Crystal structure of zwitterionic 3-(2-hydroxy-2-phosphonato-2-phosphonoethyl)imidazo[1,2-a]-pyridin-1-ium monohydrate (minodronic acid monohydrate): a redetermination

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In a previous study, the X-ray structure of the title compound, $C_9H_{12}N_2O_7P_2 \cdot H_2O$, was reported [Takeuchi *et al.*, (1998). *Chem. Pharm. Bull.* **46**, 1703–1709], but neither atomic coordinates nor details of the geometry were published. The structure has been redetermined with high precision as its detailed knowledge is essential to elucidate the presumed polymorphism of minodronic acid monohydrate at room temperature. The molecule crystallizes in a zwitterionic form with cationic imidazolium[1,2a]pyridine and anionic phosphonate groups. The dihedral angle formed by the planes of the pyridine and imidazole rings is 3.55 (9)°. A short intramolecular C—H⋯O contact is present. In the crystal, molecules are linked by O—H⋯O, N—H⋯O and C—H⋯O hydrogen bonds and π–π interactions [centroid-to-centroid distance = 3.5822 (11) Å], forming a three-dimensional structure.

1. Chemical context

Minodronic acid, (1-hydroxy-2-(imidazo[1,2-a]pyridin-3-yl)ethane-1,1-bis(phosphonic acid), has excellent bone resorption inhibitory activity, as well as anti-inflammatory, analgesic and antipyretic activities and is useful for the treatment of diseases in which an increased bone resorption participates (Tanishima & Morio, 2013; Yamane *et al.*, 2003; Ito *et al.*, 2010; Sato *et al.*, 2006). For practical uses and solid pharmaceutical preparations, the monohydrate form is preferred, giving more stable crystals with respect to the anhydrous and polyhydrate forms. By developing a pharmaceutical preparation (Takeuchi *et al.*, 1993), it was found that monohydrate crystals include two crystal forms, named *D* and *E*, having the same powder X-ray diffraction pattern but different dehydration temperatures. In fact, according to TG–DSC thermogravimetric analyses, crystal *D* has a dehydration peak temperature of 408 to 422 K, whereas for *E* it is 433 to 443 K.
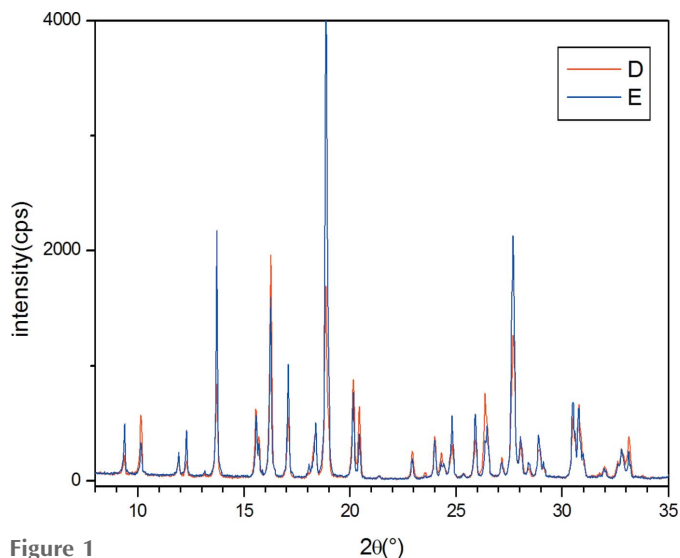

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Figure 1
Comparison of the room-temperature powder X-ray diffraction patterns of forms *D* (red line) and *E* (blue line) of the title compound.

Figure 2
The molecular structure of the title compound, showing the atom labelling. Displacement ellipsoids are drawn at the 50% probability level.

The monohydrate crystals of *D* and *E* are both produced by recrystallization of the free acid from aqueous hydrochloric acid solutions by gradual cooling of a heat-dissolved solution under mild stirring conditions, followed by drying the crystals at 313–333 K under reduced pressure. The stirring mode and cooling conditions are the key factors in determining the final crystal form.

