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4-Deoxy-4-fluoro-β-D-glucopyranose

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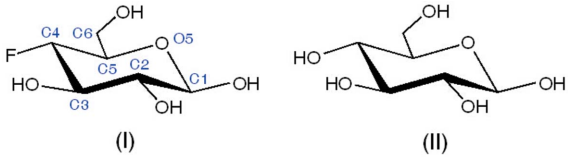
4-Deoxy-4-fluoro-β-D-glucopyranose, $C_6H_{11}FO_5$, (I), crystallizes from water at room temperature in a slightly distorted $^4C_1$ chair conformation. The observed chair distortion differs from that observed in β-D-glucopyranose [Kouwijzer, van Eijck, Kooijman & Kroon (1995). *Acta Cryst.* B**51**, 209–220], (II), with the former skewed toward a $B^{C3,O5}$ (boat) conformer and the latter toward an $^{O5}TB_{C2}$ (twist–boat) conformer, based on Cremer–Pople analysis. The exocyclic hydroxymethyl group conformations in (I) and (II) are similar; in both cases, the O—C—C—O torsion angle is ∼−60° (*gg* conformer). Intermolecular hydrogen bonding in the crystal structures of (I) and (II) is conserved in that identical patterns of donors and acceptors are observed for the exocyclic substituents and the ring O atom of each monosaccharide. Inspection of the crystal packing structures of (I) and (II) reveals an essentially identical packing configuration.

Comment

Fluorosugars find diverse applications in saccharide chemistry and biochemistry (Taylor, 1988), ranging from their use as activated donors in chemical glycosylations (*e.g.*, glycosyl fluorides) (Yokoyama, 2000) to their use as molecular probes of enzyme reaction mechanisms (*e.g.*, a covalent mechanism for lysozyme) (White *et al.*, 1996). In this laboratory, specific fluorosugars have been prepared recently to investigate the mechanisms of protein-bound saccharide rearrangements that accompany non-enzyme-catalyzed protein glycation. One of these fluorosugars, 4-deoxy-4-fluoro-β-D-glucose, (I), crystallizes from water in the β-pyranose form (Fig. 1), which is the predominant tautomer of (I) observed in aqueous solution (∼64%) based on NMR studies (Zhang & Serianni, unpublished results).

An inspection of the Cremer–Pople puckering parameters (Cremer & Pople, 1975) for (I) and for the related aldohexopyranose, β-D-glucopyranose, (II) (Kouwijzer *et al.*, 1995) (Table 1), shows that both structures are slightly distorted $^4C_1$ chair forms ($q_3 >> q_2$). The degree of distortion varies slightly with structure, with $\theta_{II} > \theta_I$. The direction of distortion, embodied in the φ value, is different for (I) and (II), with a boat-like ($B^{C3,O5}$) distortion observed in (I) and a twist–boat ($^{O5}TB_{C2}$) distortion observed in (II) (Fig. 2), based on idealized φ values of 0° for (I) and 330° for (II). Comparison with the crystal structure of 3-deoxy-β-D-*ribo*-hexopyranose (3-deoxy-β-D-glucopyranose; $\theta = 4.80\ (14)°$ and $\varphi = 59.0\ (16)°$; Zhang *et al.*, 2007) shows that C4 fluorination [$\theta = 7.16\ (13)°$] distorts the β-D-glucopyranose ring [$\theta = 8.0\ (3)°$] slightly less than does C3 deoxygenation.



