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1,N^6-Etheno-2′-deoxytubercidin hemihydrate

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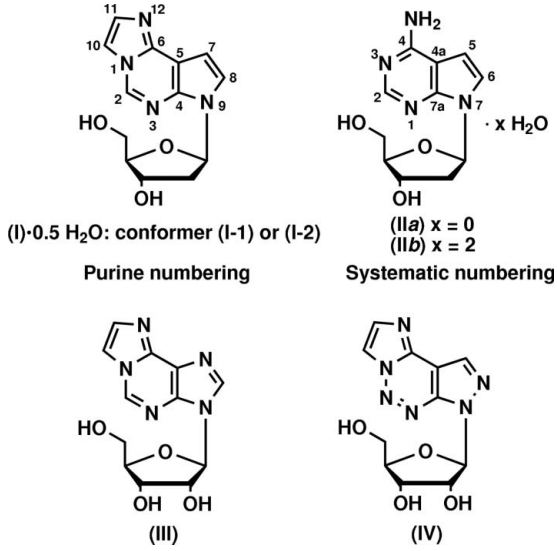
The title compound [systematic name: 7-(2-deoxy-β-D-*erythro*-pentofuranosyl)-7*H*-imidazo[1,2-*c*]pyrrolo[2,3-*d*]pyrimidine hemihydrate], $2C_{13}H_{14}N_4O_3\cdot H_2O$ or (I)·0.5H_2O, shows two similar conformations in the asymmetric unit. These two conformers are connected through one water molecule by hydrogen bonds. The N-glycosylic bonds of both conformers show an almost identical *anti* conformation with χ = −107.7 (2)° for conformer (I-1) and −107.0 (2)° for conformer (I-2). The sugar moiety adopts an unusual *N*-type (C3′-*endo*) sugar pucker for 2′-deoxyribonucleosides, with P = 36.8 (2)° and τ_m = 40.6 (1)° for conformer (I-1), and P = 34.5 (2)° and τ_m = 41.4 (1)° for conformer (I-2). Both conformers and the solvent molecule participate in the formation of a three-dimensional pattern with a 'chain'-like arrangement of the conformers. The structure is stabilized by intermolecular O—H···O and O—H···N hydrogen bonds, together with weak C—H···O contacts.

Comment

Etheno adducts have proved to be biomarkers for DNA damage arising from reactions of endogenous lipid peroxidation, chloroethylene oxide or chloroacetaldehyde (Bolt, 1994). They are also thought to initiate vinyl-chloride- and urethane-induced tumours because of their miscoding capability, leading to point mutations (Arab *et al.*, 2009; Pandya & Moriya, 1996). 1,N^6-Etheno-2′-deoxytubercidin, (I), and the corresponding congener 1,N^6-ethenoadenosine, (III), can be considered as 7-deazapurine or purine pyrrole ring annelation products with a [1,2-*c*]-ring connectivity (purine numbering is used throughout this discussion). By enlarging the aromatic system, these tricyclic nucleosides show strong fluorescence with quantum yields higher than 0.5 (Seela *et al.*, 2007). Their propensity to fluorescence makes these compounds valuable for probing the biochemical and biophysical properties of nucleosides, nucleotides and nucleic acids (Bielecki *et al.*, 2000; Inoue *et al.*, 1981; Paulsen & Wintermeyer, 1984; Secrist *et al.*, 1972; Seela *et al.*, 2007). The 7-deazapurine nucleoside, (I), shows extraordinary stability in acidic and in alkaline media compared to its 'purine' counterpart, (III) (Seela *et al.*, 2007). The synthesis of the title compound, (I), which was prepared from 2′-deoxytubercidin with chloroacetaldehyde, was reported previously (Seela *et al.*, 2007). The single-crystal structure of (I) is studied herein and is compared to the closely related crystal structures of 2′-deoxytubercidin [(II*a*) and (II*b*); Zabel *et al.*, 1987], 1,N^6-ethenoadenosine [(III); Jaskólski, 1982] and 7-deaza-2,8-diaza-1,N^6-ethenoadenosine [(IV); Lin *et al.*, 2004].