The relation between the two crystal forms deviates from the conventional concept of polymorphism by the similarity of the powder X-ray diffraction patterns. In principle, different mechanisms could be invoked to justify the different thermal behavior, amongst which a small difference in the crystal packing or in the atomic interactions could lead to it. The crystal structure of a monohydrate form of minodronic acid has been published earlier (Takeuchi *et al.*, 1998), but neither the atomic coordinates nor details of the molecular and crystal geometry were reported. In the absence of detailed information, the present study of the crystal structures of both forms, *D* and *E*, was undertaken with the aim of finding a reasonable solution to the unusual 'polymorphism' problem. Batches of the *D* and *E* crystals were prepared as described in the *Experimental* section and characterized by thermogravimetric analysis.

Powder X-ray diffraction was performed with a Thermo X'tra Diffractometer equipped with a Si(Li) solid state detector directly on the as-prepared samples without grinding (Fig. 1). This confirmed that the diffraction patterns of the two forms involve peaks occurring at the same 2θ angles, the unique difference consisting of a different intensity distribution probably originating from preferential orientation. It is noteworthy that both diffraction patterns are fully compatible with the lattice parameters reported by Takeuchi *et al.* (1998). Small single crystals suitable for XRD experiments were selected from both batches and their structures solved and refined. The analyses established that the crystal structures are perfectly comparable within experimental error, and compatible with that previously reported.
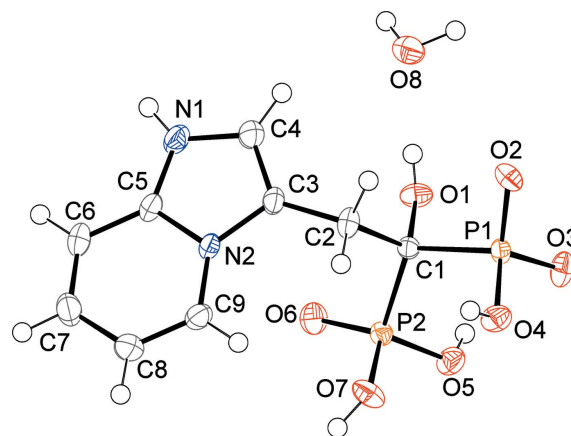
We report herein the redetermination of the crystal structure of form *D* of minodronic acid monohydrate, whereas that of form *E* has been deposited at the CCDC (Rizzoli & Calestani, 2014). On the basis of the present study, the peculiar thermal behaviour of the *D* and *E* forms of minodronic acid cannot be ascribed to structural differences, but it is probably due to morphological or microstructural features induced by the crystallization procedure and the influence of the dehydration process.

2. Structural commentary

The asymmetric unit of the title compound, Fig. 2, consists of minodronic acid and a water molecule of crystallization. The acid molecule crystallizes in a zwitterionic form with cationic imidazolium[1,2a]pyridine and anionic phosphonate groups. The fused-ring system deviates from planarity, with the dihedral angle formed by the pyridine and imidazole rings being 3.55 (9)°. An analysis of the bond lengths within the fused-ring system, indicates that the C=N and C=C double-bond distribution shown in the Scheme is the most probable, but a resonant form involving the aromatic character of the pyridine ring and the localization of the positive change on the atom N2 also exists. The values of the P—O bond lengths indicate that the negative charge is delocalized on atoms O2 and O3, whose distances [P1—O2 = 1.5197 (10), P1—O3 = 1.5001 (10) Å] are intermediate between those observed for the protonated atoms O4, O5 and O7 [mean value 1.564 (7) Å] and for the localized P=O double bond [P2—O6 = 1.4817 (10) Å]. The observed distribution of the hydrogen atoms and of the charge on the phosphonate groups differs from that deducible from the molecular plot reported previously by Takeuchi *et al.* (1998). An intramolecular C—H···O hydrogen bond is present (Table 1).

