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2-*C*-Hydroxymethyl-2,3-*O*-isopropylidene-D-mannono-1,5-lactam

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Key indicators

Single-crystal X-ray study
T = 150 K
Mean σ(C–C) = 0.002 Å
R factor = 0.030
wR factor = 0.075
Data-to-parameter ratio = 12.1

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

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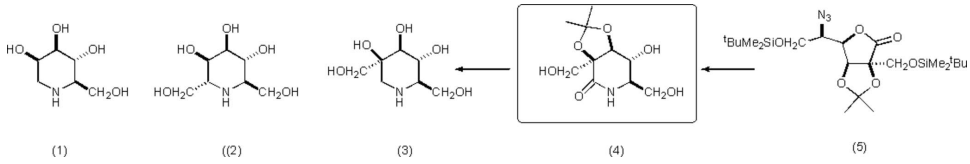
The title compound, $C_{10}H_{17}NO_6$, is an intermediate, with all the stereocentres in place, for a synthesis of a new class of glycosidase inhibitors with a branched carbon chain. Its relative configuration was determined by X-ray crystallography and the absolute configuration by the use of L-sorbose as the starting material.

Comment

Nitrogen analogues of carbohydrates, in which the ring oxygen has been replaced by a basic nitrogen are sugar mimics (Winchester *et al.*, 1992) that can act as glycosidase inhibitors. Such compounds, found widely in plants and bacteria, also have potential as chemotherapeutic agents (Asano, Nash *et al.*, 2000; Asano *et al.*, 2005; Watson *et al.*, 2001). Two natural products, deoxymannojirimycin (DMJ) (1) (Evans *et al.*, 1985) and α-homoDMJ (2) (Asano *et al.*, 2001; Asano, Nishida *et al.*, 2000) are both mannosidase and fucosidase inhibitors (Bruce *et al.*, 1992; Shilvock *et al.*, 1998).



Iso-α-HomoDMJ (3), an isomer of (2) in which a branching hydroxymethyl group is attached to C-2, is being synthesized as a potential mannosidase inhibitor. The azidolactone (5), prepared from L-sorbose, (Hotchkiss *et al.*, 2004; Soengas *et al.*, 2005) on hydrogenation gave an amine from which the silyl ether protecting groups were removed by treatment with tetrabutyl ammonium fluoride. Subsequent heating gave the crystalline lactam (4) as a key intermediate in the preparation of (3) in which all the stereocentres have been introduced. This paper reports the crystal structure of (4), unequivocally establishing the relative stereochemistry of this late-stage intermediate. The absolute configuration of (4) was set by the use of L-sorbose as the synthetic starting material.

In (4), there is a *cis* junction between the two rings and no unusual geometrical features were observed (Fig. 1). The crystal structure consists of hydrogen-bonded sheets of molecules perpendicular to the *c* axis. (Fig. 2 and Table 1) Within the sheets, hydrogen bonds form a discrete donor chain (N5 to O10 to 017 to 07), with O7 also acting as acceptor for a second hydrogen bond from O9. There are no hydrogen bonds between the sheets.

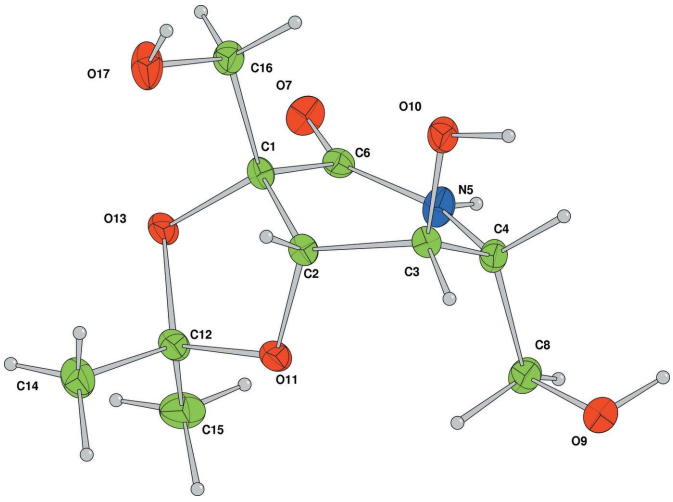


Figure 1
The molecular structure of the title compound, with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as spheres of arbitrary radius.

