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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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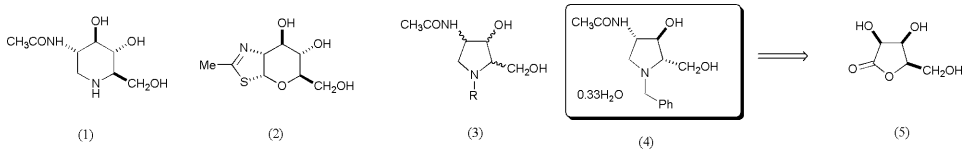
The solid-state conformation of the title compound, $C_{14}H_{20}N_2O_3\cdot0.33H_2O$, a potent hexosaminidase inhibitor, prepared from D-lyxonolactone, has been established by X-ray crystallography. The asymmetric unit contains three molecules, which have very similar conformations, together with a 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 Monosaccharides in which the ring oxygen has been replaced by nitrogen constitute a general class of glycosidase inhibitors (Watson *et al.*, 2001; Asano *et al.*, 2000).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

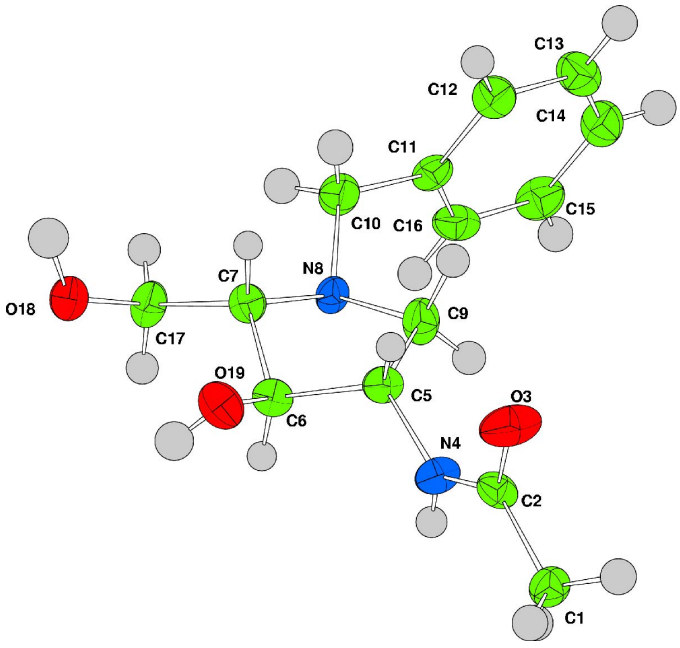


Figure 1
The structure of one molecule, with displacement ellipsoids drawn at the 50% probability level.

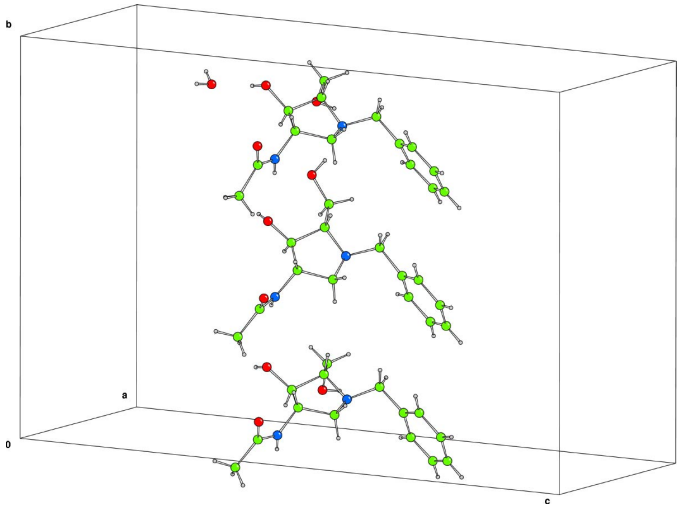


Figure 2
The asymmetric unit, containing three molecules of sugar and a solvent water molecule.

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).