3. Supramolecular features

The crystal structure of the title compound is characterized by a very effective hydrogen-bonding network which is respon-

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

$D-\text{H}\cdots A$	$D-\text{H}$	$\text{H}\cdots A$	$D\cdots A$	$D-\text{H}\cdots A$
O1—H1O···O8	0.78 (3)	1.87 (3)	2.6468 (18)	169 (2)
O4—H4O···O2^{i}	0.90 (3)	1.73 (3)	2.6116 (16)	169 (3)
O5—H5O···O3^{ii}	0.88 (3)	1.62 (3)	2.4973 (14)	175 (3)
O7—H7O···O2^{iii}	0.83 (2)	1.80 (2)	2.6183 (14)	170 (2)
O8—H81···O6^{iv}	0.82 (2)	1.99 (2)	2.8011 (15)	169 (3)
O8—H82···O6^{v}	0.91 (2)	1.83 (2)	2.7334 (16)	175 (2)
N1—H1N···O5^{vi}	0.85 (2)	2.18 (3)	2.9930 (15)	158 (2)
C2—H2B···O2	0.97	2.50	3.0224 (17)	114
C4—H4···O8	0.93	2.40	3.2079 (19)	145
C8—H8···O4^{vii}	0.93	2.51	3.1704 (17)	128

Symmetry codes: (i) $-x+1, -y, -z+1$; (ii) $-x+1, -y, -z$; (iii) $x-1, y, z$; (iv) $-x+1, -y+1, -z$; (v) $x+1, y, z$; (vi) $x, y+1, z$; (vii) $-x, -y, -z+1$.

sible for the unusually high value of the calculated density of the crystal (1.818 g cm^{-3}). As shown in Fig. 3, the crystal packing may be described as an alternate stacking along the b axis of phosphonate and organic layers forming a three-dimensional network through O—H···O, N—H···O and C—H···O hydrogen bonds (Table 1 and Fig. 3). Adjacent phosphonate layers are bridged *via* hydrogen bonds involving the water molecules, which are hosted inside channels parallel to the a axis and running between pairs of fused-ring systems connected by π–π interactions [$Cg1\cdots Cg1^{i} = 3.5822$ (11) Å; $Cg1$ is the centroid of the N2/C5–C9 ring; symmetry code: (i) $-x, -y+1, -z+1$]. The O—H···O hydrogen-bonding system within the phosphonate layer (Fig. 4) generates rings arranged in $R_2^2(8)$, $R_2^2(12)$, $R_4^2(16)$ and $R_4^4(16)$ graph-set motifs (Bernstein *et al.*, 1995).
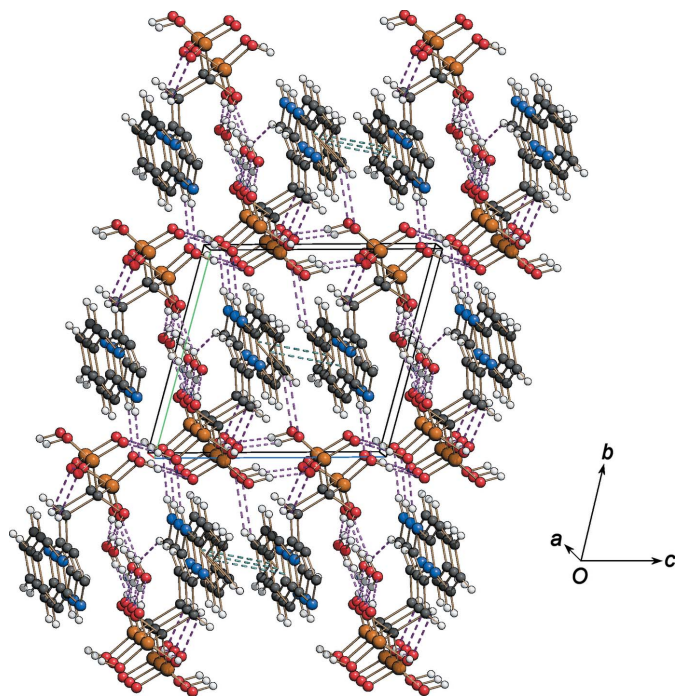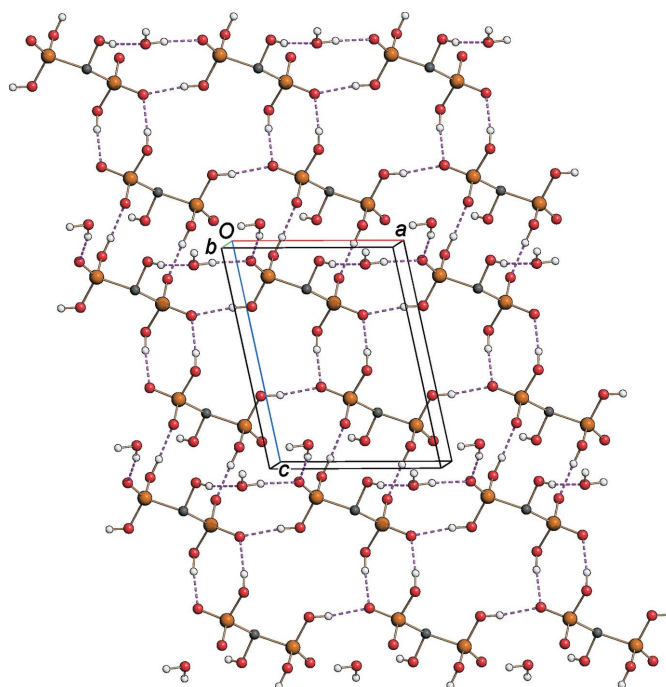