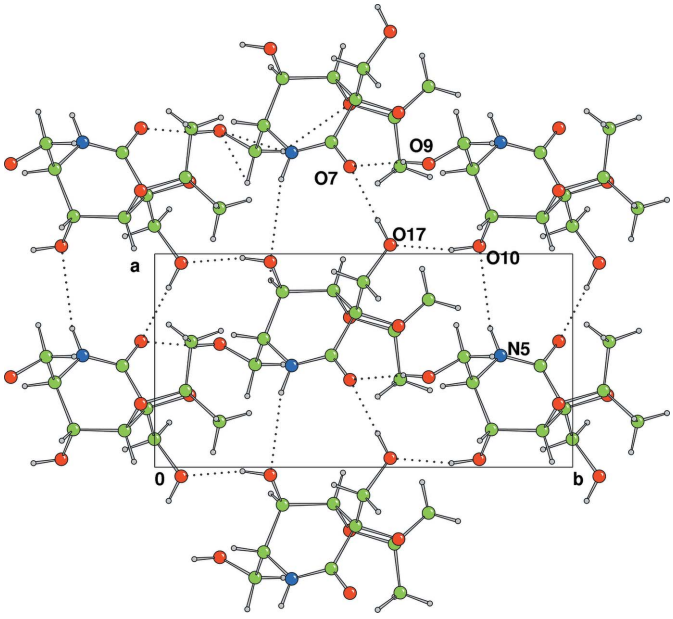


Figure 2
A sheet of molecules joined by hydrogen bonds (dashed lines), shown perpendicular to the *c* axis.

Experimental

Azidolactam (5) (1.22 g, 2.44 mmol) in 1,4-dioxane (10 ml) was hydrogenated for 5 h in the presence of palladium on carbon (10%, 260 mg). The reaction mixture was filtered and the solvent removed; the crude amine in THF (4.5 ml) was treated with tetrabutylammonium fluoride (5.37 ml, 5.3 mmol, 1 *M* solution in THF). After 12 h, the solvent was removed, the residue was dissolved in toluene (50 ml) and the reaction mixture refluxed for 6 h; the solvent was removed and the residue partitioned between dichloromethane (50 ml) and water (2 *x* 50 ml). The combined aqueous phases were evaporated to dryness and purified by flash column chromatography (15% methanol in ethyl acetate) to give the lactam (4) (472 mg, 78% over 3 steps). Crystals for the X-ray study were grown from acetonitrile; m.p. 437 K; $[\alpha]_D^{17}$+33.3 (*c*, 0.98 in MeOH); νmax (Ge plate): 3385 (O—H), 1652 (C═O) cm-1; α_H (CD_3OD, 400 MHz): 1.39, 1.41 (6H, 2 × *s*, 2 × CCH_3), 3.40 (1H, *dt*, H5, $J_{5,6b}$ 4.6 Hz, $J_{5,6a}$, $J_{5,4}$ 6.6 Hz), 3.68 (1H, *d*, H2*a*, $J_{2a,2b}$ 11.0 Hz), 3.69 (1H, *dd*, H6a, $J_{6a,6b}$ 11.3 Hz, $J_{6a,5}$ 6.1 Hz), 3.79 (1H, *d*, H2*b*, $J_{2b,2a}$ 11.0 Hz), 3.84 (1H, *dd*, H6*b*, $J_{6b,6a}$ 11.3 Hz, $J_{6b,5}$ 4.5 Hz), 3.92 (1H, *t*, H-4, $J_{4,5}$, $J_{4,3}$ 6.5 Hz), 4.39 (1H, *d*, H3, $J_{3,4}$ 5.9 Hz); δ_C (CD_3OD, 100.6 MHz): 27.5, 28.1 (2 *x* C*C*H_3), 58.1 (C5), 62.4 (C6), 65.7 (C2), 69.5 (C4), 82.6 (C3), 83.4 (C2), 111.7 (*C*(CH3)2), 173.8 (C1); *m*/*z* (ES+): 270.02 ([*M* + Na]$^+$, 40%), 306.11 ([*M* + MeCN + NH_4]$^+$, 100%); HRMS: $C_{10}H_{17}NO_6Na$ ([*M* + Na]$^+$) calculated 270.0948, found 270.0943.