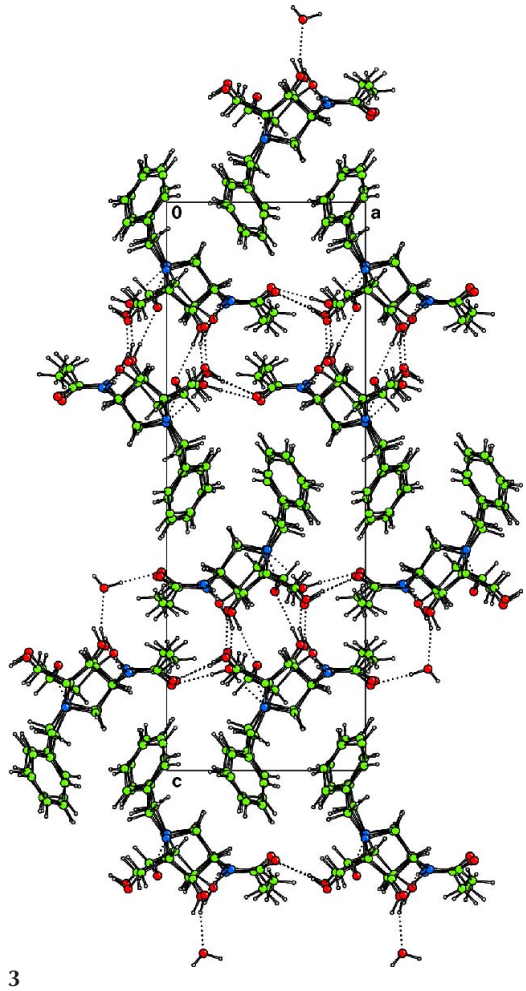


Figure 3
A view down the *b* axis, showing the extensive hydrogen bonding as dashed lines.

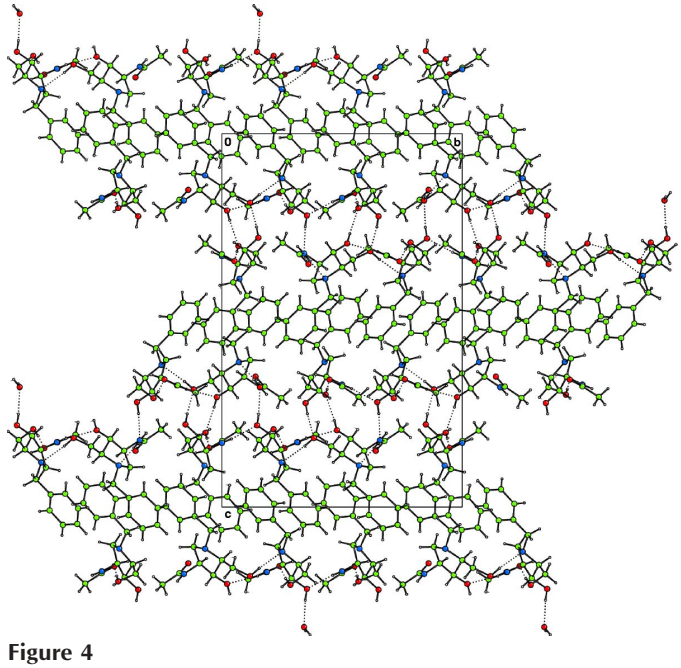


Figure 4
A view down the *a* axis, showing the extensive hydrogen bonding as dashed lines.

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°
	$h = -12 \rightarrow 12$
T_{min} = 0.98, T_{max} = 1.00	$k = -22 \rightarrow 22$
9440 measured reflections	$l = -34 \rightarrow 34$

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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supporting information

Acta Cryst. (2005). E**61**, o1683–o1685 [https://doi.org/10.1107/S1600536805014455]

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

Crystal data

$C_{14}H_{20}N_2O_3{\cdot}0.33H_2O$
$M_r = 270.33$
Orthorhombic, $P2_12_12_1$
Hall symbol: P 2ac 2ab
$a = 9.2012\ (1)$ Å
$b = 16.9571\ (3)$ Å
$c = 26.3555\ (4)$ Å
$V = 4112.13\ (10)$ Å^3
$Z = 12$
$F(000) = 1744$
$D_x = 1.310$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 5201 reflections
$\theta = 1$–$28°$
$\mu = 0.09$ mm^{-1}
$T = 190$ K
Plate, colourless
0.20 × 0.20 × 0.05 mm

Data collection

Nonius KappaCCD diffractometer
Graphite monochromator
ω scans
Absorption correction: multi-scan (DENZO/SCALEPACK; Otwinowski & Minor, 1997)
$T_{min} = 0.98$, $T_{max} = 1.00$
9440 measured reflections
5418 independent reflections
3417 reflections with $I > 2\sigma(I)$
$R_{int} = 0.019$
$\theta_{max} = 27.9°$, $\theta_{min} = 2.3°$
$h = -12 \rightarrow 12$
$k = -22 \rightarrow 22$
$l = -34 \rightarrow 34$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.046$
$wR(F^2) = 0.112$
$S = 0.81$
5394 reflections
523 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F^2) + (0.06P)^2 + 1.13P]$ where $P = (\max(F_o^2,0) + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.000285$
$\Delta\rho_{max} = 0.49$ e Å^{-3}
$\Delta\rho_{min} = -0.52$ e Å^{-3}

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

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.5149 (3)	0.25308 (17)	0.29237 (10)	0.0329
C2	0.5615 (3)	0.32281 (18)	0.32279 (10)	0.0289
O3	0.4747 (2)	0.35991 (14)	0.34941 (9)	0.0519