Figure 4
A view along the b axis of the hydrogen-bonding network (dashed lines) in the phosphonate layer (see Table 1 for detail). Nitrogen, carbon (except C1) and C- and N-bound H atoms have been omitted for clarity.

Figure 3
The crystal packing of the title compound viewed along the a axis, showing the hydrogen-bonding network (violet dashed lines) and π–π interactions (blue dashed lines); see Table 1 for details.

4. Synthesis and crystallization

Crystal form D: crystals of minodronic acid (150 g) were added to 5.6 l of 1 N hydrochloric acid (about 37.5 volumes) in a reactor equipped with mechanical stirring, and dissolved with heating. The dissolution temperature (368 K) was maintained for at least 30 min, followed by filtration of a small amount of undissolved particles. The clear filtrate was stirred at 110 r.p.m. and slowly cooled to 328 K in 4 h, and then to 295 K overnight. The crystalline precipitate was collected by filtration, washed with 300 ml of water and 300 ml of ethanol, and dried at 318 K to obtain 135 g of pure form D of minodronic acid monohydrate, as shown by the dehydration peak at 415 K (Takeuchi *et al.*, 1993). The colourless crystal sample used for X-ray analysis was selected from the batch.

Crystal form E: crystals of minodronic acid (15 g) were added to 0.6 l of 1 N hydrochloric acid (about 40 volumes) in a reactor equipped with magnetic stirring and dissolved with heating. The dissolution temperature (368 K) was maintained for at least 30 min followed by filtration of a small amount of undissolved particles. The clear filtrate was stirred slowly so that the liquid surface could not create a vortex (<110 r.p.m.) and gradually cooled down to 295 K overnight. The crystal precipitate was collected by filtration, washed with 30 ml of water and 30 ml of ethanol, and dried at 318 K to obtain 14 g of pure E form of minodronic acid monohydrate, as shown by the dehydration peak at 438 K (Takeuchi *et al.*, 1993). The colourless crystal sample used for X-ray analysis was selected from the batch.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_9H_{12}N_2O_7P_2 \cdot H_2O$
M_r	340.16
Crystal system, space group	Triclinic, $P\bar{1}$
Temperature (K)	294
a, b, c (Å)	7.3668 (11), 8.9833 (12), 9.9733 (18)
α, β, γ (°)	75.0136 (17), 77.2716 (17), 88.5706 (18)
V (Å^3)	621.54 (17)
Z	2
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.40
Crystal size (mm)	$0.18 \times 0.15 \times 0.10$
Data collection	
Diffractometer	Bruker SMART 1000 CCD
Absorption correction	Multi-scan (*SADABS*; Bruker, 2008)
T_{min}, T_{max}	0.640, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	10459, 4054, 3413
R_{int}	0.020
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.752
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.035, 0.101, 1.07
No. of reflections	4054
No. of parameters	218
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.55, −0.28

