Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

1,N^6-Etheno derivative of 7-deaza-2,8-diazaadenosine

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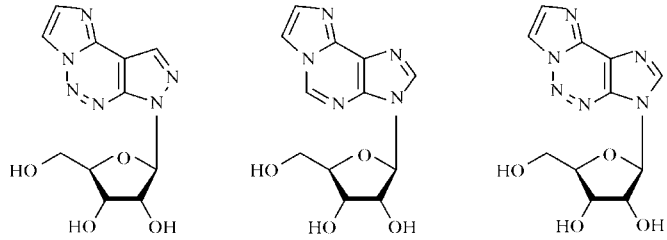
Received 6 May 2004
Accepted 10 June 2004
Online 21 July 2004

In the tricyclic nucleoside 7-(β-D-ribofuranosyl)-7*H*-imidazo[1,2-*c*]pyrazolo[4,3-*e*][1,2,3]triazine, $C_{11}H_{12}N_6O_4$, the conformation of the N-glycosyl bond is intermediate between *anti* and high *anti* [$\chi = -103.5\ (3)^\circ$]. The ribofuranose moiety adopts a $_3T^2$ sugar pucker (S-type sugar) and the conformation at the exocyclic C—C bond is *ap* (*gauche–trans*). Molecules of the title compound form a three-dimensional network *via* three medium–strong intermolecular hydrogen bonds (one O—H···N and two O—H···O bonds).

Comment

Synthetic nucleoside analogues have proved to be of great value for the therapy of human diseases and are used as structural or functional probes in molecular biology (Simons, 2001; Service, 1998). The title compound, 7-(β-D-ribofuranosyl)-7*H*-imidazo[1,2-*c*]pyrazolo[4,3-*e*][1,2,3]triazine (7-deaza-2,8-diaza-1,N^6-ethenoadenosine), (I), contains structural elements of the tricyclic nucleosides ε-adenosine, (II), and 2-aza-ε-adenosine, (III). Compounds (II) and (III) have been investigated extensively because of their strong fluorescence, which makes them useful fluorescent probes in biochemical studies (Barrio *et al.*, 1972; Secrist *et al.*, 1972), as well as because of their biological properties, such as cytotoxic activity (Tsou *et al.*, 1974). Recently, our interest became focused on 2-azapurines and their nucleosides (Sugiyama *et al.*, 2001; Seela *et al.*, 2004). Compound (I) was synthesized from 8-aza-7-deazaadenosine *via* an etheno derivative, with replacement of carbon-2 by nitrogen (Lin & Seela, 2004). In contrast to (II) and (III), compound (I) shows no significant fluorescence. We describe here the single-crystal X-ray structure determination of (I).

The preferred conformation at the N-glycosyl bond in natural purine ribonucleosides is usually in the *anti* range. The orientation of the nucleobase of (I) relative to the sugar moiety (*syn*/*anti*) is defined in analogy to purines (IUPAC–IUB Joint Commission on Biochemical Nomenclature, 1983) by the torsion angle χ (O4′—C1′—N9—C4) using the atom numbering shown in Fig. 1. The χ angle [−103.5 (3)°; Table 1] is intermediate between *anti* and high *anti*. Compound (II) exhibits an *anti* conformation (χ = −153.8°; Jaskólski, 1982). The length of the C1′—N9 glycosyl bond is 1.459 (3) Å, identical to the standard glycosyl bond length of ∼1.46 Å for purine nucleosides.



(I) (II) (III)

In contrast to the heterocyclic base moiety of (II), which is not planar but has a 'U' shape (Jaskólski, 1982), the tricyclic base moiety of (I) is nearly planar. The r.m.s. deviation of the base ring-forming atoms from their calculated least-squares plane is 0.01 Å, the maximum deviation being 0.018 (2) Å (for atom N3). Atom C1′ of the sugar moiety deviates from the tricyclic plane by 0.058 (3) Å.