N4	0.7027 (2)	0.34176 (13)	0.32091 (9)	0.0309
C5	0.7647 (3)	0.40717 (16)	0.34910 (10)	0.0282
C6	0.8564 (3)	0.46433 (16)	0.31777 (10)	0.0281
C7	0.9565 (3)	0.50019 (16)	0.35811 (10)	0.0273
N8	0.9979 (2)	0.42977 (13)	0.38835 (8)	0.0244
C9	0.8629 (3)	0.38251 (18)	0.39366 (11)	0.0358
C10	1.0585 (4)	0.45307 (18)	0.43803 (10)	0.0403
C11	1.0792 (3)	0.38655 (16)	0.47521 (10)	0.0285
C12	1.0064 (3)	0.38837 (18)	0.52135 (10)	0.0353
C13	1.0276 (4)	0.32916 (19)	0.55679 (11)	0.0401
C14	1.1226 (4)	0.26868 (19)	0.54746 (11)	0.0394
C15	1.1986 (4)	0.26671 (18)	0.50188 (12)	0.0396
C16	1.1767 (4)	0.32508 (18)	0.46606 (11)	0.0375
C17	1.0872 (3)	0.54453 (17)	0.33765 (12)	0.0341
O18	1.0444 (3)	0.61741 (12)	0.31503 (7)	0.0409
O19	0.7650 (2)	0.52132 (12)	0.29420 (7)	0.0386
N208	1.0005 (2)	0.75180 (13)	0.38063 (8)	0.0244
C207	0.9854 (3)	0.81926 (16)	0.34541 (10)	0.0266
C206	0.8675 (3)	0.78988 (16)	0.30954 (10)	0.0259
C205	0.7577 (3)	0.75339 (16)	0.34613 (9)	0.0249
C209	0.8489 (3)	0.73235 (18)	0.39399 (10)	0.0289
N204	0.6755 (2)	0.68711 (14)	0.32625 (9)	0.0299
C202	0.5288 (3)	0.68422 (18)	0.32616 (10)	0.0295
O203	0.4525 (2)	0.73913 (13)	0.34197 (8)	0.0397
C201	0.4618 (3)	0.60970 (18)	0.30615 (12)	0.0405
O219	0.8075 (2)	0.85363 (11)	0.28092 (7)	0.0359
C217	1.1263 (3)	0.84554 (17)	0.32032 (12)	0.0342
O218	1.1927 (2)	0.78501 (13)	0.29169 (8)	0.0432
C210	1.0880 (4)	0.77459 (18)	0.42535 (10)	0.0374
C211	1.0966 (3)	0.71239 (17)	0.46650 (10)	0.0285
C216	1.1992 (3)	0.65211 (17)	0.46441 (11)	0.0337
C215	1.2109 (4)	0.59832 (18)	0.50349 (11)	0.0368
C214	1.1181 (4)	0.60225 (19)	0.54500 (11)	0.0380
C213	1.0179 (4)	0.6616 (2)	0.54761 (11)	0.0411
C212	1.0074 (3)	0.71696 (19)	0.50875 (11)	0.0370
N108	1.0078 (2)	0.07278 (13)	0.38870 (8)	0.0258
C107	1.0040 (3)	0.12943 (16)	0.34668 (10)	0.0270
C106	0.8878 (3)	0.09510 (19)	0.31214 (10)	0.0311
C105	0.7724 (3)	0.06519 (17)	0.34883 (10)	0.0275
C109	0.8567 (3)	0.04715 (19)	0.39812 (10)	0.0325
N104	0.6904 (2)	−0.00024 (14)	0.32814 (8)	0.0313
C102	0.5453 (3)	−0.00048 (18)	0.32319 (11)	0.0311
O103	0.4687 (2)	0.05218 (14)	0.34146 (9)	0.0495
C101	0.4821 (3)	−0.06877 (17)	0.29502 (12)	0.0404
O119	0.8274 (2)	0.15171 (13)	0.27873 (8)	0.0480
C117	1.1487 (3)	0.14107 (18)	0.32131 (12)	0.0369
O118	1.2028 (2)	0.06854 (13)	0.30106 (7)	0.0442
C110	1.0773 (4)	0.10462 (18)	0.43404 (10)	0.0395