Computer programs: *APEX2* and *SAINT* (Bruker, 2008), *SIR97* (Altomare *et al.*, 1999), *SHELXL2014* (Sheldrick, 2008), *ORTEP-3 for Windows* (Farrugia, 2012), *SCHAKAL99* (Keller, 1999) and *publCIF* (Westrip, 2010).

5. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. All the H atoms were located in a difference Fourier map. The N- and O-bound hydrogen atoms were freely refined. The C-bound H atoms were refined using a riding model approximation, with C—H = 0.93–0.97 Å and with $U_{iso}(H) = 1.2U_{eq}(C)$.

References

Altomare, A., Burla, M. C., Camalli, M., Cascarano, G. L., Giacovazzo, C., Guagliardi, A., Moliterni, A. G. G., Polidori, G. & Spagna, R. (1999). *J. Appl. Cryst.* **32**, 115–119.
Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N. L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Bruker (2008). *APEX2, SAINT* and *SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA.
Farrugia, L. J. (2012). *J. Appl. Cryst.* **45**, 849–854.
Ito, M., Sone, T. & Fukunaga, M. (2010). *J. Bone Miner. Metab.* **28**, 334–341.
Keller, E. (1999). *SCHAKAL99.* Universität Freiburg, Germany.
Rizzoli, C. & Calestani, G. (2014). Private communication (deposition number 1037896). CCDC, Cambridge, England.
Sato, K., Yuasa, T., Nogawa, M., Kimura, S., Segawa, H., Yokota, A. & Maekawa, T. (2006). *Br. J. Cancer*, **95**, 1354–1361.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Takeuchi, M., Hamada, M., Kaneko, Y. & Yamamoto, N. (1993). Eur. Patent EP 0647649B1.
Takeuchi, M., Sakamoto, S., Kawamuki, K., Kurihara, H., Nakahara, H. & Isomura, Y. (1998). *Chem. Pharm. Bull.* **46**, 1703–1709.
Tanishima, S. & Morio, Y. (2013). *Clin. Interv. Aging*, **8**, 185–189.
Westrip, S. P. (2010). *J. Appl. Cryst.* **43**, 920–925.
Yamane, I., Hagino, H., Okano, T., Enokida, M., Yamasaki, D. & Teshima, R. (2003). *Arthritis Rheum.* **48**, 1732–1741.

supporting information

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Computing details

Data collection: *APEX2* (Bruker, 2008); cell refinement: *SAINT* (Bruker, 2008); data reduction: *SAINT* (Bruker, 2008); program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 2012) and *SCHAKAL99* (Keller, 1999); software used to prepare material for publication: *publCIF* (Westrip, 2010).

3-(2-Hydroxy-2-phosphonato-2-phosphonoethyl)imidazo[1,2-a]pyridin-1-ium monohydrate

Crystal data

$C_9H_{12}N_2O_7P_2 \cdot H_2O$	$Z = 2$
$M_r = 340.16$	$F(000) = 352$
Triclinic, $P\bar{1}$	$D_x = 1.818$ Mg m^{-3}
$a = 7.3668\ (11)$ Å	Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
$b = 8.9833\ (12)$ Å	Cell parameters from 227 reflections
$c = 9.9733\ (18)$ Å	$\theta = 8.2$–$21.3°$
$\alpha = 75.0136\ (17)°$	$\mu = 0.40$ mm^{-1}
$\beta = 77.2716\ (17)°$	$T = 294$ K
$\gamma = 88.5706\ (18)°$	Block, colourless
$V = 621.54\ (17)$ Å^3	$0.18 \times 0.15 \times 0.10$ mm

