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Crystal structure of ammonium 3'-azido-3'-deoxythymidine-5'-aminocarbonylphosphonate hemihydrate: an anti-HIV agent

Maxim V. Jasko,^a Galina V. Gurskaya,^a Marina K. Kukhanova^a and Ivan S. Bushmarinov^{b*}

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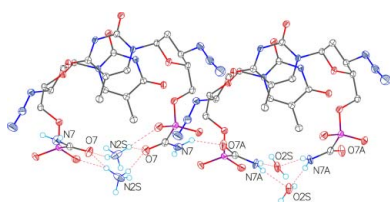
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^aEngelhardt Institute of Molecular Biology, Russian Academy of Sciences, 119991, Vavilov St 32, Moscow, Russian Federation, and ^bA.N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 119991, Vavilov St 28, Moscow, Russian Federation. *Correspondence e-mail: ib@ineos.ac.ru

The asymmetric unit of the title compound, $\text{NH}_4^+ \cdot \text{C}_{11}\text{H}_{14}\text{N}_6\text{O}_7\text{P}^- \cdot 0.5\text{H}_2\text{O}$, contains one 3'-azido-3'-deoxythymidine-5'-aminocarbonylphosphonate (ACP-AZT) anion, half of an NH_4^+ cation lying on a twofold rotation axis and in another position, occupied with equal probabilities of 0.5, an NH_4^+ cation and a water molecule. The amide group of the ACP-AZT anion is disordered (occupancy ratio 0.5:0.5), with one part forming an $\text{N}-\text{H} \cdots \text{O}$ (involving $\text{C}=\text{O} \cdots \text{H}_4\text{N}^+$) hydrogen bond and the other an $\text{O}-\text{H} \cdots \text{N}$ (involving $\text{C}-\text{NH}_2 \cdots \text{OH}_2$) hydrogen bond with the components of the split $\text{NH}_4^+/\text{H}_2\text{O}$ position. The pseudorotation parameters of ACP-AZT set it apart from previously studied AZT and thymidine. In the crystal, the various components are linked by $\text{N}-\text{H} \cdots \text{O}$, $\text{O}-\text{H} \cdots \text{O}$, $\text{N}-\text{H} \cdots \text{N}$, $\text{C}-\text{H} \cdots \text{O}$ and $\text{C}-\text{H} \cdots \text{N}$ hydrogen bonds, forming a three-dimensional framework.

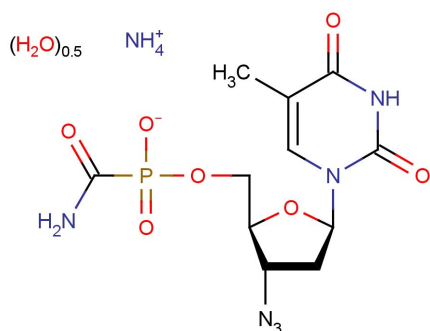
1. Chemical context

Nucleoside analogues play an important role in clinics as antiviral drugs. At present, seven nucleoside analogues have been approved by the US FDA for the treatment of HIV-infected patients, the first of which was 3'-azido-3'-deoxythymidine (AZT) (DeClercq, 2010). Despite progress in the treatment of HIV-infected patients, these drugs possess some drawbacks: AZT lifetime in patients is only one h, requiring frequent dose administration; long-term usage of AZT causes toxic side effects, *viz* anaemia, bone-marrow suppression, neuropathy and emergence of HIV-resistant strains (Stańczak *et al.*, 2006; Beaumont *et al.*, 2003). Various forms of nucleosides and nucleotides have been developed in order to reduce the toxic effects of anti-HIV drugs, to increase their oral bioavailability and to improve their pharmacokinetic properties (Kukhanova & Shirokova, 2005). Out of a large number of potential HIV drugs, only one compound has been approved by the FDA for the treatment of HIV-infected patients, namely, tenofovir disoproxil fumarate (Viread[®]; DeClercq, 2010), and one prodrug of AZT (5'-hydrogenphosphonate AZT, Nikavir[®]) has been used in clinical trials in Russia (Ivanova *et al.*, 2010; Kukhanova & Shirokova, 2005). In a continuation of the search for compounds with improved medicinal properties, we have synthesized a novel derivative form of AZT, 5'-aminocarbonylphosphonate 3'-azido-3'-deoxythymidine (ACP-AZT). Biological testing of ACP-AZT in cell cultures infected with HIV-1 showed that this compound inhibited virus replication and its toxicity was much lower compared to that of AZT and Nikavir. ACP-AZT



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displayed improved pharmacokinetic characteristics compared to AZT (Khandazhinskaya *et al.*, 2009; Kukhanova, 2012; Shirokova *et al.*, 2006). Accumulation of ACP–AZT in animal blood was slower than the accumulation of AZT, leading to a decrease in the toxic side effects displayed by AZT. The half-life of ACP–AZT in animal blood is three to four times longer than that of AZT, making it a perspective candidate as an anti-HIV drug for clinical usage. At present, the title compound is undergoing clinical trials as a potential anti-HIV drug.