C111	1.0865 (3)	0.04530 (17)	0.47656 (10)	0.0302
C116	1.1708 (3)	−0.02244 (18)	0.47184 (11)	0.0355
C115	1.1787 (4)	−0.07659 (19)	0.51094 (11)	0.0397
C114	1.1003 (4)	−0.06453 (19)	0.55490 (11)	0.0381
C113	1.0178 (4)	0.0021 (2)	0.56062 (11)	0.0391
C112	1.0117 (3)	0.05756 (18)	0.52194 (11)	0.0363
O301	0.8143 (2)	0.84175 (12)	0.17871 (8)	0.0435
H1	0.7227	0.6480	0.3156	0.0426*
H2	1.0569	0.6556	0.3365	0.0747*
H4	1.2819	0.0625	0.3156	0.0796*
H5	0.7562	0.3146	0.3021	0.0451*
H6	0.7367	−0.0399	0.3174	0.0446*
H8	0.8070	0.5322	0.2678	0.0697*
H11	0.5990	0.2295	0.2776	0.0595*
H12	0.4713	0.2153	0.3137	0.0599*
H13	0.4452	0.2688	0.2667	0.0593*
H51	0.6816	0.4362	0.3627	0.0403*
H61	0.9134	0.4349	0.2925	0.0402*
H71	0.9019	0.5366	0.3803	0.0387*
H91	0.8115	0.3957	0.4260	0.0516*
H92	0.8842	0.3257	0.3925	0.0516*
H101	1.1564	0.4776	0.4316	0.0583*
H102	0.9916	0.4911	0.4534	0.0573*
H121	0.9403	0.4309	0.5280	0.0507*
H131	0.9780	0.3307	0.5877	0.0572*
H141	1.1369	0.2293	0.5713	0.0567*
H151	1.2616	0.2256	0.4943	0.0568*
H161	1.2267	0.3237	0.4351	0.0535*
H171	1.1582	0.5548	0.3646	0.0488*
H172	1.1366	0.5114	0.3110	0.0480*
H2071	0.9472	0.8647	0.3652	0.0382*
H2061	0.9074	0.7501	0.2867	0.0361*
H2051	0.6880	0.7939	0.3544	0.0357*
H2091	0.8194	0.7634	0.4234	0.0406*
H2092	0.8406	0.6766	0.4020	0.0412*
H2171	1.1940	0.8644	0.3477	0.0482*
H2172	1.1052	0.8899	0.2971	0.0482*
H2101	1.0410	0.8220	0.4416	0.0534*
H2102	1.1867	0.7879	0.4140	0.0536*
H2161	1.2620	0.6488	0.4357	0.0478*
H2151	1.2805	0.5584	0.5020	0.0533*
H2141	1.1268	0.5648	0.5707	0.0548*
H2131	0.9561	0.6653	0.5756	0.0590*
H2121	0.9407	0.7583	0.5112	0.0530*
H1071	0.9748	0.1816	0.3600	0.0381*
H1061	0.9294	0.0509	0.2916	0.0443*
H1051	0.7063	0.1087	0.3550	0.0393*
H1091	0.8152	0.0772	0.4267	0.0468*

H1092	0.8515	−0.0091	0.4064	0.0468*
H1011	0.4044	−0.0496	0.2737	0.0731*
H1012	0.4434	−0.1070	0.3176	0.0745*
H1013	0.5540	−0.0937	0.2746	0.0739*
H1171	1.2183	0.1625	0.3457	0.0523*
H1172	1.1361	0.1790	0.2937	0.0524*
H1101	1.1781	0.1186	0.4242	0.0564*
H1102	1.0259	0.1521	0.4460	0.0565*
H1161	1.2258	−0.0319	0.4416	0.0501*
H1151	1.2372	−0.1213	0.5077	0.0562*
H1141	1.1052	−0.1017	0.5803	0.0545*
H1131	0.9685	0.0104	0.5909	0.0570*
H1121	0.9565	0.1042	0.5267	0.0514*
H3	0.8296	0.8469	0.2508	0.0654*
H58	0.8639	0.8667	0.1578	0.0786*
H67	0.7295	0.8480	0.1693	0.0784*
H7	0.8664	0.1445	0.2501	0.0856*
H2011	0.3598	0.6120	0.3030	0.0739*
H15	0.4969	0.5989	0.2729	0.0744*
H19	0.4864	0.5648	0.3257	0.0735*
H62	1.2631	0.7649	0.3092	0.0791*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0295 (16)	0.0326 (15)	0.0365 (15)	−0.0034 (15)	0.0011 (14)	−0.0034 (13)
C2	0.0233 (15)	0.0400 (17)	0.0233 (14)	−0.0007 (14)	0.0025 (13)	−0.0012 (14)
O3	0.0264 (12)	0.0688 (16)	0.0603 (14)	−0.0083 (12)	0.0053 (12)	−0.0318 (13)
N4	0.0222 (13)	0.0337 (14)	0.0369 (13)	0.0001 (11)	0.0006 (12)	−0.0104 (12)
C5	0.0222 (15)	0.0329 (15)	0.0295 (14)	−0.0006 (13)	0.0001 (13)	−0.0043 (13)
C6	0.0247 (15)	0.0315 (15)	0.0280 (14)	0.0034 (13)	−0.0023 (13)	−0.0004 (13)
C7	0.0265 (16)	0.0269 (14)	0.0284 (13)	0.0023 (13)	−0.0005 (13)	0.0024 (13)
N8	0.0211 (12)	0.0256 (11)	0.0266 (11)	−0.0056 (10)	−0.0050 (10)	0.0022 (10)
C9	0.0328 (18)	0.0376 (17)	0.0371 (16)	−0.0100 (15)	−0.0051 (15)	0.0081 (14)
C10	0.052 (2)	0.0366 (17)	0.0321 (15)	−0.0121 (17)	−0.0131 (16)	0.0043 (14)
C11	0.0265 (16)	0.0279 (15)	0.0309 (15)	−0.0037 (13)	−0.0076 (13)	−0.0041 (13)
C12	0.0343 (18)	0.0363 (17)	0.0353 (15)	0.0012 (15)	−0.0028 (15)	0.0008 (14)
C13	0.0390 (19)	0.049 (2)	0.0319 (16)	−0.0034 (18)	−0.0015 (15)	0.0038 (15)
C14	0.045 (2)	0.0359 (18)	0.0375 (17)	−0.0015 (17)	−0.0102 (16)	0.0075 (15)
C15	0.041 (2)	0.0326 (18)	0.0448 (17)	0.0073 (16)	−0.0071 (16)	−0.0041 (16)
C16	0.0405 (19)	0.0434 (18)	0.0287 (15)	−0.0020 (16)	−0.0040 (15)	−0.0075 (14)
C17	0.0318 (16)	0.0290 (16)	0.0415 (16)	−0.0058 (14)	−0.0041 (15)	0.0058 (14)
O18	0.0569 (14)	0.0285 (11)	0.0373 (11)	−0.0037 (11)	0.0019 (11)	0.0040 (10)
O19	0.0360 (12)	0.0448 (13)	0.0349 (10)	0.0071 (11)	−0.0025 (10)	0.0081 (10)
N208	0.0215 (12)	0.0256 (11)	0.0261 (11)	−0.0021 (11)	−0.0037 (10)	−0.0002 (10)
C207	0.0267 (16)	0.0226 (13)	0.0305 (14)	0.0016 (13)	0.0010 (13)	−0.0018 (12)
C206	0.0234 (15)	0.0269 (14)	0.0274 (14)	0.0033 (13)	−0.0030 (12)	0.0011 (13)
C205	0.0209 (14)	0.0270 (14)	0.0268 (14)	0.0023 (13)	−0.0045 (12)	−0.0055 (13)