The sugar moiety of (I) exhibits a pseudorotation phase angle, *P*, of 183.4° and an amplitude, τ_m, of 42.4° (Rao *et al.*, 1981), indicating that the sugar is in the south (S) conformation. The sugar has a C2′-*endo* and C3′-*exo* conformation, with the major puckering at C3′ and the minor at C2′ ($_3T^2$). The electronegative hydroxy group at atom C2′ is in a pseudo-equatorial orientation and that at C3′ is in a pseudo-axial orientation. The base is in a pseudo-equatorial orientation. Usually, ribonucleosides exhibit the N conformation, while 2′-deoxyribonucleosides prefer the S conformation. It can thus be concluded that introduction of the etheno bridge into the 7-deaza-2,8-diazaadenosine molecule significantly changes the electronic structure of its base fragment and influences even the sugar moiety by stereoelectronic effects. The C3′—C4′—C5′—O5′ torsion angle is −172.0 (2)°, which corresponds to an *ap* (*gauche–trans*) conformation according to the IUPAC–IUB recommendation. This configuration may reflect the electrostatic repulsion between atoms N8 and O5′.

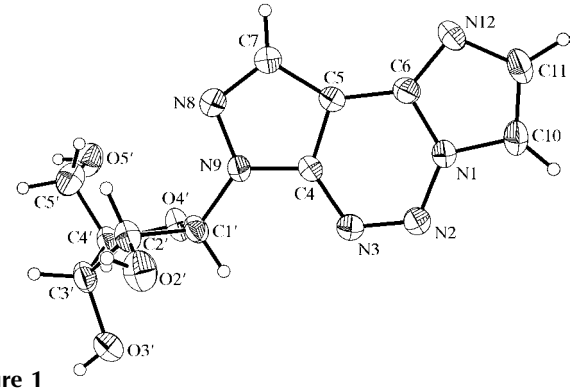


Figure 1
A perspective view of the molecule of (I), showing the atomic numbering scheme. Displacement ellipsoids of non-H atoms are drawn at the 50% probability level. H atoms are represented by spheres of arbitrary size.

  DOI: 10.1107/S010827010401409X

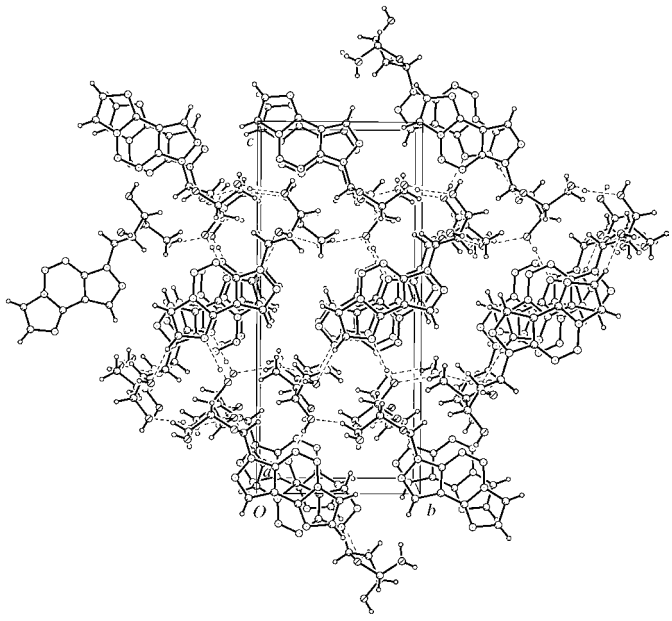


Figure 2
The crystal packing of (I), viewed along the *a* axis, showing the intermolecular hydrogen-bonding network.

In solution, the sugar puckering of (I) is in the N ↔ S pseudorotational equilibrium with 64% S, as calculated by *PSEUROT* (Van Wijk *et al.*, 1999). Thus, the solution and solid-state structures are similar and both differ from the situation typical for ribonucleosides. The other pseudo-rotational parameters of (I) are $P_N = -1.6°$, $P_S = 193.7°$, $\Psi_N = 32.0°$ and $\Psi_S = 35.0°$ (Altona & Sundaralingam, 1972).

