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7-Deaza-2′-deoxyinosine: a nucleoside showing ambiguous base-pairing properties against the four canonical DNA constituents

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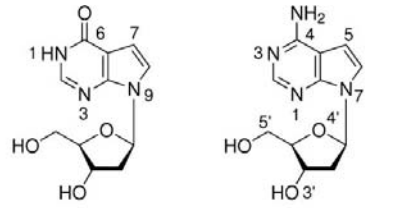
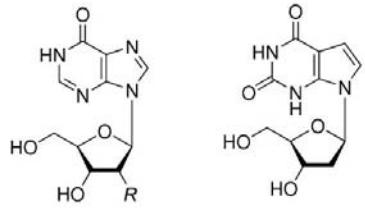
The title compound [systematic name: 7-(2-deoxy-β-D-*erythro*-pentofuranosyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one], $C_{11}H_{13}N_3O_4$, represents an acid-stable derivative of 2′-deoxyinosine. It exhibits an *anti* glycosylic bond conformation, with a χ torsion angle of 113.30 (15)°. The furanose moiety adopts an *S*-type sugar pucker $^4T_3$, with P = 221.8 (1)° and τ_m = 40.4 (1)°. The conformation at the exocyclic C4′—C5′ bond of the furanose ring is *ap* (*trans*), with γ = 167.14 (10)°. The extended structure forms a three-dimensional hydrogen-bond network involving O—H···O, N—H···O and C—H···O hydrogen bonds. The title compound forms an uncommon hydrogen bond between a CH group of the pyrrole system and the ring O atom of the sugar moiety of a neighbouring molecule.

Comment

The naturally occurring ribonucleoside inosine, (III*a*), is known to form wobble base pairs at the ambiguous positions of the anticodon of tRNAs (Crick, 1966; Topal & Fresco, 1976). The corresponding 2′-deoxyinosine, (III*b*), is the classical universal nucleoside which shows ambiguous base pairing with the four natural constituents of DNA (Topal & Fresco, 1976). The base pairing properties of 7-deaza-2′-deoxyinosine, (I), were investigated and found to be similar to those of 2′-deoxyinosine (purine numbering is used throughout this discussion). Compared with the latter, it forms an extraordinarily stable N-glycosylic bond (Seela & Mittelbach, 1999; Seela & Kaiser, 1986). Also, substituted derivatives of 7-deaza-2′-deoxyinosine have been reported with halogen substituents or alkynyl residues at the 7-position of the nucleobase (Seela & Ming, 2008). 7-Deaza-2′-deoxyinosine derivatives with a terminal triple bond in the side chain were functionalized by the Huisgen–Meldal–Sharpless azide–alkyne 'click' reaction (Seela & Ming, 2008). As nothing is known about the conformational properties of compound (I), a single-crystal X-ray analysis was performed. The conformation and molecular dimensions of (I) are compared with the similar structures (II)–(IV) (see scheme).



Purine numbering (I) Systematic numbering (II)



(III*a*) R = OH (III*b*) R = H (IV)

The three-dimensional structure of (I) is shown in Fig. 1, and selected geometric parameters are listed in Table 1. The orientation of the nucleobase relative to the sugar moiety is *anti*, with the torsion angle χ = 113.30 (15)° (χ = O4′—C1′—N9—C4; IUPAC–IUB Joint Commission on Biochemical Nomenclature, 1983). For the related 7-deazaadenosine [2′-deoxytubercidin, (II)], this conformation falls into the range between *anti* and high-*anti*, with χ = −104.4 (2)° (Zabel *et al.*, 1987). Inosine (III*a*) crystallizes in at least two distinct crystal forms, *viz*. inosine (Bugg *et al.*, 1968) and inosine dihydrate (Thewalt *et al.*, 1970). The dihydrate crystal of (III*a*) has two conformationally different molecules in the asymmetric unit (Thewalt *et al.*, 1970). Molecule *A* of inosine dihydrate adopts

