Table 3. *Selected geometric parameters (Å, °) for (II)*

S1—N2	1.575 (3)	N4—H4	0.83 (4)
S1—C10	1.751 (3)	N11—C12	1.466 (5)
N2—C3	1.325 (5)	N11—H11	0.77 (5)
C3—N11	1.325 (5)	C12—C13	1.520 (7)
C3—N4	1.368 (4)	C12—C14	1.524 (6)
N4—C5	1.389 (5)		
C3—N2—S1	120.4 (3)	C3—N4—H4	114 (3)
N2—C3—N11	121.3 (3)	C5—N4—H4	121 (3)
N2—C3—N4	122.8 (3)	C3—N11—C12	124.8 (4)
N11—C3—N4	115.9 (3)	C3—N11—H11	119 (4)
C3—N4—C5	124.0 (3)	C12—N11—H11	116 (4)
C10—S1—N2—C3	34.7 (4)	N2—C3—N11—C12	−4.9 (6)
S1—N2—C3—N11	159.9 (3)	C3—N11—C12—C13	115.4 (5)
S1—N2—C3—N4	−21.9 (5)	C3—N11—C12—C14	−117.9 (5)
N2—C3—N4—C5	−6.0 (6)	N11—C12—C14—C15	65.7 (6)
N11—C3—N4—C5	172.3 (4)		

Table 4. *Hydrogen-bonding geometry (Å, °) for (II)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N4—H4···O1^{i}	0.83 (4)	2.15 (5)	2.935 (4)	158 (4)
N11—H11···O1^{i}	0.77 (5)	2.22 (4)	2.928 (4)	151 (5)

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

H atoms were restrained (included as riding atoms) except for atoms H4 and H11 which were refined with isotropic displacement parameters fixed at $1.2U_{eq}$ of the parent atom ($1.5U_{eq}$ for the methyl-H atoms).

For both compounds, data collection: *DIF*4 (Stoe & Cie, 1987*b*); cell refinement: *DIF*4; data reduction: *REDU*4 (Stoe & Cie, 1987*c*); program(s) used to solve structures: *SHELXS*97 (Sheldrick, 1997*b*); program(s) used to refine structures: *SHELXL*97 (Sheldrick, 1997*a*); molecular graphics: *ORTEP*III (Burnett & Johnson, 1996); software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GS1050). Services for accessing these data are described at the back of the journal.

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The anomers of 8-aza-7-deaza-2′-deoxyadenosine

FRANK SEELA,[a] MATTHIAS ZULAUF,[a] HANS REUTER[b] AND GUIDO KASTNER[b]

[a]*Laboratorium für Organische und Bioorganische Chemie, Institut für Chemie, Universität Osnabrück, Barbarastraße 7, D-49069 Osnabrück, Germany, and* [b]*Anorganische Chemie II, Institut für Chemie, Universität Osnabrück, Barbarastraße 7, D-49069 Osnabrück, Germany. E-mail: fraseela@rz.uni-osnabrueck.de*

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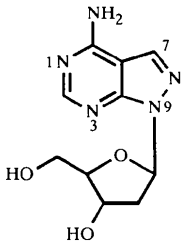
Abstract

The structures of 4-amino-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine, (I), and 4-amino-1-(2-deoxy-α-D-*erythro*-pentofuranosyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine, (II), both $C_{10}H_{13}N_5O_3$, have been determined. The sugar puckering of both compounds is C-2′-*endo*–C-3′*exo* ($^{2}T_{3'}$) (*S*-type sugar). The *N*-glycosidic torsion angle χ^1 is in the *anti* range [−106.3 (2)° for (I) and 111.5 (3)° for (II)] and the crystal structure is stabilized by hydrogen bonds.

