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6-Deoxy-6-fluoro-D-galactose

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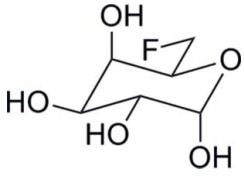
Key indicators: single-crystal X-ray study; T = 150 K; mean σ(C–C) = 0.004 Å; R factor = 0.048; wR factor = 0.119; data-to-parameter ratio = 9.0.

The crystal structure unequivocally confirms the relative stereochemistry of the title compound, $C_6H_{11}FO_5$. The absolute stereochemistry was determined by the use of D-galactose as the starting material. The compound exists as a three-dimensional O—H···O hydrogen-bonded network with each molecule acting as a donor and acceptor for four hydrogen bonds.

Related literature

For literature relating to the biotechnological interconversion of carbohydrates (Izumoring), see: Granström *et al.* (2004); Izumori (2006); Jones *et al.* (2008); Rao *et al.* (2009); Jenkinson *et al.* (2009); Gullapalli *et al.* (2010). For literature relating to fluorosugars, see: Cobb *et al.* (2005); Caravano *et al.* (2009); Brackhagen *et al.* (2001); Taylor & Kent (1958).



Experimental

Crystal data

$C_6H_{11}FO_5$
M_r = 182.15
Orthorhombic, $P2_12_12_1$
a = 6.7928 (3) Å
b = 7.5822 (3) Å
c = 14.1165 (6) Å
V = 727.06 (5) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.16 mm^{-1}
T = 150 K
0.25 × 0.15 × 0.15 mm

Data collection

Area diffractometer
Absorption correction: multi-scan (*DENZO*/*SCALEPACK*; Otwinowski & Minor, 1997)
T_{min} = 0.88, T_{max} = 0.98
6912 measured reflections
978 independent reflections
855 reflections with $I > 2\sigma(I)$
R_{int} = 0.082

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.048
$wR(F^2)$ = 0.119
S = 1.00
978 reflections
109 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.39 e Å^{-3}
$\Delta\rho_{min}$ = −0.33 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O12—H121···O8^{i}	0.82	1.95	2.769 (4)	177
O11—H111···O12^{ii}	0.84	1.96	2.781 (4)	168
O6—H61···O4^{iii}	0.84	1.91	2.747 (4)	174
O8—H81···O6^{i}	0.82	1.93	2.739 (4)	169

Symmetry codes: (i) $x-\frac{1}{2}, -y+\frac{3}{2}, -z+1$; (ii) $-x+1, y-\frac{1}{2}, -z+\frac{3}{2}$; (iii) $x+\frac{1}{2}, -y+\frac{1}{2}, -z+1$.

Data collection: *COLLECT* (Nonius, 2001); cell refinement: *DENZO*/*SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO*/*SCALEPACK*; program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *CAMERON* (Watkin *et al.*, 1996); software used to prepare material for publication: *CRYSTALS*.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: LH5035).

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6-Deoxy-6-fluoro-D-galactose

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S1. Comment

Izumoring, a strategy for the biotechnological interconversion of aldoses, ketoses and alditols (Granström *et al.* 2004, Izumori 2006) allows convenient access to rare monosaccharides. Interconversions are achieved by regioselective microbial oxidation of alditols to give the corresponding ketoses, followed by enzymatic isomerisation to aldoses. Stereochemical diversity is introduced at C-2 in the keto-aldose isomerisation step and at C-3 by the epimerisation of ketoses, catalysed by D-tagatose-3-epimerase. In addition to the simple monosaccharides, this strategy is effective for the interconversion of deoxy (Gullapalli *et al.* 2010, Rao *et al.* 2009), methyl-branched (Jones *et al.* 2008) and azido (Jenkinson *et al.* 2009) sugars.

Fluorosugars have not been isolated from natural sources and consequently, in order to study metabolic processes, their passage along various biological pathways can be effectively tracked with the detection of fluorinated metabolites by ^{19}F NMR (Cobb *et al.* 2005). The fluoro modification of sugars affects their hydrogen bonding capability and fluorosugars have been shown to resemble deoxy sugars such as fucose and rhamnose in terms of enzymatic recognition (Caravano *et al.* 2009). Application of the Izumoring strategy to fluorinated substrates would allow the bulk preparation of fluoro-sugars, an important and interesting class of carbohydrates.

