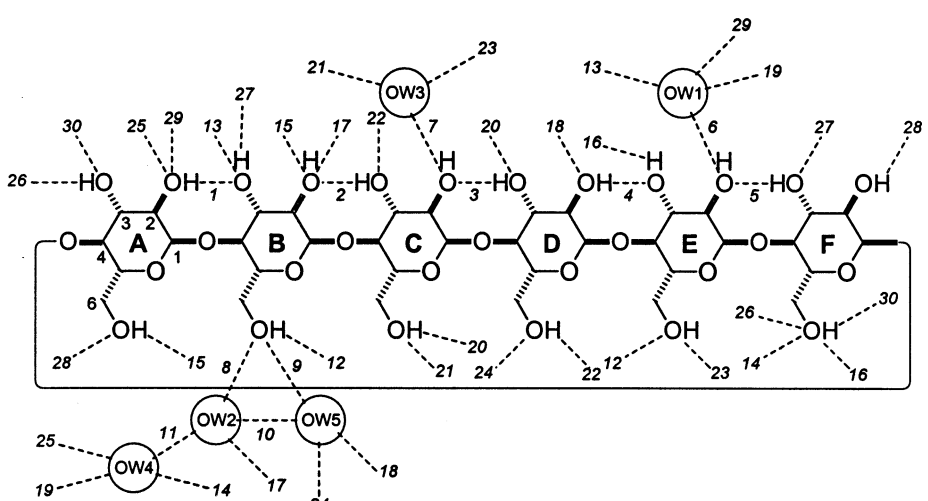



Fig. 3. Scheme of intra- and intermolecular hydrogen bonds in the solid-state structure of the α-CD–nitromethane pentahydrate inclusion complex (**1**). The individual glucose residues are labeled A–F and the water molecules OW1–OW5, the numbers in italics correspond to the indices given in Table 2; 'open-ended' lines indicate H-bonds formed between symmetry related positions. The nitromethane guest molecule is not involved in the hydrogen-bonding pattern.

Table 2
Hydrogen bonds in the solid-state structure of α-CD–nitromethane pentahydrate (**1**), listed for distances $d$(H···O) < 2.5 Å and/or $d$(O···O) < 3.2 Å only; the water molecules are labeled OW1–OW5, the glucose labeling A–F and the indices given in italics in the first column correspond to Fig. 3

| No. (cf. Fig. 3) | Hydrogen bond | $d$(H···O) (Å) [a] | $d$(O···O) (Å) | $\phi$(O–H···O) (°) [a] | Symmetry |
|---|---|---|---|---|---|
| *1* | O(2A)H···O(3B) | 2.505 | 3.177 | 152.4 | b |
| *2* | O(3C)H···O(2B) | 2.295 | 3.030 | 172.5 | b |
| *3* | O(3D)H···O(2C) | 2.308 | 2.932 | 143.1 | b |
| *4* | O(2D)H···O(3E) | 2.192 | 2.899 | 159.9 | b |
| *5* | O(3F)H···O(2E) | 2.217 | 2.949 | 172.0 | b |
| *6* | O(W1)···O(2E) | | 2.755 | | b |
| *7* | O(W3)···O(2C) | | 2.803 | | b |
| *8* | O(W2)···O(6B) | | 2.669 | | b |
| *9* | O(W5)···O(6B) | | 3.092 | | b |
| *10* | O(W5)···O(W2) | | 2.683 | | b |
| *11* | O(W4)···O(W2) | | 2.658 | | b |
| *12* | O(6B)H···O(6E) | 2.136 | 2.864 | 168.8 | c |
| *13* | O(3B)···O(W1) | | 2.834 | | c |
| *14* | O(W4)···O(6F) | | 2.978 | | c |
| *15* | O(6A)H···O(2B) | 2.117 | 2.811 | 157.1 | d |
| *16* | O(3E)H···O(6F) | 2.056 | 2.788 | 172.1 | e |
| *17* | O(2B)···O(W2) | | 2.628 | | e |
| *18* | O(2D)···O(W5) | | 2.657 | | f |
| *19* | O(W1)···O(W4) | | 3.008 | | f |
| *20* | O(6C)H···O(3D) | 2.200 | 2.820 | 142.3 | g |
| *21* | O(6C)···O(W3) | | 2.967 | | g |
| *22* | O(6D)H···O(3C) | 2.341 | 2.927 | 137.4 | h |
| *23* | O(6E)···O(W3) | | 2.780 | | h |
| *24* | O(6D)···O(W5) | | 2.646 | | i |
| *25* | O(2A)···O(W4) | | 2.852 | | j |
| *26* | O(3A)H···O(6F) | 2.262 | 2.833 | 135.1 | k |
| *27* | O(3B)H···O(3F) | 2.366 | 2.817 | 120.9 | k |
| *28* | O(2F)H···O(6A) | 2.030 | 2.744 | 163.1 | k |
| *29* | O(2A)···O(W1) | | 3.196 | | l |
| *30* | O(6F)H···O(3A) | 2.200 | 2.833 | 144.3 | l |

[a] Hydrogen bond H···O distances and O–H···O angles omitted if hydrogen atoms were not located explicitly. Symmetry operations: [b] $x, y, z$. [c] $x, y+1, z$. [d] $x-1, y, z$. [e] $x+1, y, z$. [f] $x+1, y-1, z$. [g] $-x+1, y+1/2, -z+3/2$. [h] $-x+1, y-1/2, -z+3/2$. [i] $-x, y-1/2, -z+3/2$. [j] $x+1/2, -y+3/2, -z+2$. [k] $x+1/2, -y+1/2, -z+2$. [l] $x-1/2, -y+1/2, -z+2$.