C209	0.0242 (15)	0.0363 (17)	0.0261 (14)	−0.0024 (13)	0.0010 (12)	0.0013 (13)
N204	0.0220 (13)	0.0307 (13)	0.0369 (13)	−0.0010 (11)	−0.0026 (12)	−0.0008 (12)
C202	0.0263 (16)	0.0364 (16)	0.0256 (14)	0.0012 (14)	−0.0072 (14)	0.0074 (14)
O203	0.0241 (11)	0.0481 (13)	0.0468 (12)	0.0036 (11)	−0.0008 (10)	−0.0061 (11)
C201	0.0290 (17)	0.0357 (18)	0.0567 (19)	−0.0059 (15)	−0.0143 (16)	0.0047 (16)
O219	0.0411 (13)	0.0340 (11)	0.0328 (10)	0.0106 (10)	−0.0008 (10)	0.0051 (9)
C217	0.0321 (16)	0.0335 (16)	0.0371 (16)	−0.0010 (14)	0.0007 (15)	0.0013 (15)
O218	0.0337 (13)	0.0512 (13)	0.0447 (12)	−0.0003 (11)	0.0045 (11)	−0.0075 (11)
C210	0.0388 (18)	0.0368 (17)	0.0366 (16)	−0.0084 (16)	−0.0126 (15)	0.0034 (14)
C211	0.0249 (15)	0.0313 (15)	0.0294 (14)	−0.0027 (14)	−0.0080 (13)	−0.0005 (13)
C216	0.0290 (16)	0.0427 (18)	0.0293 (15)	−0.0016 (15)	−0.0040 (14)	−0.0079 (14)
C215	0.0416 (19)	0.0318 (16)	0.0369 (17)	0.0042 (16)	−0.0102 (16)	−0.0040 (14)
C214	0.0398 (19)	0.0429 (18)	0.0313 (16)	−0.0037 (17)	−0.0121 (15)	0.0035 (15)
C213	0.0312 (18)	0.061 (2)	0.0305 (15)	0.0033 (18)	−0.0027 (15)	−0.0012 (16)
C212	0.0305 (17)	0.0433 (17)	0.0373 (16)	0.0095 (16)	−0.0093 (15)	−0.0046 (15)
N108	0.0212 (12)	0.0284 (12)	0.0278 (11)	−0.0041 (11)	−0.0051 (11)	0.0012 (10)
C107	0.0255 (16)	0.0255 (14)	0.0300 (14)	0.0007 (13)	−0.0035 (13)	0.0001 (13)
C106	0.0206 (15)	0.0456 (18)	0.0270 (14)	0.0077 (14)	−0.0022 (13)	0.0057 (14)
C105	0.0189 (14)	0.0345 (15)	0.0291 (14)	0.0016 (13)	−0.0017 (12)	−0.0013 (13)
C109	0.0262 (16)	0.0454 (18)	0.0259 (14)	−0.0046 (15)	−0.0004 (13)	0.0024 (14)
N104	0.0241 (13)	0.0320 (13)	0.0377 (13)	0.0008 (11)	−0.0028 (11)	−0.0047 (12)
C102	0.0192 (15)	0.0392 (17)	0.0348 (15)	0.0019 (14)	−0.0046 (13)	0.0028 (15)
O103	0.0235 (11)	0.0550 (14)	0.0699 (15)	0.0083 (11)	−0.0075 (11)	−0.0238 (13)
C101	0.0325 (17)	0.0360 (17)	0.0526 (19)	−0.0030 (16)	−0.0099 (16)	−0.0039 (16)
O119	0.0326 (12)	0.0733 (16)	0.0379 (11)	0.0153 (12)	0.0012 (10)	0.0228 (12)
C117	0.0296 (16)	0.0410 (18)	0.0402 (17)	−0.0024 (15)	−0.0004 (15)	0.0103 (16)
O118	0.0261 (11)	0.0673 (16)	0.0392 (11)	0.0075 (12)	−0.0021 (10)	−0.0088 (12)
C110	0.045 (2)	0.0384 (18)	0.0353 (16)	−0.0112 (16)	−0.0175 (16)	0.0008 (15)
C111	0.0321 (16)	0.0309 (16)	0.0275 (14)	−0.0084 (14)	−0.0133 (14)	−0.0001 (13)
C116	0.0394 (18)	0.0383 (17)	0.0288 (15)	−0.0034 (16)	−0.0056 (14)	−0.0036 (14)
C115	0.0407 (19)	0.0382 (18)	0.0400 (17)	0.0059 (16)	−0.0068 (16)	−0.0024 (15)
C114	0.0433 (19)	0.0409 (18)	0.0301 (15)	−0.0017 (17)	−0.0095 (15)	0.0071 (15)
C113	0.0358 (19)	0.0520 (19)	0.0294 (14)	−0.0033 (18)	−0.0050 (14)	−0.0014 (16)
C112	0.0309 (17)	0.0375 (17)	0.0404 (17)	0.0021 (15)	−0.0069 (15)	−0.0058 (15)
O301	0.0327 (12)	0.0586 (15)	0.0392 (12)	−0.0022 (11)	−0.0009 (11)	0.0154 (11)