In the asymmetric unit of (I)·0.5H_2O, two conformers with a slightly different sugar puckering exist which are connected through a water molecule by hydrogen bonds. They are defined as types 1 and 2, and denoted (I-1) and (I-2), respectively. The three-dimensional structures of the molecules of (I-1) and (I-2) are shown in Figs. 1 and 2, and selected geometric parameters are summarized in Table 1.

Conformers (I-1) and (I-2) exhibit almost identical torsion angles χ (O4′—C1′—N9—C4) of −107.7 (2) and −107.0 (2)°, respectively, which indicate conformations situated between *anti* and high-*anti* (IUPAC-IUB Joint Commission on Biochemical Nomenclature, 1983). These values are close to that of the water-free crystal of (II*a*) [χ = −104.4 (2)°], whereas the torsion angle of dihydrate (II*b*) [χ = −115.5 (3)°] falls into the *anti* range (Zabel *et al.*, 1987). The length of the glycosylic N9—C1′ bond is 1.451 (2) Å for (I-1) and 1.449 (2) Å for (I-2), which is almost identical to the bond length observed for 2′-deoxytubercidin [1.449 (2) Å in (II*a*) and 1.446 (4) Å in (II*b*); Zabel *et al.*, 1987]. The parent ribonucleoside, (III), adopts a slightly longer glycosylic bond [1.455 (4) Å; Jaskólski, 1982].

The heterocyclic base moiety of 1,N^6-ethenoadenosine, (III), forms a 'U'-shaped structure when looking from the edge side, with a maximum deviation of 0.064 (4) Å out of the

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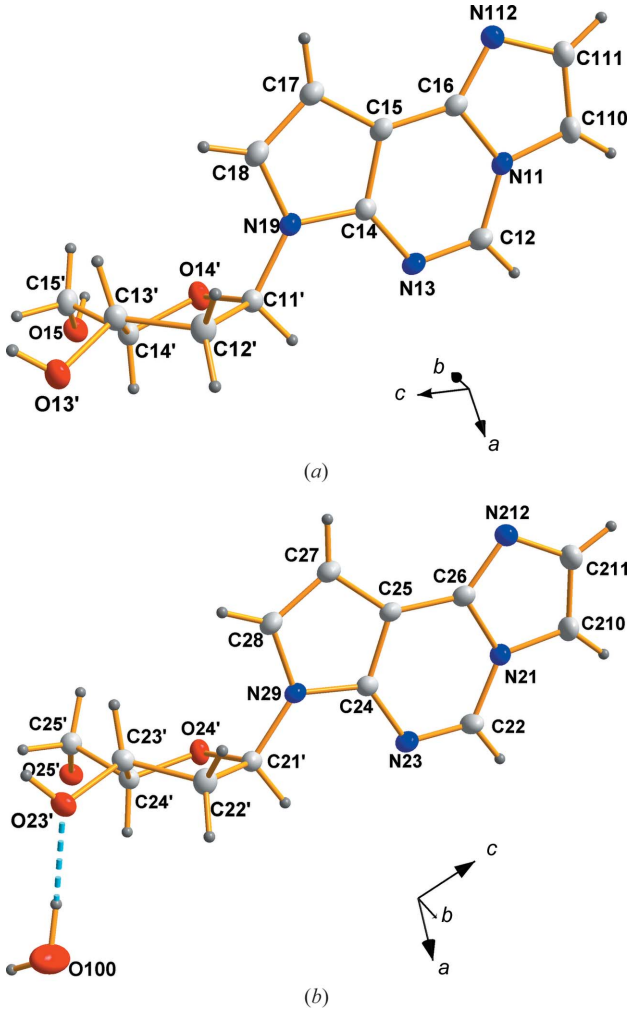

Figure 1
Perspective views of (*a*) conformer (I-1) and (*b*) conformer (I-2), showing the atom-numbering schemes. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary size.

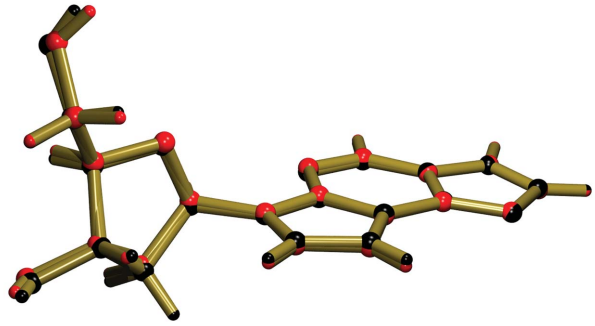

Figure 2
Overlay of molecules (I-1) and (I-2).