2. Structural commentary

The molecular structure of the title compound, ACP–AZT, is illustrated in Fig. 1. The comparative analysis of the crystal structure conformation of the title ACP–AZT molecule with the conformation of AZT and natural thymidine molecules (Young *et al.*, 1969) is discussed below. The main differences are observed in the carbohydrate fragments of the molecules. In terms of pseudorotation (IUPAC–IUB, 1983), the conformation of the furanose ring in the ACP–AZT molecule is

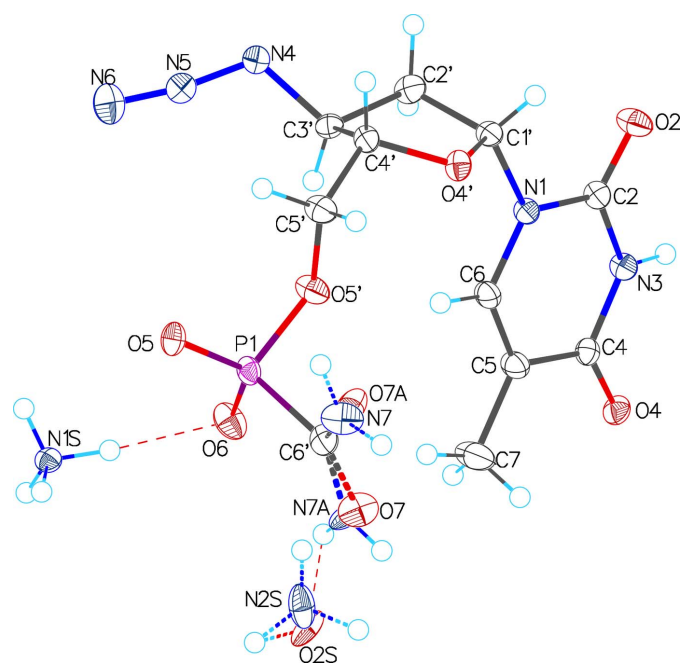


Figure 1
A view of the molecular structure of the title salt, showing the atom numbering. Displacement ellipsoids are drawn at the 50% probability level. The ammonium cation, N1S, lies on a twofold rotation axis.

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

<i>D</i> –H··· <i>A</i>	<i>D</i> –H	H··· <i>A</i>	<i>D</i> ··· <i>A</i>	<i>D</i> –H··· <i>A</i>
N1S–H1SA···O4 ⁱ	0.85 (2)	2.01 (2)	2.8565 (19)	173 (2)
N1S–H1SB···O6	0.94 (3)	1.86 (3)	2.780 (2)	168 (2)
N3–H3···O5 ⁱⁱ	0.90 (3)	1.90 (3)	2.781 (2)	167 (3)
O2S–H2SA···O5 ⁱⁱⁱ	0.87 (2)	2.00 (2)	2.868 (11)	176 (3)
N2S–H2SA···O5 ⁱⁱⁱ	0.93 (2)	2.00 (2)	2.857 (11)	154 (3)
N2S–H2SC···O6	0.94 (3)	2.21 (4)	3.013 (12)	143 (5)
N2S–H2SC···O7	0.94 (3)	2.20 (5)	2.901 (16)	130 (5)
O2S–H2SB···O2 ^{iv}	0.93 (2)	1.91 (2)	2.822 (11)	166 (3)
N2S–H2SB···O2 ^{iv}	0.95 (2)	1.91 (2)	2.818 (12)	159 (3)
N2S–H2SD···O7 ^v	0.95 (3)	1.99 (3)	2.902 (16)	162 (5)
N7–H7A···N7 ^{vi}	0.91 (3)	1.93 (5)	2.67 (3)	136 (5)
N7–H7B···N2S ^{vii}	0.92 (3)	2.66 (6)	3.265 (17)	124 (5)
N7A–H7AA···O2S ^v	0.90 (3)	2.00 (3)	2.887 (18)	167 (6)
N7A–H7AB···O2S	0.91 (3)	2.03 (3)	2.856 (15)	150 (4)
C1′–H1′···O6 ^{viii}	0.90 (3)	2.53 (2)	3.100 (2)	122.3 (19)
C3′–H3′···N4 ^{iv}	0.92 (2)	2.65 (2)	3.274 (3)	125.1 (19)
C4′–H4′···O4 ^{ix}	1.00	2.51	3.257 (2)	131
C6–H6···O5′	0.95	2.47	3.402 (2)	168

Symmetry codes: (i) $-x + \frac{3}{2}, y - \frac{1}{2}, -z + \frac{5}{4}$; (ii) $y + \frac{1}{2}, -x + \frac{3}{2}, z + \frac{3}{4}$; (iii) $-y + 1, -x + 1, -z + \frac{1}{2}$; (iv) $-y + \frac{3}{2}, x - \frac{1}{2}, z + \frac{1}{4}$; (v) $y, x, -z + 1$; (vi) $y, x, -z$; (vii) $-x + 1, -y + 1, z - \frac{1}{2}$; (viii) $y + \frac{1}{2}, -x + \frac{3}{2}, z - \frac{1}{4}$; (ix) $x, y, z - 1$.