Crystal data

$C_{10}H_{17}NO_6$
M_r = 247.25
Orthorhombic, $P2_12_12_1$
a = 6.3477 (2) Å
b = 12.4398 (3) Å
c = 14.1469 (5) Å
V = 1117.10 (6) Å^3
Z = 4
D_x = 1.470 Mg m^{-3}
Mo *Kα* radiation
μ = 0.12 mm^{-1}
T = 150 K
Needle, colourless
0.60 × 0.30 × 0.20 mm

Data collection

Nonius Kappa CCD diffractometer
ω scans
Absorption correction: multi-scan (*DENZO/SCALEPACK*; Otwinowski & Minor, 1997)
T_{min} = 0.761, T_{max} = 0.976
6703 measured reflections
1866 independent reflections
1705 reflections with $I > 2\sigma(I)$
R_{int} = 0.027
θ_{max} = 30.0°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.030
$wR(F^2)$ = 0.075
S = 0.99
1858 reflections
154 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F^2) + (0.04P)^2 + 0.2P]$
where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.32 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O10—H1···O17^{i}	0.84	1.91	2.7297 (14)	164
O17—H3···O7^{ii}	0.85	1.82	2.6712 (16)	176
O9—H4···O7^{iii}	0.89	2.04	2.9199 (14)	169
N5—H2···O10^{iv}	0.90	2.50	3.321 (2)	152

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

Five reflections at sin(θ)/λ <0.01 were eliminated as being partially obscured by the incident beam trap. Reflection 022, with F_o = 27.3 and F_c = 34.6, was manually excluded as an outlier. In the absence of significant anomalous scattering, Friedel pairs were merged and the absolute configuration assigned from the known starting material. The H atoms were all located in a difference map, but those attached to C 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 = 0.93–98, N—H = 0.86–0.89 and O—H = 0.82 Å) and isotropic displacement parameters [U_{iso}(H) = 1.2 or 1.5 times U_{eq}(parent atom)], after which they were refined with riding constraints.

Data collection: *COLLECT* (Nonius, 2001); cell refinement: *DENZO/SCALEPACK*; data reduction: *DENZO/SCALEPACK*

(Otwinowski & Minor, 1997); 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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References

Altomare, A., Cascarano, G., Giacovazzo, G., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.

Asano, N., Nash, R. J., Molyneux, R. J. & Fleet, G. W. J. (2000). *Tetrahedron Asymmetry*, **11**, 1645–1680.

Asano, N., Nishida, M., Miyauchi, M., Ikeda, K., Yamamoto, M., Kizu, H., Kameda, Y., Watson, A. A., Nash, R. J. & Fleet, G. W. J. (2000). *Phytochemistry*, **53**, 379–382.

Asano, N., Yamauchi, T., Kagamifuchi, K., Shimizu, N., Takahashi, S., Takatsuka, H., Ikeda, K., Kizu, H., Chuakul, W., Kettawan, A. & Okamoto, T. (2005). *J. Nat. Prod.* **68**, 1238–1242.