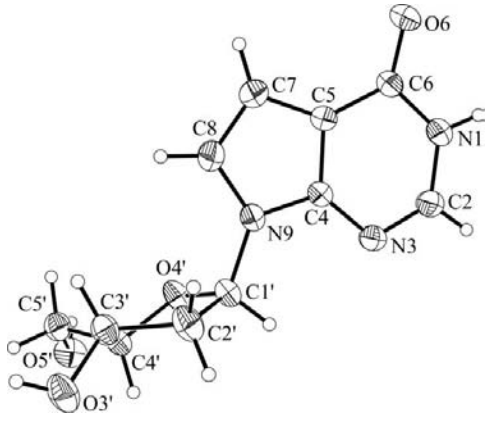


Figure 1
A perspective view of compound (I), showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as spheres of arbitrary size.

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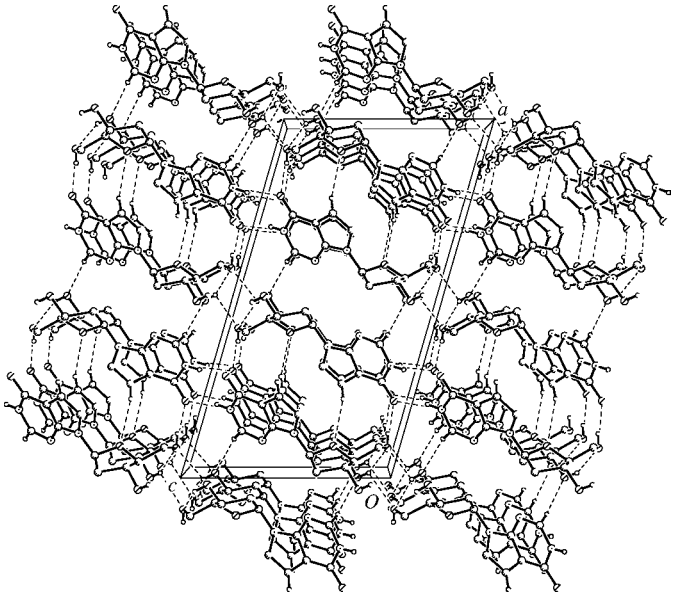

Figure 2
The intermolecular hydrogen-bonding network in the crystal structure of (I), viewed parallel to the *b* axis. Hydrogen bonds are indicated by dashed lines and H atoms not involved in hydrogen bonding have been omitted.

an *anti* conformation, with $\chi = -133.18\ (1)^\circ$, while molecule *B* shows a *syn* conformation [$\chi = -58.40\ (1)^\circ$; Thewalt *et al.*, 1970]. Similarly, 7-deaza-2′-deoxyxanthosine, (IV), shows the *syn* conformation [$\chi = 61.9\ (4)^\circ$; Seela *et al.*, 2002]. In contrast, in the absence of water, the conformation of inosine is *anti* with $\chi = -174.26\ (5)^\circ$ (Munns & Tollin, 1970). The length of the N9—C1′ glycosylic bond of (I) is 1.4509 (15) Å, which is within the range of the corresponding bonds in compounds (II) [1.449 (2) Å; Zabel *et al.*, 1987] and (III*a*) [1.477 (4) Å for inosine; 1.462 Å for molecule *A* and 1.452 Å for molecule *B* of inosine dihydrate; Munns & Tollin, 1970; Thewalt *et al.*, 1970].

According to common rules, the displacement of the sugar ring atoms is *endo* when lying on the same side of the sugar plane as atom C5′, or *exo* when lying on the opposite side. The most frequently observed sugar ring conformations of purine nucleosides are C2′-*endo* and C3′-*endo*, also called *S* (south) and *N* (north) (Arnott & Hukins, 1972). The pseudorotation phase angle *P* and the maximum puckering amplitude τ_m (Rao *et al.*, 1981) show that the sugar ring of (I) adopts an *S* conformation with an unsymmetrical twist of C3′-*exo*–C4′-*endo* ($^4T_3$), with $P = 221.8\ (1)^\circ$ and $\tau_m = 40.4\ (1)^\circ$. This pucker is consistent with that observed in solution (69% *S*; Ramzaeva *et al.*, 1999). In the case of (II), the sugar ring conformation is $^2T_1$ (*S*), with $P = 186.6\ (2)^\circ$ (Zabel *et al.*, 1987). The sugar moiety of compound (IV) also adopts an *S* ($^2T_3$) conformation, with $P = 155.4\ (3)^\circ$ and $\tau_m = 35.9\ (2)^\circ$ (Seela *et al.*, 2002), while compound (III*a*) displays the *N* conformation in the anhydrous crystal ($P = 7.8^\circ$ and $\tau_m = 41.8^\circ$, C2′-*exo*–C3′-*endo*; Munns & Tollin, 1970) and the *S* conformation (C2′-*endo*) for both independent molecules of inosine dihydrate (Thewalt *et al.*, 1970).

