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7-Deaza-2′-deoxyguanosine

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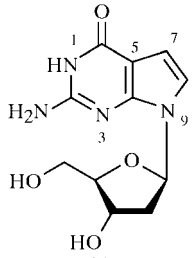
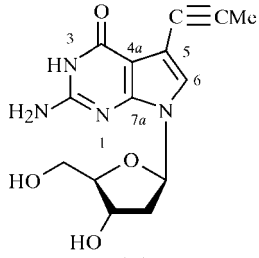
In the title compound, 2-amino-7-(2-deoxy-β-D-*erythro*-pentofuranosyl)-3,7-dihydropyrrolo[2,3-*d*]pyrimidin-4-one, $C_{11}H_{14}N_4O_4$, the N-glycosylic bond torsion angle, χ, is *anti* [−106.5 (3)°]. The 2′-deoxyribofuranosyl moiety adopts the $^3T_4$ (N-type) conformation, with $P = 39.1°$ and $\tau_m = 40.3°$. The conformation around the exocyclic C—C bond is *ap* (*trans*), with a torsion angle, γ, of −173.8 (3)°. The nucleoside forms a hydrogen-bonded network, leading to a close-packed multiple-layer structure with a head-to-head arrangement of the bases. The nucleobase interplanar O=C—C···NH_2 distance is 3.441 (1) Å.

Comment

7-Deaza-2′-deoxyguanosine, (I), is one of the most applicable modified nucleosides being used in chemistry, molecular biology and nanotechnology (purine numbering is used throughout the manuscript). The synthesis of (I) was reported by Winkeler & Seela (1983). The first oligonucleotide incorporating (I) was reported three years later (Seela & Driller, 1986). Compound (I) is known for applications in the form of its 5′-triphosphate in the Sanger DNA sequencing (Barr *et al.*, 1986; Mizusawa, *et al.*, 1986). 7-Alkynylamino derivatives of the corresponding 2′,3′-dideoxy nucleoside triphosphate carrying fluorescent reporter groups are used as chain terminators in automatized DNA/RNA sequencing machines (Prober *et al.*, 1987; Cocuzza, 1988; Hobbs, 1989). As nucleoside (I) cannot form dG-tetrads (Seela & Mersmann, 1993), band compression is reduced during gel electrophoresis. Moreover, the replacement of 2′-deoxyguanosine by (I) increases the sensitivity of MALDI-TOF (matrix-assisted laser desorption time-of-flight) mass spectra performed on DNA fragments (Schneider & Chait, 1995). In addition, the fluorescence of ethidium bromide is strongly quenched by (I) (Li *et al.*, 2004), and 7-deaza-2′,3′-dideoxyguanosine triphosphate proved to be an effective inhibitor of HIV reverse transcriptase (Seela *et al.*, 1990). The incorporation of the 7-substituted derivatives of (I) into oligonucleotides results in an increase of DNA duplex stability (Seela *et al.*, 1995; Ramzaeva & Seela, 1996; Seela & Shaikh, 2005), as well as of DNA–RNA duplexes (Buhr *et al.*, 1996). Oligonucleotide triplexes are also stabilized when (I) is part of the 7-deazaguanine–guanine–cytosine triplet motif (Milligan *et al.*, 1993). Thus, (I) and 7-substituted derivatives are applied in antisense technology (Lamm *et al.*, 1991; Uhlmann *et al.*, 2000) as well as in DNA/RNA diagnostics (Bailly & Waring, 1998). Consequently, it was of interest to perform a single-crystal X-ray analysis and report the structure.