6-Deoxy-6-fluoro-D-galactose was prepared from D-galactose diacetonide **1** (Fig. 1). Fluoride was introduced nucleophilically to give the protected fluorogalactose **2** in 68% yield as previously described for the enantiomer (Brackhagen *et al.* 2001). Dowex resin (H^+) catalysed hydrolysis of the diacetonide gave the free 6-deoxy-6-fluoro-D-galactose **3** in 98% yield.

X-ray crystallography unequivocally confirmed the relative stereochemistry of the title compound. The absolute stereochemistry was determined by the use of D-galactose as the starting material. The compound exists as an extensively hydrogen-bonded lattice with each molecule acting as a donor and acceptor for 4 hydrogen bonds. Only classical hydrogen bonding is considered.

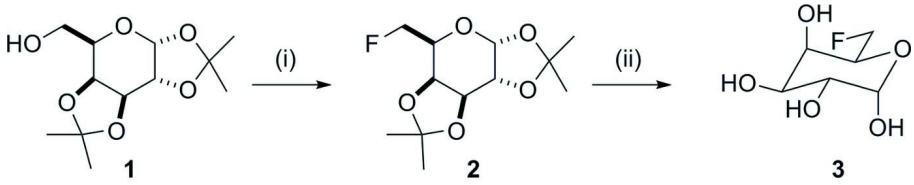
S2. Experimental

The title compound was recrystallised by vapour diffusion from a mixture of ethanol and water [m.p. 431-433 K;$[\alpha]_D^{25}$ initial: +119.8, equilibrium: +69.4 (*c* 1.12, H_2O) {Lit. (Taylor & Kent, 1958) m.p. 433 K; $[\alpha]_D^{20}$ initial: +135, equilibrium: +76.5 (*c* 0.967, H_2O)].

S3. Refinement

In the absence of significant anomalous scattering, Friedel pairs were merged and the absolute configuration was assigned from the use of D-galactose as the starting material.

The H atoms were all located in a difference map, but those attached to carbon atoms were repositioned geometrically. The H atoms were initially refined with soft restraints on the bond lengths and angles to regularize their geometry (C—H in the range 0.93–0.98, O—H = 0.82 Å) and U_{iso}(H) (in the range 1.2–1.5 times U_{eq} of the parent atom), after which the positions were refined with riding constraints.



Reagents and conditions: (i) $(CF_3SO_2)_2O$, pyridine, DCM, -30°C; then TBAF, THF; (ii) Dowex (H^+), H_2O, 1,4-dioxane.

Figure 1
Synthetic Scheme.

