Acta Cryst E STRUCTURE REPORTS

ISSN 1600-5368

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

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Received 25 September 2014
Accepted 11 October 2014

Edited by H. Stoeckli-Evans, University of Neuchâtel, Switzerland

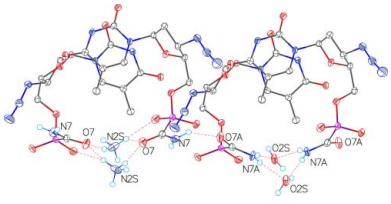
Keywords: crystal structure; anti-HIV agent; deoxythymidine; aminocarbonylphosphonate; ammonium salt

CCDC reference: 1028847
Supporting information: this article has supporting information at journals.iucr.org/e

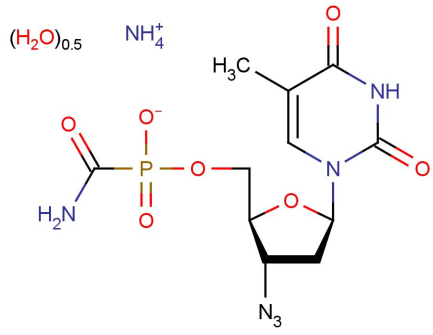
The asymmetric unit of the title compound, $NH_4^+ \cdot C_{11}H_{14}N_6O_7P^- \cdot 0.5H_2O$, contains one 3′-azido-3′-deoxythymidine-5′aminocarbonylphosphonate (ACP–AZT) anion, half of an NH_4^+ cation lying on a twofold rotation axis and in another position, occupied with equal probabilities of 0.5, 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 N—H···O (involving C=O···H_4N^+) hydrogen bond and the other an O—H···N (involving C—NH_2···OH_2) hydrogen bond with the components of the split NH_4^+/H_2O 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 N—H···O, O—H···O, N—H···N, C—H···O and C—H···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



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 described by the phase angle of pseudorotation, $P = 25.2°$, and the degree of pucker, $\Psi_m = 35.0°$. 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 $\chi_{ACP-AZT}$(O4′—C1′—N1—C2) = −147.75 (16)°. The geometric parameters of the azido residue and the orientation relative to the deoxyribose ring in ACP–AZT and AZT coincide within experimental error.

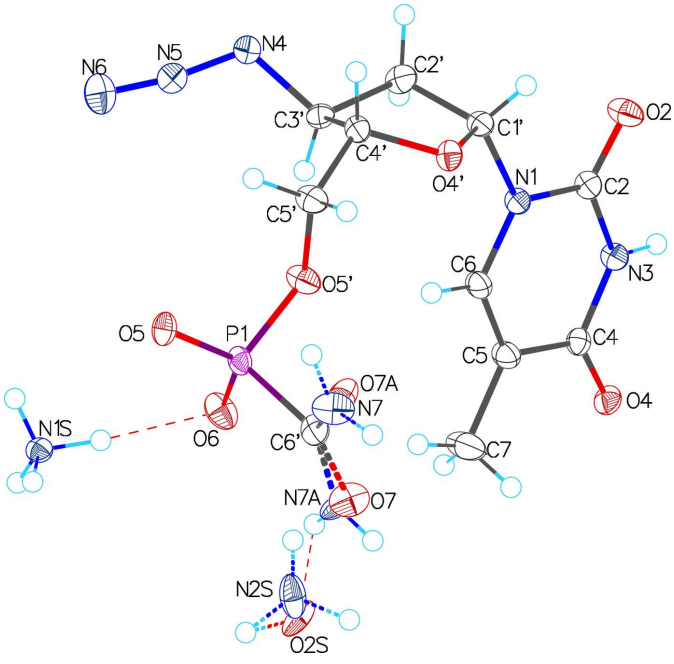


Figure 1
A view of the molecular structure of the title salt, showing the atom numbering. Displacement ellipsoids are drawn at the 50% probability level. The ammonium cation, N1*S*, lies on a twofold rotation axis.

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1*S*—H1*SA*···O4^{i}	0.85 (2)	2.01 (2)	2.8565 (19)	173 (2)
N1*S*—H1*SB*···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)
O2*S*—H2*SA*···O5^{iii}	0.87 (2)	2.00 (2)	2.868 (11)	176 (3)
N2*S*—H2*SA*···O5^{iii}	0.93 (2)	2.00 (2)	2.857 (11)	154 (3)
N2*S*—H2*SC*···O6	0.94 (3)	2.21 (4)	3.013 (12)	143 (5)
N2*S*—H2*SC*···O7	0.94 (3)	2.20 (5)	2.901 (16)	130 (5)
O2*S*—H2*SB*···O2^{iv}	0.93 (2)	1.91 (2)	2.822 (11)	166 (3)
N2*S*—H2*SB*···O2^{iv}	0.95 (2)	1.91 (2)	2.818 (12)	159 (3)
N2*S*—H2*SD*···O7^{v}	0.95 (3)	1.99 (3)	2.902 (16)	162 (5)
N7—H7*A*···N7^{vi}	0.91 (3)	1.93 (5)	2.67 (3)	136 (5)
N7—H7*B*···N2*S*^{vii}	0.92 (3)	2.66 (6)	3.265 (17)	124 (5)
N7*A*—H7*AA*···O2*S*^{v}	0.90 (3)	2.00 (3)	2.887 (18)	167 (6)
N7*A*—H7*AB*···O2*S*	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) $x, y, z-1$.

