Synthesis and crystallographic characterization of 6-hydroxy-1,2-dihydropyridin-2-one
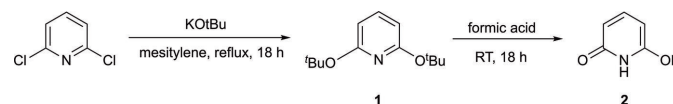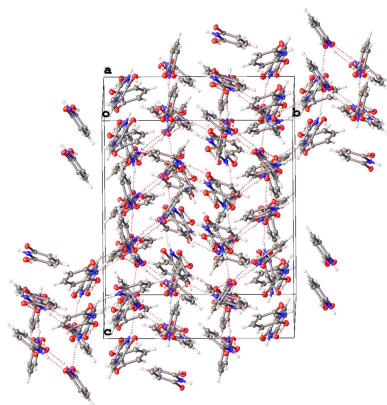
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The title compound, $C_5H_5NO_2$, is a hydroxylated pyridine ring that has been studied for its involvement in microbial degradation of nicotinic acid. Here we describe its synthesis as a formic acid salt, rather than the standard hydrochloride salt that is commercially available, and its spectroscopic and crystallographic characterization.

1. Chemical context

6-Hydroxy-1,2-dihydropyridin-2-one, more commonly known as 2,6-dihydroxypyridine (2,6-DHP), is a derivative of nicotinic acid, a common compound found within personal care products (Behrman & Stanier, 1957; Hicks *et al.*, 2016; Nakamoto *et al.*, 2019). Recent work has focused on the bacterial hydrolysis of nicotinic acid for use in bioremediation efforts (Bokor *et al.*, 2022). Synthesis of 2,6-DHP can be accomplished by reaction between 2,6-dichloropyridine and potassium *tert*-butoxide to afford 2,6-di-*tert*-butoxypyridine (**1**) followed by reaction with formic acid to produce the product **2** as the pyridone tautomer (Scheme 1; Kocienski, 1994). The identification of **2** was confirmed by ^{1}H, ^{13}C and IR spectroscopy. The ^{1}H NMR spectrum suggested a non-symmetric pyridone molecule with an N—H proton at δ = 11.47 ppm. The aromatic region of the spectrum suggested that each of the three protons on the aromatic backbone of **2** were in different chemical environments highlighted by their different chemical shifts of δ = 7.66, 6.91 and 6.60 ppm. These shifts, along with their splitting patterns and coupling constants, are consistent with the structure of **2**. IR spectroscopic data of **2** were also consistent with the overall structure of a pyridone tautomer. Crystals of **2** were grown from slow evaporation of a saturated methanol solution. The solid-state structure of **2** was consistent with the solution state as the title molecule crystallized as the keto tautomer.

Scheme 1

2. Structural commentary

The structure of 2,6-dihydroxypyridine (Fig. 1) shows the expected 2,6-disubstitution of the pyridine ring. The bond

Table 1
Selected geometric parameters (Å, °) for **2**.

O9—C21	1.2789 (12)	N5—C21	1.3688 (12)
O10—C25	1.3193 (12)	N5—C25	1.3557 (12)
C25—N5—C21	124.86 (9)	N5—C21—C22	116.60 (8)
C21—N5—H5	117.3 (8)	O10—C25—N5	114.23 (8)
C25—N5—H5	117.8 (8)	O10—C25—C24	126.58 (9)
O9—C21—N5	117.12 (9)	N5—C25—C24	119.19 (9)
O9—C21—C22	126.28 (9)		

lengths and angles are routine for nitrogen-containing aromatic compounds (Table 1).

3. Supramolecular features

There are six independent molecules in the asymmetric unit of **2**; of these, two pairs of molecules are each held together by O—H···O hydrogen bonds. In both instances, the H atoms in the hydrogen bonds are disordered over two positions with refined occupancies of 0.51 (3) and 0.49 (3) at the O6 and O7 sites, respectively, and 0.39 (3) and 0.61 (3) at the O2 and O3
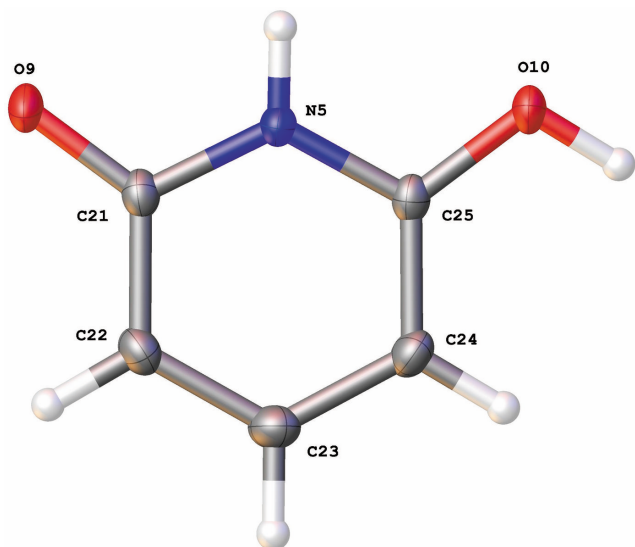
Table 2
Hydrogen-bond geometry (Å, °) for **2**.