described by the phase angle of pseudorotation, $P = 25.2^\circ$, and the degree of pucker, $\Psi_m = 35.0^\circ$. These results correspond to a C3′-endo-C4′-exo (3T_4) conformation of the sugar cycle. Atoms C3′ and C4′ deviate from the plane of atoms C1′/O4′/C2′ by 0.458 and -0.101 Å, respectively. Unlike the AZT molecules and the molecule of thymidine, which exhibit a C3′-exo- class of pucker, the ACP–AZT molecule exhibits a C3′-endo pucker. The orientation of the thymine base relative to the deoxyribose ring in the ACP–AZT molecule is *anti*, similar to that in natural thymidine and AZT, the glycosyl torsion angle $\chi_{\text{ACP-AZT}}(\text{O4′}–\text{C1′}–\text{N1}–\text{C2}) = -147.75$ (16) $^\circ$. The geometric parameters of the azido residue and the orientation relative to the deoxyribose ring in ACP–AZT and AZT coincide within experimental error.

3. Supramolecular features

The C(O)NH₂ group of ACP–AZT is disordered, one part forming a C=O···H₄N⁺ hydrogen bond and the other a C–

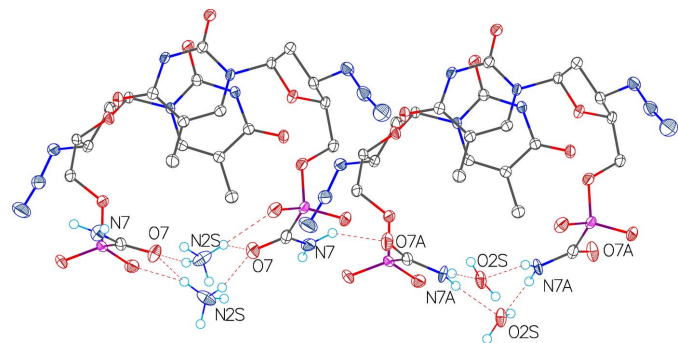


Figure 2
The hydrogen bonds involving the disordered water and ammonia molecules in the crystal packing of ACP–AZT (see Table 1 for details). A fragment of the hypothetically ordered ‘supercell’ is shown.

NH₂···OH₂ hydrogen bond with the components of the NH₄⁺/H₂O position (Table 1 and Fig. 2). In the crystal, the various components are linked by N—H···O, O—H···O, N—H···N, C—H···O and C—H···N hydrogen bonds (Table 1), forming a three-dimensional framework. The structure can be described by an ordered supercell doubled in the *c* direction (Fig. 2); however, this was not observed in the diffraction experiment.

4. Database survey

Earlier, in 1986, we studied the crystal and molecular structures of AZT and then some other HIV replication inhibitors by X-ray analysis (Gurskaya *et al.*, 1986, 1990, 1991, 1992). AZT structures obtained later by four other laboratories were similar to our structure (Camerman *et al.*, 1987; Birnbaum *et al.*, 1987; Parthasarathy *et al.*, 1988; Van Roey *et al.*, 1988).

5. Synthesis and crystallization

The title compound was synthesized as described earlier (Shirokova *et al.*, 2004). The crystals for X-ray analysis were selected from a highly dispersed (fine crystals) batch of ACP–AZT prepared for clinical usage.

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. The C-bound H atoms were included in calculated positions and treated as riding, with C—H = 0.95–1.00 Å and $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$ for methyl H atoms and $1.2U_{\text{eq}}(\text{C})$ for other H atoms. The other distance restraints and SIMU parameters are given below: DFIX 1.234 0.005 O7A C6' O7 C6'; DFIX 0.9 N7 H7a N7 H7b; DFIX 0.95 N2S H2Sc N2S H2Sd N2S H2Sa N2S H2Sb O2S H2Sb O2S H2Sa; DFIX 1.325 0.005 N7 C6' N7A C6'; DFIX 0.9 N7A H7Aa N7A H7Ab; SIMU 0.01 0.005 1.7 N2S O2S; SIMU 0.01 0.005 1.7 N7A O7 O7A N7. The split NH₄⁺/H₂O position was refined with an occupancy of 0.5 for each atom.

Acknowledgements

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Table 2
Experimental details.