The structural parameters for (I) and (II) are compared in Table 2. The endocyclic C—C bond lengths vary by ∼0.01 Å between the two structures, with the C1—C2, C2—C3 and C4—C5 bonds elongated and the C3—C4 bond shortened in the fluorosugar. The exocyclic C5—C6 bond is essentially unchanged in the two structures. The endocyclic C1—O5 bond

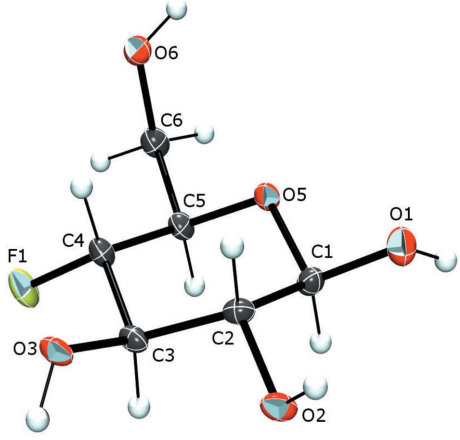


Figure 1
The structure of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. The minor component of the disorder has been removed for clarity.

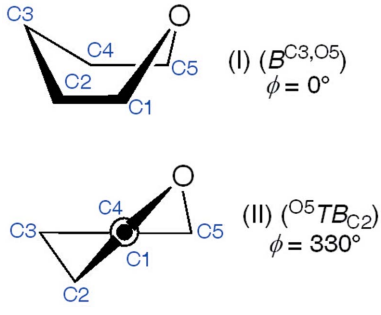


Figure 2
Ring distortions observed in compounds (I) and (II), based on Cremer–Pople parameters. *B* denotes the boat form and *TB* denotes the twist–boat form. The definition of φ is given in Cremer & Pople (1975).

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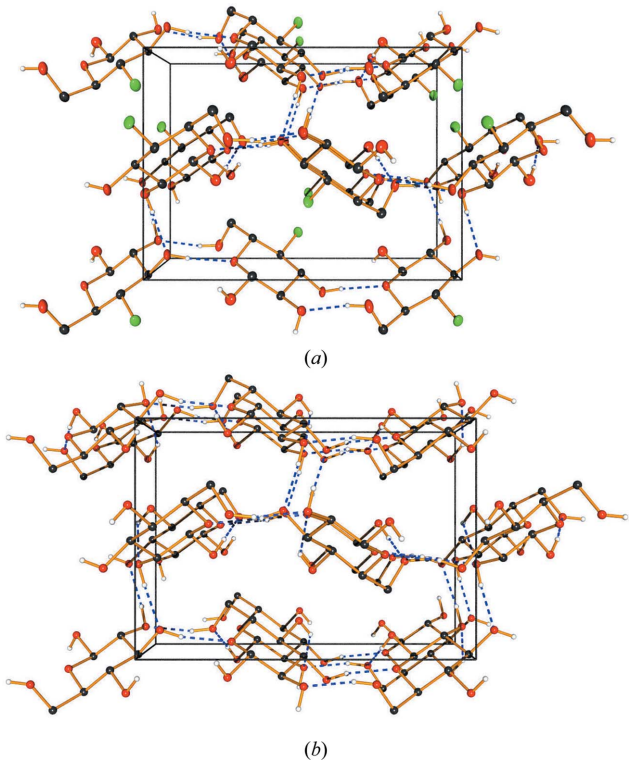

Figure 3
Packing diagrams of (*a*) (I) and (*b*) (II), viewed along the *a* axis. Dashed lines indicate hydrogen bonds.

is ∼0.01 Å longer in (I), whereas the C5—O5 bond is ∼0.01 Å shorter. It is noteworthy that the largest difference in exocyclic C—O bond lengths occurs for C1—O1, which is nearly 0.03 Å shorter in the fluorosugar, (I). This latter effect is notable, considering that the site of F substitution is maximally displaced from the C1—O1 bond in terms of numbers of intervening covalent bonds. As expected, the exocyclic C4—F bond in (I) is about 0.02 Å shorter than the corresponding C4—O4 bond in (II).

Of the three endocyclic C—C—C bond angles, the C3—C4—C5 angle shows the greatest change, increasing by 2.5° in the fluorosugar. In contrast, the exocyclic C4—C5—C6 angle is 1.9° smaller in the fluorosugar. The C4—C5—O5 and C5—O5—C1 angles are essentially the same in (I) and (II).

