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Crystal structure of mono[3-(2-imidazolylthio)]-*altro*-β-cyclodextrin: elliptical distortion of the cavity and unique 'Yin–Yang' stacking†‡

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The title compound is elliptically distorted due to the unusual $^1C_4$ geometry of the altrose portion. In packing, a unique fourfold helical structure is elaborated with head-to-head dimers as the repeating motif. The imidazolyl moieties mutually reside on each other's cavities thereby resembling the Yin–Yang type balancing of antagonisms.

In an effort to improve and extend the binding and catalytic capabilities of cyclodextrins (CDs), chemical modifications have been studied to alternate the size and shape of or introduce additional functional moieties to the CD molecule.[1] One way to do this is to convert the CDs to the corresponding 2,3-manno- or 2,3-alloepoxides and then open the epoxide rings with appropriate nucleophiles.[2,3] In each case, a pair of ring-opening products are formed, one with a modified glucopyranoside residue and another with a modified altroside residue (*altro*-CD). These *altro*-CDs have very interesting molecular recognition properties, *e.g. altro*-β-CD can restrict the orientation of a flat guest–substrate molecule, and alter its own conformation to fit better the geometry of a spherical guest.[4,5] However, structural information about these *altro*-CDs is still scarce. The only *altro*-CD derivative X-rayed hitherto has been the mono(3-amino-3-deoxy)-*altro*-α-CD,[6] in which the altrose portion adopts the $^{3,O}B$ twist–boat conformation and the whole molecule has a cavity closely resembling that of α-CD. We here describe the unique X-ray structure of mono[3-deoxy-3-(2-imidazolylthio)]-*altro*-β-CD **1** (Fig. 1) in which the macrocycle is severely distorted towards an elliptical shape and the molecules stack in a novel 'Yin–Yang' packing mode to form fourfold helical columns.

Compound **1** crystallizes with 15.5 H_2O in a tetragonal system (space group $P4_12_12$).§ As shown in Fig. 2, the

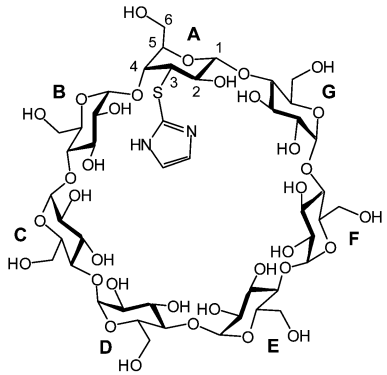

Fig. 1 Chemical structure and numbering scheme of **1**.

2-imidazolylthio group is attached on the C3 of the altrose residue and stretches horizontally over the cavity with its N1 and N2 H-bonded to the O2A and O2B atoms, respectively. The altrose residue is not disordered and a comparison of the dihedral angles around the altropyranose rings elaborates on the fairly perfect adoption of a $^1C_4$ chair conformation. The *trans*-diaxial disposition of O4a and C6a is especially notable and the dihedral angle O4A–C4A–C5A–C6A = 168.3° is indicative of their nearly antiparallel orientations. The equatorial dispositions of O2A, O3A and O4G are strongly supported by their corresponding dihedral angles O5A–C1A–C2A–O2A, O2A–C2A–C3A–C4A, C1A–C2A–C3A–S3A, S3A–C3A–C4A–C5A, O4G–C1A–C2A–C3A and O4G–C1A–O5A–C5A all having the size of 175 ± 3°. The $^1C_4$ chair conformation of altrose residues in the solid state is rare. The only documented case is the crystalline α-cycloaltrin in which the $^1C_4$ and $^4C_1$ conformers coexist.[7]

The $^1C_4$ chair conformation of the altrose part does not affect the $^4C_1$ chair geometries of the six glucose units, as shown with the Cremer–Pople puckering parameters[8] Q, θ (Table 1). However, it causes significant torsional changes of the glycosidic links and thus substantially alters the overall frame of

† Electronic supplementary information (ESI) available: the preparation procedure, NMR spectral data and a crystal cell (Fig. 3S) of compound **1**; 3D chime graphics of the dimeric structure. See http://www.rsc.org/suppdata/cc/b3/b303788f/

‡ According to daoist belief, Yin and Yang are the positive and negative aspects of the universe. Each depends on the other to exist as they are balanced by each other.