Crystal data	
Chemical formula	NH ₄ ⁺ ·C ₁₁ H ₁₄ N ₆ O ₇ P [−] ·0.5H ₂ O
<i>M_r</i>	400.30
Crystal system, space group	Tetragonal, <i>P</i> 4 ₁ 2 ₁ 2
Temperature (K)	100
<i>a</i> , <i>c</i> (Å)	18.5564 (6), 10.1139 (4)
<i>V</i> (Å ³)	3482.6 (3)
<i>Z</i>	8
Radiation type	Mo <i>K</i> α
μ (mm ^{−1})	0.21
Crystal size (mm)	0.21 × 0.20 × 0.20
Data collection	
Diffractometer	Bruker APEXII CCD
Absorption correction	Multi-scan (<i>SADABS</i> ; Bruker, 2009)
<i>T</i> _{min} , <i>T</i> _{max}	0.670, 0.746
No. of measured, independent and observed [<i>I</i> > 2σ(<i>I</i>)] reflections	47562, 5322, 4822
<i>R</i> _{int}	0.047
(sin θ/λ) _{max} (Å ^{−1})	0.714
Refinement	
<i>R</i> [<i>F</i> ² > 2σ(<i>F</i> ²)], <i>wR</i> (<i>F</i> ²), <i>S</i>	0.032, 0.079, 1.09
No. of reflections	5322
No. of parameters	315
No. of restraints	32
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{\text{max}}$, $\Delta\rho_{\text{min}}$ (e Å ^{−3})	0.34, −0.29
Absolute structure	Flack <i>x</i> determined using 1919 quotients [(<i>I</i> ⁺)−(<i>I</i> [−])]/[(<i>I</i> ⁺)+(<i>I</i> [−])] (Parsons <i>et al.</i> , 2013)
Absolute structure parameter	0.00 (3)

Computer programs: *APEX2* and *SAINT* (Bruker, 2009), *SHELXS2014* and *SHELXL2014* (Sheldrick, 2008) and *OLEX2* (Dolomanov *et al.*, 2009).

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Computing details

Data collection: *APEX2* (Bruker, 2009); cell refinement: *SAINTE* (Bruker, 2009); data reduction: *SAINTE* (Bruker, 2009); program(s) used to solve structure: *SHELXS2014* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2008); molecular graphics: *OLEX2* (Dolomanov *et al.*, 2009); software used to prepare material for publication: *OLEX2* (Dolomanov *et al.*, 2009).

Ammonium 3'-azido-3'-deoxythymidine-5'-aminocarbonylphosphonate hemihydrate

Crystal data

$\text{NH}_4^+\cdot\text{C}_{11}\text{H}_{14}\text{N}_6\text{O}_7\text{P}^- \cdot 0.5\text{H}_2\text{O}$

$M_r = 400.30$

Tetragonal, $P4_12_12$

$a = 18.5564$ (6) Å

$c = 10.1139$ (4) Å

$V = 3482.6$ (3) Å³

$Z = 8$

$F(000) = 1672$

$D_x = 1.527$ Mg m⁻³

Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å

Cell parameters from 9998 reflections

$\theta = 2.3\text{--}30.3^\circ$

$\mu = 0.21$ mm⁻¹

$T = 100$ K

Prism, colourless

0.21 × 0.20 × 0.20 mm

Data collection

Bruker APEXII CCD

diffractometer

Radiation source: sealed tube

Graphite monochromator

Detector resolution: 8 pixels mm⁻¹

φ and ω scans

Absorption correction: multi-scan

(*SADABS*; Bruker, 2009)

$T_{\min} = 0.670$, $T_{\max} = 0.746$

47562 measured reflections

5322 independent reflections

4822 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.047$

$\theta_{\max} = 30.5^\circ$, $\theta_{\min} = 2.2^\circ$

$h = -26 \rightarrow 26$

$k = -26 \rightarrow 26$

$l = -14 \rightarrow 14$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.032$

$wR(F^2) = 0.079$

$S = 1.09$

5322 reflections

315 parameters

32 restraints

Primary atom site location: structure-invariant

direct methods

Secondary atom site location: difference Fourier map

Hydrogen site location: mixed

H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0415P)^2 + 0.5648P]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} = 0.001$