Asano, N., Yasuda, K., Kizu, H., Kato, A., Fan, J. Q., Nash, R. J., Fleet, G. W. J. & Molyneux, R. J. (2001). *Eur. J. Biochem.* **268**, 35–41.

Betteridge, P. W., Carruthers, J. R., Cooper, R. I., Prout, K. & Watkin, D. J. (2003). *J. Appl. Cryst.* **36**, 1487.

Bruce, I., Fleet, G. W. J., di Bello, I. C. & Winchester, B. (1992). *Tetrahedron*, **48**, 10191–10200.

Evans, S. V., Fellows, L. E., Fleet, G. W. J. & Shing, T. K. M. (1985). *Phytochemistry*, **24**, 1953–1956.

Hotchkiss, D., Soengas, R., Simone, M. I., van Ameijde, J., Hunter, S., Cowley, A. R. & Fleet, G. W. J. (2004). *Tetrahedron Lett.* **45**, 9461–9464.

Nonius (2001). *COLLECT*. Nonius BV, Delft, The Netherlands.

Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.

Shilvock, J. P., Nash, R. J., Lloyd, J. D., Winters, A. L., Asano, N. & Fleet, G. W. J. (1998). *Tetrahedron Asymmetry*, **19**, 3505–3516.

Soengas, R., Izumori, K., Simone, M. I., Watkin, D. J., Skytte, U. P., Soetaert, W. & Fleet, G. W. J. (2005). *Tetrahedron Lett.* **46**, 5755–5759.

Watkin, D. J., Prout, C. K. & Pearce, L. J. (1996). *CAMERON*. Chemical Crystallography Laboratory, Oxford, England.

Watson, A. A., Nash, R. J. & Fleet, G. W. J. (2001). *Phytochemistry*, **56**, 265–295.

Winchester, B. & Fleet, G. W. J. (1992). *Glycobiology*, **2**, 199–210.

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$c = 14.1469$ (5) Å
$V = 1117.10$ (6) Å^3
$Z = 4$
$F(000) = 528$
$D_x = 1.470$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 1590 reflections
$\theta = 1$–30°
$\mu = 0.12$ mm^{-1}
$T = 150$ K
Needle, colourless
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Data collection

Nonius Kappa CCD diffractometer
Graphite monochromator
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1866 independent reflections
1705 reflections with $I > 2\sigma(I)$
$R_{int} = 0.027$
$\theta_{max} = 30.0°$, $\theta_{min} = 2.2°$
$h = -8\rightarrow8$
$k = -17\rightarrow17$
$l = -19\rightarrow19$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.030$
$wR(F^2) = 0.075$
$S = 0.99$
1858 reflections
154 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F^2) + (0.04P)^2 + 0.2P]$ where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max} = 0.000183$
$\Delta\rho_{max} = 0.32$ e Å^{-3}
$\Delta\rho_{min} = -0.20$ e Å^{-3}

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

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.7247 (2)	0.48062 (10)	0.25243 (9)	0.0135
C2	0.8285 (2)	0.42768 (10)	0.33750 (9)	0.0141
C3	0.8234 (2)	0.30590 (10)	0.33514 (10)	0.0145
C4	0.6020 (2)	0.26077 (10)	0.31981 (9)	0.0157
N5	0.4765 (2)	0.32757 (9)	0.25597 (9)	0.0188