*Crystal structure determination.*—Suitable crystals for solid-state structural analysis were obtained by slow crystallization from a 9:1 water–nitromethane solution. A colorless single crystal, of dimensions 0.25 × 0.175 × 0.15 mm, was sealed in the presence of the mother liquor in a thin glass capillary, and then mounted on an Enraf–Nonius CAD-4 diffractometer with graphite-monochromated Mo $K_\alpha$ ($\lambda = 0.71093$ Å) radiation: prisms, orthorhombic, space group $P2_12_12_1$ with $a = 9.452(4)$, $b = 14.299(3)$, and $c = 37.380(10)$ Å, $V = 5052.1(27)$ Å$^3$, $Z = 4$, $T = 298(2)$ K, $\mu$(Mo $K_\alpha$) = 0.126 mm$^{-1}$, and $D_x = 1.465$ Mg m$^{-3}$. A total of 5158 reflections were collected of which 5004 were independent ($R_{int} = 0.1236$). The structure was solved by direct methods using SHELXS-86 [17] and successive Fourier difference synthesis. Refinement (on $F^2$) was performed by full-matrix least-squares method with SHELXL-93 [18]. $R(F) = 0.0812$ for 3270 reflections with $I \geq 2\sigma I$, $\omega R(F^2) = 0.2762$ for 5004 reflections with $\omega = 1/(\sigma^2(F_o^2) + (0.1747P)^2 + 12.1519P$; where $P = (F_o^2 + 2F_c^2)/3$. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were considered in calculated positions with the $1.2 \times U_{eq}$ value of the corresponding atom; hydroxyl protons on the cyclodextrin were treated as idealized OH groups. Data reduction was

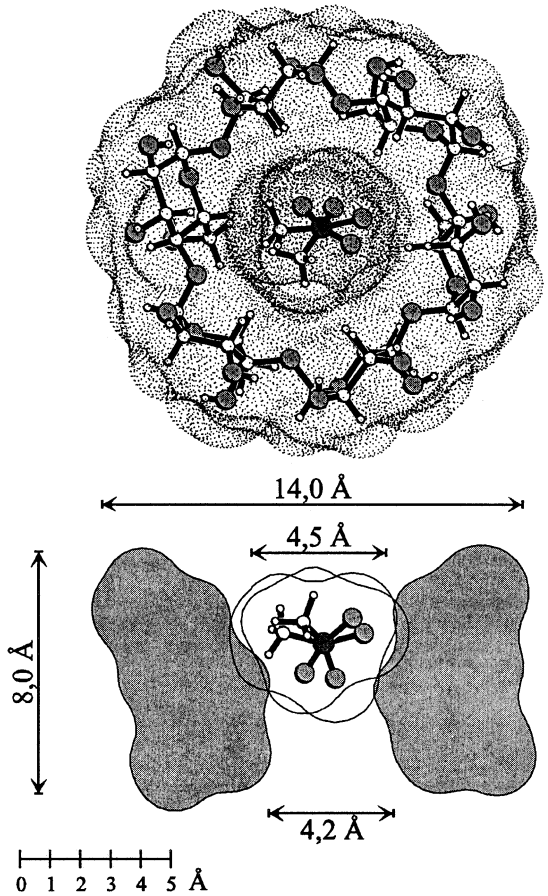



Fig. 4. Topology of the α-CD–nitromethane inclusion complex (**1**) with the water molecules located at the CD outside left off for clarity. Top: Contact surfaces in dotted form with a ball-and-stick model insert, viewed from the wider opening (2-OH/3-OH side) of the truncated cone; oxygen and nitrogen atoms are shaded. — Bottom: Side-view surface cross sections through the complex (2-OH/3-OH face at top); approximate molecular dimensions are given in Å.

done by a Stoe-REDU4 program, for atomic coordinates any further details see Section 5. The molecular graphics of Figs. 1, 2 and 4 were generated by the MolArch$^+$ program [19].

## 5. Supplementary material

Table of atomic coordinates, bond lengths and bond angles have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 136109. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk). Supporting information and additional molecular representations will be provided on the Internet in our graphics gallery at: http://caramel.oc.chemie.tu-darmstadt.de/immel/molcad/gallery.html.

## Acknowledgements

The authors thank the Fonds der Chemischen Industrie, Frankfurt, for support of this work, Mrs Sabine Foro for collecting the crystallographic data, and Dr. T. Wimmer, Wacker-Chemie, Burghausen, for a generous gift of α-CD.

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