Endocyclic torsion angles (absolute values) range from 50 to 66° in both (I) and (II), indicative of non-ideal chair conformations. Exocyclic hydroxymethyl conformations in (I) and (II) are *gg* (H5 *anti* to O6), with virtually identical O5—C5—C6—O6 torsion angles [−59.56 (16) and −60.4 (3)°].

All of the hydroxy H atoms in (I) serve as intermolecular hydrogen-bond donors, and atoms O2, O3, O5 and O6 serve as mono-acceptors in intermolecular hydrogen bonds, which link the molecules into a three-dimensional network. Atoms O1 and F do not act as hydrogen-bond acceptors within the hydrogen-bonding scheme. In comparison, all of the hydroxy H atoms in (II) serve as hydrogen-bond donors [the O4···O2′ distance and O4—H4···O2′ angle are 3.122 (3) Å and 140 (4)°, respectively] and atoms O1 and O4 do not act as hydrogen-bond acceptors. Remarkably, the overall packing motifs of (I) and (II) are essentially identical (Fig. 3) and the primary differences are minor changes in the cell parameters, notably a slight contraction of the *b* axis [9.2055 (3) *cf* 9.014 (2) Å] and an expansion of the *c* axis [12.6007 (3) *cf* 12.720 (2) Å] on going from (I) to (II).

The hydroxy atom O1 was found to be disordered over two positions, with the second very minor position with occupancy 0.06 (1) corresponding with the α-anomer. NMR spectra indicate that (I) is chemically pure. However, saccharides are known to undergo spontaneous anomerization in aqueous solution and it is plausible that this occurred during crystallization, resulting in the minor component observed.

Experimental

Synthesis details for the preparation of 4-deoxy-4-fluoro-D-[2-^{13}C]-glucopyranose are given in the *Supplementary material*. After isolation and purification, this ^{13}C isotopomer of (I) was dissolved in a minimal volume of distilled water and the solution was left at room temperature. Crystals of the title β-pyranose, (I), formed slowly and were harvested for structure determination.

Table 1
Cremer–Pople puckering parameters for (I) and (II).

Compound	θ (°)	φ (°)	*Q* (Å)	q_2 (Å)	q_3 (Å)
(I)	7.16 (13)	9.5 (11)	0.5775 (14)	0.0726 (13)	0.5730 (14)
(II)	8.0 (3)	319 (2)	0.580 (3)	0.080 (3)	0.575 (3)

Table 2
Comparison of structural parameters in (I) and (II).

	4-Fluoro-β-D-Glc*p*, (I)	β-D-Glc*p*, (II)
Bond lengths (Å)		
C1—C2	1.5208 (18)	1.511 (4)
C2—C3	1.5286 (19)	1.513 (4)
C3—C4	1.5158 (19)	1.531 (4)
C4—C5	1.5348 (18)	1.519 (4)
C5—C6	1.515 (2)	1.513 (4)
C1—O1	1.3682 (17)	1.394 (4)
C1—O5	1.4415 (16)	1.431 (3)
C2—O2	1.4228 (16)	1.429 (3)
C3—O3	1.4272 (16)	1.427 (3)
C4—F/O4	1.4019 (16)	1.422 (3)
C5—O5	1.4285 (17)	1.439 (3)
C6—O6	1.4286 (19)	1.424 (4)
Bond angles (°)		
C1—C2—C3	111.63 (11)	113.1 (2)
C2—C3—C4	110.13 (11)	109.8 (2)
C3—C4—C5	111.98 (12)	109.5 (2)
C4—C5—O5	108.32 (11)	108.3 (2)
C5—O5—C1	112.60 (10)	112.0 (2)
O5—C1—C2	107.84 (11)	109.3 (2)
C4—C5—C6	113.09 (12)	115.0 (2)
Torsion angles (°)		
C1—C2—C3—C4	−50.81 (14)	−49.7 (3)
C1—O5—C5—C4	64.47 (14)	66.5 (3)
C2—C3—C4—C5	49.68 (14)	52.6 (3)
C2—C1—O5—C5	−65.54 (13)	−61.9 (3)
C3—C4—C5—O5	−55.55 (14)	−60.5 (3)
C3—C2—C1—O5	57.15 (14)	53.2 (3)
C3—C4—C5—C6	−174.82 (12)	−179.8 (3)
O5—C5—C6—O6	−59.56 (15) (*gg*)†	−60.4 (3) (*gg*)†