C6	0.5244 (2)	0.42276 (11)	0.21906 (9)	0.0143
O7	0.40987 (18)	0.46718 (8)	0.15911 (8)	0.0205
C8	0.4821 (3)	0.24032 (11)	0.41182 (11)	0.0212
O9	0.5776 (2)	0.15570 (8)	0.46372 (7)	0.0237
O10	0.96288 (17)	0.27672 (8)	0.25926 (7)	0.0195
O11	0.70317 (18)	0.46678 (8)	0.41412 (7)	0.0182
C12	0.6407 (3)	0.57383 (11)	0.39106 (9)	0.0173
O13	0.66274 (18)	0.58309 (8)	0.28953 (7)	0.0171
C14	0.7858 (3)	0.65522 (12)	0.43653 (11)	0.0264
C15	0.4115 (3)	0.58741 (14)	0.41841 (11)	0.0263
C16	0.8685 (2)	0.49940 (11)	0.16772 (11)	0.0173
O17	1.04251 (18)	0.56346 (8)	0.19536 (8)	0.0257
H21	0.9743	0.4504	0.3444	0.0163*
H31	0.8757	0.2777	0.3943	0.0169*
H41	0.6201	0.1893	0.2899	0.0185*
H81	0.3335	0.2214	0.3957	0.0256*
H82	0.4814	0.3071	0.4511	0.0259*
H141	0.7465	0.7256	0.4157	0.0386*
H142	0.9297	0.6397	0.4163	0.0385*
H143	0.7735	0.6469	0.5040	0.0388*
H151	0.3608	0.6581	0.3991	0.0393*
H152	0.3309	0.5335	0.3865	0.0395*
H153	0.3924	0.5736	0.4868	0.0393*
H161	0.9169	0.4290	0.1456	0.0204*
H162	0.7908	0.5347	0.1144	0.0207*
H1	0.9812	0.2099	0.2655	0.0299*
H2	0.3498	0.3028	0.2372	0.0249*
H3	1.1580	0.5333	0.1808	0.0396*
H4	0.5689	0.0948	0.4314	0.0381*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0136 (6)	0.0111 (5)	0.0157 (6)	0.0012 (5)	−0.0012 (6)	−0.0012 (5)
C2	0.0124 (6)	0.0140 (5)	0.0158 (5)	0.0002 (5)	−0.0007 (6)	−0.0010 (5)
C3	0.0146 (6)	0.0136 (5)	0.0154 (5)	0.0001 (5)	−0.0005 (6)	−0.0004 (5)
C4	0.0167 (6)	0.0127 (5)	0.0177 (6)	−0.0018 (5)	0.0006 (6)	0.0009 (5)
N5	0.0151 (6)	0.0180 (5)	0.0233 (6)	−0.0043 (5)	−0.0055 (6)	0.0028 (5)
C6	0.0127 (6)	0.0157 (5)	0.0146 (5)	0.0010 (5)	0.0013 (5)	−0.0009 (5)
O7	0.0163 (5)	0.0232 (5)	0.0220 (5)	0.0004 (4)	−0.0050 (5)	0.0038 (4)
C8	0.0236 (7)	0.0170 (6)	0.0230 (7)	−0.0008 (6)	0.0058 (7)	0.0017 (5)
O9	0.0321 (6)	0.0188 (5)	0.0201 (5)	−0.0026 (5)	0.0029 (5)	0.0015 (4)
O10	0.0199 (5)	0.0138 (4)	0.0249 (5)	0.0019 (4)	0.0076 (5)	0.0001 (4)
O11	0.0252 (5)	0.0148 (4)	0.0148 (4)	0.0033 (4)	0.0015 (5)	−0.0014 (4)
C12	0.0210 (7)	0.0148 (6)	0.0161 (6)	0.0020 (6)	0.0002 (6)	−0.0023 (5)
O13	0.0223 (5)	0.0127 (4)	0.0162 (4)	0.0043 (4)	0.0003 (4)	−0.0018 (3)
C14	0.0368 (9)	0.0201 (6)	0.0223 (7)	−0.0062 (7)	−0.0042 (8)	−0.0037 (6)
C15	0.0239 (8)	0.0316 (8)	0.0235 (7)	0.0056 (7)	0.0046 (7)	−0.0008 (6)

C16	0.0163 (7)	0.0151 (5)	0.0205 (6)	−0.0004 (6)	0.0026 (6)	0.0001 (5)
O17	0.0162 (5)	0.0171 (5)	0.0437 (6)	−0.0042 (4)	0.0085 (6)	−0.0033 (5)