D—H···A	D—H	H···A	D···A	D—H···A
O2—H2A···O3	0.84 (2)	1.60 (2)	2.4317 (10)	174 (4)
N1—H1···O9[i]	0.88 (1)	1.98 (1)	2.8606 (11)	175 (1)
O3—H3···O2	0.87 (2)	1.57 (2)	2.4317 (10)	176 (3)
O4—H4···O5[ii]	0.981 (14)	1.500 (14)	2.4768 (10)	173.5 (14)
N2—H2···O1[iii]	0.89 (1)	1.89 (1)	2.7554 (11)	166 (1)
O6—H6···O7	0.86 (1)	1.58 (1)	2.4381 (10)	177 (3)
N3—H3B···O11[iv]	0.87 (1)	1.95 (1)	2.8155 (11)	170 (1)
O7—H7A···O6	0.88 (2)	1.56 (2)	2.4381 (10)	179 (3)
O8—H8A···O9[v]	0.91 (1)	1.58 (1)	2.4803 (10)	175 (1)
N4—H4A···O10[i]	0.87 (1)	2.07 (1)	2.8999 (11)	161 (1)
O10—H10···O11[iv]	0.95 (1)	1.52 (1)	2.4690 (9)	176 (1)
N5—H5···O2[i]	0.88 (1)	1.90 (1)	2.7699 (11)	167 (1)
O12—H12A···O1[iii]	0.90 (1)	1.61 (1)	2.5057 (10)	178 (2)
N6—H6A···O5[vi]	0.88 (1)	1.91 (1)	2.7893 (11)	172 (1)

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

sites, respectively. The molecules pack together in the solid state with intermolecular O—H···O and N—H···O inter-actions (Table 2 and Fig. 2). The crystal packing of the title compound involves no π–π ring interactions (Fig. 3).

4. Hirshfeld surface analysis

The Hirshfeld surface analysis of **2** was performed and the associated two-dimensional fingerprint plots were generated using *Crystal Explorer 21.5* software (Spackman *et al.*, 2021). Visualizations used a red–white–blue color scheme where red indicates shorter contacts, while blue indicates longer contacts. There are four red spots on the d_{norm} surface (Fig. 4*a*) and these spots indicate the direction and strength of the inter-

Figure 1
A view of **2** showing the atom-numbering scheme for one independent molecule. Displacement ellipsoids are drawn at the 50% probability level.
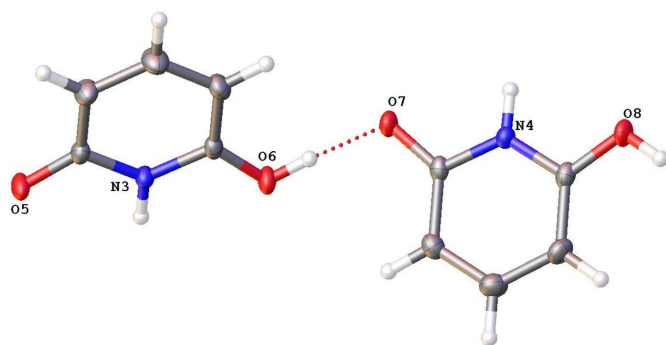

Figure 2
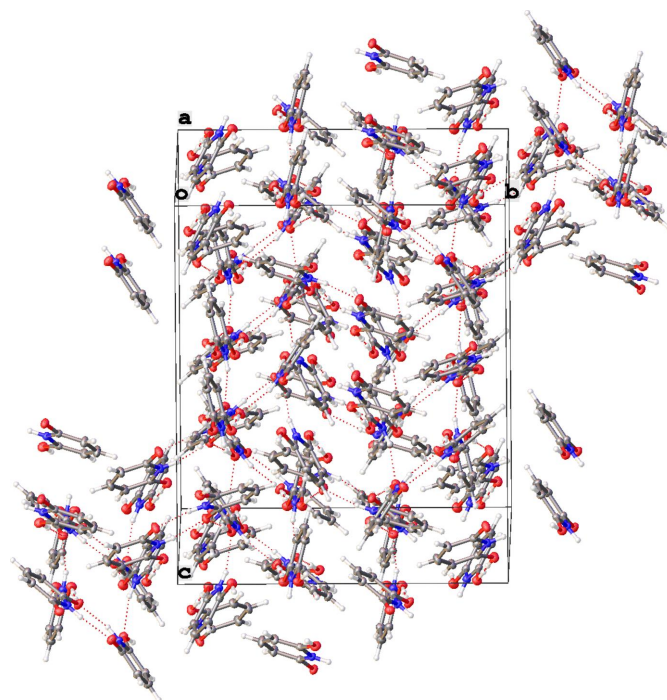A view of the intermolecular interactions in **2**.

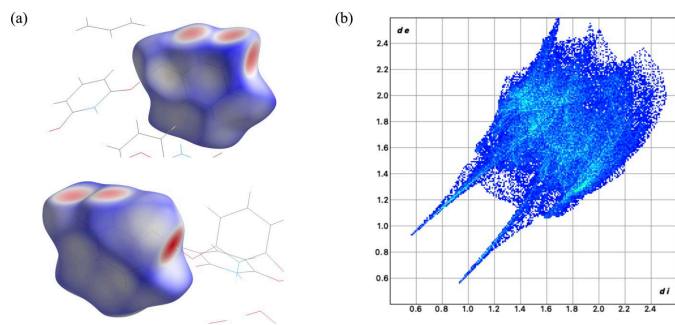

Figure 3
A view of the molecular packing in **2**.

Figure 4
(*a*) Hirshfeld surface representations of **2** with the function d_{norm} plotted onto the surface indicating the $E-H\cdots O$ (E = N, O) interactions; (*b*) two-dimensional fingerprint plot.

molecular $E-H\cdots O$ (E = N, O). The two-dimensional fingerprint plots are shown in Fig. 4*b*. The resulting fingerprint plot indicates strong $O\cdots H$ interactions, as shown by the two prominent spikes on either side of the diagonal. The $N\cdots H$ interactions are shown in the 'wings' of the plot and are not as prominent as the $O\cdots H$ interactions.