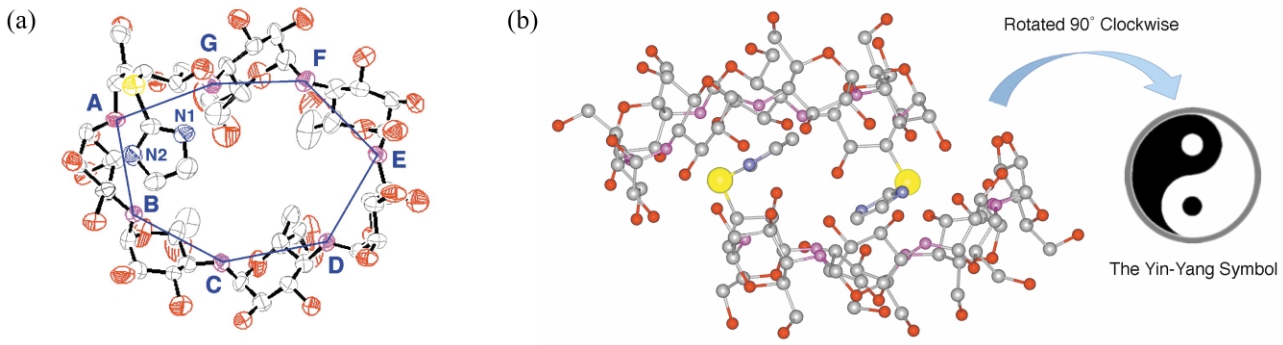

Fig. 2 Crystal structure of **1** with the H atoms and solvent water molecules omitted for clarity. (a) Stereostructure of **1** viewed from the secondary hydroxyl side. Displacement ellipsoids are drawn at the 30% probability level. (b) The novel mutual-locked dimer viewed along the crystallographic C_2 axis with C gray, N blue, O red, O4 pink and S yellow. The scheme on the right is the Yin–Yang symbol of daoism.

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Table 1 Geometrical parameters

Residue	R/Å	φ/°	Q/Å	θ/°	d/Å	ϕ/°	ψ/°	τ/°
A	6.21 (2)	90.8 (1)	0.55	178.7	0.815 (4)	89.8 (7)	162.7 (6)	94.9
B	5.23 (2)	132.7 (1)	0.59	3.4	−0.350 (4)	105.8 (8)	129.7 (8)	115.7
C	4.62 (2)	134.0 (1)	0.53	5.3	−0.555 (4)	111.4 (8)	125.2 (8)	122.6
D	5.15 (2)	131.2 (1)	0.54	6.6	0.517 (4)	95.3 (7)	100.6 (8)	113.1
E	5.75 (2)	105.5 (1)	0.56	9.1	0.568 (4)	89.4 (8)	174.6 (7)	76.4
F	4.13 (2)	124.8 (1)	0.60	4.7	−0.931 (4)	110.2 (8)	135.8 (8)	132.6
G	3.61 (2)	162.7 (1)	0.56	5.4	−0.064 (4)	85.9 (7)	98.5 (8)	134.8
β-CD[a]	5.06 (1)	128.3 (2)	0.56	3.7	0.0 (1)	109.8 (4)	127.6 (8)	101.0

R = distance between O4X and the gravity centre of the seven O4 atoms; φ = vertex angle O4(X−1)–O4X–O4(X+1); Q and θ = Cremer–Pople puckering amplitude; d = deviation of O4X atom from the least-squares mean plane of O4 atoms; ϕ = torsion angle O5(X+1)–C1(X+1)–O4X–C4X; ψ = torsion angle C1(X+1)–O4X–C4X–C3X; τ = angle between the O4 mean plane and the mean plane through the atoms C1X, C2X, C3X, C4X, C5X and O5X.[a] Average values of β-CD hydrate from reference 10.