Geometric parameters (Å, º)

C1—C2	1.5220 (18)	C8—H82	1.000
C1—C6	1.535 (2)	O9—H4	0.887
C1—O13	1.4335 (15)	O10—H1	0.844
C1—C16	1.525 (2)	O11—C12	1.4271 (17)
C2—C3	1.5156 (18)	C12—O13	1.4477 (16)
C2—O11	1.4297 (16)	C12—C14	1.512 (2)
C2—H21	0.972	C12—C15	1.515 (2)
C3—C4	1.529 (2)	C14—H141	0.957
C3—O10	1.4381 (17)	C14—H142	0.977
C3—H31	0.967	C14—H143	0.963
C4—N5	1.4633 (18)	C15—H151	0.976
C4—C8	1.529 (2)	C15—H152	0.957
C4—H41	0.992	C15—H153	0.990
N5—C6	1.3295 (17)	C16—O17	1.4170 (17)
N5—H2	0.901	C16—H161	0.980
C6—O7	1.2462 (17)	C16—H162	1.002
C8—O9	1.4196 (18)	O17—H3	0.849
C8—H81	0.998		

C2—C1—C6	113.50 (11)	C4—C8—H82	109.7
C2—C1—O13	102.35 (10)	O9—C8—H82	109.3
C6—C1—O13	107.60 (11)	H81—C8—H82	108.6
C2—C1—C16	115.37 (12)	C8—O9—H4	109.9
C6—C1—C16	109.04 (11)	C3—O10—H1	104.8
O13—C1—C16	108.41 (10)	C2—O11—C12	107.38 (10)
C1—C2—C3	113.95 (11)	O11—C12—O13	105.92 (10)
C1—C2—O11	102.20 (10)	O11—C12—C14	111.01 (12)
C3—C2—O11	110.18 (11)	O13—C12—C14	108.07 (12)
C1—C2—H21	111.4	O11—C12—C15	108.20 (13)
C3—C2—H21	108.2	O13—C12—C15	109.70 (12)
O11—C2—H21	110.8	C14—C12—C15	113.66 (12)
C2—C3—C4	112.94 (12)	C12—O13—C1	108.60 (10)
C2—C3—O10	104.81 (11)	C12—C14—H141	108.8
C4—C3—O10	111.55 (11)	C12—C14—H142	108.2
C2—C3—H31	109.7	H141—C14—H142	109.5
C4—C3—H31	107.8	C12—C14—H143	107.5
O10—C3—H31	110.1	H141—C14—H143	112.5
C3—C4—N5	112.31 (11)	H142—C14—H143	110.2
C3—C4—C8	113.45 (12)	C12—C15—H151	110.2
N5—C4—C8	110.41 (12)	C12—C15—H152	108.3
C3—C4—H41	106.5	H151—C15—H152	108.9
N5—C4—H41	108.0	C12—C15—H153	110.4
C8—C4—H41	105.8	H151—C15—H153	112.9

C4—N5—C6	128.58 (12)	H152—C15—H153	105.9
C4—N5—H2	118.3	C1—C16—O17	109.64 (12)
C6—N5—H2	113.1	C1—C16—H161	107.6
C1—C6—N5	119.10 (12)	O17—C16—H161	110.3
C1—C6—O7	118.97 (12)	C1—C16—H162	111.3
N5—C6—O7	121.92 (13)	O17—C16—H162	110.2
C4—C8—O9	110.54 (12)	H161—C16—H162	107.8
C4—C8—H81	108.4	C16—O17—H3	110.9
O9—C8—H81	110.3		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O10—H1···O17^{i}	0.84	1.91	2.7297 (14)	164
O17—H3···O7^{ii}	0.85	1.82	2.6712 (16)	176
O9—H4···O7^{iii}	0.89	2.04	2.9199 (14)	169
N5—H2···O10^{iv}	0.90	2.50	3.321 (2)	152

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