Comment

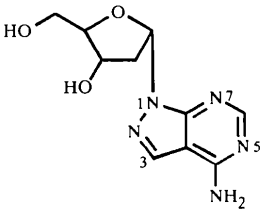
Oligonucleotides containing 8-aza-7-deaza-2′-deoxyadenosine, (I) (Seela & Kaiser, 1988), or C-7-modified 8-aza-7-deazapurine β-D-nucleosides (purine skeleton numbering is used throughout) show enhanced stability of duplexes with antiparallel (aps) chain orientation (Seela *et al.*, 1997; Seela & Becher, 1998; Seela, Becher & Zulauf, 1999; Seela & Zulauf, 1999). The X-ray structures of 7-substituted 8-aza-7-deazaguanine 2′-deoxynucleosides show that, apart from anomeric and *gauche* effects, the steric and stereoelectronic effects of the nucleobase are responsible for the high-*anti* conformation (Seela, Becher, Rosemeyer *et al.*, 1999). In this context, it was of interest to evaluate the crystal structure of 8-aza-7-deaza-2′-deoxyadenosine, (I), not carrying a substituent at C7. As duplexes with parallel (ps) chains can be formed when one oligonucleotide strand contains the sugar in an α-D-configuration (Im-

bach *et al.*, 1989) and since these oligonucleotides show nuclease resistance, it was of interest to study the conformational properties of the α-D-anomer 9-(2-deoxy-α-D-*erythro*-pentofuranosyl)-8-aza-7-deazaadenine, (II), as well.



(I)

Purine numbering



(II)

Systematic numbering

The ribonucleoside 8-aza-7-deaza-2′-deoxyadenosine (8-azatubercidin) exhibits a nearly symmetrical C1′-*exo*–C2′-*endo* ($^2T_{1'}$) pucker (Sprang *et al.*, 1978). In contrast to this observation, an unsymmetrical C2′-*endo*–C3′-*exo* ($^2T_{3'}$) (*S*-type sugar) sugar-ring conformation was observed for compounds (I) and (II). This half-chair conformation was also found for 2′-deoxytubercidin (Zabel *et al.*, 1987; Seela *et al.*, 1996), but not for 2′-deoxyadenosine (C3′-*endo*) (Sato, 1984). The puckering amplitude, τ_m, and the pseudorotation phase angle, *P* (Rao *et al.*, 1981), for (I) are τ_m = 41.2 (1)° and *P* = 182.2 (2)°, while for (II), τ_m = 33.1 (2)° and *P* = 183.9 (3)°. The orientation of the base relative to the sugar (*syn*/*anti*) is defined by the torsion angle χ^1 (O4′—C1′—N9—C4) (IUPAC–IUB Joint Commission on Biochemical Nomenclature, 1983); the preferred conformation around the *N*-glycosidic bond of a natural 2′-deoxynucleoside is usually in the *anti* range. It has been shown that Coulombic repulsion between the nonbonding electron pairs of O4′ and N8 of 8-azatubercidin (Sprang *et al.*, 1978), formycin (Prusiner *et al.*, 1973) and 7-halogenated 8-aza-7-deaza-2′-deoxypurines (Seela & Becher, 1998; Seela & Zulauf, 1999) forces the *N*-glycosidic conformation into the high-*anti* (−*sc*) (Klyne & Prelog, 1960) range. Compounds (I) and (II) adopt a conformation in the *anti* range between the perfect *anti* and the high-*anti* orientation [χ^1 = −106.3 (2)° for (I) and 111.5 (3)° for (II)] which was also found for 2′-deoxytubercidin (χ^1 = −104.4°; Zabel *et al.*, 1987), although 2′-deoxyadenosine adopts an almost perfect *anti* orientation (χ^1 = −165.1°; Sato, 1984). The conformation about the C4′—C5′ bond of (I) is in the *trans* (−*ap*) range [γ = −178.7 (16)°], whereas for (II), a *gauche* (+*sc*) conformation [γ = 62.9 (3)°] can be deduced. Since other torsion angles in (I) are also comparable to those of 2′-deoxytubercidin (Zabel *et al.*, 1987; Seela *et al.*, 1996), it can be deduced that compound (I) exhibits conformational similarities to this nucleoside but not to 8-azatubercidin (Sprang *et al.*, 1978) or to 2′-deoxyadenosine (Sato, 1984; Seela *et al.*, 1996).