The crystal structure of (I) is stabilized by three medium–strong hydrogen bonds (listed in Table 2 and shown in Fig. 2), which arrange the nucleoside molecules into a compact three-dimensional network, with the aromatic nucleobases stacked head-to-tail.

Experimental

The title compound was prepared from 8-aza-7-deazaadenosine (Lin & Seela, 2004) and crystals suitable for X-ray analysis were grown from a solution in ethanol and water (m.p. 483 K).

Crystal data

$C_{11}H_{12}N_6O_4$
$M_r = 292.27$
Orthorhombic, $P2_12_12_1$
$a = 6.8229\ (5)$ Å
$b = 8.9565\ (11)$ Å
$c = 20.310\ (6)$ Å
$V = 1241.2\ (4)$ Å^3
$Z = 4$
$D_x = 1.564$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 49 reflections
$\theta = 4.7$–$15.0°$
$\mu = 0.12$ mm^{-1}
$T = 293\ (2)$ K
Block, colourless
0.52 × 0.40 × 0.36 mm

Data collection

Bruker *P*4 diffractometer
$2\theta/\omega$ scans
2583 measured reflections
1927 independent reflections
1520 reflections with $I > 2\sigma(I)$
$R_{int} = 0.046$
$\theta_{max} = 29.0°$
$h = -9 \rightarrow 1$
$k = -1 \rightarrow 12$
$l = -1 \rightarrow 27$
3 standard reflections
every 97 reflections
intensity decay: none

Table 1
Selected geometric parameters (Å, °).

N1—N2	1.377 (3)	C7—N8	1.327 (3)
N1—C10	1.378 (3)	N8—N9	1.356 (3)
N1—C6	1.398 (3)	N9—C1′	1.459 (3)
N2—N3	1.279 (3)	C10—C11	1.350 (4)
N3—C4	1.355 (3)	C11—N12	1.394 (3)
C4—N9	1.361 (3)	C1′—O4′	1.425 (3)
C4—C5	1.393 (3)	C1′—C2′	1.512 (4)
C5—C6	1.411 (3)	C2′—C3′	1.530 (4)
C5—C7	1.415 (3)	C3′—C4′	1.533 (4)
C6—N12	1.319 (3)	O4′—C4′	1.456 (3)
N2—N1—C6	128.0 (2)	C7—N8—N9	106.4 (2)
C10—N1—C6	107.9 (2)	N8—N9—C4	111.0 (2)
N3—N2—N1	117.1 (2)	C11—C10—N1	105.0 (2)
N2—N3—C4	118.1 (2)	C10—C11—N12	111.9 (2)
N3—C4—C5	128.7 (2)	C6—N12—C11	105.3 (2)
N9—C4—C5	107.2 (2)	O4′—C1′—C2′	107.1 (2)
C4—C5—C6	113.8 (2)	C1′—C2′—C3′	100.7 (2)
C4—C5—C7	104.4 (2)	C2′—C3′—C4′	100.6 (2)
N12—C6—N1	109.9 (2)	C1′—O4′—C4′	108.8 (2)
N1—C6—C5	114.2 (2)	O4′—C4′—C3′	104.7 (2)
N8—C7—C5	111.0 (2)		
C6—N1—N2—N3	0.4 (5)	N3—C4—N9—N8	−179.8 (3)
N1—N2—N3—C4	−1.6 (4)	N1—C6—N12—C11	0.0 (4)
N2—N3—C4—C5	1.5 (4)	C5—C6—N12—C11	180.0 (3)
N3—C4—C5—C6	0.1 (4)	N8—N9—C1′—O4′	73.7 (3)
N9—C4—C5—C6	−180.0 (2)	C4—N9—C1′—O4′	−103.5 (3)
N3—C4—C5—C7	−180.0 (3)	N8—N9—C1′—C2′	−46.5 (4)
N9—C4—C5—C7	−0.1 (3)	C4—N9—C1′—C2′	136.4 (3)
N2—N1—C6—N12	−178.8 (3)	O4′—C1′—C2′—C3′	33.4 (2)
C10—N1—C6—N12	−0.1 (3)	C1′—C2′—C3′—C4′	−41.3 (2)
N2—N1—C6—C5	1.2 (4)	C2′—C1′—O4′—C4′	−11.1 (3)
C10—N1—C6—C5	180.0 (3)	C1′—O4′—C4′—C3′	−16.1 (2)
C4—C5—C6—N1	−1.3 (4)	C2′—C3′—C4′—O4′	36.0 (2)
C7—C5—C6—N1	178.9 (4)	O4′—C4′—C5′—O5′	70.4 (3)
C4—C5—C7—N8	−0.2 (4)	C3′—C4′—C5′—O5′	−172.0 (2)
C5—C7—N8—N9	0.4 (3)		

