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# The α-D anomer of 5-aza-7-deaza-2′-deoxyguanosine

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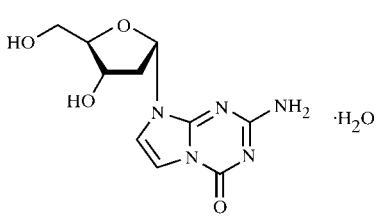
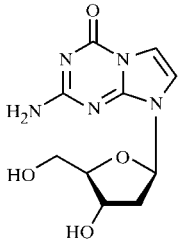
In the monohydrate of 2-amino-8-(2-deoxy-α-D-*erythro*-pentofuranosyl)-8*H*-imidazo[1,2-*a*][1,3,5]triazin-4-one, $C_{10}H_{13}N_5O_4\cdot H_2O$, denoted (I) or $\alpha Z_d$, the conformation of the *N*-glycosylic bond is in the high-*anti* range [$\chi$ = 87.5 (3)°]. The 2′-deoxyribofuranose moiety adopts a C2′-*endo*,C3′-*exo*($^{2'}T_{3'}$) sugar puckering (*S*-type sugar) and the conformation at the C4′—C5′ bond is −*sc* (*trans*).

## Comment

5-Aza-7-deazapurines [imidazo[1,2-*a*][1,3,5]-triazines, *e.g.* (I)] can be formally constructed by transposition of the purine N-7 atom to the bridgehead 5-position (Seela & Rosemeyer, 2002). 5-Aza-7-deaza-2′-deoxyguanosine [(II), purine numbering is used throughout discussion] (Rosemeyer & Seela, 1987) is a structural analogue of both 2′-deoxyguanosine and 7-deaza-2′-deoxyguanosine. Therefore, it is isosteric with 2′-deoxyguanosine but shows an altered Watson–Crick recognition site.




(I)




(II)

Within oligodeoxynucleotides, the β-D-configured 5-aza-7-deaza-2′-deoxyguanosine [$\beta Z_d$, (II)] forms strong tridentate 'purine–purine' base pairs with 2′-deoxyguanosine (neutral conditions), with parallel (ps) chain orientations (Seela & Melenewski, 1999). However, antiparallel tridentate base pairs are formed between $\beta Z_d$ and 2′-deoxycytidine (dC) under acidic (pH 5) conditions (Seela & Melenewski, 1999). Duplexes with parallel strands can be formed when all the sugar moieties in one oligonucleotide strand are in an α-D configuration (Imbach *et al.*, 1989). These oligonucleotides show nuclease resistance.

Nucleoside (I) was synthesized according to Rosemeyer & Seela (1987) and crystallizes from water as the monohydrate (Fig. 1 and Table 1). The orientation of the nucleobase relative to the sugar (*syn*/*anti*) is defined by the torsion angle $\chi^1$(O4′—C1′—N9—C4) (IUPAC–IUB Joint Commission on Biochemical Nomenclature, 1983). The preferred conformation at the *N*-glycosylic bond in natural 2′-deoxynucleosides is usually in the *anti* range ($-150° \le \chi^1 \le -140°$). For an α-D nucleoside, the 'perfect' *anti* range is $140° \le \chi^1 \le 150°$. In the case of compound (I), $\chi^1$ is 87.5 (3)°. This indicates that the title compound adopts a high-*anti* conformation, with the C1′—C2′ and N9—C8 bonds nearly eclipsed [torsion angle C1′—C2′—N9—C8 = 30.3 (4)°].

This conformation is quite unusual. It is displayed by 8-azapurine-2′-deoxy-β-D-ribofuranosides and 8-aza-7-deazapurine-2′-deoxy-β-D-ribofuranosides, where it is attributed to Coulombic repulsion between non-bonding electron pairs at O4′ and N8 (Seela *et al.*, 1999, 1999*a*,*b*). The β-D-ribonucleoside of 5-aza-7-deazaguanine shows an *anti* conformation. The reason for the difference between the β-D-ribonucleoside and the α-D-2′-deoxyribonucleoside is still unknown.

