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The high-*anti* conformation of 8-aza-1,3-dideaza-2′-deoxyadenosine

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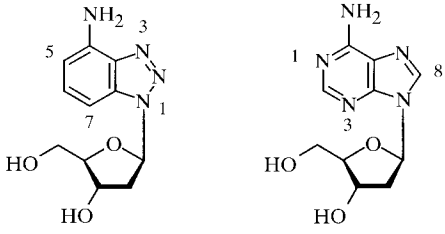
In the title compound, 4-amino-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)-1*H*-benzotriazole, $C_{11}H_{14}N_4O_3$, the conformation of the N-glycosidic bond is in the high-*anti* range [χ = −77.1 (4)°] and the 2′-deoxyribofuranose moiety adopts a 2′-*endo* (^2E) sugar puckering. The 5′-hydroxyl group is disordered and has conformations *ap* with γ = 171.1 (3)° [occupation of 61.4 (3)%] and +*sc* with γ = 52.4 (6)° [occupation of 38.6 (3)%]. The nucleobases are stacked in the crystal state.

Comment

8-Aza-1,3-dideaza-2′-deoxyadenosine, (I), can be considered as an analogue of the DNA constituent dA, (II). It shows a similar shape to the parent DNA constituent but cannot develop bidentate Watson–Crick hydrogen bonds with dT. Nevertheless, it should be well accommodated in a DNA duplex. Its preparation from 4-amino- or 4-nitrobenzotriazole has been described (Kazimierczuk & Seela, 1990), and the kinetics and mechanism of its acid-catalyzed hydrolysis have been investigated (Käppi *et al.*, 1991).



(I) Systematic numbering (II) Purine numbering

The structure of (I) is shown in Fig. 1. Some geometrical parameters are summarized in Table 1 (systematic numbering is used throughout). For the normal purine nucleosides, the orientation of the base relative to the sugar (*syn*/*anti*) is defined by the torsion angle χ(O4′—C1′—N9—C4) (IUPAC–IUB Joint Commission on Biochemical Nomenclature, 1983). The preferred conformation around the N-glycosidic bond of purine 2′-deoxynucleosides is usually *anti*. 2′-Deoxyadenosine, (II), shows a χ value of −165.1° (Sato, 1984). In the case of compound (I), the torsion angle χ(O4′—C1′—N1—C7a) (systematic numbering) is −77.1 (4)°. This indicates that the title compound adopts a high-*anti* conformation. As it contains an N atom at position 8 (purine numbering), the particular conformation is in accordance with the high-*anti* conformation of other *ortho* azanucleosides (Abola & Sundaralingam, 1973; Schwalbe & Saenger, 1973; Singh & Hodgson, 1974*a*,*b*, 1977; Seela, Becher *et al.*, 1999). 8-Aza-7-deaza-7-iodo-2′-deoxyadenosine (χ = −73.2°) and 8-aza-7-bromo-7-deaza-2′-deoxyadenosine (χ = −74.1°) show similar values (Seela *et al.*, 2000). The high-*anti* conformation results from Coulomb repulsion between non-bonding electron pairs of O4′ and N8 (Seela *et al.*, 2000). In contrast, the conformation of 8-aza-7-deaza-2′-deoxyadenosine (χ = −106.3°; Seela, Zulauf *et al.*, 1999) belongs to the *anti* range. The glycosidic bond length (N1—C1′) of (I) is 1.454 (3) Å, which is shorter than the corresponding bond of compound (II) (1.474 Å; Sato, 1984).

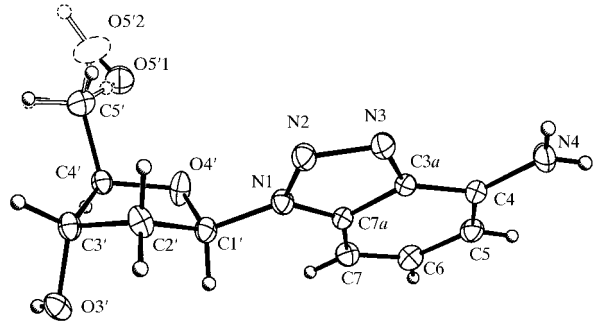


Figure 1
Perspective view of (I). Displacement ellipsoids of non-H atoms are drawn at the 25% probability level. H atoms are shown as spheres of an arbitrary size. Conformation 1 of the C4′—C5′ bond is represented by full bonds and an O5′1 atom with octants. Conformation 2 is represented by open bonds and an O5′2 atom without octants.