Geometric parameters (Å, º)

C1—C2	1.491 (4)	O219—H3	0.828
C1—H11	0.954	C217—O218	1.413 (3)
C1—H12	0.941	C217—H2171	1.004
C1—H13	0.970	C217—H2172	0.988
C2—O3	1.235 (3)	O218—H62	0.865
C2—N4	1.339 (4)	C210—C211	1.515 (4)
N4—C5	1.452 (3)	C210—H2101	1.009
N4—H5	0.837	C210—H2102	0.982
C5—C6	1.527 (4)	C211—C216	1.393 (4)
C5—C9	1.539 (4)	C211—C212	1.386 (4)

C5—H51	0.977	C216—C215	1.380 (4)
C6—C7	1.533 (4)	C216—H2161	0.953
C6—O19	1.424 (3)	C215—C214	1.390 (4)
C6—H61	0.984	C215—H2151	0.932
C7—N8	1.485 (3)	C214—C213	1.366 (4)
C7—C17	1.517 (4)	C214—H2141	0.932
C7—H71	0.988	C213—C212	1.393 (4)
N8—C9	1.485 (3)	C213—H2131	0.933
N8—C10	1.477 (3)	C212—H2121	0.933
C9—H91	1.001	N108—C107	1.466 (3)
C9—H92	0.983	N108—C109	1.477 (3)
C10—C11	1.506 (4)	N108—C110	1.459 (3)
C10—H101	1.006	C107—C106	1.520 (4)
C10—H102	0.980	C107—C117	1.503 (4)
C11—C12	1.388 (4)	C107—H1071	0.989
C11—C16	1.396 (4)	C106—C105	1.523 (4)
C12—C13	1.385 (4)	C106—O119	1.416 (3)
C12—H121	0.960	C106—H1061	1.000
C13—C14	1.370 (4)	C105—C109	1.544 (4)
C13—H131	0.933	C105—N104	1.448 (4)
C14—C15	1.390 (5)	C105—H1051	0.970
C14—H141	0.927	C109—H1091	0.987
C15—C16	1.383 (4)	C109—H1092	0.980
C15—H151	0.929	N104—C102	1.342 (4)
C16—H161	0.937	N104—H6	0.845
C17—O18	1.427 (3)	C102—O103	1.235 (3)
C17—H171	0.981	C102—C101	1.493 (4)
C17—H172	1.007	C101—H1011	0.966
O18—H2	0.866	C101—H1012	0.950
O19—H8	0.816	C101—H1013	0.952
N208—C207	1.480 (3)	O119—H7	0.843
N208—C209	1.476 (4)	C117—O118	1.430 (4)
N208—C210	1.479 (3)	C117—H1171	0.977
C207—C206	1.523 (4)	C117—H1172	0.979
C207—C217	1.522 (4)	O118—H4	0.829
C207—H2071	0.995	C110—C111	1.508 (4)
C206—C205	1.528 (4)	C110—H1101	0.992
C206—O219	1.429 (3)	C110—H1102	0.986
C206—H2061	0.976	C111—C116	1.392 (4)
C205—C209	1.557 (4)	C111—C112	1.396 (4)
C205—N204	1.453 (3)	C116—C115	1.382 (4)
C205—H2051	0.965	C116—H1161	0.958
C209—H2091	0.975	C115—C114	1.380 (4)
C209—H2092	0.971	C115—H1151	0.934
N204—C202	1.350 (4)	C114—C113	1.369 (4)
N204—H1	0.842	C114—H1141	0.920
C202—O203	1.238 (3)	C113—C112	1.388 (4)
C202—C201	1.502 (4)	C113—H1131	0.929

