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2-Acetamido-*N*-benzyl-1,4-imino-1,2,4-trideoxy-L-arabinitol 0.33-hydrate

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Key indicators

Single-crystal X-ray study
T = 190 K
Mean σ(C–C) = 0.004 Å
R factor = 0.046
wR factor = 0.112
Data-to-parameter ratio = 10.3

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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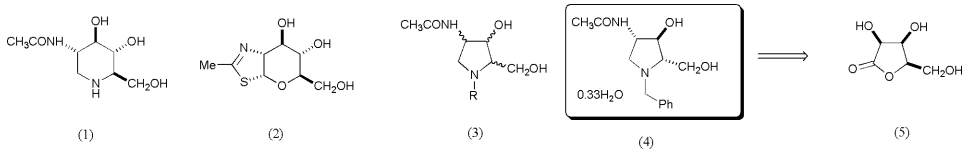
The solid-state conformation of the title compound, $C_{14}H_{20}N_2O_3\cdot0.33H_2O$, a potent hexosaminidase inhibitor, prepared from D-lyxonolactone, has been established by X-ray crystallography. The asymmetric unit contains three molecules, which have very similar conformations, together with a molecule of water.

Comment

β-*N*-Acetylglucosaminidases (NAGs) have attracted considerable research interest as therapeutic targets for some lysosomal storage diseases (Tropak *et al.*, 2004), cancer (Woynarowska *et al.*, 1992) and osteoarthritis (Liu *et al.*, 2001), and as antifungal agents (Horsch *et al.*, 1997) and catalysts for biomass degradation (Kato, Uno *et al.*, 2005). Monosaccharides in which the ring oxygen has been replaced by nitrogen constitute a general class of glycosidase inhibitors (Watson *et al.*, 2001; Asano *et al.*, 2000). All potent inhibitors of NAGs in this class have hitherto been pyranose analogues of NAG such as the piperidine (1) (Fleet *et al.*, 1986) and NAG-thiazoline (Knapp *et al.*, 1996); other heterocyclic compounds containing a pyranose ring (Terinek & Vasella, 2005; van den Berg *et al.*, 2004) also show promise as potential chemotherapeutic agents. In contrast few five-ring pyrrolidine analogues, none of which are potent, have been reported (Croucher *et al.*, 1994; Liessem *et al.*, 1993; Liu *et al.*, 2004).



(1) (2) (3) (4) (5)

A systematic study of the stereoisomers of a set of pyrrolidine analogues, (3), as potential NAG inhibitors (Harding *et al.*, 2005) is in progress. Both enantiomers of imino sugars are frequently inhibitors of the same enantiospecific enzyme (Kato, Kato *et al.*, 2005; Asano *et al.*, 2005; Yu *et al.*, 2004). Solid-state and solution studies of the conformations of the diastereomers of (3) may yield an understanding of this phenomenon; this paper reports the crystal structure of the title compound, (4), which is a potent inhibitor of a number of hexosaminidases, prepared from D-lyxonolactone (5).

The asymmetric unit of (4) contains three sugar molecules (Figs. 1 and 2), together with a solvent water molecule. The water molecule is involved in the hydrogen bonding, and forms part of a hydrophilic layer which is surrounded by the hydrophobic benzyl groups (Figs. 3 and 4). The three independent molecules differ only slightly in conformation from each other, the main difference being that the hydroxyl group

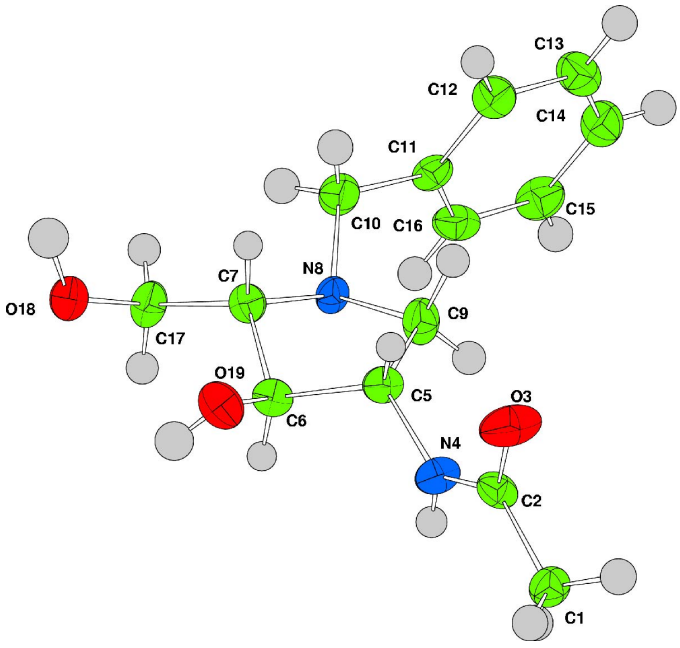


Figure 1
The structure of one molecule, with displacement ellipsoids drawn at the 50% probability level.