5. Database survey

A search for the pyridone tautomers of relatively simple dihydroxy-substituted pyridines in the Cambridge Structure Database (CSD version 5.44, last update April 2023; Groom *et al.*, 2016) revealed 23 crystal structures. Nearly all these structures have $N-H\cdots O$ and $O-H\cdots O$ hydrogen-bonding motifs, similar to those observed in the title compound. The structures with dissimilar motifs involve intermolecular inter-actions with solvent molecules or intramolecular hydrogen bonding. The closest analogues to **2** were found to be GUBKIZ and NOQGOR (Gerhardt & Bolte, 2015); these structures contain $N-H\cdots O$ and $O-H\cdots O$(solvent) hydrogen-bonding motifs.

6. Synthesis and crystallization

1: A 100 mL round-bottom flask equipped with a stir bar was charged with 2,6-dichloropyridine (1.00 g, 6.80 mmol, 1 eq) and 15 mL of mesitylene solvent. To the solution was added potassium *tert*-butoxide (1.52 g, 13.6 mmol, 2.1 eq). The solution was then refluxed under N_2 for 18 h. A color change from colorless to deep red was observed. After 18 h, the solution was allowed to cool to room temperature and the solution was washed with water (3 × 20 mL). The organic layer was collected, dried over sodium sulfate and used without purification in step 2.

2: To the crude solution from step 1 in a 20 mL scintillation vial was added formic acid (1.00 mL, 17.8 mmol, 2.6 eq). The bi-layered solution was stirred in air at high speed for 18 h when a solid precipitate formed. The solid was collected and dried under vacuum to yield 0.180 g (17% over 2 steps).

Table 3
Experimental details.

Crystal data	
Chemical formula	$C_{30}H_{30}N_6O_{12}$
M_r	666.60
Crystal system, space group	Monoclinic, $P2_1/n$
Temperature (K)	100
a, b, c (Å)	9.58785 (4), 16.83642 (8), 19.55978 (10)
β (°)	103.7319 (5)
V (Å^3)	3067.19 (3)
Z	4
Radiation type	Cu $K\alpha$
μ (mm^{-1})	0.97
Crystal size (mm)	0.38 × 0.12 × 0.10
Data collection	
Diffractometer	XtaLAB Synergy, Dualflex, HyPix
Absorption correction	Gaussian (*CrysAlis PRO*; Rigaku OD, 2021)
T_{min}, T_{max}	0.453, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	83138, 6554, 6155
R_{int}	0.035
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.635
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.032, 0.083, 1.02
No. of reflections	6554
No. of parameters	477
No. of restraints	14
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}, \Delta\rho_{min}$ (e Å^{-3})	0.19, −0.35

Computer programs: *CrysAlis PRO* (Rigaku OD, 2021), *SHELXT2014/5* (Sheldrick, 2015*a*), *SHELXL2016/6* (Sheldrick, 2015*b*), and *OLEX2* (Dolomanov *et al.*, 2009).

^{1}H NMR (300 MHz, ppm), 11.47 (*bs*, 1H NH), 7.68 (*t*, 1H), 6.91 (*d*, 1H), 6.60 (*d*, 1H). ^{13}C NMR (75 MHz, ppm), 163.7, 147.0, 142.2, 114.9, 108.5. IR (cm^{-1}): 1596 *m*, 1333 *m*, 825 *w*, 772 *w*, 706 *s*.

Crystals suitable for X-ray analysis were grown from slow evaporation of a saturated methanol solution. The melting point of 2,6-DHP was measured at 460–465 K.

7. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 3. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms bonded to carbon were included in calculated positions and refined using a riding model. Hydrogen atoms bound to N and O were located in the difference-Fourier map, and refined semi-freely with the help of distance restraints.

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Synthesis and crystallographic characterization of 6-hydroxy-1,2-dihydro-pyridin-2-one

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Computing details

6-Hydroxy-1,2-dihydropyridin-2-one

Crystal data

$C_{30}H_{30}N_6O_{12}$	$F(000) = 1392$
$M_r = 666.60$	$D_x = 1.444$ Mg m^{-3}
Monoclinic, $P2_1/n$	Cu $K\alpha$ radiation, $\lambda = 1.54184$ Å
$a = 9.58785$ (4) Å	Cell parameters from 59431 reflections
$b = 16.83642$ (8) Å	$\theta = 3.5$–78.0°
$c = 19.55978$ (10) Å	$\mu = 0.97$ mm^{-1}
$\beta = 103.7319$ (5)°	$T = 100$ K
$V = 3067.19$ (3) Å^3	Block, clear colourless
$Z = 4$	$0.38 \times 0.12 \times 0.10$ mm

Data collection

XtaLAB Synergy, Dualflex, HyPix diffractometer	$T_{min} = 0.453$, $T_{max} = 1.000$
	83138 measured reflections
Radiation source: micro-focus sealed X-ray tube, PhotonJet (Cu) X-ray Source	6554 independent reflections
	6155 reflections with $I > 2\sigma(I)$
Mirror monochromator	$R_{int} = 0.035$
Detector resolution: 10.0000 pixels mm^{-1}	$\theta_{max} = 78.1°$, $\theta_{min} = 3.5°$
ω scans	$h = -11 \rightarrow 12$
Absorption correction: gaussian (CrysAlisPro; Rigaku OD, 2021)	$k = -21 \rightarrow 21$
	$l = -24 \rightarrow 24$