The shortening of the glycosidic bond of *ortho* azanucleosides has already been discussed (Sundaralingam, 1966; Lin *et al.*, 1971). The puckering of the deoxyribose ring of (I) is C2′-*endo* (^2E), with P = 163.3 (3)° and τ_m = 41.9 (2)°, observed for anomers of 8-aza-7-deaza-2′-deoxyadenosine (Seela, Zulauf *et al.*, 1999) but not for 2′-deoxyadenosine (C3′-*endo*; Sato, 1984). This is the typical South conformation. The sugar moiety of the title compound shows a disorder of the hydroxyl group. There are two alternative conformations, defined as conformations 1 and 2; both are staggered. The γ(O5′1—C5′1—C4′—C3′) value of conformation 1 [occupation factor 0.614 (3)] is 171.1 (3)°, which corresponds to *ap*. For conformation 2 [occupation factor 0.386 (3)], the γ(O5′2—C5′1—C4′—C3′) value is 52.4 (6)°, which corresponds to +*sc*. The preponderant *ap* conformation means that the nucleobase and the CH_2OH group undergo a disrotatory motion so that the Coulomb repulsion between N8 (purine numbering) and O5′, as well as O4′, is minimized.

Another distinct attribute of the structure is a nearly parallel orientation of the base moieties, which is probably caused by π-electron interactions between the aromatic ring systems of adjacent molecules. The least-squares plane of the base moiety (atoms N1, N2, N3, C3a, C4, N4, C5, C6, C7 and C7a) results in a plane nearly orthogonal to the *a* axis [89.10 (6)°]. Because of the space-group symmetry, the molecules can take two alternative orientations, here called (*a*) and (*b*). The asymmetric unit and translation equivalent molecules are in orientation (*a*). The molecules generated by the screw-axis have orientation (*b*). The base moieties of molecules of the same orientation are naturally parallel. The base moieties of molecules of different orientation [(*a*) and (*b*)] form an interplanar angle of 1.80 (12)°. A view along the *a* axis shows the stacking of the base moieties (Fig. 2). Interestingly, the average distance between those nearly parallel base moieties stacked along the *a* axis is 3.48 Å (= 0.5*a*), very close to the distance between adjacent base pairs in DNA duplexes (3.4 Å). However, there is no helical twist in the crystal structure of (I) as is found for the base pairs in a DNA duplex.

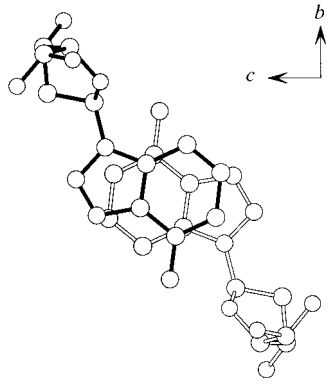


Figure 2
The stacking of the base moieties of (I) viewed against the *a* axis.

The molecules of the title compound are linked by several hydrogen bonds (Table 2), forming two-dimensional networks perpendicular to the *c* axis. The molecules are linked along the screw axis parallel to **a** by the bifurcated hydrogen-bond system N4—H41···O5′1/O4′. A further hydrogen bond is found linking molecules parallel to the *a* axis (O5′1—H5′1···O3′). Finally, there are further hydrogen bonds that connect molecules along the *b* axis or *via* the screw axis parallel to **b**, namely O3′—H3′···N3, N4—H42···O3′ and the bifurcated contact O5′2—H5′2···N2/N3.

Experimental

Crystal data

$C_{11}H_{14}N_4O_3$
M_r = 250.26
Orthorhombic, $P2_12_12_1$
a = 6.959 (1) Å
b = 8.564 (1) Å
c = 18.734 (3) Å
V = 1116.5 (3) Å^3
Z = 4
D_x = 1.489 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 38 reflections
θ = 2.6–17.3°
μ = 0.11 mm^{-1}
T = 293 (2) K
Prism, colourless
0.48 × 0.16 × 0.15 mm