$\Delta\rho_{\max} = 0.34$ e Å⁻³

$\Delta\rho_{\min} = -0.29$ e Å⁻³

Absolute structure: Flack x determined using
1919 quotients $[(F^+)-(F^-)]/[(F^+)+(F^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter: 0.00 (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 (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$	Occ. (<1)
P1	0.68921 (3)	0.49006 (3)	0.20527 (5)	0.01645 (10)	
O2	0.92567 (8)	0.79475 (9)	0.50029 (14)	0.0247 (3)	
O2S	0.5859 (5)	0.4368 (6)	0.5786 (9)	0.0241 (17)	0.5
O4	0.79798 (8)	0.68215 (7)	0.82247 (13)	0.0194 (3)	
O4'	0.81753 (7)	0.69188 (7)	0.21627 (13)	0.0172 (3)	
O5	0.68747 (8)	0.45502 (8)	0.07236 (14)	0.0229 (3)	
O5'	0.74688 (8)	0.55407 (8)	0.20885 (14)	0.0234 (3)	
O6	0.70278 (9)	0.44576 (8)	0.32578 (14)	0.0257 (3)	
O7	0.5715 (9)	0.5389 (8)	0.3380 (10)	0.026 (2)	0.5
O7A	0.5847 (6)	0.5815 (6)	0.1427 (10)	0.0303 (19)	0.5
N1	0.85030 (9)	0.70295 (9)	0.43868 (15)	0.0156 (3)	
N1S	0.69819 (9)	0.30181 (9)	0.2500	0.0156 (4)	
H1SA	0.7013 (13)	0.2684 (13)	0.308 (2)	0.018 (6)*	
H1SB	0.7014 (14)	0.3480 (14)	0.287 (3)	0.025 (6)*	
H3	0.8853 (15)	0.7633 (15)	0.719 (3)	0.029*	
H2SA	0.5720 (15)	0.3982 (11)	0.536 (3)	0.029*	
H2SC	0.619 (3)	0.461 (3)	0.478 (4)	0.029*	0.5
H2SB	0.6270 (12)	0.4260 (15)	0.628 (2)	0.029*	
H2SD	0.570 (3)	0.477 (3)	0.590 (5)	0.029*	0.5
N2S	0.5985 (7)	0.4395 (7)	0.5538 (11)	0.028 (2)	0.5
N3	0.86108 (9)	0.73708 (9)	0.65883 (15)	0.0163 (3)	
N4	0.94590 (10)	0.55785 (9)	0.10114 (18)	0.0229 (4)	
N5	0.92571 (10)	0.49900 (10)	0.05676 (19)	0.0266 (4)	
N6	0.91507 (14)	0.44520 (13)	0.0082 (3)	0.0464 (6)	
N7	0.5716 (7)	0.5749 (8)	0.1320 (14)	0.0259 (17)	0.5
H7A	0.597 (3)	0.578 (3)	0.055 (4)	0.037 (16)*	0.5
H7B	0.531 (2)	0.604 (3)	0.133 (6)	0.038 (16)*	0.5
N7A	0.5747 (10)	0.5256 (10)	0.3488 (11)	0.0199 (17)	0.5
H7AA	0.532 (2)	0.549 (3)	0.361 (6)	0.033 (17)*	0.5
H7AB	0.593 (2)	0.494 (2)	0.407 (4)	0.011 (11)*	0.5
C1'	0.87645 (10)	0.70731 (10)	0.30064 (18)	0.0166 (3)	
H1'	0.8922 (13)	0.7528 (14)	0.290 (2)	0.016 (6)*	
C2	0.88180 (10)	0.74798 (10)	0.52988 (18)	0.0164 (3)	
C2'	0.93586 (11)	0.65280 (11)	0.26815 (19)	0.0206 (4)	
H2'A	0.9735	0.6747	0.2116	0.025*	