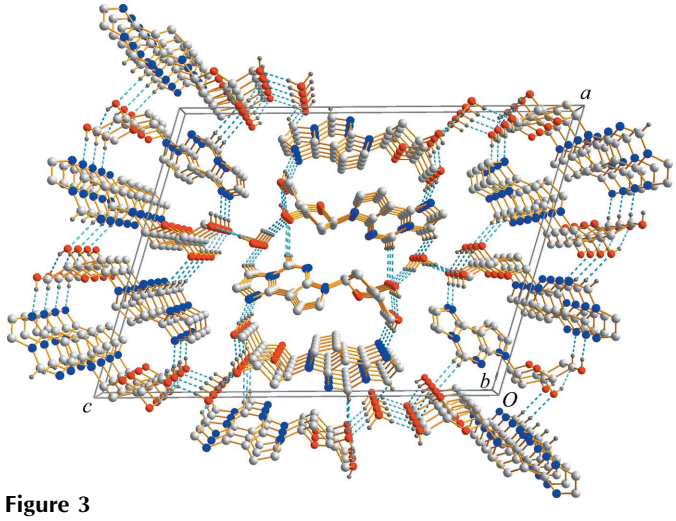

Figure 3
The crystal packing showing the intermolecular hydrogen-bonding network (parallel to the *ac* plane).

plane (Jaskólski, 1982). In contrast, the 7-deazapurine moieties of (I-1) and (I-2) are nearly planar. The r.m.s. deviations of the ring atoms from their calculated least-squares planes are 0.0121 Å for (I-1) and 0.0206 Å for (I-2). Maximum deviations of 0.0185 (2) and 0.0365 (2) Å were found for atom C112 of (I-1) and atom N29 of (I-2), respectively.

For both conformers, the torsion angle about the exocyclic C4′—C5′ bond, which is defined as γ (O5′—C5′—C4′—C3′), adopts an antiperiplanar (*gauche*, *trans*) conformation with γ = −168.7 (2)° for (I-1) and γ = −167.1 (2)° for (I-2). In the crystal structures of (II*a*) and (II*b*), the torsion angles γ are also within the antiperiplanar range [−179.6 (2) and −173.6 (3)°; *trans*] (Zabel *et al.*, 1987).

Usually, the sugar conformation of ribonucleosides adopts the *N*-type pucker, whereas 2′-deoxyribonucleosides prefer the *S* conformation. In solution, the predominant conformation of compound (I) shows the *S*-type conformation (75% *S*). The sugar conformation of compound (I) was determined from the vicinal ^3J(H,H) coupling constants of the ^{1}H NMR spectra measured in D_2O, applying the program *PSEUROT6.3* (Van Wijk *et al.*, 1999). It has to be noted that both conformers exhibit sugar moieties with the *N* conformation in the crystalline state. For conformer (I-1), the sugar pucker is $^4T_3$ (C4′-*exo*–C3′-*endo*) (Altona & Sundaralingam, 1972), with a phase angle of pseudorotation of P = 36.8 (2)° and a maximum amplitude of puckering of τ_m = 40.6 (1)°. In conformer (I-2), the sugar moiety adopts a slightly different *N*-type sugar pucker ($^3T_4$; C3′-*endo*–C4′-*exo*), with P = 34.5 (2)° and τ_m = 41.4 (1)°. In contrast, the parent 2′-deoxytubercidins, (II*a*) and (II*b*), adopt *S* conformations with P = 186.6 (2) ($^3T_2$; C3′-*exo*–C2′-*endo*) and 215.1 (3)° ($^3T_4$; C3′-*exo*–C4′-*endo*), respectively. A similar influence on the sugar conformation was also found for the ribonucleoside 1,N^6-etheno derivatives, (III) and (IV), which adopt the *S* conformation (C2′-*endo*) instead of the usual *N*-type conformation of ribonucleosides. The ribose ring of nucleoside (III) is characterized by P = 163.5° ($^2T_3$; C2′-*endo*–C3′-*exo*) and τ_m = 44.3° (Jaskólski, 1982), while P = 183.4° ($^3T_2$; C3′-*exo*–C2′-*endo*) and τ_m = 42.4° for compound (IV) (Lin *et al.*, 2004).