Refinement

Refinement on F^2	Hydrogen site location: mixed
Least-squares matrix: full	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)] = 0.032$	
$wR(F^2) = 0.083$	$w = 1/[\sigma^2(F_o^2) + (0.0411P)^2 + 1.0736P]$
$S = 1.02$	where $P = (F_o^2 + 2F_c^2)/3$
6554 reflections	$(\Delta/\sigma)_{max} = 0.001$
477 parameters	$\Delta\rho_{max} = 0.19$ e Å^{-3}
14 restraints	$\Delta\rho_{min} = -0.35$ e Å^{-3}
Primary atom site location: dual	

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

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

	x	*y*	*z*	U_{iso}*/U_{eq}	Occ. (<1)
O1	0.99326 (7)	0.14764 (4)	0.52810 (4)	0.02046 (15)	
O2	0.52056 (7)	0.20046 (5)	0.45281 (4)	0.02307 (16)	
H2A	0.433 (2)	0.190 (2)	0.449 (2)	0.028*	0.39 (3)
N1	0.75397 (8)	0.16938 (5)	0.49622 (4)	0.01657 (16)	
H1	0.7731 (13)	0.2085 (7)	0.4701 (6)	0.020*	
C1	0.86759 (10)	0.12574 (6)	0.53339 (5)	0.01703 (19)	
C2	0.83551 (11)	0.06266 (6)	0.57353 (5)	0.0215 (2)	
H2B	0.910124	0.031089	0.601141	0.026*	
C3	0.69311 (11)	0.04690 (6)	0.57242 (6)	0.0228 (2)	
H3A	0.671749	0.004190	0.599998	0.027*	
C4	0.58049 (10)	0.09106 (6)	0.53259 (5)	0.0196 (2)	
H4B	0.483773	0.078550	0.532377	0.024*	
C5	0.61270 (10)	0.15408 (6)	0.49300 (5)	0.01704 (19)	
O3	0.26881 (7)	0.17595 (5)	0.44883 (4)	0.02250 (16)	
H3	0.3589 (19)	0.1824 (14)	0.4497 (13)	0.027*	0.61 (3)
O4	−0.19312 (7)	0.12596 (5)	0.35615 (4)	0.02344 (16)	
H4	−0.2704 (15)	0.1017 (8)	0.3202 (7)	0.028*	
N2	0.04226 (8)	0.14771 (5)	0.39488 (4)	0.01710 (16)	
H2	0.0221 (13)	0.1564 (8)	0.4363 (6)	0.021*	
C6	0.18169 (10)	0.15386 (6)	0.39087 (5)	0.01790 (19)	
C7	0.21482 (11)	0.13432 (6)	0.32713 (6)	0.0213 (2)	
H7	0.310669	0.137636	0.321914	0.026*	
C8	0.10467 (11)	0.11005 (7)	0.27185 (6)	0.0239 (2)	
H8	0.126899	0.095290	0.228771	0.029*	
C9	−0.03761 (11)	0.10639 (6)	0.27684 (5)	0.0219 (2)	
H9	−0.111893	0.090907	0.237695	0.026*	
C10	−0.06756 (10)	0.12600 (6)	0.34062 (5)	0.01782 (19)	
O5	1.10984 (8)	0.44209 (4)	0.77157 (4)	0.02427 (17)	
O6	0.69473 (7)	0.46139 (4)	0.60703 (4)	0.02291 (16)	
H6	0.633 (3)	0.4403 (16)	0.5726 (11)	0.027*	0.51 (3)
N3	0.90320 (8)	0.44362 (5)	0.68705 (4)	0.01738 (17)	
H3B	0.8924 (13)	0.4921 (7)	0.7009 (7)	0.021*	
C11	1.02185 (10)	0.40333 (6)	0.72324 (5)	0.01834 (19)	
C12	1.03646 (12)	0.32439 (6)	0.70413 (6)	0.0254 (2)	
H12	1.116169	0.293498	0.727941	0.030*	
C13	0.93248 (13)	0.29207 (7)	0.64981 (6)	0.0295 (2)	
H13	0.942521	0.238376	0.636833	0.035*	
C14	0.81402 (11)	0.33486 (6)	0.61347 (6)	0.0240 (2)	
H14	0.744993	0.311212	0.576036	0.029*	