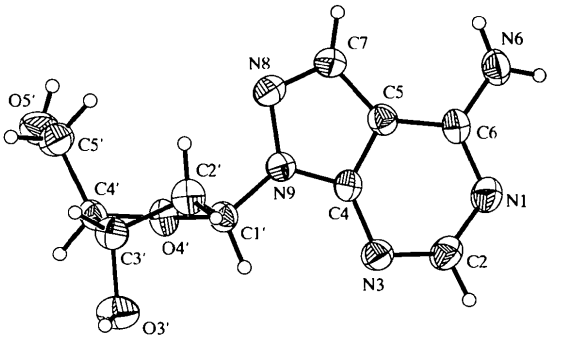


Fig. 1. Perspective view of (I) showing the atomic numbering scheme. Displacement ellipsoids of non-H atoms are drawn at the 50% probability level and H atoms are shown as spheres of small arbitrary size.

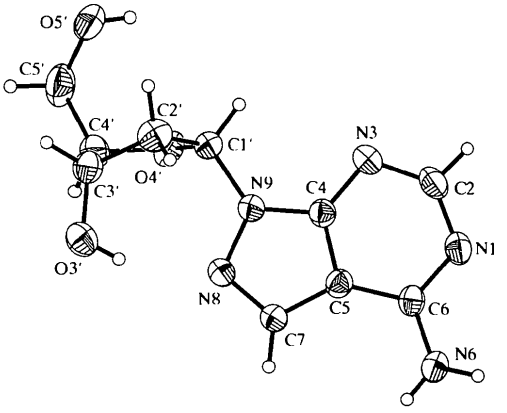


Fig. 2. Perspective view of (II) showing the atomic numbering scheme. Displacement ellipsoids of non-H atoms are drawn at the 50% probability level and H atoms are shown as spheres of small arbitrary size.

Hydrogen bonds in (I) and (II) provide additional crystal stabilization (see Tables 2 and 4). The 8-aza-7-deazaadenine base of (I) and (II) is planar. The deviations of C and N atoms from the least-squares plane are in the range of −0.020–0.021 Å.

Experimental

Compound (I) was prepared from 1-[2-deoxy-3,5-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl]-4-methoxy-1*H*-pyrazolo-[3,4-*d*]pyrimidine (300 mg, 0.60 mmol) (Seela & Steker, 1985) by treatment with 25% aqueous NH_3/1,4-dioxane (160 ml, 3:1 *v*/*v*) for 6 h at 363 K in an autoclave. The solvent was evaporated and the residue purified by flash chromatography on silica gel (column 12 × 3 cm; methanol–dichloromethane, 1:9). Crystallization from ^{i}PrOH yielded colourless crystals (81 mg, 54%) showing ^{1}H and ^{13}C NMR data identical

with a known sample (Seela & Steker, 1985). Compound (II) was prepared from 1-[2-deoxy-3,5-di-*O*-(*p*-toluoyl)-α-D-*erythro*-pentofuranosyl]-4-methoxy-1*H*-pyrazolo[3,4-*d*]-pyrimidine (200 mg, 0.40 mmol) (Seela & Steker, 1985) by treatment with 25% aqueous NH_3/1,4-dioxane (160 ml, 3:1 *v*/*v*) as described for (I). The solvent was evaporated and the residue purified by flash chromatography on silica gel (column 12 × 3 cm; methanol–dichloromethane, 1:9). Crystallization from ^{i}PrOH furnished colourless crystals (49 mg, 49%). For the diffraction experiments, single crystals were fixed at the top of Lindemann capillaries with epoxy resin. For (II): m.p. 460–461 K; R_f (methanol–dichloromethane, 1:9) 0.21; UV, λ_{max}(MeOH)/nm: 260 (ε dm^{-3} mol^{-1} cm^{-1} 9200) and 276 (11 100); ^{1}H NMR (250 MHz, DMSO-d_6, p.p.m.): 2.58 (*m*, 1H, C2′-H$_\alpha$), 2.70 (*m*, 1H, C2′-H$_\beta$), 3.40 (*m*, 2H, C5′-H$_{\alpha,\beta}$), 3.93 (*m*, 1H, C4′-H), 4.13 (*m*, 1H, C3′-H), 4.71 (*t*, 1H, C5′-OH, *J* = 5.6 Hz), 5.67 (*d*, 1H, C3′-OH, *J* = 7.5 Hz), 6.47 (*dd*, C1′-H, *J* = 5.1 and 7.0 Hz), 7.80 (*br s*, 2H, NH_2), 8.19 (*s*, 1H, C3-H), 8.20 (*s*, 1H, C6-H); ^{13}C NMR (125 MHz, DMSO-d_6, p.p.m.): 38.2 (C2′), 61.5 (C5′), 70.5 (C3′), 84.5 (C1′), 86.8 (C4′), 100.6 (C5), 133.2 (C7), 153.5 (C4), 156.3 (C2), 158.3 (C6); analytical data for $C_{10}H_{13}N_5O_3$, calculated: C 47.81, H 5.22, N 27.88%; found: C 47.68, H 5.20; N 27.78%.