The title compound forms a three-dimensional network, which is generated by numerous hydrogen bonds involving conformers (I-1) and (I-2) and the water molecule (Fig. 3 and

Table 2). Within the *ac* plane, (I-1) and (I-2) are located in a 'chain'-like arrangement. Each chain is composed of molecules of identical conformation, either (I-1) or (I-2), and the chains are ordered in an alternating fashion. Furthermore, within the chains, the individual molecules are arranged in a head-to-tail fashion. The different chains are connected to each other *via* hydrogen bonding between the two conformers. The individual chains are also stabilized by hydrogen bonds, while the water molecule participates in both intra- and interchain hydrogen bonds. Conformers (I-1) and (I-2) show a different hydrogen-bonding pattern. Hydrogen bonds are formed to neighbouring molecules of identical conformation (O13′—H13′···O15′^{i}, O15′—H15′···N112^{ii}, O23′—H23′···O25′^{iii} and O25′—H25′···N212^{iv}; for symmetry codes and geometry see Table 2), while those to the water molecule (O100) employ different atoms as acceptors. For (I-1), atom O15′ functions as acceptor (O100—H102···O15′^{i}), whereas atom O23′ is the acceptor for (I-2) (O100—H101···O23′). Additional weak contacts (Steiner, 2002) were observed for both conformers, including that of conformer (I-2) to atom O100 of the water molecule (C210—H210···O100^{vi}, C12—H12···O13′^{v} and C22—H22···O23′^{vi}).

Experimental

Compound (I) was synthesized as reported previously (Seela *et al.*, 2007). Slow crystallization from aqueous methanol afforded (I)·0.5H_2O as colourless crystals (m.p. 442 K). For the diffraction experiment, a single crystal was mounted on a MiTeGen MicroMountsfibre in a thin smear of oil.

Crystal data

$2C_{13}H_{14}N_4O_3·H_2O$
M_r = 566.58
Monoclinic, *C*2
a = 19.6476 (12) Å
b = 5.2979 (3) Å
c = 26.3354 (16) Å
β = 106.865 (3)°
V = 2623.4 (3) Å^3
Z = 4
Mo *Kα* radiation
μ = 0.11 mm^{-1}
T = 130 K
0.30 × 0.20 × 0.10 mm

Data collection

Bruker APEXII CCD diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2008)
T_{min} = 0.969, T_{max} = 0.989
46138 measured reflections
4214 independent reflections
3987 reflections with $I > 2\sigma(I)$
R_{int} = 0.033

Table 1
Selected geometric parameters (Å, °).

N11—C16	1.396 (3)	N21—C26	1.394 (3)
C16—N112	1.322 (2)	C26—N212	1.325 (2)
N19—C11′	1.451 (2)	N29—C21′	1.449 (2)
O13′—C13′—C14′	112.06 (17)	O23′—C23′—C24′	111.71 (16)
O15′—C15′—C14′	111.68 (18)	O25′—C25′—C24′	110.91 (17)
C12—N11—C16—N112	178.6 (2)	C22—N21—C26—N212	176.1 (2)
C14—C15—C16—N112	−179.5 (2)	C24—C25—C26—N212	−177.3 (2)
C14—N19—C11′—O14′	−107.7 (2)	C24—N29—C21′—O24′	−107.0 (2)
C13′—C14′—C15′—O15′	−168.66 (16)	C23′—C24′—C25′—O25′	−167.05 (16)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O13′—H13′···O15′^{i}	0.84	2.01	2.800 (2)	156
O15′—H15′···N112^{ii}	0.84	1.87	2.705 (2)	175
O23′—H23′···O25′^{iii}	0.84	1.84	2.665 (2)	165
O25′—H25′···N212^{iv}	0.84	1.84	2.675 (2)	174
O100—H101···O23′	0.96	1.91	2.823 (3)	157
O100—H102···O15′^{i}	0.96	1.92	2.868 (2)	169
C12—H12···O13′^{v}	0.95	2.37	3.241 (3)	153
C22—H22···O23′^{vi}	0.95	2.47	3.295 (3)	145
C210—H210···O100^{vi}	0.95	2.47	3.230 (4)	138