The C2′-*endo* (*N*) and C3′-*endo* (*S*) puckerings are the most frequently observed sugar-ring conformations of nucleosides. Among these, 2′-deoxy-α-D-ribonucleosides often show C2′-*endo* sugar puckering with either a half-chair or envelope conformation (Seela *et al.*, 1999*a*; Hamor *et al.*, 1977; Revankar *et al.*, 1990; Leumann *et al.*, 1995; Marfurt *et al.*, 1996). The puckering of the deoxyribose ring of (I) is C2′-*endo*,C3′-*exo* ($^{2'}T_{3'}$), with $P$ = 177.43° and $\tau_m$ = 30.5° (Rao *et al.*, 1981). The γ(O5′—C5′—C4′—C3′) torsion angle is −71.6 (3)°, which corresponds to −*sc*, a conformation often found in nucleosides with $^{2'}T_{3'}$ sugar puckering. The confor-

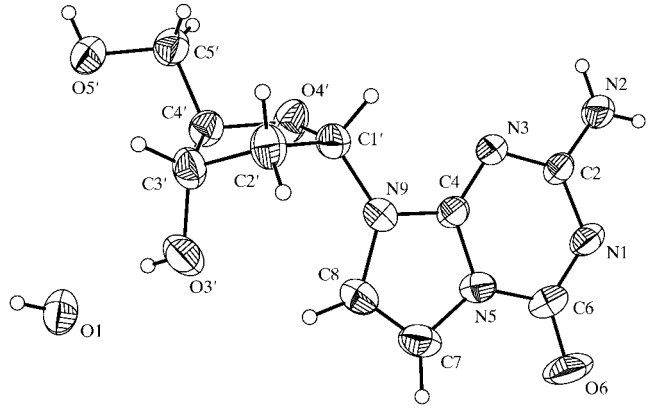



**Figure 1**
Perspective view of the α-D anomer of 5-aza-7-deaza-2′-deoxyguanosine monohydrate. Displacement ellipsoids of non-H atoms are drawn at the 50% probability level. H atoms are shown as spheres of arbitrary radii. One H atom of the water molecule is eclipsed.

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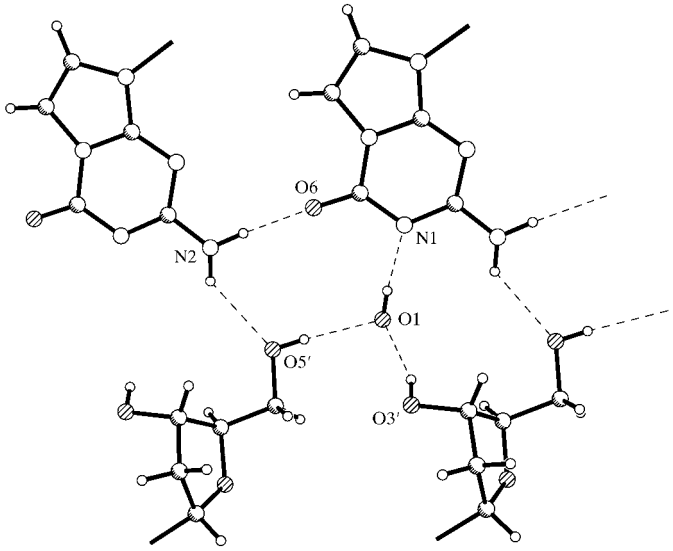


**Figure 2**
Detail of the hydrogen bonding within one monolayer in the crystal structure of (I).

mational parameters of (I) in the crystal are generally identical to those in solution (Seela *et al.*, 2001).

The base moiety of (I) is nearly planar. The average deviation of the ring atoms from the least-squares plane is ±0.014 Å. The ring substituents were not used for calculation of the plane; they deviate as follows: amino N2 −0.061 Å and carboxy O6 0.004 Å. In the crystalline state, the structure of (I) is stabilized by several hydrogen bonds (listed in Table 2 and shown in Fig. 2), leading to the formation of double layers. Within each monolayer, the molecules of (I) are interconneted with each other and the water molecules by four strong hydrogen bonds: N2—H22···O6, N1—H11···O1, O1···H3′—O3′ and O1···O5′—H5′. Because of steric hindrance, however, the second H atom of the $NH_2$ group can only form a weak hydrogen bond, N2—H21···O5′, which is characterized by a narrow angle at the H atom and a long donor–acceptor distance. Only one hydrogen bond exists between two of these monolayers, O1—H12···N3; this is also weak and connects the water molecule with the nucleoside in the neigbouring layer and *vice versa*.

## Experimental

The title compound was prepared according to Rosemeyer & Seela (1987) and was recrystallized from water.