H2'B	0.9586	0.6341	0.3498	0.025*
C3'	0.89591 (10)	0.59331 (10)	0.19471 (19)	0.0168 (3)
H3'	0.8762 (13)	0.5614 (14)	0.255 (2)	0.018 (6)*
C4	0.81153 (10)	0.68706 (10)	0.70369 (17)	0.0154 (3)
C4'	0.83606 (10)	0.63509 (10)	0.12478 (17)	0.0163 (3)
H4'	0.8557	0.6569	0.0419	0.020*
C5	0.77850 (11)	0.64287 (11)	0.60195 (19)	0.0204 (4)
C5'	0.76867 (12)	0.59301 (11)	0.09211 (19)	0.0211 (4)
H5'A	0.7298	0.6262	0.0640	0.025*
H5'B	0.7784	0.5589	0.0189	0.025*
C6	0.79969 (11)	0.65210 (10)	0.47609 (19)	0.0198 (4)
H6	0.7790	0.6224	0.4097	0.024*
C6'	0.60339 (12)	0.53904 (11)	0.23020 (18)	0.0207 (4)
C7	0.72211 (16)	0.58965 (16)	0.6417 (2)	0.0416 (7)
H7C	0.7422	0.5562	0.7070	0.062*
H7D	0.7061	0.5627	0.5638	0.062*
H7E	0.6810	0.6152	0.6805	0.062*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
P1	0.0215 (2)	0.0144 (2)	0.01346 (19)	-0.00265 (18)	-0.00230 (17)	-0.00192 (16)
O2	0.0285 (8)	0.0300 (8)	0.0157 (6)	-0.0136 (6)	-0.0020 (6)	0.0018 (6)
O2S	0.024 (3)	0.033 (3)	0.015 (2)	0.017 (2)	0.0025 (18)	-0.0010 (17)
O4	0.0261 (7)	0.0193 (6)	0.0127 (6)	0.0011 (5)	0.0019 (5)	-0.0005 (5)
O4'	0.0213 (6)	0.0177 (6)	0.0125 (5)	0.0009 (5)	-0.0039 (5)	-0.0014 (5)
O5	0.0287 (8)	0.0212 (7)	0.0189 (6)	-0.0021 (6)	0.0005 (6)	-0.0088 (5)
O5'	0.0289 (8)	0.0269 (7)	0.0143 (6)	-0.0122 (6)	-0.0027 (6)	0.0011 (6)
O6	0.0348 (8)	0.0200 (7)	0.0223 (7)	-0.0033 (6)	-0.0079 (6)	0.0049 (5)
O7	0.026 (2)	0.033 (5)	0.018 (2)	0.008 (3)	-0.0044 (19)	0.0120 (19)
O7A	0.041 (5)	0.031 (3)	0.019 (2)	0.012 (3)	0.007 (3)	0.000 (2)
N1	0.0213 (7)	0.0161 (7)	0.0095 (6)	-0.0030 (6)	-0.0009 (6)	-0.0001 (5)
N1S	0.0175 (6)	0.0175 (6)	0.0119 (9)	-0.0014 (8)	0.0005 (6)	0.0005 (6)
N2S	0.025 (4)	0.018 (2)	0.042 (6)	0.006 (2)	-0.015 (4)	-0.008 (3)
N3	0.0190 (8)	0.0190 (8)	0.0110 (6)	-0.0029 (6)	-0.0028 (6)	-0.0001 (6)
N4	0.0264 (9)	0.0184 (8)	0.0239 (8)	-0.0024 (7)	0.0071 (7)	-0.0026 (7)
N5	0.0293 (9)	0.0229 (9)	0.0276 (9)	-0.0021 (7)	0.0081 (8)	-0.0030 (7)
N6	0.0528 (14)	0.0334 (11)	0.0529 (14)	-0.0122 (10)	0.0144 (12)	-0.0194 (11)
N7	0.016 (3)	0.039 (3)	0.023 (3)	-0.002 (2)	-0.0084 (18)	0.008 (3)
N7A	0.022 (3)	0.028 (5)	0.009 (2)	0.009 (3)	0.005 (2)	0.006 (2)
C1'	0.0214 (8)	0.0183 (8)	0.0101 (7)	-0.0043 (7)	0.0002 (6)	-0.0005 (6)
C2	0.0182 (8)	0.0173 (8)	0.0138 (8)	-0.0007 (7)	-0.0025 (7)	0.0002 (7)
C2'	0.0184 (9)	0.0276 (10)	0.0158 (8)	-0.0021 (7)	-0.0014 (7)	-0.0026 (7)
C3'	0.0189 (8)	0.0182 (8)	0.0132 (7)	-0.0005 (7)	0.0022 (7)	0.0014 (7)
C4	0.0171 (8)	0.0142 (7)	0.0148 (7)	0.0017 (7)	-0.0009 (7)	0.0002 (6)
C4'	0.0227 (9)	0.0156 (8)	0.0107 (7)	-0.0021 (7)	-0.0011 (7)	-0.0001 (6)
C5	0.0241 (10)	0.0205 (9)	0.0165 (8)	-0.0068 (8)	0.0012 (7)	-0.0017 (7)
C5'	0.0260 (10)	0.0251 (10)	0.0123 (7)	-0.0080 (8)	-0.0019 (7)	0.0012 (7)

C6	0.0226 (9)	0.0186 (9)	0.0182 (9)	-0.0066 (7)	0.0015 (7)	-0.0037 (7)
C6'	0.0277 (10)	0.0203 (9)	0.0140 (8)	-0.0016 (7)	-0.0016 (7)	-0.0009 (7)
C7	0.0536 (16)	0.0472 (15)	0.0242 (11)	-0.0338 (13)	0.0121 (11)	-0.0092 (11)

Geometric parameters (Å, °)