(I)
purine numbering



(II)
systematic numbering

Earlier efforts were made to grow a single crystal of (I). Recently, we were able to crystallize (I) as colorless needles from an aqueous solution of (I) at room temperature. The three-dimensional structure of (I) [systematic numbering: 2-amino-7-(2-deoxy-β-D-*erythro*-pentofuranosyl)-3,7-dihydropyrrolo[2,3-*d*]pyrimidin-4-one] is shown in Fig. 1, and selected bond lengths and angles are summarized in Table 1. The orientation of the nucleobase relative to the sugar moiety (*syn*/*anti*) is defined in analogy to the purine nucleosides by the torsion angle χ (O4′—C1′—N9—C4) (IUPAC–IUB Joint Commission on Biochemical Nomenclature, 1983). In the crystalline state of (I), the glycosylic bond torsion angle is in the *anti* range [χ = −106.5 (3)°], which is similar to that of recently reported 7-deaza-2′-deoxy-7-propynylguanosine, (II) (Seela *et al.*, 2004), in which the propynyl group is slightly tilted [C4—C5—C7—C71 = 177.2 (5)°], and the 8-methyl derivative of 7-deaza-2′-deoxyguanosine (Seela *et al.*, 1997), as well as that of queuosine 5′-monophosphate (Yokoyama *et al.*, 1979). The sugar ring in (I) is puckered, as shown by the C3′—C4′—O4′—C1′ [34.5 (3)°] and C4′—O4′—C1′—C2′ [−14.4 (3)°] torsion angles. The pseudorotation phase angle

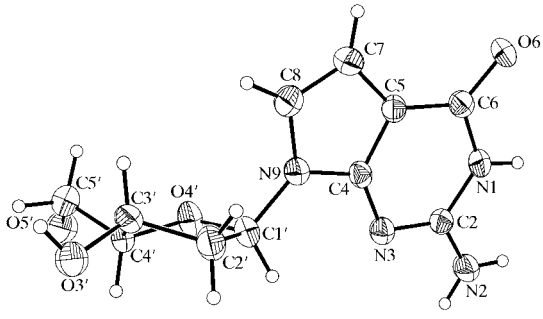


Figure 1
A perspective view of (I). Displacement ellipsoids for non-H atoms are drawn at the 50% probability level and H atoms are shown as spheres of arbitrary size.

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(P) of 39.1° and amplitude (τ_m) of 40.3° indicate an N-type sugar conformation (3′-*endo*-4′-*exo*, $^3T_4$), which is an unusual sugar puckering compared with the canonical nucleosides (Rao *et al.*, 1981). The torsion angle γ [O5′—C5′—C4′—C3′ = −173.8 (3)°] describing the orientation of the 5′-hydroxy group relative to the sugar ring shows that the C4′—C5′ bond is in an *ap* (*trans*) orientation (Saenger, 1984). The N-type sugar pucker of (I) found in the solid state is in contrast to the conformation found in solution (70% S). In this case, the conformational analysis was carried out on the basis of ^{1}H NMR vicinal [^{1}H,^{1}H] coupling constants using the *PSEUROT6.3* program (Van Wijk *et al.*, 1999). The base moiety of (I) is nearly planar, the r.m.s. deviation of the ring atoms from their calculated least-squares planes being 0.0323 Å [N1 0.030 (2) Å, C2 −0.027 (2) Å, N3 −0.009 (2) Å, C4 −0.014 (3) Å, C5 −0.049 (3) Å, C6 0.042 (2) Å, C7 −0.033 (3) Å, C8 0.019 (3) Å and N9 0.043 (2) Å]. The O6 substituent of (I) lies 0.144 (4) Å above and the N atom of the 2-amino group lies −0.103 (4) Å below this plane. The structure of (I) is stabilized by several intermolecular hydrogen bonds, leading to a three-dimensional multiple-layer network (Fig. 2 and Table 2). In the close-packed network of nucleoside (I), the head-to-head stacking patterns are strikingly similar to the head-to-head stacking of nucleobases observed for (II) (Seela *et al.*, 2004). The nucleobases are not skewed and the closest separation of the stacked bases for (I) is 3.441 (1) Å (C5 and N2), while the closest separation for (II) is 3.728 (1) Å (C5 and N2) (Fig. 3). This corresponds to a plane separation that is similar to the average base pair stacking distance in B-DNA (3.5 Å). Within each monolayer, the molecules of (I) are interconnected with one another by five strong hydrogen bonds, as listed in Table 2, *viz.* three N—H···O and two O—H···O interactions. As there are two lone electron pairs on atom O6, it can form bifurcated hydrogen bonds with the H1—N1 and H5′—O5′ groups. In addition, another hydrogen-bond interaction, between atom O6 and the H2*A*—N2 group, is observed. C—H···O^{v} (H···O = 2.52 Å) and C—H···π(C=C)^{v} (H···C = 2.77 Å) interactions complete the hydrogen bonding [symmetry code: (v) $-\frac{1}{2}+x, \frac{1}{2}-y, -z$].