Data collection

Bruker SMART 1000 CCD diffractometer	4054 independent reflections
ω scan	3413 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (SADABS; Bruker, 2008)	$R_{int} = 0.020$
	$\theta_{max} = 32.3°$, $\theta_{min} = 2.2°$
$T_{min} = 0.640$, $T_{max} = 0.746$	$h = -11 \rightarrow 10$
10459 measured reflections	$k = -12 \rightarrow 13$
	$l = -14 \rightarrow 14$

Refinement

Refinement on F^2	Hydrogen site location: mixed
Least-squares matrix: full	H atoms treated by a mixture of independent
$R[F^2 > 2\sigma(F^2)] = 0.035$	and constrained refinement
$wR(F^2) = 0.101$	$w = 1/[\sigma^2(F_o^2) + (0.060P)^2 + 0.1062P]$
$S = 1.07$	where $P = (F_o^2 + 2F_c^2)/3$
4054 reflections	$(\Delta/\sigma)_{max} = 0.001$
218 parameters	$\Delta\rho_{max} = 0.55$ e Å^{-3}
0 restraints	$\Delta\rho_{min} = -0.28$ e Å^{-3}

Special details

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

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($Å^2$)

	x	*y*	*z*	U_{iso}*/U_{eq}
P1	0.51328 (4)	−0.00236 (4)	0.28423 (3)	0.01430 (9)
P2	0.17313 (4)	0.13064 (4)	0.15681 (3)	0.01514 (9)
O1	0.49943 (14)	0.25308 (12)	0.08484 (10)	0.0206 (2)
H1O	0.576 (3)	0.303 (3)	0.098 (2)	0.039 (6)*
O2	0.67125 (13)	0.05492 (12)	0.33555 (10)	0.0208 (2)
O3	0.56833 (15)	−0.09174 (12)	0.17446 (11)	0.0232 (2)
O4	0.37247 (14)	−0.10822 (11)	0.41416 (11)	0.0214 (2)
H4O	0.349 (4)	−0.080 (3)	0.496 (3)	0.070 (8)*
O5	0.22204 (14)	0.01195 (11)	0.06740 (11)	0.0213 (2)
H5O	0.298 (4)	0.044 (3)	−0.016 (3)	0.072 (8)*
O6	0.10307 (14)	0.27806 (12)	0.08260 (12)	0.0258 (2)
O7	0.03415 (14)	0.04399 (13)	0.29628 (11)	0.0240 (2)
H7O	−0.079 (3)	0.054 (3)	0.300 (3)	0.050 (7)*
O8	0.77583 (16)	0.42957 (14)	0.09502 (14)	0.0301 (3)
H81	0.800 (3)	0.515 (3)	0.038 (3)	0.049 (7)*
H82	0.884 (3)	0.379 (3)	0.086 (2)	0.049 (6)*
N1	0.25482 (18)	0.67430 (14)	0.19284 (13)	0.0225 (2)
H1N	0.277 (3)	0.769 (3)	0.148 (2)	0.047 (6)*
N2	0.09082 (15)	0.46468 (12)	0.31543 (12)	0.0158 (2)
C1	0.38347 (17)	0.16943 (14)	0.21539 (13)	0.0138 (2)
C2	0.34325 (19)	0.26352 (15)	0.32898 (14)	0.0189 (2)
H2A	0.2507	0.2061	0.4098	0.023*
H2B	0.4565	0.2705	0.3619	0.023*