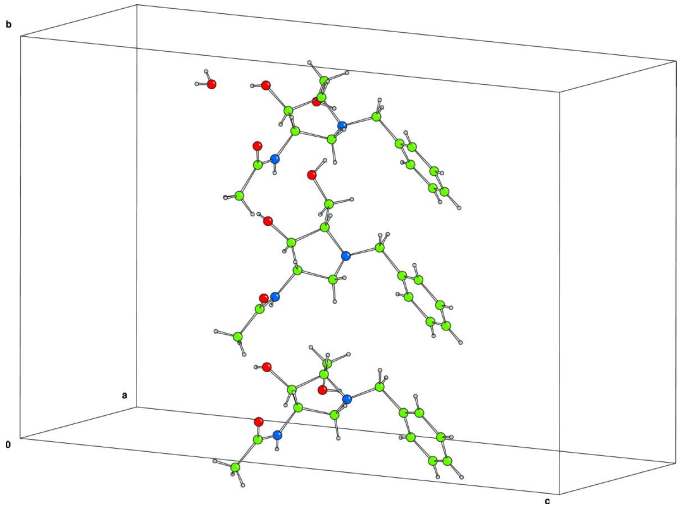


Figure 2
The asymmetric unit, containing three molecules of sugar and a solvent water molecule.

of the middle molecule in Fig. 2 points almost in the opposite direction from that of its counterparts in the other two molecules.

Experimental

A solution of the title compound was dissolved in acetonitrile. The vial was placed inside another vial containing cyclohexane and closed to the atmosphere. This system was then left to undergo competitive diffusion for two weeks. Small amounts of water also found their way into the system. This yielded small plate-like clear crystals of the hydrated title compound. The full experimental method will be published separately (Rountree *et al.*, 2005).

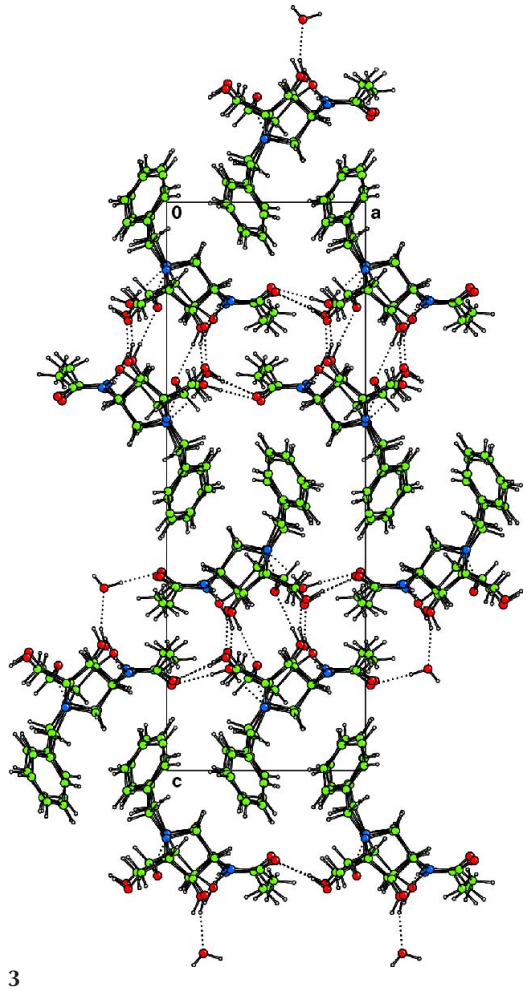


Figure 3
A view down the *b* axis, showing the extensive hydrogen bonding as dashed lines.