C201—H2011	0.943	C112—H1121	0.947
C201—H15	0.951	O301—H58	0.831
C201—H19	0.946	O301—H67	0.826
C2—C1—H11	108.5	C202—C201—H19	112.8
C2—C1—H12	110.0	H2011—C201—H19	108.6
H11—C1—H12	107.7	H15—C201—H19	105.4
C2—C1—H13	110.3	C206—O219—H3	107.8
H11—C1—H13	111.5	C207—C217—O218	112.8 (2)
H12—C1—H13	108.8	C207—C217—H2171	108.0
C1—C2—O3	121.6 (3)	O218—C217—H2171	110.3
C1—C2—N4	116.7 (3)	C207—C217—H2172	108.9
O3—C2—N4	121.7 (3)	O218—C217—H2172	107.9
C2—N4—C5	123.1 (2)	H2171—C217—H2172	108.9
C2—N4—H5	117.4	C217—O218—H62	109.0
C5—N4—H5	119.5	N208—C210—C211	114.7 (2)
N4—C5—C6	115.2 (2)	N208—C210—H2101	108.3
N4—C5—C9	114.4 (2)	C211—C210—H2101	105.9
C6—C5—C9	105.1 (2)	N208—C210—H2102	108.7
N4—C5—H51	105.3	C211—C210—H2102	109.2
C6—C5—H51	108.1	H2101—C210—H2102	110.0
C9—C5—H51	108.5	C210—C211—C216	121.2 (3)
C5—C6—C7	102.1 (2)	C210—C211—C212	120.4 (3)
C5—C6—O19	109.9 (2)	C216—C211—C212	118.3 (3)
C7—C6—O19	112.9 (2)	C211—C216—C215	120.6 (3)
C5—C6—H61	109.8	C211—C216—H2161	119.1
C7—C6—H61	110.5	C215—C216—H2161	120.3
O19—C6—H61	111.3	C216—C215—C214	120.5 (3)
C6—C7—N8	102.0 (2)	C216—C215—H2151	120.2
C6—C7—C17	115.2 (2)	C214—C215—H2151	119.3
N8—C7—C17	112.7 (2)	C215—C214—C213	119.3 (3)
C6—C7—H71	110.6	C215—C214—H2141	119.1
N8—C7—H71	108.4	C213—C214—H2141	121.5
C17—C7—H71	107.7	C214—C213—C212	120.4 (3)
C7—N8—C9	105.7 (2)	C214—C213—H2131	120.1
C7—N8—C10	110.9 (2)	C212—C213—H2131	119.5
C9—N8—C10	112.1 (2)	C213—C212—C211	120.8 (3)
C5—C9—N8	105.8 (2)	C213—C212—H2121	120.1
C5—C9—H91	108.2	C211—C212—H2121	119.1
N8—C9—H91	110.8	C107—N108—C109	107.3 (2)
C5—C9—H92	111.1	C107—N108—C110	112.7 (2)
N8—C9—H92	111.0	C109—N108—C110	112.6 (2)
H91—C9—H92	109.8	N108—C107—C106	102.6 (2)
N8—C10—C11	115.1 (2)	N108—C107—C117	113.6 (2)
N8—C10—H101	107.4	C106—C107—C117	114.0 (2)
C11—C10—H101	107.9	N108—C107—H1071	109.0
N8—C10—H102	107.8	C106—C107—H1071	111.3
C11—C10—H102	107.6	C117—C107—H1071	106.3