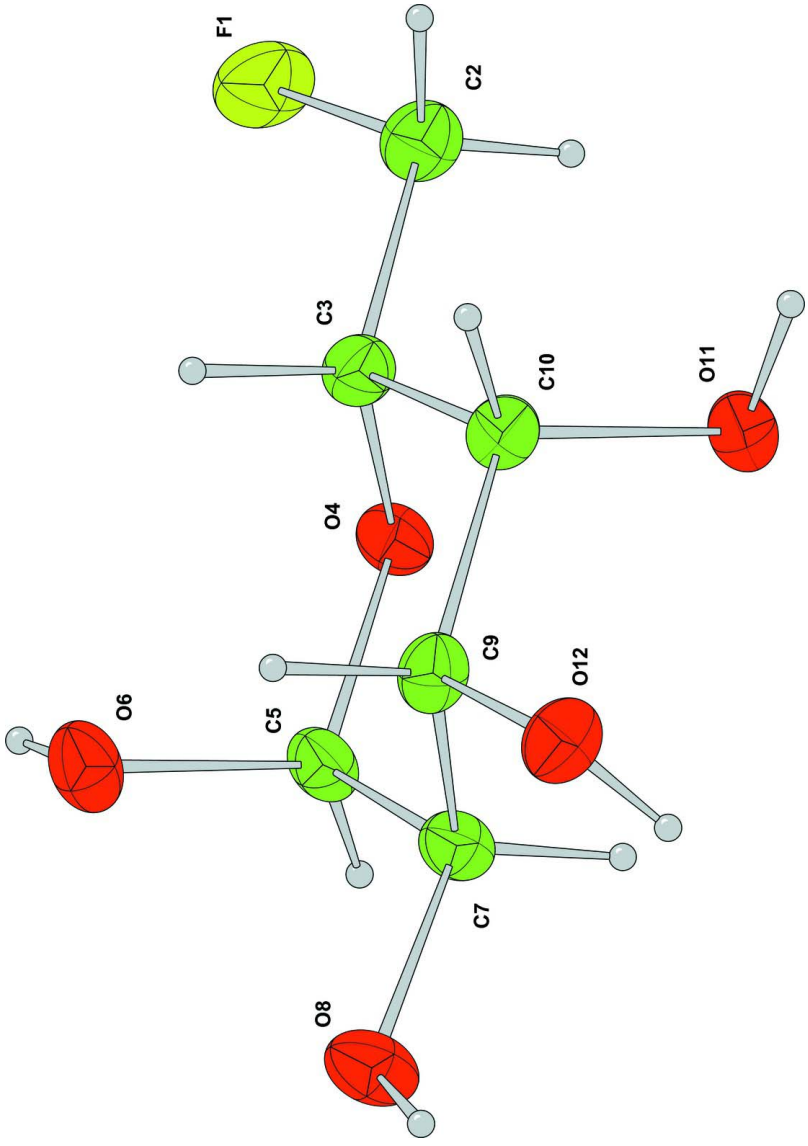


Figure 2

The title compound with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as spheres of arbitrary radius.

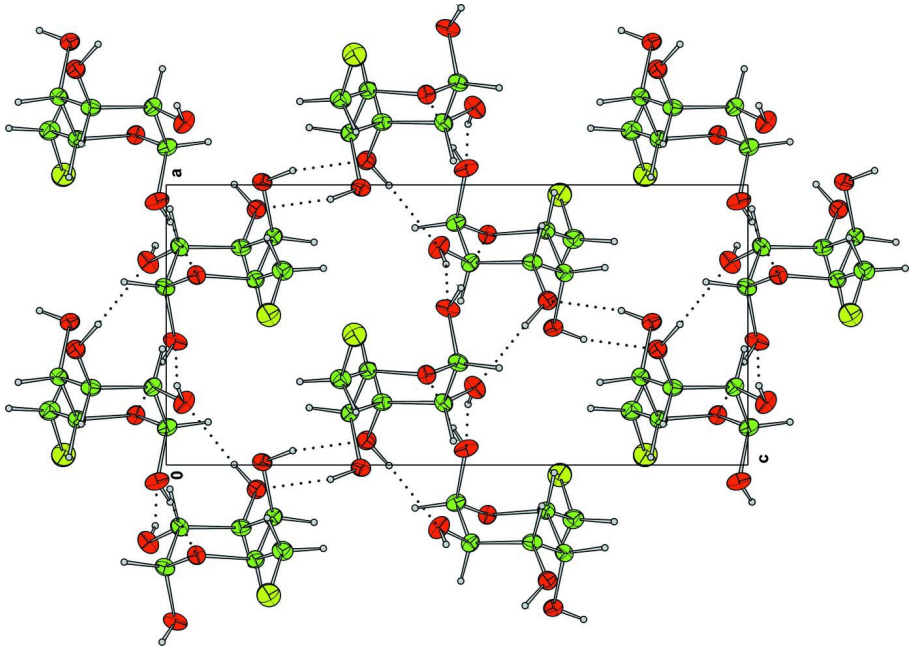


Figure 3

Packing diagram of the title compound projected along the *b*-axis. Hydrogen bonds are shown by dotted lines.