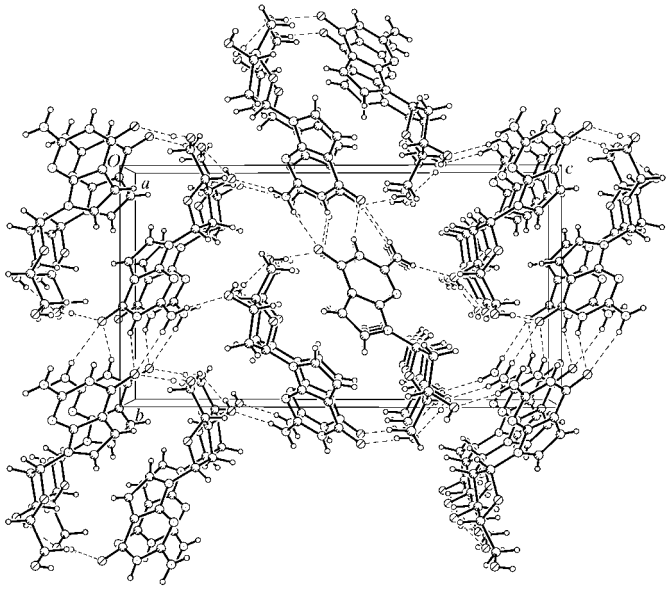

Figure 2
Details of the three-dimensional multilayered network, showing the hydrogen bonds (dashed lines) within the monolayers and the stacking of nucleobases.

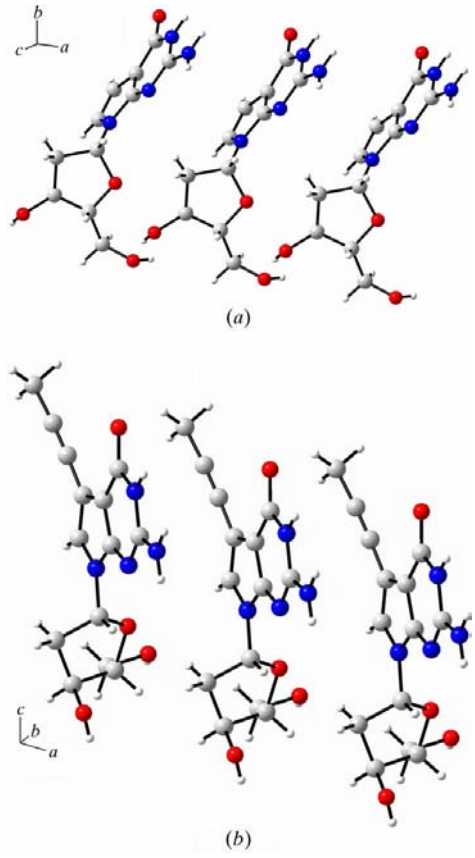

Figure 3
Views showing (*a*) head-to-head nucleobase stacking in nucleoside (I) and (*b*) head-to-head nucleobase stacking in nucleoside (II).

