

7-Vinyl-8-aza-7-deaza-2'-deoxy-  
adenosine monohydrateFrank Seela,<sup>a\*</sup> Yunlong Zhang,<sup>a</sup> Kuiying Xu<sup>a</sup> and Henning  
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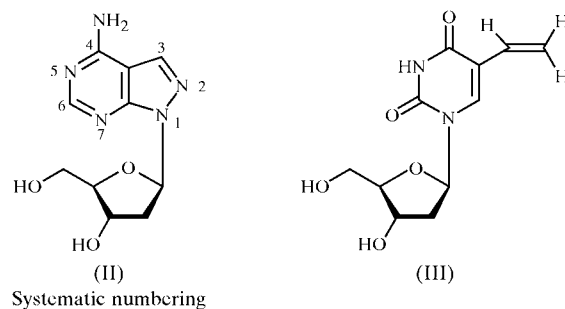
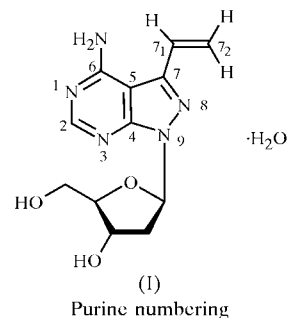
In the title compound, 4-amino-1-(2-deoxy- $\beta$ -D-erythro-pentofuranosyl)-3-vinyl-1H-pyrazolo[3,4-d]pyrimidine monohydrate, C<sub>12</sub>H<sub>15</sub>N<sub>5</sub>O<sub>3</sub>·H<sub>2</sub>O, the conformation of the glycosyl bond is *anti*. The furanose moiety is in an *S* conformation with an unsymmetrical twist, and the conformation at the exocyclic C—C(OH) bond is *+sc* (*gauche*, *gauche*). The vinyl side chain is bent out of the heterocyclic ring plane by 147.5 (5)°. The three-dimensional packing is stabilized by O—H···O, O—H···N and N—H···O hydrogen bonds.

## Comment

The 7-substituted 8-aza-7-deazapurine 2'-deoxyribonucleosides (3-substituted pyrazolo[3,4-d]pyrimidine 2'-deoxyribonucleosides) are studied as analogues of natural DNA constituents. Compound (II) (Seela & Steker, 1985; Seela, Zulauf *et al.*, 1999; Seela & Kaiser, 1988) has attracted attention as it is an ideal shape mimic of 2'-deoxyadenosine. Purine numbering is used throughout the manuscript. The 7-substituted derivatives of compound (II) have a stabilizing effect on oligonucleotide duplexes (Seela, Becher & Zulauf, 1999; Seela & Zulauf, 1999). Thus, the 7-position of an 8-aza-7-deazapurine 2'-deoxyribonucleoside is an attractive site for modification as it is the 5-position of a pyrimidine nucleoside (Gourlain *et al.*, 2001). Cheng *et al.* (1976) reported that 5-vinyl-2'-deoxyuridine, (III), has the capacity for viral and tumour inhibition. A single-crystal X-ray analysis of (III) was reported by Hamor *et al.* (1978). The present manuscript reports the single-crystal X-ray structure of the title compound, (I), containing a vinyl side chain in the 7-position.

Canonical purine 2'-deoxyribonucleosides tend to adopt an *anti* conformation. The orientation of the base relative to the sugar moiety (*syn/anti*) of purine nucleosides is defined by the torsion angle  $\chi$  (O4'—C1'—N9—C4) (IUPAC—IUB Joint Commission on Biochemical Nomenclature, 1983). In the crystal structure of (I) (Fig. 1 and Table 1), the conformation of the glycosyl bond is between *anti* and high *anti* [ $\chi =$