C15	0.79897 (10)	0.41320 (6)	0.63325 (5)	0.01727 (19)	
O7	0.51409 (7)	0.40623 (4)	0.50930 (4)	0.02113 (15)	
H7A	0.579 (3)	0.4265 (17)	0.5446 (12)	0.025*	0.49 (3)
O8	0.06505 (7)	0.32983 (5)	0.41128 (4)	0.02330 (16)	
H8A	−0.0264 (13)	0.3226 (8)	0.4150 (7)	0.028*	
N4	0.28349 (8)	0.37226 (5)	0.46665 (4)	0.01696 (17)	
H4A	0.3118 (13)	0.3515 (8)	0.4316 (6)	0.020*	
C16	0.38461 (10)	0.41017 (6)	0.51679 (5)	0.01732 (19)	
C17	0.33735 (11)	0.44811 (6)	0.57103 (5)	0.0218 (2)	
H17	0.402967	0.476182	0.606926	0.026*	
C18	0.19353 (12)	0.44388 (7)	0.57127 (6)	0.0260 (2)	
H18	0.161676	0.469269	0.608196	0.031*	
C19	0.09332 (11)	0.40380 (7)	0.51941 (6)	0.0239 (2)	
H19	−0.004815	0.401025	0.521012	0.029*	
C20	0.14144 (10)	0.36826 (6)	0.46563 (5)	0.01835 (19)	
O9	0.18597 (7)	0.69692 (4)	0.58239 (4)	0.02126 (15)	
O10	0.66116 (7)	0.66705 (4)	0.66883 (4)	0.01849 (15)	
H10	0.7367 (13)	0.6395 (8)	0.6998 (7)	0.022*	
N5	0.42153 (8)	0.67871 (5)	0.63253 (4)	0.01655 (16)	
H5	0.4396 (13)	0.7114 (7)	0.6004 (6)	0.020*	
C21	0.28056 (10)	0.66605 (6)	0.63264 (5)	0.01715 (19)	
C22	0.25389 (10)	0.61994 (6)	0.68815 (5)	0.0203 (2)	
H22	0.158220	0.610105	0.691582	0.024*	
C23	0.36839 (11)	0.58916 (6)	0.73752 (6)	0.0224 (2)	
H23	0.349750	0.558253	0.775009	0.027*	
C24	0.51056 (11)	0.60179 (6)	0.73441 (5)	0.0203 (2)	
H24	0.587906	0.579291	0.768459	0.024*	
C25	0.53506 (10)	0.64807 (6)	0.68018 (5)	0.01634 (18)	
O11	0.64103 (7)	0.09175 (4)	0.75468 (4)	0.01983 (15)	
O12	0.20548 (7)	0.07976 (5)	0.60556 (4)	0.02324 (16)	
H12A	0.1306 (14)	0.1044 (8)	0.5774 (7)	0.028*	
N6	0.42400 (8)	0.09381 (5)	0.67740 (4)	0.01662 (16)	
H6A	0.4165 (13)	0.0440 (7)	0.6899 (7)	0.020*	
C26	0.54837 (10)	0.13190 (6)	0.70929 (5)	0.01743 (19)	
C27	0.56380 (12)	0.21052 (6)	0.68974 (6)	0.0260 (2)	
H27	0.649710	0.238977	0.708997	0.031*	
C28	0.45219 (13)	0.24630 (7)	0.64195 (6)	0.0304 (3)	
H28	0.462424	0.300102	0.629325	0.036*	
C29	0.32527 (12)	0.20661 (7)	0.61155 (6)	0.0249 (2)	
H29	0.249173	0.232717	0.579442	0.030*	
C30	0.31366 (10)	0.12804 (6)	0.62962 (5)	0.01851 (19)	

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0114 (3)	0.0298 (4)	0.0185 (3)	0.0016 (3)	0.0002 (2)	0.0008 (3)
O2	0.0104 (3)	0.0268 (4)	0.0301 (4)	0.0005 (3)	0.0013 (3)	0.0117 (3)
N1	0.0118 (4)	0.0194 (4)	0.0174 (4)	−0.0001 (3)	0.0013 (3)	0.0032 (3)