P1—O5	1.4936 (14)	N4—C3'	1.480 (3)
P1—O5'	1.5991 (14)	N5—N6	1.130 (3)
P1—O6	1.4916 (15)	N7—H7A	0.91 (3)
P1—C6'	1.851 (2)	N7—H7B	0.92 (3)
O2—C2	1.227 (2)	N7—C6'	1.333 (6)
O2S—H2SA	0.874 (19)	N7A—H7AA	0.90 (3)
O2S—H2SB	0.93 (2)	N7A—H7AB	0.91 (3)
O4—C4	1.231 (2)	N7A—C6'	1.336 (5)
O4'—C1'	1.416 (2)	C1'—H1'	0.90 (3)
O4'—C4'	1.444 (2)	C1'—C2'	1.532 (3)
O5'—C5'	1.442 (2)	C2'—H2'A	0.9900
O7—C6'	1.241 (6)	C2'—H2'B	0.9900
O7A—C6'	1.234 (5)	C2'—C3'	1.523 (3)
N1—C1'	1.480 (2)	C3'—H3'	0.92 (2)
N1—C2	1.375 (2)	C3'—C4'	1.528 (3)
N1—C6	1.384 (2)	C4—C5	1.452 (3)
N1S—H1SA	0.85 (2)	C4'—H4'	1.0000
N1S—H1SB	0.94 (3)	C4'—C5'	1.511 (3)
N2S—H2SA	0.93 (2)	C5—C6	1.343 (3)
N2S—H2SC	0.94 (3)	C5—C7	1.494 (3)
N2S—H2SB	0.95 (2)	C5'—H5'A	0.9900
N2S—H2SD	0.95 (3)	C5'—H5'B	0.9900
N3—H3	0.90 (3)	C6—H6	0.9500
N3—C2	1.375 (2)	C7—H7C	0.9800
N3—C4	1.383 (2)	C7—H7D	0.9800
N4—N5	1.239 (2)	C7—H7E	0.9800
O5—P1—O5'	110.99 (8)	C3'—C2'—C1'	103.47 (15)
O5—P1—C6'	108.53 (9)	C3'—C2'—H2'A	111.1
O5'—P1—C6'	102.01 (9)	C3'—C2'—H2'B	111.1
O6—P1—O5	119.94 (9)	N4—C3'—C2'	109.21 (16)
O6—P1—O5'	106.13 (8)	N4—C3'—H3'	112.6 (15)
O6—P1—C6'	107.73 (9)	N4—C3'—C4'	112.67 (15)
H2SA—O2S—H2SB	109 (3)	C2'—C3'—H3'	109.6 (15)
C1'—O4'—C4'	110.47 (14)	C2'—C3'—C4'	102.23 (15)
C5'—O5'—P1	122.76 (12)	C4'—C3'—H3'	109.9 (15)
C2—N1—C1'	117.39 (15)	O4—C4—N3	120.38 (17)
C2—N1—C6	121.29 (16)	O4—C4—C5	124.32 (17)
C6—N1—C1'	121.17 (15)	N3—C4—C5	115.30 (16)
H1SA—N1S—H1SB	113 (2)	O4'—C4'—C3'	104.29 (14)
H2SA—N2S—H2SC	113 (4)	O4'—C4'—H4'	109.2
H2SA—N2S—H2SB	103 (3)	O4'—C4'—C5'	108.68 (16)

H2SA—N2S—H2SD	113 (4)	C3'—C4'—H4'	109.2
H2SC—N2S—H2SB	122 (4)	C5'—C4'—C3'	116.14 (16)
H2SC—N2S—H2SD	103 (5)	C5'—C4'—H4'	109.2
H2SB—N2S—H2SD	101 (4)	C4—C5—C7	118.58 (17)
C2—N3—H3	114.9 (18)	C6—C5—C4	118.44 (18)
C2—N3—C4	126.57 (16)	C6—C5—C7	122.99 (18)
C4—N3—H3	118.3 (18)	O5'—C5'—C4'	108.18 (15)
N5—N4—C3'	115.73 (17)	O5'—C5'—H5'A	110.1
N6—N5—N4	171.6 (2)	O5'—C5'—H5'B	110.1
H7A—N7—H7B	113 (5)	C4'—C5'—H5'A	110.1
C6'—N7—H7A	116 (4)	C4'—C5'—H5'B	110.1
C6'—N7—H7B	130 (4)	H5'A—C5'—H5'B	108.4
H7AA—N7A—H7AB	124 (5)	N1—C6—H6	118.5
C6'—N7A—H7AA	112 (4)	C5—C6—N1	123.00 (17)
C6'—N7A—H7AB	124 (3)	C5—C6—H6	118.5
O4'—C1'—N1	107.70 (14)	O7—C6'—P1	121.9 (6)
O4'—C1'—H1'	111.8 (15)	O7—C6'—N7	116.4 (11)
O4'—C1'—C2'	107.03 (15)	O7A—C6'—P1	117.2 (6)
N1—C1'—H1'	105.5 (16)	O7A—C6'—N7A	130.6 (9)
N1—C1'—C2'	113.71 (15)	N7—C6'—P1	121.6 (8)
C2'—C1'—H1'	111.1 (15)	N7A—C6'—P1	111.9 (7)
O2—C2—N1	123.25 (17)	C5—C7—H7C	109.5
O2—C2—N3	121.39 (17)	C5—C7—H7D	109.5
N3—C2—N1	115.35 (16)	C5—C7—H7E	109.5
C1'—C2'—H2'A	111.1	H7C—C7—H7D	109.5
C1'—C2'—H2'B	111.1	H7C—C7—H7E	109.5
H2'A—C2'—H2'B	109.0	H7D—C7—H7E	109.5
P1—O5'—C5'—C4'	-165.61 (14)	C1'—O4'—C4'—C3'	24.84 (18)
O4—C4—C5—C6	-177.9 (2)	C1'—O4'—C4'—C5'	149.32 (15)
O4—C4—C5—C7	2.6 (3)	C1'—N1—C2—O2	6.0 (3)
O4'—C1'—C2'—C3'	-18.00 (19)	C1'—N1—C2—N3	-173.72 (16)
O4'—C4'—C5'—O5'	-68.8 (2)	C1'—N1—C6—C5	174.96 (19)
O5—P1—O5'—C5'	25.85 (19)	C1'—C2'—C3'—N4	151.29 (15)
O5—P1—C6'—O7	139.4 (11)	C1'—C2'—C3'—C4'	31.75 (18)
O5—P1—C6'—O7A	-52.1 (6)	C2—N1—C1'—O4'	-147.75 (16)
O5—P1—C6'—N7	-38.8 (8)	C2—N1—C1'—C2'	93.8 (2)
O5—P1—C6'—N7A	132.9 (11)	C2—N1—C6—C5	-0.5 (3)
O5'—P1—C6'—O7	-103.3 (11)	C2—N3—C4—O4	179.38 (18)
O5'—P1—C6'—O7A	65.2 (6)	C2—N3—C4—C5	-0.6 (3)
O5'—P1—C6'—N7	78.4 (8)	C2'—C3'—C4'—O4'	-34.79 (18)
O5'—P1—C6'—N7A	-109.8 (11)	C2'—C3'—C4'—C5'	-154.33 (16)
O6—P1—O5'—C5'	157.72 (16)	C3'—C4'—C5'—O5'	48.3 (2)
O6—P1—C6'—O7	8.1 (11)	C4—N3—C2—O2	178.93 (18)
O6—P1—C6'—O7A	176.6 (6)	C4—N3—C2—N1	-1.3 (3)
O6—P1—C6'—N7	-170.1 (8)	C4—C5—C6—N1	-1.6 (3)
O6—P1—C6'—N7A	1.6 (11)	C4'—O4'—C1'—N1	-126.92 (15)
N1—C1'—C2'—C3'	100.81 (17)	C4'—O4'—C1'—C2'	-4.29 (19)