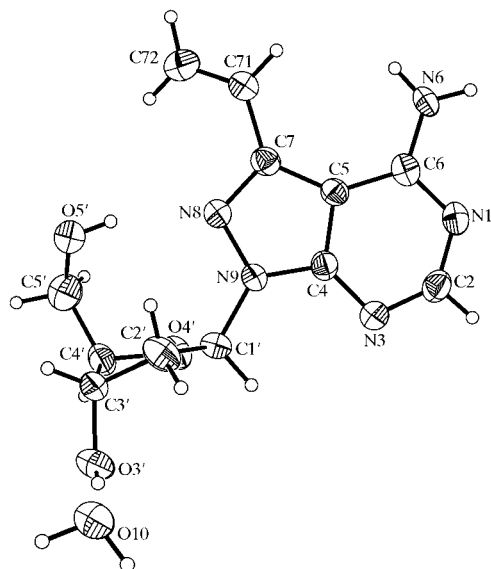
−106.9 (5)°]. A similar conformation was observed for the parent 8-aza-7-deazapurine 2'-deoxyribonucleoside (II) [ $\chi =$  −106.3 (2)°; Seela, Zulauf *et al.*, 1999]. Halogen substituents at the 7-position drive the conformation to high *anti* [ $\chi =$  −74.1 (4)° (7-bromo) and −73.2 (4)° (7-iodo) (Seela *et al.*, 2000)]. This phenomenon might be caused by stereoelectronic effects of the base. As the vinyl group has an electron-withdrawing influence on the heterocyclic base, the  $pK_a$  value of protonation is decreased from 4.0 in (II) to 3.54 in (I). The glycosyl bond length in (I) [N9—C1' = 1.460 (4) Å] is slightly longer than that in (II) [1.442 (2) Å].



The pseudorotation phase,  $P$ , and the puckering amplitude,  $\tau$ , angles (Rao *et al.*, 1981) show that the sugar ring of (I) adopts an *S* conformation, with an unsymmetrical twist of the C4'-*endo*—C3'-*exo* bond (between  $^3E$  and  $^3T^4$ ), having a  $P$  value of 205.6 (4)° and a  $\tau$  value of 30.2 (2)°. In (II), the sugar ring conformation is  $^3T^2$  [ $P = 182.2$  (2)° and  $\tau = 41.2$  (2)°]. The conformation about the C4'—C5' bond of (I) is *+sc* (*gauche*, *gauche*), with a dihedral angle,  $\gamma$ , of 42.1 (4)°, whereas in (II), the C4'—C5' bond adopts a *−ap* (*trans*) conformation, with  $\gamma$  equal to −178.73 (16)°.

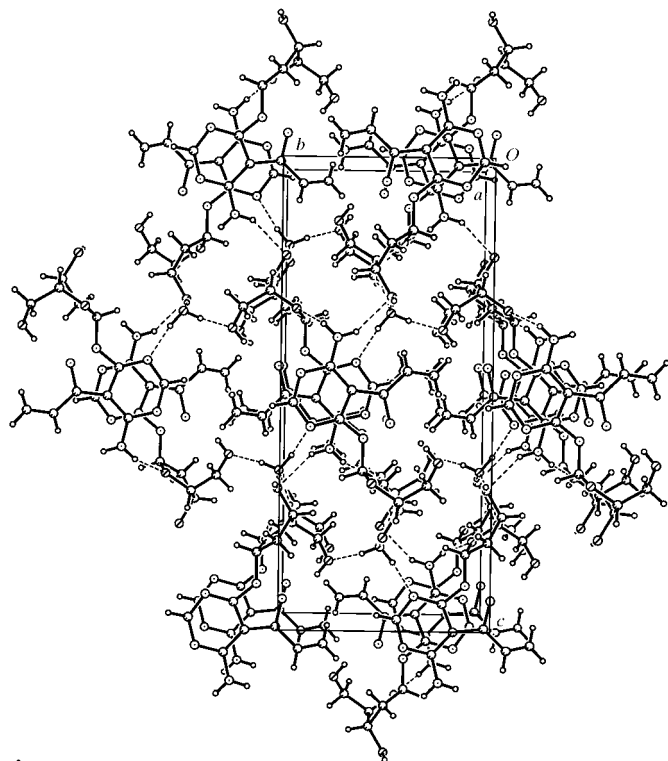
The base moiety of (I) is nearly planar, but the vinyl side chain deviates from the plane. The r.m.s. deviation of ring atoms N9, N8, C7, C5, C6, N1, C2, N3 and C4 from the least-squares plane through these atoms is 0.012 Å, with a maximum deviation of −0.024 (4) Å (atom C6). Atom C1' is displaced from this plane by −0.014 (6) Å. The C5—C7—C71=C72 torsion angle linking the vinyl group and the heterocycle is 147.5 (5)°. In (III), the vinyl group is inclined by 12° to the pyrimidine ring plane (Hamor *et al.*, 1978). Such a deviation was also observed in the propynyl group in 8-aza-7-deaza-7-propynyladenosine (Lin *et al.*, 2005). The conformation of the conjugated diene system (N8=C7—C71=C72) is *s-Z*. This conformation occurs because of the steric repulsion between the vinyl chain and the 6-amino group.