Data collection

Bruker $P4$ diffractometer
$2\theta/\omega$ scans
1169 measured reflections
1169 independent reflections
1058 reflections with $I > 2\sigma(I)$
R_{int} = 0.041
θ_{max} = 25.0°
$h = -8 \rightarrow 8$
$k = -10 \rightarrow 10$
$l = -22 \rightarrow 22$
3 standard reflections
every 97 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.113
S = 1.10
1169 reflections
179 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0756P)^2 + 0.0595P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.28 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N1—C1′	1.454 (3)		
N2—N1—C7a	110.9 (2)	C7a—N1—C1′	125.7 (2)
N2—N1—C1′	123.1 (2)		
C7a—N1—N2—N3	0.4 (3)	C2′—C3′—C4′—O4′	26.1 (3)
C1′—N1—N2—N3	174.6 (3)	O3′—C3′—C4′—C5′1	150.2 (3)
N1—N2—N3—C3a	−0.5 (3)	O3′—C3′—C4′—C5′2	150.2 (3)
N2—N1—C1′—O4′	109.5 (3)	C2′—C1′—O4′—C4′	−24.5 (3)
C7a—N1—C1′—O4′	−77.1 (4)	C3′—C4′—O4′—C1′	−1.2 (3)
O4′—C1′—C2′—C3′	39.7 (3)	C3′—C4′—C5′1—O5′1	171.1 (3)
C1′—C2′—C3′—C4′	−39.1 (3)	C3′—C4′—C5′1—O5′2	52.4 (6)

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

D—H···A	D—H	H···A	D···A	D—H···A
N4—H41···O5′1^{i}	0.86	2.28	3.134 (5)	170
N4—H41···O4′^{i}	0.86	2.66	3.125 (4)	116
N4—H42···O3′^{ii}	0.86	2.68	3.460 (4)	151
O3′—H3′···N3^{iii}	0.82	2.04	2.854 (3)	171
O5′1—H5′1···O3′^{iv}	0.82	1.92	2.706 (4)	160
O5′2—H5′2···N2^{v}	0.82	2.38	3.164 (7)	159
O5′2—H5′2···N3^{v}	0.82	2.54	3.331 (7)	162

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

In the absence of suitable anomalous scatterers, the measured Friedel data could not be used to determine the absolute structure. Because of this, the Friedel reflections were merged. Comparison with the known configuration of the parent molecule indicates that the proposed configuration is correct. All H atoms except H511 and H521 were located in difference Fourier synthesis. The localization of H511 and H521 failed because their electron density is hidden behind the electron density of the disordered O5′ atom (H511 is covered by O5′2 and H21 is covered by O5′1). In order to optimize the data/parameter ratio, all H atoms were calculated at geometrically reasonable positions and refined as riding on the parent atoms. Their displacement parameters were fixed at 1.2 times the (equivalent) isotropic displacement parameter of the parent atoms.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *SHELXTL* (Sheldrick, 1997); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL* and *DIAMOND* (Brandenburg, 1999); software used to prepare material for publication: *SHELXTL*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: JZ1443). Services for accessing these data are described at the back of the journal.

References

Abola, J. & Sundaralingam, M. (1973). *Acta Cryst.* B**29**, 697–703.
Brandenburg, K. (1999). *DIAMOND*. Release 2.1c. Crystal Impact GbR, Bonn, Germany.
IUPAC-IUB Joint Commission on Biochemical Nomenclature (1983). *Eur. J. Biochem.* **131**, 9–15.
Käppi, R., Kazimierczuk, Z., Seela, F. & Lönnberg, H. (1991). *Nucleosides Nucleotides*, **10**, 571–572.
Kazimierczuk, Z. & Seela, F. (1990). *Helv. Chim. Acta*, **73**, 316–325.
Lin, G. H.-Y., Sundaralingam, M. & Arora, S. K. (1971). *J. Am. Chem. Soc.* **93**, 1235–1241.
Sato, T. (1984). *Acta Cryst.* C**40**, 880–881.
Schwalbe, C. H. & Saenger, W. (1973). *J. Mol. Biol.* **75**, 129–143.
Seela, F., Becher, G., Rosemeyer, H., Reuter, H., Kastner, G. & Mikhailopulo, I. (1999). *Helv. Chim. Acta*, **82**, 105–124.
Seela, F., Zulauf, M., Reuter, H. & Kastner, G. (1999). *Acta Cryst.* C**55**, 1947–1950.
Seela, F., Zulauf, M., Reuter, H. & Kastner, G. (2000). *Acta Cryst.* C**56**, 489–491.
Sheldrick, G. M. (1990). *SHELXS*86. University of Göttingen, Germany.
Sheldrick, G. M. (1993). *SHELXL*93. University of Göttingen, Germany.
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.
Singh, P. & Hodgson, D. J. (1974*a*). *J. Am. Chem. Soc.* **96**, 1239–1241.
Singh, P. & Hodgson, D. J. (1974*b*). *J. Am. Chem. Soc.* **96**, 5276–5278.
Singh, P. & Hodgson, D. J. (1977). *J. Am. Chem. Soc.* **99**, 4807–4815.
Sundaralingam, M. (1966). *Acta Cryst.* **21**, 495–505.