The torsion angle γ (O5′—C5′—C4′—C3′) characterizes the orientation of the exocyclic 5′-hydroxyl group relative to the 2′-deoxyribose ring. In the crystal structures of compounds (I) and (II), γ is 167.14 (10) and 179.6 (2)°, respectively. These values show that both C4′—C5′ bonds are in an antiperiplanar (+*ap*, *gauche*, *trans*) orientation, while the exocyclic 5′-hydroxyl group of compound (IV) falls into the +*sc* conformation with a torsion angle $\gamma = 51.9\ (4)^\circ$. However, for anhydrous inosine (III*a*), the conformation of the torsion angle around the C4′—C5′ bond is $\gamma = -168.9\ (4)^\circ$ (*gauche–trans*; Munns & Tollin, 1970), while both independent molecules in the crystal structure of inosine dihydrate adopt a *trans–gauche* conformation, with $\gamma = -55.34\ (1)$ and $-73.38\ (1)^\circ$ for molecules *A* and *B*, respectively (Thewalt *et al.*, 1970).

The 7-deazapurine ring of (I) is nearly planar. The deviations of the ring atoms from the least-squares plane (N1/C2/N3/C4/C5–C8/N9) range from −0.0132 (14) (C5) to 0.0190 (12) Å (C6), with an r.m.s. deviation of 0.0093 Å. The C1′ substituent and atom O6 lie 0.049 (2) and 0.066 (2) Å, respectively, above this plane.

The structure of nucleoside (I) is stabilized by several intermolecular hydrogen bonds, leading to the formation of an infinite three-dimensional hydrogen-bond network (Table 2 and Fig. 2). Within one layer, the nucleobases are arranged head-to-tail and are stacked. Compound (I) has six principle hydrogen donor sites, *viz.* N1—H, C2—H, C7—H, C8—H, O3′—H and O5′—H, but five acceptor sites, *viz.* N3, O6, O3′, O4′ and O5′. However, only five of the donors and four of the acceptors are involved in the interactions. Hydrogen bonds are formed between adjacent sugar–sugar, base–base and sugar–base moieties. The C8—H group does not take part in hydrogen bonding, which is different to the crystal structure of inosine (Munns & Tollin, 1970). Instead, compound (I) forms a hydrogen bond between C7—H7 of the pyrrole system and ring atom O4′ of the sugar moiety of a neighbouring molecule.

Experimental

Compound (I) was prepared as described by Seela & Mittelbach (1999). Slow crystallization from an aqueous solution afforded colourless crystals [m.p. 508–509 K (decomposition)].

Crystal data

$C_{11}H_{13}N_3O_4$
$M_r = 251.24$
Monoclinic, *C*2
$a = 19.9633\ (6)$ Å
$b = 5.2733\ (2)$ Å
$c = 11.2390\ (4)$ Å
$\beta = 106.109\ (2)^\circ$
$V = 1136.70\ (7)$ Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.11$ mm^{-1}
$T = 296\ (2)$ K
0.3 × 0.2 × 0.2 mm

Data collection

Bruker APEXII CCD area-detector diffractometer
62751 measured reflections
1829 independent reflections
1793 reflections with $I > 2\sigma(I)$
$R_{int} = 0.026$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.032$
$wR(F^2) = 0.094$
$S = 1.10$
1829 reflections
165 parameters
1 restraint
H-atom parameters constrained
$\Delta\rho_{max} = 0.27$ e Å^{-3}
$\Delta\rho_{min} = -0.23$ e Å^{-3}

Table 1
Selected torsion angles (°).