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

D—H···A	D—H	H···A	D···A	D—H···A
O5′—H5′···O3′^{i}	0.82 (3)	1.93 (3)	2.720 (3)	162 (4)
O3′—H3′···N12^{ii}	0.820 (14)	1.941 (13)	2.758 (3)	174 (2)
O2′—H2′···O5′^{iii}	0.820 (16)	1.955 (17)	2.761 (3)	167.2 (14)

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

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.044$
$wR(F^2) = 0.114$
$S = 1.02$
1927 reflections
202 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.054P)^2 + 0.3012P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.23$ Å^{-3}
$\Delta\rho_{min} = -0.26$ Å^{-3}

In the absence of suitable anomalous scatterers, Friedel equivalents could not be used to determine the absolute structure. Therefore, Friedel equivalents were merged before the final refinement and the known configuration of the parent molecule was used to define the enantiomer of the final model. All H atoms were initially found in a difference Fourier synthesis. In order to maximize the data/parameter ratio, H atoms bonded to C atoms were placed in idealized

positions (C—H = 0.93–0.98 Å) and constrained to ride on their parent atoms, with U_{iso}(H) values of $1.2U_{eq}$(C). Hydroxy H atoms, initially placed in the difference-map positions, were later positioned geometrically and assumed to ride on their parent O atoms, under the constraint that the O—H distances be equal.

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: HJ1011). Services for accessing these data are described at the back of the journal.

References

Altona, C. & Sundaralingam, M. (1972). *J. Am. Chem. Soc.* **94**, 8205–8212.

Barrio, J. R., Secrist, J. A. III & Leonard, N. J. (1972). *Biochem. Biophys. Res. Commun.* **46**, 597–604.

IUPAC–IUB Joint Commission on Biochemical Nomenclature (1983). *Eur. J. Biochem.* **131**, 9–15.

Jaskólski, M. (1982). *Acta Cryst.* B**38**, 3171–3174.

Lin, W. & Seela, F. (2004). In preparation.

Rao, S. T., Westhof, E. & Sundaralingam, M. (1981). *Acta Cryst.* A**37**, 421–425.

Secrist, J. A. III, Barrio, J. R., Leonard, N. J. & Weber, G. (1972). *Biochemistry*, **11**, 3499–3506.

Seela, F., Lindner, M., Glacon, V. & Lin, W. (2004). *J. Org. Chem.* In the press.

Service, R. F. (1998). *Science*, **282**, 396–401.

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.

Simons, C. (2001). In *Nucleoside Mimetics: Their Chemistry and Biological Properties.* Amsterdam: Gordon and Breach Science Publishers.

Spek, A. L. (1999). *PLATON* for Windows. Utrecht University, The Netherlands. 32-Bit Windows implentation by L. J. Farrugia, University of Glasgow, Scotland.

Sugiyama, T., Schweinberger, E., Kazimierczuk, Z., Ramzaeva, N., Rosemeyer, H. & Seela, F. (2001). *Chem. Eur. J.* **6**, 369–378.

Tsou, K. C., Yip, K. F., Miller, E. E. & Lo, K. W. (1974). *Nucleic Acids Res.* **1**, 531–547.

Van Wijk, L., Haasnoot, C. A. G., de Leeuw, F. A. A. M., Huckriede, B. D., Westra Hoekzema, A. J. A. & Altona, C. (1999). *PSEUROT.* Version 6.3. Leiden Institute of Chemistry, Leiden University, The Netherlands.