N3—C4—C5—C6	2.0 (3)	C6—N1—C1'—O4'	36.6 (2)
N3—C4—C5—C7	-177.5 (2)	C6—N1—C1'—C2'	-81.8 (2)
N4—C3'—C4'—O4'	-151.88 (15)	C6—N1—C2—O2	-178.36 (19)
N4—C3'—C4'—C5'	88.6 (2)	C6—N1—C2—N3	1.9 (3)
N5—N4—C3'—C2'	164.58 (18)	C6'—P1—O5'—C5'	-89.59 (17)
N5—N4—C3'—C4'	-82.6 (2)	C7—C5—C6—N1	177.9 (2)

Hydrogen-bond geometry (\AA , $^\circ$)

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
N1S—H1SA \cdots O4 ⁱ	0.85 (2)	2.01 (2)	2.8565 (19)	173 (2)
N1S—H1SB \cdots O6	0.94 (3)	1.86 (3)	2.780 (2)	168 (2)
N3—H3 \cdots O5 ⁱⁱ	0.90 (3)	1.90 (3)	2.781 (2)	167 (3)
O2S—H2SA \cdots O5 ⁱⁱⁱ	0.87 (2)	2.00 (2)	2.868 (11)	176 (3)
N2S—H2SA \cdots O5 ⁱⁱⁱ	0.93 (2)	2.00 (2)	2.857 (11)	154 (3)
N2S—H2SC \cdots O6	0.94 (3)	2.21 (4)	3.013 (12)	143 (5)
N2S—H2SC \cdots O7	0.94 (3)	2.20 (5)	2.901 (16)	130 (5)
O2S—H2SB \cdots O2 ^{iv}	0.93 (2)	1.91 (2)	2.822 (11)	166 (3)
N2S—H2SB \cdots O2 ^{iv}	0.95 (2)	1.91 (2)	2.818 (12)	159 (3)
N2S—H2SD \cdots O7 ^v	0.95 (3)	1.99 (3)	2.902 (16)	162 (5)
N7—H7A \cdots N7 ^{vi}	0.91 (3)	1.93 (5)	2.67 (3)	136 (5)
N7—H7B \cdots N2S ^{vii}	0.92 (3)	2.66 (6)	3.265 (17)	124 (5)
N7A—H7AA \cdots O2S ^v	0.90 (3)	2.00 (3)	2.887 (18)	167 (6)
N7A—H7AB \cdots O2S	0.91 (3)	2.03 (3)	2.856 (15)	150 (4)
C1'—H1' \cdots O6 ^{viii}	0.90 (3)	2.53 (2)	3.100 (2)	122.3 (19)
C3'—H3' \cdots N4 ^{iv}	0.92 (2)	2.65 (2)	3.274 (3)	125.1 (19)
C4'—H4' \cdots O4 ^{ix}	1.00	2.51	3.257 (2)	131
C6—H6 \cdots O5'	0.95	2.47	3.402 (2)	168

Symmetry codes: (i) $-x+3/2, y-1/2, -z+5/4$; (ii) $y+1/2, -x+3/2, z+3/4$; (iii) $-y+1, -x+1, -z+1/2$; (iv) $-y+3/2, x-1/2, z+1/4$; (v) $y, x, -z+1$; (vi) $y, x, -z$; (vii) $-x+1, -y+1, z-1/2$; (viii) $y+1/2, -x+3/2, z-1/4$; (ix) $x, y, z-1$.