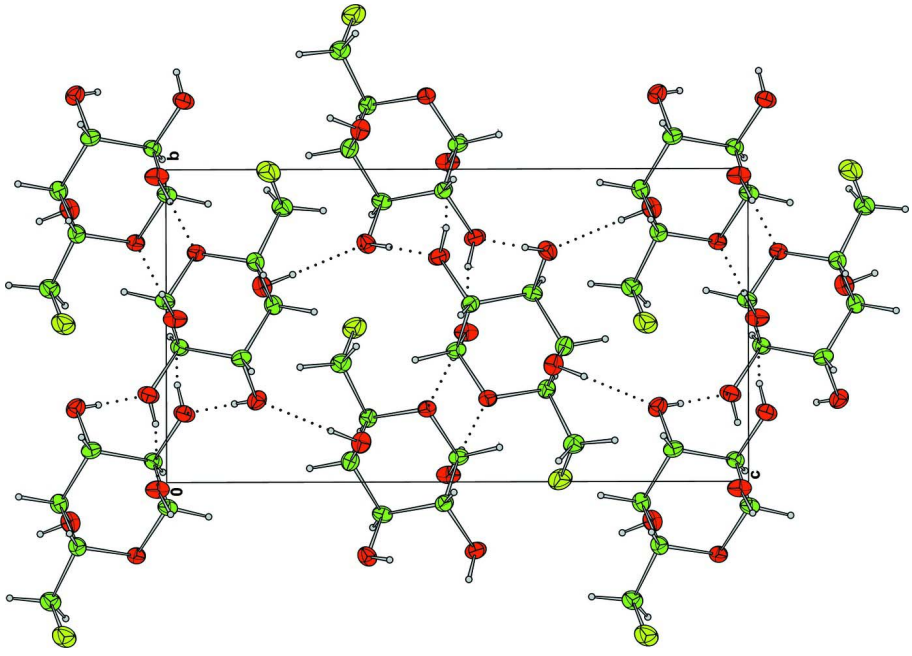


Figure 4

Packing diagram of the title compound projected along the *a*-axis. Hydrogen bonds are shown by dotted lines.

6-Deoxy-6-fluoro-D-galactose

Crystal data

$C_6H_{11}FO_5$
M_r = 182.15

Orthorhombic, $P2_12_12_1$
Hall symbol: P 2ac 2ab

a = 6.7928 (3) Å
b = 7.5822 (3) Å
c = 14.1165 (6) Å
V = 727.06 (5) Å^3
Z = 4
F(000) = 384
D_x = 1.664 Mg m^{-3}

Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 976 reflections
θ = 5–27°
μ = 0.16 mm^{-1}
T = 150 K
Plate, colourless
0.25 × 0.15 × 0.15 mm

Data collection

Area diffractometer
Graphite monochromator
ω scans
Absorption correction: multi-scan (*DENZO*/*SCALEPACK*; Otwinowski & Minor, 1997)
T_{min} = 0.88, T_{max} = 0.98

6912 measured reflections
978 independent reflections
855 reflections with $I > 2\sigma(I)$
R_{int} = 0.082
θ_{max} = 27.4°, θ_{min} = 5.1°
h = −8→8
k = −9→9
l = −18→18

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.048
$wR(F^2)$ = 0.119
S = 1.00
978 reflections
109 parameters
0 restraints
Primary atom site location: structure-invariant direct methods

Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
Method = Modified Sheldrick $w = 1/[\sigma^2(F^2) + (0.06P)^2 + 0.71P]$, where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max}$ = 0.000180
$\Delta\rho_{max}$ = 0.39 e Å^{-3}
$\Delta\rho_{min}$ = −0.33 e Å^{-3}

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	y	z	U_{iso}*/U_{eq}
F1	0.9642 (3)	0.0074 (3)	0.67642 (15)	0.0322
C2	0.8064 (5)	0.1203 (4)	0.7000 (2)	0.0241
C3	0.8368 (5)	0.2957 (4)	0.6533 (2)	0.0197
O4	0.8221 (3)	0.2665 (3)	0.55221 (14)	0.0197
C5	0.8651 (5)	0.4205 (4)	0.4981 (2)	0.0199
O6	1.0586 (3)	0.4776 (3)	0.51563 (17)	0.0249
C7	0.7217 (5)	0.5681 (4)	0.5230 (2)	0.0193
O8	0.7765 (3)	0.7197 (3)	0.46922 (16)	0.0253
C9	0.7242 (5)	0.6033 (4)	0.6292 (2)	0.0196
C10	0.6857 (5)	0.4332 (4)	0.6843 (2)	0.0207
O11	0.4899 (3)	0.3738 (3)	0.66532 (15)	0.0234
O12	0.5874 (3)	0.7379 (3)	0.65554 (15)	0.0225
H21	0.6889	0.0662	0.6738	0.0302*
H22	0.7979	0.1319	0.7701	0.0295*
H31	0.9723	0.3377	0.6670	0.0229*
H51	0.8463	0.3902	0.4278	0.0240*
H71	0.5858	0.5333	0.5064	0.0246*
H91	0.8539	0.6454	0.6460	0.0234*
H101	0.7044	0.4557	0.7541	0.0250*