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

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.039
$wR(F^2)$ = 0.106
S = 1.12
4214 reflections
374 parameters
1 restraint
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.33 e Å^{-3}
$\Delta\rho_{min}$ = −0.33 e Å^{-3}
Absolute structure: established by known chemical absolute configuration

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 for this parameter [0.2 (7)]. Therefore, Friedel equivalents (2881) 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. In order to maximize the data/parameter ratio, the H atoms were placed in geometrically idealized positions (C—H = 0.95–1.00 Å) and constrained to ride on their parent atoms, with U_{iso}(H) = 1.2U_{eq}(C). The OH groups were refined as rigid groups, allowed to rotate but not tip (AFIX 147 instruction in the XL routine of *SHELXTL*; Sheldrick, 2008), with O—H = 0.84 Å and U_{iso}(H) = 1.5U_{eq}(O). The water H atoms were located from difference maps, and the parameters of the water H atoms were first refined freely. Owing to the low reflection/refined parameter ratio, the O—H distances were constrained [AFIX 3 (*m* = 0)] to 0.96 Å and with U_{iso}(H) = 1.5U_{eq}(O) in the final cycles of refinement.

Data collection: *APEX2* (Bruker, 2008); cell refinement: *SAINT* (Bruker, 2008); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 2008); program(s) used to refine structure: *SHELXTL*; molecular graphics: *DIAMOND* (Brandenburg, 1999); software used to prepare material for publication: *SHELXTL* and *PLATON* (Spek, 2009).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GD3377). 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.
Arab, K., Pedersen, M., Nair, J., Meerang, M., Knudsen, L. E. & Bartsch, H. (2009). *Carcinogenesis*, **30**, 282–285.
Bielecki, L., Skalski, B., Zagorowska, I., Verrall, R. E. & Adamiak, R. W. (2000). *Nucleosides Nucleotides Nucleic Acids*, **19**, 1735–1750.
Bolt, H. M. (1994). *DNA Adducts*: *Identification and Biological Significance*, Vol. 125, edited by K. Hemminki, A. Dipple, D. E. G. Shuker, F. F. Kadlubar, D. Segerback & H. Bartsch, pp. 141–150. Lyon: IARC.

Brandenburg, K. (1999). *DIAMOND*. Crystal Impact GbR, Bonn, Germany.
Bruker (2008). *APEX2* (Version 2008/5), *SADABS* (Version 2008/1) and *SAINT* (Version 7.56a). Bruker AXS Inc., Madison, Wisconsin, USA.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Inoue, Y., Kuramochi, T. & Imakubo, K. (1981). *Chem. Lett.* **10**, 1161–1164.
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., Eickmeier, H. & Reuter, H. (2004). *Acta Cryst.* C**60**, o566–o568.
Pandya, G. A. & Moriya, M. (1996). *Biochemistry*, **35**, 11487–11492.
Paulsen, H. & Wintermeyer, W. (1984). *Eur. J. Biochem.* **138**, 125–130.
Secrist, J. A., Barrio, J. R., Leonard, N. J. & Weber, G. (1972). *Biochemistry*, **11**, 3499–3506.
Seela, F., Schweinberger, E., Xu, K., Sirivolu, V. R., Rosemeyer, H. & Becker, E.-M. (2007). *Tetrahedron*, **63**, 3471–3482.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Spek, A. L. (2009). *Acta Cryst.* D**65**, 148–155.
Steiner, T. (2002). *Angew. Chem. Int. Ed.* **41**, 48–76.
Van Wijk, L., Haasnoot, C. A. G., de Leeuw, F. A. A. M., Huckriede, B. D., Westra Hoekzema, A. J. A. & Altona, C. (1999). *PSEUROT6.3*. Leiden Institute of Chemistry, Leiden University, The Netherlands.
Zabel, V., Saenger, W. & Seela, F. (1987). *Acta Cryst.* C**43**, 131–134.