C3	0.27645 (18)	0.42267 (15)	0.28236 (14)	0.0176 (2)
C4	0.3748 (2)	0.55521 (16)	0.20766 (15)	0.0219 (3)
H4	0.5030	0.5637	0.1723	0.026*
C5	0.08150 (19)	0.62025 (15)	0.25700 (14)	0.0182 (2)
C6	−0.0888 (2)	0.69424 (16)	0.27288 (16)	0.0236 (3)
H6	−0.0965	0.7984	0.2295	0.028*
C7	−0.2424 (2)	0.60818 (17)	0.35401 (17)	0.0260 (3)
H7	−0.3572	0.6541	0.3670	0.031*
C8	−0.2293 (2)	0.44988 (17)	0.41874 (16)	0.0240 (3)
H8	−0.3350	0.3937	0.4766	0.029*
C9	−0.06486 (19)	0.37863 (15)	0.39786 (15)	0.0200 (3)
H9	−0.0576	0.2737	0.4385	0.024*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
P1	0.01367 (15)	0.01350 (15)	0.01500 (15)	0.00313 (11)	−0.00231 (11)	−0.00340 (11)
P2	0.01371 (15)	0.01476 (16)	0.01648 (16)	0.00114 (11)	−0.00367 (11)	−0.00301 (11)
O1	0.0207 (5)	0.0207 (5)	0.0165 (4)	−0.0069 (4)	−0.0002 (4)	−0.0004 (4)
O2	0.0134 (4)	0.0274 (5)	0.0221 (5)	0.0026 (4)	−0.0045 (4)	−0.0072 (4)
O3	0.0304 (5)	0.0192 (5)	0.0202 (5)	0.0075 (4)	−0.0029 (4)	−0.0084 (4)
O4	0.0239 (5)	0.0183 (5)	0.0185 (4)	−0.0037 (4)	−0.0016 (4)	−0.0008 (4)
O5	0.0248 (5)	0.0190 (5)	0.0213 (5)	−0.0009 (4)	−0.0038 (4)	−0.0084 (4)
O6	0.0243 (5)	0.0199 (5)	0.0327 (6)	0.0059 (4)	−0.0123 (4)	−0.0016 (4)
O7	0.0138 (5)	0.0324 (6)	0.0216 (5)	−0.0010 (4)	−0.0005 (4)	−0.0024 (4)
O8	0.0204 (5)	0.0258 (6)	0.0404 (7)	−0.0019 (4)	−0.0044 (5)	−0.0036 (5)
N1	0.0259 (6)	0.0131 (5)	0.0244 (6)	−0.0003 (4)	0.0008 (5)	−0.0028 (4)
N2	0.0186 (5)	0.0112 (5)	0.0179 (5)	0.0024 (4)	−0.0037 (4)	−0.0044 (4)
C1	0.0132 (5)	0.0131 (5)	0.0142 (5)	0.0004 (4)	−0.0017 (4)	−0.0028 (4)
C2	0.0235 (6)	0.0156 (6)	0.0192 (6)	0.0063 (5)	−0.0070 (5)	−0.0060 (5)
C3	0.0188 (6)	0.0149 (6)	0.0198 (6)	0.0035 (4)	−0.0034 (5)	−0.0070 (5)
C4	0.0206 (6)	0.0193 (6)	0.0247 (7)	0.0010 (5)	−0.0007 (5)	−0.0077 (5)
C5	0.0236 (6)	0.0121 (5)	0.0183 (6)	0.0021 (4)	−0.0033 (5)	−0.0040 (4)
C6	0.0277 (7)	0.0164 (6)	0.0273 (7)	0.0077 (5)	−0.0080 (6)	−0.0059 (5)
C7	0.0221 (7)	0.0264 (7)	0.0324 (7)	0.0079 (5)	−0.0074 (6)	−0.0121 (6)
C8	0.0197 (6)	0.0240 (7)	0.0271 (7)	−0.0017 (5)	−0.0015 (5)	−0.0075 (5)
C9	0.0222 (6)	0.0153 (6)	0.0211 (6)	−0.0018 (5)	−0.0029 (5)	−0.0038 (5)

Geometric parameters (Å, º)