3. Supramolecular features

The C(O)NH$_2$ group of ACP–AZT is disordered, one part forming a C═O···H$_4$N$^+$ hydrogen bond and the other a C—

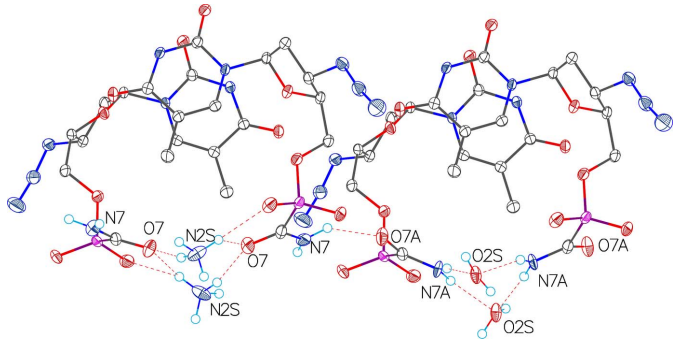


Figure 2
The hydrogen bonds involving the disordered water and ammonia molecules in the crystal packing of ACP–AZT (see Table 1 for details). A fragment of the hypothetically ordered 'supercell' is shown.

$NH_2\cdots OH_2$ hydrogen bond with the components of the NH_4^+/H_2O 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_{iso}(H) = 1.5U_{eq}(C) for methyl H atoms and 1.2U_{eq}(C) for other H atoms. The other distance restraints and SIMU parameters are given below: DFIX 1.234 0.005 O7*A* C6′ O7 C6′; DFIX 0.9 N7 H7a N7 H7b; DFIX 0.95 N2*S* H2Sc N2*S* H2Sd N2*S* H2Sa N2*S* H2Sb O2*S* H2Sb O2*S* H2Sa; DFIX 1.325 0.005 N7 C6′ N7*A* C6′; DFIX 0.9 N7*A* H7Aa N7*A* H7Ab; SIMU 0.01 0.005 1.7 N2*S* O2*S*; SIMU 0.01 0.005 1.7 N7*A* O7 O7*A* N7. The split NH_4^+/H_2O position was refined with an occupancy of 0.5 for each atom.

Table 2
Experimental details.

Crystal data	
Chemical formula	$NH_4^+\cdot C_{11}H_{14}N_6O_7P^-\cdot 0.5H_2O$
M_r	400.30
Crystal system, space group	Tetragonal, $P4_12_12$
Temperature (K)	100
a, *c* (Å)	18.5564 (6), 10.1139 (4)
V (Å^3)	3482.6 (3)
Z	8
Radiation type	Mo *Kα*
μ (mm^{-1})	0.21
Crystal size (mm)	0.21 × 0.20 × 0.20
Data collection	
Diffractometer	Bruker APEXII CCD
Absorption correction	Multi-scan (*SADABS*; Bruker, 2009)
T_{min}, T_{max}	0.670, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	47562, 5322, 4822
R_{int}	0.047
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.714
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, *S*	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
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.34, −0.29
Absolute structure	Flack x determined using 1919 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 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).

Acknowledgements

This work was supported by the Russian Foundation for Basic Research (Project 12–04-00581), and the project of Presidium RAN 'Molecular and Cellular Biology'.

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supporting information

Acta Cryst. (2014). E**70**, 396-399 [doi:10.1107/S1600536814022405]

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Computing details

Data collection: *APEX2* (Bruker, 2009); cell refinement: *SAINT* (Bruker, 2009); data reduction: *SAINT* (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

$NH_4^+ \cdot C_{11}H_{14}N_6O_7P^- \cdot 0.5H_2O$
M_r = 400.30
Tetragonal, $P4_12_12$
a = 18.5564 (6) Å
c = 10.1139 (4) Å
V = 3482.6 (3) Å^3
Z = 8
$F(000)$ = 1672
D_x = 1.527 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 9998 reflections
θ = 2.3–30.3°
μ = 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_{int} = 0.047
θ_{max} = 30.5°, θ_{min} = 2.2°
h = −26→26
k = −26→26
l = −14→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 $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (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 (Å²)

	x	*y*	*z*	U_{iso}*/U_{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, º)

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 (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1*S*—H1*SA*···O4^{i}	0.85 (2)	2.01 (2)	2.8565 (19)	173 (2)
N1*S*—H1*SB*···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)
O2*S*—H2*SA*···O5^{iii}	0.87 (2)	2.00 (2)	2.868 (11)	176 (3)
N2*S*—H2*SA*···O5^{iii}	0.93 (2)	2.00 (2)	2.857 (11)	154 (3)
N2*S*—H2*SC*···O6	0.94 (3)	2.21 (4)	3.013 (12)	143 (5)
N2*S*—H2*SC*···O7	0.94 (3)	2.20 (5)	2.901 (16)	130 (5)
O2*S*—H2*SB*···O2^{iv}	0.93 (2)	1.91 (2)	2.822 (11)	166 (3)
N2*S*—H2*SB*···O2^{iv}	0.95 (2)	1.91 (2)	2.818 (12)	159 (3)
N2*S*—H2*SD*···O7^{v}	0.95 (3)	1.99 (3)	2.902 (16)	162 (5)
N7—H7*A*···N7^{vi}	0.91 (3)	1.93 (5)	2.67 (3)	136 (5)
N7—H7*B*···N2*S*^{vii}	0.92 (3)	2.66 (6)	3.265 (17)	124 (5)
N7*A*—H7*AA*···O2*S*^{v}	0.90 (3)	2.00 (3)	2.887 (18)	167 (6)
N7*A*—H7*AB*···O2*S*	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*+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.