Crystal structure of mono(3-amino-3-deoxy)-α-cyclodextrin 5.5 hydrate. Evidence for the ^{3,0}B boat conformation of the altrosamine residue

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The crystal structure of the title compound reveals that the altrosamine residue has a skew ^{3,0}B boat conformation in the elliptically distorted macrocyclic ring.

The chemical modification of cyclodextrins has been extensively studied to improve their unique characteristics by altering the macrocyclic structure or to create new functional materials such as artificial enzymes.[1,2] Cyclodextrins have many hydroxy groups and regioselective modification is essential for the synthesis of functionalized cyclodextrins. The modification of the secondary hydroxy group side, which is wider than the primary hydroxy group side, has received particular attention because the guest molecule can be inserted more easily into the macrocyclic cavity from the wider, secondary hydroxy group side. Amino derivatives are useful as intermediates in the preparation of cyclodextrin derivatives. A commonly used procedure is the ammonolysis of 2,3-manno-epoxide derived from a sulfonyl compound by the treatment with aq. ammonia, which produces an altrosamine residue because of the diaxal opening of the epoxide.[3–5] The conformation of the altrosamine residue has been investigated by NMR spectroscopy and the $^1C_4$ chair conformation has been proposed[5,6] although the possibility of the presence of non-chair geometry is still controversial.[7] X-Ray analysis of mono-(3-amino-3-deoxy)-α-cyclodextrin has been performed to determine the conformation of the altrosamine residue and to evaluate the effect of regioselective modification on the macrocyclic structure.§

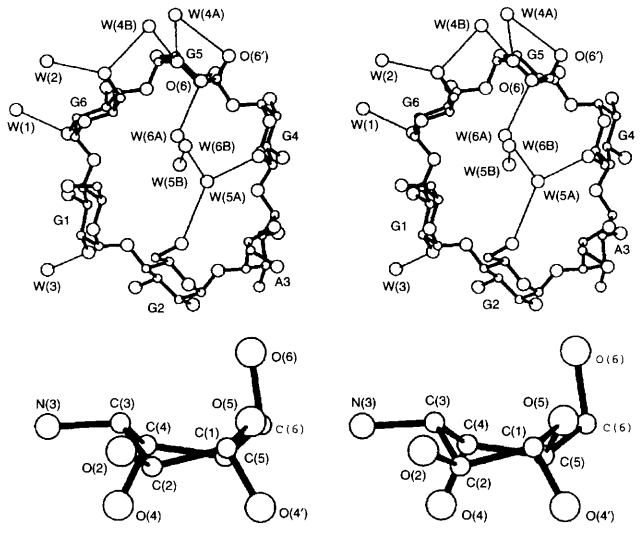

Fig. 1 Stereo-drawing of the structures of mono-(3-amino-3-deoxy)-α-cyclodextrin 5.5 hydrate (upper) and the A3 altrosamine residue (lower). Water molecules are denoted by W(1), W(2)..., with A and B for disordered sites. The disorder of the primary hydroxy group of G5 is denoted by O(6) and O(6'). Host molecules are stacked along the *a* axis to form a head-to-tail channel-type structure and W(5A), W(5B), W(6A) and W(6B) are included in the host column.

Table 1 Torsion angles (°) in the pyranose ring

	^{3,0}B	$^4C_1$[a]
C(1)–C(2)–C(3)–C(4)	70.1	−53.8
C(2)–C(3)–C(4)–C(5)	−44.6	50.8
C(3)–C(4)–C(5)–O(5)	−19.3	−52.1
C(4)–C(5)–O(5)–C(1)	66.1	60.5
C(5)–O(5)–C(1)–C(2)	−40.0	−62.9
O(5)–C(1)–C(2)–C(3)	−26.2	57.3

[a] Values in the G6 residue.

As shown in Fig. 1, the altrosamine residue (A3) is in a skew ^{3,0}B boat conformation. The torsion angles in the ^{3,0}B pyranose ring are given in Table 1 in comparison with those of the $^4C_1$ chair conformation. The C(2)–O(2), C(3)–N(3) and C(5)–C(6) bonds are equatorial while two bonds, C(1)–O(4') and C(4)–O(4), involving the glycosidic linkage, are axial. The amino group is hydrogen-bonded to O(2) of the G2 residue (3.24 Å), but the O(2) hydroxy group is too far from O(3) of the G4 residue (3.58 Å) to form a hydrogen bond. The macrocyclic ring is elliptically distorted. The distance from the centre of the hexagon, composed of six O(4) atoms, to each O(4) atom varies from 3.77 [to O(4) of G4] to 4.86 Å [to O(4) of A3]. The side of the hexagon is in the range 4.08 (G4 residue) to 4.43 (G2 residue) Å. The $O(4_{i-1})$—$O(4_i)$—$O(4_{i+1})$ angle, which is ideally 120°, is 100° at O(4) (A3) and 141° at O(4) (G4). The other four angles are in the range of 111–131°. This geometrical data demonstrates that the conversion of a glucose residue to an altrosamine residue causes a marked change in macrocyclic conformation. The cylindrical shape of the cavity is still conserved because of the equatorial orientation of the C(2)–O(2), C(3)–N(3) and C(5)–C(6) bonds. The stable conformation of altrose has been considered to be $^1C_4$ or $^4C_1$. In the $^4C_1$ conformation, the C(2)–O(2) and C(3)–N(3) bonds are axial and the amino group inside the cavity causes steric hindrance with hydrogen atoms of the adjacent residues. On the other hand, the $^1C_4$ conformation requires the severe distortion of the macrocyclic ring because of the axial C(4)–O(4) bond and equatorial C(1)–O(4') bond. The boat conformation is a less stable intermediate state between the two chair conformations, but when compiled in the cyclodextrin ring it relieves the unfavourable effect, such as the steric hindrance with adjacent residues and the distortion of the macrocycle, which might be caused by the chair conformation.

Footnotes

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§ *Crystal data* for: $C_{36}H_{61}NO_{29}\cdot 5.5H_2O$, M = 1069.9, monoclinic, space group $P2_1$, a = 7.955(1), b = 24.989(2), c = 13.106(1) Å, β = 98.15(1)°, U = 2599(2) Å^3, Z = 2, D_c = 1.367 g cm^{-3}. The crystal was obtained from a 70% aqueous propan-1-ol solution by slow evaporation. X-Ray diffraction data were measured on an Enraf-Nonius CAD4 diffractometer equipped

with an Elliott GX21 generator (40 kV, 50 mA, Cu-Kα radiation, and focal spot size 0.3 × 3 mm) and 3977 unique reflections were collected up to 120° in 2θ. The structure was solved by the molecular replacement method using a computer-generated model of α-cyclodextrin with 6-fold symmetry,[8] and refined by the block-diagonal least-squares method to the R-value of 0.088 for 686 parameters and 3304 reflections with $|F_o| > 3\sigma(F)$. Hydrogen atom positions of methine and methylene groups were calculated and included in the structure factor calculation. The O(6) atom of the G5 residue and water molecules, W(4), W(5) and W(6) were disordered and their occupancy factor was estimated from the peak density in the electron density map. A considerably high temperature factor was observed for the C(6) and O(6) atoms in the G2 residue, however, each of these atoms was observed as a single peak in the electron density map. The computer program used in the structure determination and refinement were those developed in the authors' laboratory. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/180.

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