P1—O3	1.5001 (10)	N2—C9	1.3743 (17)
P1—O2	1.5197 (10)	N2—C5	1.3744 (16)
P1—O4	1.5745 (10)	N2—C3	1.4004 (17)
P1—C1	1.8534 (13)	C1—C2	1.5558 (17)
P2—O6	1.4817 (10)	C2—C3	1.4914 (18)
P2—O5	1.5468 (10)	C2—H2A	0.9700
P2—O7	1.5625 (10)	C2—H2B	0.9700
P2—C1	1.8426 (13)	C3—C4	1.3580 (19)
O1—C1	1.4233 (15)	C4—H4	0.9300
O1—H1O	0.78 (2)	C5—C6	1.4022 (19)
O4—H4O	0.90 (3)	C6—C7	1.360 (2)
O5—H5O	0.88 (3)	C6—H6	0.9300
O7—H7O	0.83 (2)	C7—C8	1.412 (2)
O8—H81	0.83 (3)	C7—H7	0.9300
O8—H82	0.91 (2)	C8—C9	1.356 (2)
N1—C5	1.3363 (18)	C8—H8	0.9300
N1—C4	1.3700 (18)	C9—H9	0.9300
N1—H1N	0.85 (2)		
O3—P1—O2	116.20 (6)	P2—C1—P1	115.68 (7)
O3—P1—O4	107.20 (6)	C3—C2—C1	116.39 (11)

O2—P1—O4	109.85 (6)	C3—C2—H2A	108.2
O3—P1—C1	110.32 (6)	C1—C2—H2A	108.2
O2—P1—C1	106.68 (6)	C3—C2—H2B	108.2
O4—P1—C1	106.17 (6)	C1—C2—H2B	108.2
O6—P2—O5	115.07 (6)	H2A—C2—H2B	107.3
O6—P2—O7	113.46 (6)	C4—C3—N2	105.72 (11)
O5—P2—O7	105.64 (6)	C4—C3—C2	129.60 (13)
O6—P2—C1	109.47 (6)	N2—C3—C2	124.62 (12)
O5—P2—C1	107.81 (6)	C3—C4—N1	109.01 (13)
O7—P2—C1	104.75 (6)	C3—C4—H4	125.5
C1—O1—H1O	111.6 (16)	N1—C4—H4	125.5
P1—O4—H4O	116.9 (17)	N1—C5—N2	107.39 (11)
P2—O5—H5O	116.7 (18)	N1—C5—C6	131.56 (13)
P2—O7—H7O	118.0 (17)	N2—C5—C6	121.04 (12)
H81—O8—H82	105 (2)	C7—C6—C5	117.60 (13)
C5—N1—C4	109.26 (12)	C7—C6—H6	121.2
C5—N1—H1N	121.0 (15)	C5—C6—H6	121.2
C4—N1—H1N	129.6 (15)	C6—C7—C8	120.72 (13)
C9—N2—C5	120.93 (11)	C6—C7—H7	119.6
C9—N2—C3	130.37 (11)	C8—C7—H7	119.6
C5—N2—C3	108.59 (11)	C9—C8—C7	120.97 (13)
O1—C1—C2	112.48 (10)	C9—C8—H8	119.5
O1—C1—P2	101.50 (8)	C7—C8—H8	119.5
C2—C1—P2	112.69 (8)	C8—C9—N2	118.63 (12)
O1—C1—P1	106.38 (8)	C8—C9—H9	120.7
C2—C1—P1	107.91 (8)	N2—C9—H9	120.7

Hydrogen-bond geometry (Å, °)

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1O···O8	0.78 (3)	1.87 (3)	2.6468 (18)	169 (2)
O4—H4O···O2[i]	0.90 (3)	1.73 (3)	2.6116 (16)	169 (3)
O5—H5O···O3[ii]	0.88 (3)	1.62 (3)	2.4973 (14)	175 (3)
O7—H7O···O2[iii]	0.83 (2)	1.80 (2)	2.6183 (14)	170 (2)
O8—H81···O6[iv]	0.82 (2)	1.99 (2)	2.8011 (15)	169 (3)
O8—H82···O6[v]	0.91 (2)	1.83 (2)	2.7334 (16)	175 (2)
N1—H1N···O5[vi]	0.85 (2)	2.18 (3)	2.9930 (15)	158 (2)
C2—H2B···O2	0.97	2.50	3.0224 (17)	114
C4—H4···O8	0.93	2.40	3.2079 (19)	145
C8—H8···O4[vii]	0.93	2.51	3.1704 (17)	128

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