In the three-dimensional network, the bases are stacked (3.3 Å apart; Fig. 2). Each nucleoside is connected to one water molecule, which is coordinated by hydrogen bonds. The water molecule acts as an acceptor (O10) of a hydrogen bond from atom O3' and as a donor of two H atoms in bonds to atoms N3 and O5' (Table 2). Hence, three nucleosides are connected by one water molecule. There is an intramolecular



**Figure 1**

A perspective view of (I). Displacement ellipsoids of non-H atoms are drawn at the 50% probability level and H atoms are shown as spheres of arbitrary size.



**Figure 2**

The crystal packing of (I), viewed down the *a* axis, showing the hydrogen bonds as dashed lines.

hydrogen bond between the O5'—H5' group and atom N8, which we have not observed in related nucleosides. Other inter- and intramolecular hydrogen bonds are summarized in Table 2.

## Experimental

Compound (I) was synthesized according to a known procedure (Seela & Zulauf, 1998) and was crystallized as the monohydrate from aqueous methanol. For the diffraction experiment, a single crystal was fixed at the top of a Lindemann capillary with epoxy resin.

### Crystal data

$C_{12}H_{15}N_5O_3 \cdot H_2O$   
 $M_r = 295.31$   
 Orthorhombic,  $P2_12_12_1$   
 $a = 6.6513$  (8) Å  
 $b = 9.603$  (5) Å  
 $c = 21.481$  (3) Å  
 $V = 1372.1$  (7) Å<sup>3</sup>  
 $Z = 4$   
 $D_x = 1.430$  Mg m<sup>-3</sup>

Mo  $K\alpha$  radiation  
 Cell parameters from 28 reflections  
 $\theta = 4.9$ – $12.5^\circ$   
 $\mu = 0.11$  mm<sup>-1</sup>  
 $T = 293$  (2) K  
 Block, colourless  
 $0.42 \times 0.28 \times 0.20$  mm

### Data collection

Bruker *P4* diffractometer  
 $2\theta/\omega$  scans  
 2800 measured reflections  
 2100 independent reflections  
 1180 reflections with  $I > 2\sigma(I)$   
 $R_{int} = 0.040$   
 $\theta_{max} = 29.0^\circ$

$h = -1 \rightarrow 9$   
 $k = -1 \rightarrow 13$   
 $l = -29 \rightarrow 1$   
 3 standard reflections  
 every 97 reflections  
 intensity decay: none

### Refinement

Refinement on  $F^2$   
 $R[F^2 > 2\sigma(F^2)] = 0.058$   
 $wR(F^2) = 0.113$   
 $S = 1.02$   
 2100 reflections  
 205 parameters  
 H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0349P)^2]$   
 where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{max} < 0.001$   
 $\Delta\rho_{max} = 0.22$  e Å<sup>-3</sup>  
 $\Delta\rho_{min} = -0.21$  e Å<sup>-3</sup>  
 Extinction correction: *SHELXL97*  
 Extinction coefficient: 0.0074 (11)

**Table 1**

Selected geometric parameters (Å, °).