*Crystal data*

$C_{10}H_{13}N_5O_4·H_2O$
$M_r$ = 285.27
Monoclinic, $P2_1$
$a$ = 8.5397 (14) Å
$b$ = 7.1025 (14) Å
$c$ = 10.7187 (16) Å
$\beta$ = 107.460 (13)°
$V$ = 620.17 (18) Å$^3$
$Z$ = 2
$D_x$ = 1.528 Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 38 reflections
$\theta$ = 4.9–17.2°
$\mu$ = 0.12 mm$^{-1}$
$T$ = 293 (2) K
Prism, colourless
0.5 × 0.4 × 0.2 mm

*Data collection*

Siemens $P4$ diffractometer
$2\theta/\omega$ scans
Absorption correction: empirical *via* $\psi$ scan (*SHELXTL*; Sheldrick, 1997*a*)
$T_{min}$ = 0.296, $T_{max}$ = 0.359
2526 measured reflections
1194 independent reflections
1123 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.049
$\theta_{max}$ = 25.0°
$h = -10 \rightarrow 10$
$k = -8 \rightarrow 8$
$l = -12 \rightarrow 12$
3 standard reflections
every 97 reflections
intensity decay: none

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.030
$wR(F^2)$ = 0.076
$S$ = 1.09
1194 reflections
204 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0256P)^2 + 0.0846P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.13 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.19 e Å$^{-3}$
Extinction correction: *SHELXL*97
Extinction coefficient: 0.041 (4)
Absolute structure: Flack (1983)
Flack parameter = −0.9 (17)

**Table 1**
Selected geometric parameters (Å, °).

| | | | |
|---|---|---|---|
| N1—C6 | 1.337 (4) | C8—N9 | 1.404 (4) |
| N1—C2 | 1.350 (4) | N9—C1′ | 1.461 (4) |
| C2—N2 | 1.326 (4) | C1′—O4′ | 1.408 (3) |
| C2—N3 | 1.364 (3) | C1′—C2′ | 1.525 (3) |
| N3—C4 | 1.318 (4) | C2′—C3′ | 1.518 (3) |
| C4—N9 | 1.349 (3) | C3′—O3′ | 1.419 (4) |
| C4—N5 | 1.354 (4) | C3′—C4′ | 1.518 (4) |
| N5—C7 | 1.397 (4) | C4′—O4′ | 1.452 (3) |
| N5—C6 | 1.406 (3) | C4′—C5′ | 1.513 (4) |
| C6—O6 | 1.222 (4) | C5′—O5′ | 1.426 (3) |
| C7—C8 | 1.329 (5) | | |
| | | | |
| H11—O1—H12 | 104 (2) | | |
| | | | |
| C7—C8—N9—C4 | 0.8 (3) | C8—N9—C1′—C2′ | 30.0 (4) |
| C7—C8—N9—C1′ | 178.7 (3) | C3′—C4′—C5′—O5′ | −71.9 (3) |
| C4—N9—C1′—O4′ | 87.6 (3) | | |

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| N2—H22···O6$^{i}$ | 0.914 (18) | 1.864 (19) | 2.775 (4) | 175 (3) |
| O5′—H5′1···O1$^{i}$ | 0.83 (2) | 2.06 (2) | 2.889 (4) | 176 (3) |
| N2—H21···O5′$^{ii}$ | 0.914 (18) | 2.35 (3) | 3.073 (3) | 135 (4) |
| O1—H11···N1$^{iii}$ | 0.802 (14) | 1.993 (16) | 2.782 (3) | 168 (3) |
| O1—H12···N3$^{iv}$ | 0.802 (14) | 2.35 (3) | 3.010 (3) | 140 (4) |
| O3′—H3′2···O1 | 0.83 (2) | 1.93 (3) | 2.713 (3) | 156 (4) |

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

In the absence of suitable anomalous scatterers, the measured Friedel data ($h\bar{k}l$, $hk\bar{l}$, $\bar{h}kl$, $\bar{h}k\bar{l}$) could not be used to determine the absolute structure. However, comparison with the known configuration of the parent molecule indicated that the proposed configuration was correct. Friedel-opposite reflections were merged. All H atoms were found in a difference Fourier synthesis and were included in the structure model in the usual fashion; H atoms on C atoms were positioned geometrically and allowed for as riding (C—H = 0.93–0.98 Å), and H atoms on O and N atoms were refined freely with restraints.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *SHELXTL* (Sheldrick, 1997*a*); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997*b*); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997*b*); molecular graphics: *DIAMOND* (Brandenburg, 1999) and *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: JZ1477). Services for accessing these data are described at the back of the journal.

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