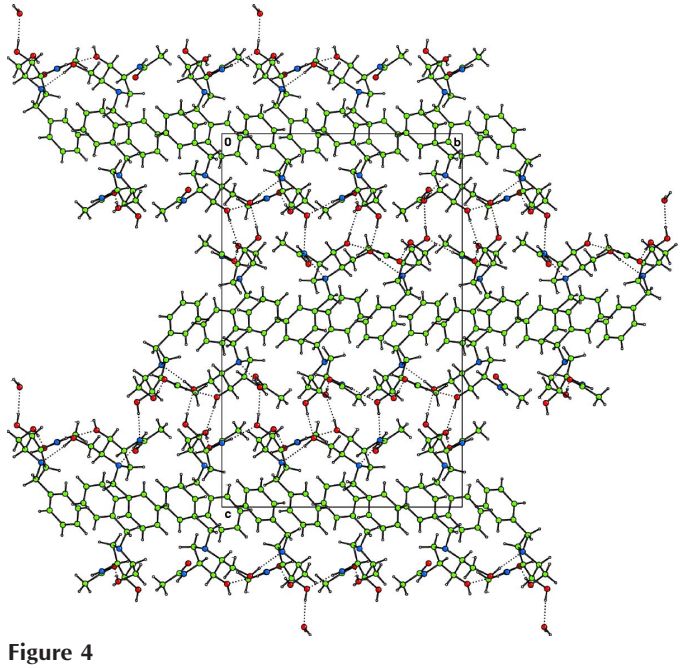


Figure 4
A view down the *a* axis, showing the extensive hydrogen bonding as dashed lines.

Crystal data

$C_{14}H_{20}N_2O_3\cdot H_2O$	D_x = 1.310 Mg m^{-3}
M_r = 270.33	Cell parameters from 5201 reflections
Orthorhombic, $P2_12_12_1$	θ = 1–28°
a = 9.2012 (1) Å	μ = 0.09 mm^{-1}
b = 16.9571 (3) Å	T = 190 K
c = 26.3555 (4) Å	Plate, colourless
V = 4112.13 (10) Å^3	0.20 × 0.20 × 0.05 mm
Z = 12	

Data collection

Nonius KappaCCD diffractometer	5418 independent reflections
ω scans	3417 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (*DENZO*/*SCALEPACK*; Otwinowski & Minor, 1997)	R_{int} = 0.019
	θ_{max} = 27.9°
T_{min} = 0.98, T_{max} = 1.00	$h = -12 \rightarrow 12$
9440 measured reflections	$k = -22 \rightarrow 22$
	$l = -34 \rightarrow 34$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F^2) + (0.06P)^2 + 1.13P]$ where $P = (\max(F_o^2,0) + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.046	
$wR(F^2)$ = 0.112	
S = 0.81	$(\Delta/\sigma)_{max} < 0.001$
5394 reflections	$\Delta\rho_{max}$ = 0.49 e Å^{-3}
523 parameters	$\Delta\rho_{min}$ = −0.52 e Å^{-3}
H-atom parameters constrained	

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

D—H···A	D—H	H···A	D···A	D—H···A
O18—H2···N208	0.87	2.07	2.889 (3)	157
O118—H4···O103^{i}	0.83	1.86	2.683 (3)	174
N104—H6···O219^{ii}	0.85	2.15	2.975 (3)	167
O19—H8···O118^{iii}	0.82	1.92	2.652 (3)	149
O219—H3···O301	0.83	1.91	2.702 (3)	161
O301—H58···N8^{iii}	0.83	2.06	2.887 (3)	174
O301—H67···O3^{iv}	0.83	1.96	2.778 (3)	177
O119—H7···O18^{v}	0.84	1.96	2.799 (3)	175
O218—H62···O203^{i}	0.87	1.99	2.841 (3)	167
N204—H1···O19	0.84	2.25	3.049 (3)	157

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

H atoms were observed in difference electron density maps. They were initially refined with soft restraints on the bond lengths and angles to regularize their geometry [C—H = 0.93–98 Å, N—H = 0.86–0.89 Å and O—H = 0.82 Å, and with U_{iso}(H) in the range 1.2–1.5U_{eq} of the parent atom], after which they were refined with riding constraints. In the absence of significant anomalous scattering effects, Friedel pairs were merged. The absolute configuration is known from the synthesis. Several low-angle reflections were omitted from the refinement because they appeared to be obscured by the beam-stop.

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*.

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