C1	0.0133 (4)	0.0214 (5)	0.0148 (4)	0.0020 (3)	0.0000 (3)	−0.0032 (3)
C2	0.0195 (5)	0.0217 (5)	0.0210 (5)	0.0054 (4)	0.0002 (4)	0.0031 (4)
C3	0.0237 (5)	0.0199 (5)	0.0244 (5)	0.0007 (4)	0.0050 (4)	0.0050 (4)
C4	0.0157 (4)	0.0202 (5)	0.0229 (5)	−0.0015 (3)	0.0041 (4)	0.0014 (4)
C5	0.0127 (4)	0.0191 (4)	0.0181 (4)	0.0002 (3)	0.0013 (3)	−0.0003 (4)
O3	0.0113 (3)	0.0326 (4)	0.0218 (4)	−0.0029 (3)	0.0005 (3)	−0.0013 (3)
O4	0.0125 (3)	0.0331 (4)	0.0237 (4)	−0.0050 (3)	0.0022 (3)	−0.0064 (3)
N2	0.0123 (4)	0.0207 (4)	0.0177 (4)	−0.0014 (3)	0.0024 (3)	−0.0020 (3)
C6	0.0127 (4)	0.0177 (4)	0.0222 (5)	0.0001 (3)	0.0019 (3)	0.0020 (4)
C7	0.0164 (4)	0.0239 (5)	0.0247 (5)	0.0015 (4)	0.0069 (4)	0.0037 (4)
C8	0.0255 (5)	0.0271 (5)	0.0205 (5)	0.0003 (4)	0.0082 (4)	0.0002 (4)
C9	0.0205 (5)	0.0246 (5)	0.0187 (5)	−0.0031 (4)	0.0008 (4)	−0.0023 (4)
C10	0.0144 (4)	0.0167 (4)	0.0209 (5)	−0.0019 (3)	0.0011 (4)	−0.0001 (4)
O5	0.0181 (3)	0.0227 (4)	0.0261 (4)	0.0047 (3)	−0.0066 (3)	−0.0051 (3)
O6	0.0158 (3)	0.0241 (4)	0.0241 (4)	0.0013 (3)	−0.0048 (3)	−0.0018 (3)
N3	0.0143 (4)	0.0166 (4)	0.0193 (4)	0.0007 (3)	0.0001 (3)	−0.0023 (3)
C11	0.0146 (4)	0.0211 (5)	0.0179 (4)	0.0013 (3)	0.0010 (3)	0.0003 (4)
C12	0.0238 (5)	0.0218 (5)	0.0274 (5)	0.0069 (4)	−0.0004 (4)	−0.0019 (4)
C13	0.0319 (6)	0.0213 (5)	0.0319 (6)	0.0038 (4)	0.0007 (5)	−0.0073 (4)
C14	0.0225 (5)	0.0238 (5)	0.0227 (5)	−0.0027 (4)	−0.0002 (4)	−0.0059 (4)
C15	0.0133 (4)	0.0219 (5)	0.0158 (4)	−0.0022 (3)	0.0019 (3)	0.0006 (4)
O7	0.0119 (3)	0.0277 (4)	0.0218 (4)	−0.0025 (3)	0.0001 (3)	−0.0025 (3)
O8	0.0117 (3)	0.0300 (4)	0.0265 (4)	−0.0043 (3)	0.0012 (3)	−0.0042 (3)
N4	0.0128 (4)	0.0200 (4)	0.0176 (4)	−0.0006 (3)	0.0026 (3)	−0.0009 (3)
C16	0.0146 (4)	0.0174 (4)	0.0181 (4)	−0.0012 (3)	0.0001 (3)	0.0039 (3)
C17	0.0226 (5)	0.0223 (5)	0.0189 (5)	−0.0026 (4)	0.0020 (4)	−0.0014 (4)
C18	0.0267 (5)	0.0274 (5)	0.0261 (5)	−0.0009 (4)	0.0108 (4)	−0.0036 (4)
C19	0.0168 (4)	0.0271 (5)	0.0299 (5)	−0.0009 (4)	0.0093 (4)	−0.0003 (4)
C20	0.0134 (4)	0.0181 (4)	0.0224 (5)	−0.0010 (3)	0.0020 (4)	0.0037 (4)
O9	0.0110 (3)	0.0253 (4)	0.0252 (4)	−0.0008 (3)	−0.0002 (3)	0.0068 (3)
O10	0.0106 (3)	0.0242 (3)	0.0193 (3)	0.0011 (3)	0.0008 (2)	0.0022 (3)
N5	0.0120 (4)	0.0197 (4)	0.0171 (4)	0.0001 (3)	0.0017 (3)	0.0038 (3)
C21	0.0126 (4)	0.0175 (4)	0.0204 (5)	−0.0004 (3)	0.0020 (3)	−0.0008 (4)
C22	0.0152 (4)	0.0232 (5)	0.0237 (5)	−0.0004 (4)	0.0070 (4)	0.0016 (4)
C23	0.0236 (5)	0.0242 (5)	0.0207 (5)	0.0012 (4)	0.0077 (4)	0.0050 (4)
C24	0.0182 (5)	0.0231 (5)	0.0180 (5)	0.0041 (4)	0.0014 (4)	0.0036 (4)
C25	0.0132 (4)	0.0179 (4)	0.0168 (4)	0.0007 (3)	0.0013 (3)	−0.0022 (3)
O11	0.0143 (3)	0.0197 (3)	0.0214 (3)	−0.0014 (3)	−0.0040 (3)	0.0039 (3)
O12	0.0131 (3)	0.0304 (4)	0.0222 (4)	−0.0006 (3)	−0.0038 (3)	0.0036 (3)
N6	0.0130 (4)	0.0185 (4)	0.0166 (4)	0.0002 (3)	0.0000 (3)	0.0022 (3)
C26	0.0146 (4)	0.0203 (5)	0.0159 (4)	0.0001 (3)	0.0008 (3)	−0.0004 (4)
C27	0.0254 (5)	0.0202 (5)	0.0264 (5)	−0.0045 (4)	−0.0055 (4)	0.0018 (4)
C28	0.0369 (6)	0.0184 (5)	0.0291 (6)	−0.0001 (4)	−0.0058 (5)	0.0038 (4)
C29	0.0249 (5)	0.0234 (5)	0.0213 (5)	0.0067 (4)	−0.0045 (4)	0.0021 (4)
C30	0.0138 (4)	0.0254 (5)	0.0151 (4)	0.0031 (4)	0.0010 (3)	−0.0012 (4)

Geometric parameters (Å, º)