† *gg* is *gauche–gauche*.

Table 3
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1···O6^{i}	0.84	1.85	2.6855 (14)	174
O2—H2···O3^{ii}	0.84	1.85	2.6847 (14)	169
O3—H3···O5^{iii}	0.84	1.92	2.7511 (13)	173
O6—H6···O2^{iv}	0.84	1.85	2.6796 (14)	170

Symmetry codes: (i) $x-1, y, z$; (ii) $x-\frac{1}{2}, -y-\frac{1}{2}, -z+1$; (iii) $-x+\frac{1}{2}, -y, z+\frac{1}{2}$; (iv) $-x+\frac{1}{2}, -y, z-\frac{1}{2}$.

Crystal data

$C_6H_{11}FO_5$
M_r = 182.15
Orthorhombic, $P2_12_12_1$
a = 6.5323 (2) Å
b = 9.2055 (3) Å
c = 12.6007 (3) Å
V = 757.72 (4) Å^3
Z = 4
Cu $K\alpha$ radiation
μ = 1.35 mm^{-1}
T = 100 K
0.34 × 0.15 × 0.10 mm

Data collection

Bruker APEX diffractometer
Absorption correction: numerical (*SADABS*; Sheldrick, 2008)
T_{min} = 0.725, T_{max} = 0.928
7231 measured reflections
1387 independent reflections
1370 reflections with $I > 2\sigma(I)$
R_{int} = 0.022

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.025
$wR(F^2)$ = 0.067
S = 1.08
1387 reflections
114 parameters
1 restraint
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.28 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}
Absolute structure: Flack (1983), with 542 Friedel pairs
Flack parameter: 0.10 (17)

Hydroxy atom O1 was found to be partially disordered with a very minor α-anomer component. The model was refined with the site occupancies of atoms O1 and O1*A* constrained to sum to unity, yielding values of 0.94 (1) and 0.06 (1), respectively. Due to the weak electron density at the minor component site, the C—O bond distances were restrained to be the same within experimental error and atom O1*A* was refined isotropically. The minor-component bond distances and angles are reported in the archived CIF. H atoms were positioned geometrically and treated as riding, with C—H = 0.99–1.00 Å and O—H = 0.84 Å, and with U_{iso}(H) = 1.2U_{eq}(C,O). The absolute stereochemistry was determined by the known configuration of the initial compound (methyl α-D-[2-^{13}C]galactopyranoside). The stereochemistry was retained throughout the synthesis and the structure of the title compound is in agreement with this assessment. A measurement of the Hooft *y* parameter (Hooft *et al.*, 2008) gives a value of 0.09 (5), and *P*2(true) and *P*3(true) values of 1.000 and 1.000, respectively.

Data collection: *APEX2* (Bruker–Nonius, 2008); cell refinement: *SAINT* (Bruker–Nonius, 2008); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *XP* (Sheldrick, 2008), *POV-Ray* (Cason, 2003) and *DIAMOND* (Brandenburg, 2009); software used to prepare material for publication: *XCIF* (Sheldrick, 2008), *enCIFer* (Allen *et al.*, 2004), *publCIF* (Westrip, 2010) and *PLATON* (Spek, 2009).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FN3060). Services for accessing these data are described at the back of the journal.

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