C2—N1—C6—O6	−176.92 (17)	C8—N9—C1′—O4′	−68.2 (2)
C7—C5—C6—O6	0.1 (3)	O4′—C4′—C5′—O5′	−75.63 (13)
C5—C7—C8—N9	−0.2 (2)	C3′—C4′—C5′—O5′	167.14 (10)
C4—N9—C1′—O4′	113.30 (15)		

Table 2
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···O6^{i}	0.86	2.01	2.8511 (17)	168
O3′—H3′*A*···O5′^{ii}	0.82	2.12	2.8835 (18)	155
O5′—H5′*A*···O6^{iii}	0.82	1.92	2.7353 (15)	174
C2—H2···O3′^{iv}	0.93	2.29	3.1395 (19)	151
C7—H7···O4′^{v}	0.93	2.54	3.4005 (17)	153

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

In the absence of suitable anomalous scattering, Friedel equivalents could not be used to determine the absolute structure. Refinement of the Flack (1983) parameter led to inconclusive values (Flack & Bernardinelli, 2000) for this parameter [0.7 (6)]. Therefore, Friedel equivalents (1499) were merged before the final refinement. The known configuration of the parent molecule was used to define the enantiomer employed in the refined model. All H atoms were found in a difference Fourier synthesis. Subsequently, the H atoms were placed in geometrically idealized positions, with C—H = 0.93–0.98 Å and N—H = 0.86 Å (AFIX 43 in *SHELXTL*; Sheldrick, 2008), and constrained to ride on their parent atoms, with U_{iso}(H) = 1.2U_{eq}(parent atom). The hydroxy groups were refined as rigid groups allowed to rotate but not tip (AFIX 147 in *SHELXTL*), with O—H = 0.82 Å and U_{iso}(H) = 1.5U_{eq}(O).

Data collection: *APEX2* (Bruker, 2006); cell refinement: *APEX2*; data reduction: *APEX2*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 2008); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL* and *PLATON* (Spek, 2003).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: LN3105). Services for accessing these data are described at the back of the journal.

References

Arnott, S. & Hukins, D. W. L. (1972). *Biochem. J.* **130**, 453–465.
Bruker (2006). *APEX2*. Bruker AXS Inc., Madison, Wisconsin, USA.
Bugg, C. E., Thewalt, U. T. & Marsh, R. E. (1968). *Biochem. Biophys. Res. Commun.* **33**, 436–440.
Crick, F. H. C. (1966). *J. Mol. Biol.* **19**, 548–555.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Flack, H. D. & Bernardinelli, G. (2000). *J. Appl. Cryst.* **33**, 1143–1148.
IUPAC–IUB Joint Commission on Biochemical Nomenclature (1983). *Eur. J. Biochem.* **131**, 9–15.
Munns, A. R. I. & Tollin, P. (1970). *Acta Cryst.* B**26**, 1101–1113.
Ramzaeva, N., Mittelbach, C. & Seela, F. (1999). *Helv. Chim. Acta*, **82**, 12–18.
Rao, S. T., Westhof, E. & Sundaralingam, M. (1981). *Acta Cryst.* A**37**, 421–425.
Seela, F. & Kaiser, K. (1986). *Nucleic Acids Res.* **14**, 1825–1844.
Seela, F. & Ming, X. (2008). *Helv. Chim. Acta*. In the press.
Seela, F. & Mittelbach, C. (1999). *Nucleosides Nucleotides*, **18**, 425–441.
Seela, F., Wiglenda, T., Rosemeyer, H., Eickmeier, H. & Reuter, H. (2002). *Angew. Chem. Int. Ed.* **41**, 603–605.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Thewalt, U., Bugg, C. E. & Marsh, R. E. (1970). *Acta Cryst.* B**26**, 1089–1101.
Topal, M. D. & Fresco, J. R. (1976). *Nature (London)*, **263**, 289–293.
Zabel, V., Saenger, W. & Seela, F. (1987). *Acta Cryst.* C**43**, 131–134.