O1—C1	1.2875 (12)	O7—H7A	0.879 (18)
O2—H2A	0.839 (19)	O7—C16	1.2858 (12)
O2—C5	1.2956 (12)	O8—H8A	0.905 (12)
N1—H1	0.880 (12)	O8—C20	1.3098 (12)
N1—C1	1.3708 (12)	N4—H4A	0.868 (12)
N1—C5	1.3655 (12)	N4—C16	1.3630 (12)
C1—C2	1.3978 (15)	N4—C20	1.3590 (12)
C2—H2B	0.9500	C16—C17	1.4026 (15)
C2—C3	1.3859 (15)	C17—H17	0.9500
C3—H3A	0.9500	C17—C18	1.3819 (15)
C3—C4	1.3879 (14)	C18—H18	0.9500
C4—H4B	0.9500	C18—C19	1.3946 (15)
C4—C5	1.3908 (14)	C19—H19	0.9500
O3—H3	0.867 (17)	C19—C20	1.3811 (15)
O3—C6	1.2928 (12)	O9—C21	1.2789 (12)
O4—H4	0.981 (14)	O10—H10	0.948 (11)
O4—C10	1.3096 (12)	O10—C25	1.3193 (12)
N2—H2	0.888 (12)	N5—H5	0.882 (12)
N2—C6	1.3616 (12)	N5—C21	1.3688 (12)
N2—C10	1.3556 (12)	N5—C25	1.3557 (12)
C6—C7	1.3971 (15)	C21—C22	1.4067 (14)
C7—H7	0.9500	C22—H22	0.9500
C7—C8	1.3818 (15)	C22—C23	1.3795 (14)
C8—H8	0.9500	C23—H23	0.9500
C8—C9	1.3919 (15)	C23—C24	1.3952 (14)
C9—H9	0.9500	C24—H24	0.9500
C9—C10	1.3850 (15)	C24—C25	1.3805 (14)
O5—C11	1.2856 (12)	O11—C26	1.2884 (12)
O6—H6	0.861 (14)	O12—H12A	0.897 (12)
O6—C15	1.2949 (12)	O12—C30	1.3139 (12)
N3—H3B	0.874 (12)	N6—H6A	0.881 (12)
N3—C11	1.3686 (12)	N6—C26	1.3671 (12)
N3—C15	1.3672 (12)	N6—C30	1.3622 (12)
C11—C12	1.3966 (14)	C26—C27	1.3955 (14)
C12—H12	0.9500	C27—H27	0.9500
C12—C13	1.3843 (15)	C27—C28	1.3810 (15)
C13—H13	0.9500	C28—H28	0.9500
C13—C14	1.3896 (15)	C28—C29	1.3919 (16)
C14—H14	0.9500	C29—H29	0.9500
C14—C15	1.3916 (15)	C29—C30	1.3805 (15)
C5—O2—H2A	117 (3)	C16—O7—H7A	114.1 (19)
C1—N1—H1	117.4 (8)	C20—O8—H8A	111.5 (9)
C5—N1—H1	117.1 (8)	C16—N4—H4A	117.0 (8)
C5—N1—C1	125.31 (9)	C20—N4—H4A	118.0 (8)
O1—C1—N1	116.42 (9)	C20—N4—C16	124.96 (9)

O1—C1—C2	126.71 (9)	O7—C16—N4	115.79 (9)
N1—C1—C2	116.88 (9)	O7—C16—C17	127.13 (9)
C1—C2—H2B	120.5	N4—C16—C17	117.07 (9)
C3—C2—C1	118.94 (9)	C16—C17—H17	120.6
C3—C2—H2B	120.5	C18—C17—C16	118.75 (9)
C2—C3—H3A	118.7	C18—C17—H17	120.6
C2—C3—C4	122.58 (9)	C17—C18—H18	118.7
C4—C3—H3A	118.7	C17—C18—C19	122.56 (10)
C3—C4—H4B	120.8	C19—C18—H18	118.7
C3—C4—C5	118.37 (9)	C18—C19—H19	121.1
C5—C4—H4B	120.8	C20—C19—C18	117.81 (9)
O2—C5—N1	116.12 (9)	C20—C19—H19	121.1
O2—C5—C4	126.02 (9)	O8—C20—N4	113.69 (9)
N1—C5—C4	117.85 (9)	O8—C20—C19	127.49 (9)
C6—O3—H3	119.1 (16)	N4—C20—C19	118.83 (9)
C10—O4—H4	114.4 (8)	C25—O10—H10	111.5 (8)
C6—N2—H2	118.0 (8)	C25—N5—C21	124.86 (9)
C10—N2—H2	117.5 (8)	C21—N5—H5	117.3 (8)
C10—N2—C6	124.49 (9)	C25—N5—H5	117.8 (8)
O3—C6—N2	114.22 (9)	O9—C21—N5	117.12 (9)
O3—C6—C7	127.87 (9)	O9—C21—C22	126.28 (9)
N2—C6—C7	117.89 (9)	N5—C21—C22	116.60 (8)
C6—C7—H7	120.8	C21—C22—H22	120.4
C8—C7—C6	118.33 (9)	C23—C22—C21	119.17 (9)
C8—C7—H7	120.8	C23—C22—H22	120.4
C7—C8—H8	118.7	C22—C23—H23	118.8
C7—C8—C9	122.55 (10)	C22—C23—C24	122.38 (9)
C9—C8—H8	118.7	C24—C23—H23	118.8
C8—C9—H9	121.0	C23—C24—H24	121.1
C10—C9—C8	117.96 (9)	C25—C24—C23	117.76 (9)
C10—C9—H9	121.0	C25—C24—H24	121.1
O4—C10—N2	113.87 (9)	O10—C25—N5	114.23 (8)
O4—C10—C9	127.39 (9)	O10—C25—C24	126.58 (9)
N2—C10—C9	118.74 (9)	N5—C25—C24	119.19 (9)
C15—O6—H6	112.0 (19)	C30—O12—H12A	112.5 (9)
C11—N3—H3B	116.6 (8)	C26—N6—H6A	116.1 (8)
C15—N3—H3B	118.0 (8)	C30—N6—H6A	119.5 (8)
C15—N3—C11	125.33 (9)	C30—N6—C26	124.46 (9)
O5—C11—N3	116.65 (9)	O11—C26—N6	116.90 (9)
O5—C11—C12	126.15 (9)	O11—C26—C27	125.87 (9)
N3—C11—C12	117.21 (9)	N6—C26—C27	117.24 (9)
C11—C12—H12	120.7	C26—C27—H27	120.5
C13—C12—C11	118.67 (10)	C28—C27—C26	118.93 (10)
C13—C12—H12	120.7	C28—C27—H27	120.5
C12—C13—H13	118.6	C27—C28—H28	118.7
C12—C13—C14	122.76 (10)	C27—C28—C29	122.56 (10)
C14—C13—H13	118.6	C29—C28—H28	118.7
C13—C14—H14	120.8	C28—C29—H29	121.1