Experimental

Compound (I) was synthesized from 7-(2-deoxy-β-D-*erythro*-pentofuranosyl)-4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidin-2-amine according to the method of Winkeler & Seela (1983). Compound (I) was crystallized slowly from a dilute solution in double distilled water at room temperature over a period of one week as colorless needles (m.p. 535–538 K). For the diffraction experiment, a single crystal was fixed at the top of a Lindemann capillary with epoxy resin.

Crystal data

$C_{11}H_{14}N_4O_4$
M_r = 266.26
Orthorhombic, $P2_12_12_1$
a = 5.4146 (12) Å
b = 10.969 (2) Å
c = 19.968 (4) Å
V = 1185.9 (4) Å^3
Z = 4
D_x = 1.491 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 51 reflections
θ = 2.0–15.2°
μ = 0.12 mm^{-1}
T = 293 K
Needle, colorless
0.53 × 0.33 × 0.26 mm

Data collection

Bruker *P*4 diffractometer
$2\theta/\omega$ scans
2301 measured reflections
1679 independent reflections
1204 reflections with $I > 2\sigma(I)$
$R_{int} = 0.043$
$\theta_{max} = 28.0^\circ$
$h = -7 \rightarrow 1$
$k = -14 \rightarrow 1$
$l = -26 \rightarrow 1$
3 standard reflections
every 97 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.051$
$wR(F^2) = 0.120$
$S = 1.03$
1679 reflections
179 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0542P)^2 + 0.1063P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.20$ e Å^{-3}
$\Delta\rho_{min} = -0.21$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N1—C2	1.375 (4)	C5—C7	1.431 (5)
N1—C6	1.380 (4)	C6—O6	1.261 (3)
C2—N3	1.316 (4)	C4—N9	1.376 (4)
C2—N2	1.343 (4)	N9—C8	1.393 (4)
N3—C4	1.343 (4)	C7—C8	1.355 (5)
C4—C5	1.397 (4)	C3′—O3′	1.422 (4)
C5—C6	1.409 (4)	C5′—O5′	1.429 (5)
N3—C4—N9	123.4 (3)	C4—N9—C8	108.3 (3)
N3—C4—C5	129.1 (3)	C4—N9—C1′	125.0 (3)
N9—C4—C5	107.5 (3)	C8—N9—C1′	126.5 (3)
C4—C5—C6	116.8 (3)	C5—C7—C8	106.7 (3)
C4—C5—C7	107.7 (3)	C7—C8—N9	109.7 (3)
C6—C5—C7	135.1 (3)	C1′—O4′—C4′	108.1 (2)
C7—C8—N9—C1′	175.4 (3)	O3′—C3′—C4′—O4′	−160.0 (2)
C8—N9—C1′—O4′	77.9 (4)	C2′—C3′—C4′—C5′	−159.2 (3)
C8—N9—C1′—C2′	−40.5 (5)	N9—C1′—O4′—C4′	−137.6 (3)
O4′—C1′—C2′—C3′	−11.1 (3)	C2′—C1′—O4′—C4′	−14.4 (3)
N9—C1′—C2′—C3′	108.3 (3)	C3′—C4′—C5′—O5′	−173.8 (3)

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O6^{i}	0.86	2.04	2.847 (4)	155
N2—H2A···O6^{i}	0.86	2.38	3.085 (4)	140
N2—H2B···O3′^{ii}	0.86	2.06	2.907 (4)	169
O3′—H3′···O5′^{iii}	0.82 (3)	1.97 (2)	2.767 (3)	162 (2)
O5′—H5′···O6^{iv}	0.819 (8)	1.990 (12)	2.794 (3)	167 (3)

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

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, *viz.* −1 (2). Therefore, Friedel pairs were merged before the final refinements. The known configuration of the parent molecule was used to define the enantiomer used in the refined model. In order to maximize the data/parameter ratio, H atoms bonded to C atoms were placed in geometrically 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). The hydroxy H atoms were initially placed in their difference map positions, then refined so that the chemically equivalent O—H bond lengths were restrained to 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: GG1237). Services for accessing these data are described at the back of the journal.

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