H101—C10—H102	111.2	C107—C106—C105	103.7 (2)
C10—C11—C12	119.5 (3)	C107—C106—O119	112.9 (3)
C10—C11—C16	121.8 (3)	C105—C106—O119	110.3 (2)
C12—C11—C16	118.5 (3)	C107—C106—H1061	110.0
C11—C12—C13	120.4 (3)	C105—C106—H1061	111.2
C11—C12—H121	118.8	O119—C106—H1061	108.7
C13—C12—H121	120.7	C106—C105—C109	104.5 (2)
C12—C13—C14	120.8 (3)	C106—C105—N104	112.3 (2)
C12—C13—H131	119.9	C109—C105—N104	115.3 (2)
C14—C13—H131	119.3	C106—C105—H1051	106.9
C13—C14—C15	119.6 (3)	C109—C105—H1051	108.9
C13—C14—H141	120.5	N104—C105—H1051	108.6
C15—C14—H141	119.9	C105—C109—N108	105.8 (2)
C14—C15—C16	120.0 (3)	C105—C109—H1091	110.3
C14—C15—H151	121.1	N108—C109—H1091	109.9
C16—C15—H151	118.9	C105—C109—H1092	110.8
C11—C16—C15	120.7 (3)	N108—C109—H1092	111.7
C11—C16—H161	119.0	H1091—C109—H1092	108.3
C15—C16—H161	120.4	C105—N104—C102	123.9 (3)
C7—C17—O18	111.0 (2)	C105—N104—H6	118.3
C7—C17—H171	110.9	C102—N104—H6	117.8
O18—C17—H171	109.5	N104—C102—O103	121.8 (3)
C7—C17—H172	109.2	N104—C102—C101	116.0 (3)
O18—C17—H172	108.4	O103—C102—C101	122.2 (3)
H171—C17—H172	107.7	C102—C101—H1011	108.4
C17—O18—H2	109.7	C102—C101—H1012	111.3
C6—O19—H8	104.1	H1011—C101—H1012	108.5
C207—N208—C209	103.5 (2)	C102—C101—H1013	110.8
C207—N208—C210	110.4 (2)	H1011—C101—H1013	109.5
C209—N208—C210	112.5 (2)	H1012—C101—H1013	108.1
N208—C207—C206	101.7 (2)	C106—O119—H7	106.9
N208—C207—C217	114.8 (2)	C107—C117—O118	111.2 (2)
C206—C207—C217	115.6 (2)	C107—C117—H1171	109.7
N208—C207—H2071	107.6	O118—C117—H1171	109.7
C206—C207—H2071	109.1	C107—C117—H1172	108.2
C217—C207—H2071	107.6	O118—C117—H1172	109.2
C207—C206—C205	102.2 (2)	H1171—C117—H1172	108.8
C207—C206—O219	110.8 (2)	C117—O118—H4	103.9
C205—C206—O219	112.6 (2)	N108—C110—C111	112.7 (2)
C207—C206—H2061	110.0	N108—C110—H1101	106.5
C205—C206—H2061	111.0	C111—C110—H1101	107.5
O219—C206—H2061	110.0	N108—C110—H1102	110.7
C206—C205—C209	104.3 (2)	C111—C110—H1102	109.6
C206—C205—N204	115.5 (2)	H1101—C110—H1102	109.7
C209—C205—N204	113.3 (2)	C110—C111—C116	121.0 (3)
C206—C205—H2051	107.1	C110—C111—C112	120.6 (3)
C209—C205—H2051	109.8	C116—C111—C112	118.3 (3)
N204—C205—H2051	106.6	C111—C116—C115	120.7 (3)

C205—C209—N208	105.4 (2)	C111—C116—H1161	120.5
C205—C209—H2091	111.7	C115—C116—H1161	118.8
N208—C209—H2091	109.4	C116—C115—C114	120.0 (3)
C205—C209—H2092	110.9	C116—C115—H1151	120.2
N208—C209—H2092	110.1	C114—C115—H1151	119.8
H2091—C209—H2092	109.3	C115—C114—C113	120.3 (3)
C205—N204—C202	123.3 (3)	C115—C114—H1141	118.9
C205—N204—H1	117.4	C113—C114—H1141	120.8
C202—N204—H1	119.2	C114—C113—C112	120.1 (3)
N204—C202—O203	122.6 (3)	C114—C113—H1131	119.4
N204—C202—C201	116.2 (3)	C112—C113—H1131	120.5
O203—C202—C201	121.2 (3)	C111—C112—C113	120.5 (3)
C202—C201—H2011	113.9	C111—C112—H1121	120.1
C202—C201—H15	110.2	C113—C112—H1121	119.4
H2011—C201—H15	105.3	H58—O301—H67	104.7

Hydrogen-bond geometry (Å, º)

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) $x+1, y, z$; (ii) $x, y-1, z$; (iii) $-x+2, y+1/2, -z+1/2$; (iv) $-x+1, y+1/2, -z+1/2$; (v) $-x+2, y-1/2, -z+1/2$.