C13—C14—C15	118.38 (9)	C30—C29—C28	117.79 (9)
C15—C14—H14	120.8	C30—C29—H29	121.1
O6—C15—N3	115.11 (9)	O12—C30—N6	113.73 (9)
O6—C15—C14	127.23 (9)	O12—C30—C29	127.30 (9)
N3—C15—C14	117.65 (9)	N6—C30—C29	118.97 (9)
O1—C1—C2—C3	−179.28 (10)	O7—C16—C17—C18	−178.06 (10)
N1—C1—C2—C3	1.34 (14)	N4—C16—C17—C18	1.06 (14)
C1—N1—C5—O2	−177.46 (9)	C16—N4—C20—O8	178.71 (9)
C1—N1—C5—C4	2.61 (15)	C16—N4—C20—C19	−1.01 (15)
C1—C2—C3—C4	0.39 (16)	C16—C17—C18—C19	−0.44 (17)
C2—C3—C4—C5	−0.75 (16)	C17—C18—C19—C20	−0.91 (17)
C3—C4—C5—O2	179.42 (10)	C18—C19—C20—O8	−178.08 (10)
C3—C4—C5—N1	−0.66 (14)	C18—C19—C20—N4	1.60 (15)
C5—N1—C1—O1	177.61 (9)	C20—N4—C16—O7	178.86 (9)
C5—N1—C1—C2	−2.95 (14)	C20—N4—C16—C17	−0.35 (14)
O3—C6—C7—C8	178.33 (10)	O9—C21—C22—C23	178.40 (10)
N2—C6—C7—C8	0.10 (14)	N5—C21—C22—C23	−1.37 (14)
C6—N2—C10—O4	−178.47 (9)	C21—N5—C25—O10	178.72 (9)
C6—N2—C10—C9	1.86 (15)	C21—N5—C25—C24	−1.47 (15)
C6—C7—C8—C9	1.70 (16)	C21—C22—C23—C24	−0.27 (16)
C7—C8—C9—C10	−1.75 (16)	C22—C23—C24—C25	1.14 (16)
C8—C9—C10—O4	−179.62 (10)	C23—C24—C25—O10	179.46 (9)
C8—C9—C10—N2	0.00 (15)	C23—C24—C25—N5	−0.31 (15)
C10—N2—C6—O3	179.62 (9)	C25—N5—C21—O9	−177.48 (9)
C10—N2—C6—C7	−1.91 (15)	C25—N5—C21—C22	2.31 (14)
O5—C11—C12—C13	−178.89 (11)	O11—C26—C27—C28	−177.73 (11)
N3—C11—C12—C13	0.80 (16)	N6—C26—C27—C28	2.43 (16)
C11—N3—C15—O6	179.01 (9)	C26—N6—C30—O12	179.47 (9)
C11—N3—C15—C14	0.10 (15)	C26—N6—C30—C29	−0.36 (15)
C11—C12—C13—C14	−0.03 (19)	C26—C27—C28—C29	−1.01 (19)
C12—C13—C14—C15	−0.74 (18)	C27—C28—C29—C30	−1.18 (19)
C13—C14—C15—O6	−178.07 (11)	C28—C29—C30—O12	−177.96 (11)
C13—C14—C15—N3	0.70 (15)	C28—C29—C30—N6	1.84 (16)
C15—N3—C11—O5	178.86 (9)	C30—N6—C26—O11	178.32 (9)
C15—N3—C11—C12	−0.86 (15)	C30—N6—C26—C27	−1.83 (15)

Hydrogen-bond geometry (Å, º)

D—H···A	D—H	H···A	D···A	D—H···A
O2—H2A···O3	0.84 (2)	1.60 (2)	2.4317 (10)	174 (4)
N1—H1···O9[i]	0.88 (1)	1.98 (1)	2.8606 (11)	175 (1)
O3—H3···O2	0.87 (2)	1.57 (2)	2.4317 (10)	176 (3)
O4—H4···O5[ii]	0.981 (14)	1.500 (14)	2.4768 (10)	173.5 (14)
N2—H2···O1[iii]	0.89 (1)	1.89 (1)	2.7554 (11)	166 (1)
O6—H6···O7	0.86 (1)	1.58 (1)	2.4381 (10)	177 (3)
N3—H3B···O11[iv]	0.87 (1)	1.95 (1)	2.8155 (11)	170 (1)
O7—H7A···O6	0.88 (2)	1.56 (2)	2.4381 (10)	179 (3)

O8—H8*A*⋯O9ᵛ	0.91 (1)	1.58 (1)	2.4803 (10)	175 (1)
N4—H4*A*⋯O10ⁱ	0.87 (1)	2.07 (1)	2.8999 (11)	161 (1)
O10—H10⋯O11ⁱᵛ	0.95 (1)	1.52 (1)	2.4690 (9)	176 (1)
N5—H5⋯O2ⁱ	0.88 (1)	1.90 (1)	2.7699 (11)	167 (1)
O12—H12*A*⋯O1ⁱⁱⁱ	0.90 (1)	1.61 (1)	2.5057 (10)	178 (2)
N6—H6*A*⋯O5ᵛⁱ	0.88 (1)	1.91 (1)	2.7893 (11)	172 (1)

Symmetry codes: (i) −*x*+1, −*y*+1, −*z*+1; (ii) *x*−3/2, −*y*+1/2, *z*−1/2; (iii) *x*−1, *y*, *z*; (iv) −*x*+3/2, *y*+1/2, −*z*+3/2; (v) −*x*, −*y*+1, −*z*+1; (vi) −*x*+3/2, *y*−1/2, −*z*+3/2.