C7—C71	1.461 (4)	N8—N9	1.370 (3)
C71—C72	1.306 (5)	N9—C1'	1.460 (4)
N8—C7—C5	109.3 (3)	C5—C7—C71	129.6 (3)
N8—C7—C71	121.1 (3)	C72—C71—C7	123.8 (4)
N8—C7—C71—C72	−30.6 (7)	C4—N9—C1'—C2'	134.0 (5)
C5—C7—C71—C72	147.5 (5)	N8—N9—C1'—C2'	−48.3 (6)
C4—N9—C1'—O4'	−106.9 (5)	O4'—C4'—C5'—O5'	−76.7 (4)
N8—N9—C1'—O4'	70.7 (5)	C3'—C4'—C5'—O5'	42.1 (4)

In the absence of suitable anomalous scattering, Friedel equivalents could not be used to determine the absolute structure. Therefore, Friedel pairs were merged before the final refinements. The known configuration of the parent molecule was used to define the enantiomer of the final nucleoside. All H atoms were initially found in a difference Fourier synthesis. H atoms bonded to C and N atoms were placed in idealized positions (C—H = 0.93–0.98 Å and N—H = 0.86 Å) and constrained to ride on their parent atoms, with  $U_{iso}(H)$  values of  $1.2U_{eq}(C)$  and  $1.5U_{eq}(N)$ . The H-atom positions were found

**Table 2**  
Hydrogen-bonding 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>
N6—H6A...O4 <sup>ii</sup>	0.86	2.39	2.995 (4)	128
N6—H6B...O3 <sup>ii</sup>	0.86	2.24	3.010 (4)	150
O3'—H3'...O10	0.82 (2)	1.88 (2)	2.698 (5)	174 (5)
O5'—H5'...N8	0.83 (4)	2.02 (4)	2.832 (4)	164 (4)
O10—H10A...N3 <sup>iii</sup>	0.91 (3)	1.93 (3)	2.831 (4)	169 (4)
O10—H10B...O5 <sup>iv</sup>	0.91 (3)	1.86 (3)	2.755 (4)	169 (5)

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

in a difference Fourier map and were geometrically idealized and constrained (DFIX). The  $U_{\text{iso}}(\text{H})$  values were constrained to be 1.5 times  $U_{\text{eq}}(\text{O})$ .

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *SHELXTL* (Sheldrick, 1997); program(s) used to solve structure: *SHELXTL*; program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL* and *PLATON* (Spek, 1999).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GA1089). Services for accessing these data are described at the back of the journal.

## References

- Cheng, Y. C., Domin, B. A., Sharma, R. A. & Bobek, M. (1976). *Antimicrob. Agents Chemother.* **10**, 119–122.
- Gourlain, T., Sidorov, A., Mignet, N., Thorpe, S. J., Lee, S. E., Grasby, J. A. & Williams, D. M. (2001). *Nucleic Acids Res.* **29**, 1898–1905.
- Hamor, T. A., O'Leary, M. K. & Walker, R. T. (1978). *Acta Cryst.* **B34**, 1627–1630.
- IUPAC–IUB Joint Commission on Biochemical Nomenclature (1983). *Eur. J. Biochem.* **131**, 9–15.
- Lin, W., Xu, K., Seela, F. & Eickmeier, H. (2005). *Acta Cryst.* **C61**. In preparation.
- Rao, S. T., Westhof, E. & Sundaralingam, M. (1981). *Acta Cryst.* **A37**, 421–425.
- Seela, F., Becher, G. & Zulauf, M. (1999). *Nucleosides Nucleotides*, **18**, 1399–1400.
- Seela, F. & Kaiser, K. (1988). *Helv. Chim. Acta*, **71**, 1813–1823.
- Seela, F. & Steker, H. (1985). *Helv. Chim. Acta*, **68**, 563–570.
- Seela, F. & Zulauf, M. (1998). *J. Chem. Soc. Perkin Trans 1*, pp. 3233–3239.
- Seela, F. & Zulauf, M. (1999). *J. Chem. Soc. Perkin Trans. 1*, pp. 479–488.
- Seela, F., Zulauf, M., Reuter, H. & Kastner, G. (1999). *Acta Cryst.* **C55**, 1947–1950.
- Seela, F., Zulauf, M., Reuter, H. & Kastner, G. (2000). *Acta Cryst.* **C56**, 489–491.
- Sheldrick, G. M. (1997). *SHELXTL*. Release 5.1. Bruker AXS Inc., Madison, Wisconsin, USA.
- Siemens (1996). *XSCANS*. Release 2.2. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
- Spek, A. L. (1999). *PLATON for Windows*. Utrecht University, The Netherlands. (32-bit Windows Implementation by L. J. Farrugia, University of Glasgow, Scotland.)