the macromolecule towards an ellipsoid. This is clearly reflected in the non-regular heptagon formed by the seven intersaccharide oxygens, most notably the very large variations of the vertex angles φ (mean angle 126.0°, max. variation 36.7°). The largest angle O4F–O4G–O4A amounts to 162.7° while ∠O4G–O4A–O4B (90.8°) measures only half this value. The ∠O4D–O4E–O4F (105.5°) on the opposite side is also much smaller than the mean value. In addition, the very large differences in the radii R (distances from seven O4 atoms to their gravity centre, Table 1) also reflect the elliptical distortion of the macrocycle.

The torsion angles[9] ϕ and ψ significantly deviate from the average values of β-CD,[10] indicative of the significant twist of the disaccharide structures. Remarkable deviations of the seven O4 atoms from their mean plane were also detected (Table 1, Fig. 2b). The angle τ between the O4-mean plane and the mean planes through the pyranose ring atoms characterises the relative orientation of the glycosides with respect to the mean plane of the macrocycle. The large positive angles found for glucoses C, F and G indicate that these residues are rotated severely with their C6 side towards the inside of the macrocycle, breaking all other inter-unit O3X···O2(X+1) H-bonds except those within the B–C and F–G disaccharide structures. As a result, the side view of the macrocycle has an elliptically shaped structure in which the glucose E is lifted upwards to the secondary hydroxy side.

The crystal structures of substituted CDs reported hitherto are classified into three types according to the mode of interaction of the substituent group with CD.[11] One is the self-inclusion type in which the substituent is bent into the CD cavity to form an intramolecular host–guest complex. Another is the layer-type in which the CDs are arranged to form molecular layers while the substituents, instead of acting as guests, reside in the intermolecular space of the adjacent layers. The third and most frequently observed structure is the polymeric chain type in which each molecule uses its cavity to accommodate the substituent of the preceding molecule while inserting its own substituent into the cavity of the next. In the present case, two CD molecules related by a crystallographic twofold axis stack together to form a unique mutual-locked dimer which is reminiscent of the 'Yin–Yang' symbol of daoism‡ (Fig. 2b). The imidazolyl group is reciprocally located at the secondary hydroxy side of the counterpart macrocycle. It does not penetrate but resides almost horizontally at the entrance of the counterpart cavity. Intermolecular hydrophobic interaction is suggested by the short distances between the atoms of the imidazolyl and the C and O atoms of the duplicate counterpart. In addition, strong intermolecular H-bonding interactions are detected between O2A···O2A′, O2A···O4G′, O2B···O2E′, O4G···O2A′ and O2E···O2B′. Therefore, the dimeric structure is maintained by intermolecular H-bonding and hydrophobic interactions. This dimer unit is the repeating motif stacking along the fourfold screw axis to form an infinite helix, and within the helical structure is rotated 90° around the column axis with respect to its preceding one (Fig. 3S showing the crystal cell is available as supplementary material†).

In conclusion, we have described the unique solid state structure of mono[3-deoxy-3-(2-imidazolylthio)]-*altro*-β-CD, in which the altroside adopts a fairly perfect $^1C_4$ conformation, not significantly affecting the $^4C_1$ chair geometries of the six glucose residues but distorting the cavity towards an elliptical shape. Two molecules stack together in a novel 'Yin–Yang' mode to form a complementary CD dimer which reiterates towards infinite fourfold helical columns.

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Notes and references

§ Crystal data for $C_{45}H_{72}N_2O_{34}S·15.5H_2O$: M = 1496.35, tetragonal, $P4_12_12$, a = 15.7589(8), b = 53.461(5) Å, V = 13276.7(17) Å^3, T = 173(2) K, Z = 8, λ (Mo-Kα) = 0.71073 Å, 11892 reflections measured, 6735 reflections independent, 2521 reflections with $I > 2\sigma(I)$, R_{int} = 0.0399, $wR(F^2)$ = 0.1294. CCDC 208377. See http://www.rsc.org/suppdata/cc/b3/b303788f/ for crystallographic data in .cif format.

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