H121	0.4980	0.7488	0.6170	0.0346*
H111	0.4489	0.3361	0.7175	0.0347*
H61	1.1320	0.3983	0.4931	0.0374*
H81	0.7170	0.8119	0.4811	0.0389*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
F1	0.0339 (11)	0.0274 (10)	0.0352 (11)	0.0100 (9)	0.0011 (9)	0.0051 (9)
C2	0.0227 (16)	0.0222 (15)	0.0273 (15)	0.0057 (15)	0.0012 (14)	0.0016 (13)
C3	0.0187 (14)	0.0211 (14)	0.0193 (14)	0.0019 (13)	0.0003 (12)	0.0014 (12)
O4	0.0221 (11)	0.0165 (10)	0.0205 (10)	−0.0024 (9)	0.0011 (9)	0.0005 (9)
C5	0.0189 (15)	0.0168 (14)	0.0241 (14)	−0.0029 (12)	0.0029 (12)	0.0020 (12)
O6	0.0193 (12)	0.0195 (10)	0.0359 (12)	0.0006 (9)	0.0060 (10)	−0.0002 (9)
C7	0.0205 (16)	0.0171 (14)	0.0204 (14)	0.0006 (12)	0.0028 (12)	0.0018 (12)
O8	0.0307 (12)	0.0176 (10)	0.0277 (11)	0.0021 (10)	0.0077 (10)	0.0035 (9)
C9	0.0172 (15)	0.0171 (14)	0.0246 (15)	0.0033 (13)	0.0001 (12)	−0.0020 (12)
C10	0.0192 (16)	0.0228 (15)	0.0203 (14)	0.0005 (13)	−0.0016 (12)	0.0012 (12)
O11	0.0185 (11)	0.0281 (12)	0.0236 (11)	−0.0034 (10)	0.0013 (9)	0.0023 (10)
O12	0.0220 (11)	0.0230 (11)	0.0226 (10)	0.0054 (10)	−0.0005 (9)	−0.0038 (10)

Geometric parameters (Å, º)

F1—C2	1.412 (4)	C7—O8	1.428 (4)
C2—C3	1.499 (4)	C7—C9	1.522 (4)
C2—H21	0.971	C7—H71	0.988
C2—H22	0.995	O8—H81	0.824
C3—O4	1.448 (3)	C9—C10	1.528 (4)
C3—C10	1.527 (4)	C9—O12	1.430 (4)
C3—H31	0.992	C9—H91	0.967
O4—C5	1.426 (4)	C10—O11	1.430 (4)
C5—O6	1.406 (4)	C10—H101	1.008
C5—C7	1.524 (4)	O11—H111	0.838
C5—H51	1.027	O12—H121	0.820
O6—H61	0.843		
F1—C2—C3	109.2 (3)	C5—C7—C9	110.4 (2)
F1—C2—H21	106.2	O8—C7—C9	112.3 (2)
C3—C2—H21	108.7	C5—C7—H71	110.3
F1—C2—H22	109.4	O8—C7—H71	109.4
C3—C2—H22	111.5	C9—C7—H71	106.9
H21—C2—H22	111.7	C7—O8—H81	116.5
C2—C3—O4	106.8 (2)	C7—C9—C10	110.5 (3)
C2—C3—C10	112.8 (3)	C7—C9—O12	112.0 (2)
O4—C3—C10	109.9 (2)	C10—C9—O12	111.0 (2)
C2—C3—H31	109.1	C7—C9—H91	108.1
O4—C3—H31	107.8	C10—C9—H91	108.0
C10—C3—H31	110.3	O12—C9—H91	107.0

C3—O4—C5	112.9 (2)	C9—C10—C3	108.4 (3)
O4—C5—O6	110.4 (3)	C9—C10—O11	109.2 (3)
O4—C5—C7	110.3 (2)	C3—C10—O11	110.9 (3)
O6—C5—C7	109.3 (2)	C9—C10—H101	109.5
O4—C5—H51	108.0	C3—C10—H101	108.1
O6—C5—H51	110.8	O11—C10—H101	110.7
C7—C5—H51	107.9	C10—O11—H111	104.6
C5—O6—H61	105.5	C9—O12—H121	112.3
C5—C7—O8	107.6 (2)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C2—H21···O12^{i}	0.97	2.60	3.318 (4)	131
C5—H51···O11^{ii}	1.03	2.59	3.320 (4)	128
O12—H121···O8^{iii}	0.82	1.95	2.769 (4)	177
O11—H111···O12^{iv}	0.84	1.96	2.781 (4)	168
O6—H61···O4^{ii}	0.84	1.91	2.747 (4)	174
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Symmetry codes: (i) $x, y-1, z$; (ii) $x+1/2, -y+1/2, -z+1$; (iii) $x-1/2, -y+3/2, -z+1$; (iv) $-x+1, y-1/2, -z+3/2$.