Compound (I)

Crystal data

$C_{10}H_{13}N_5O_3$
M_r = 251.25
Orthorhombic
$P2_12_12_1$
a = 7.2420 (14) Å
b = 10.862 (2) Å
c = 14.2846 (16) Å
V = 1123.7 (3) Å^3
Z = 4
D_x = 1.485 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 37 reflections
θ = 4.68–12.50°
μ = 0.113 mm^{-1}
T = 293 (2) K
Thin plate
0.8 × 0.8 × 0.2 mm
Colourless

Data collection

Siemens *P*4 diffractometer
$2\theta/\omega$ scans
Absorption correction: none
2263 measured reflections
1946 independent reflections
1822 reflections with $I > 2\sigma(I)$
R_{int} = 0.022

θ_{max} = 25°
$h = -8 \rightarrow 8$
$k = -12 \rightarrow 12$
$l = -16 \rightarrow 16$
3 standard reflections every 97 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.033
$wR(F^2)$ = 0.088
S = 1.065
1946 reflections
165 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0492P)^2 + 0.1041P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.152 e Å^{-3}
$\Delta\rho_{min}$ = −0.160 e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997*a*)
Extinction coefficient: 0.031 (3)
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

N9—C1′	1.442 (2)		
C4—N9—C1′—O4′	−106.3 (2)	O3′—C3′—C4′—C5′	157.95 (16)
N8—N9—C1′—O4′	68.3 (2)	C2′—C1′—O4′—C4′	−11.6 (2)
O4′—C1′—C2′—C3′	32.76 (19)	C3′—C4′—O4′—C1′	−14.66 (19)
C1′—C2′—C3′—C4′	−40.44 (18)	O4′—C4′—C5′—O5′	64.1 (2)
C2′—C3′—C4′—O4′	34.50 (18)	C3′—C4′—C5′—O5′	−178.73 (16)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N6—H61···O3′^{i}	0.85	2.22	2.983 (2)	150
N6—H62···O5′^{ii}	0.86	2.07	2.909 (3)	165
O3′—H3′O···O4′^{iii}	0.82	1.98	2.7820 (17)	165
O5′—H5′O···N3^{iv}	0.82	1.96	2.778 (2)	176

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

Compound (II)

Crystal data

$C_{10}H_{13}N_5O_3$
M_r = 251.25
Orthorhombic
$P2_12_12_1$
a = 5.8690 (6) Å
b = 10.8869 (13) Å
c = 17.5477 (14) Å
V = 1121.2 (2) Å^3
Z = 4
D_x = 1.488 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 27 reflections
θ = 4.58–12.43°
μ = 0.114 mm^{-1}
T = 293 (2) K
Block
0.5 × 0.3 × 0.3 mm
Colourless

Data collection

Siemens *P*4 diffractometer
$2\theta/\omega$ scans
Absorption correction: none
4060 measured reflections
1966 independent reflections
1785 reflections with $I > 2\sigma(I)$
R_{int} = 0.031

θ_{max} = 24.98°
$h = -6 \rightarrow 6$
$k = -12 \rightarrow 12$
$l = -20 \rightarrow 20$
3 standard reflections every 97 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.110
S = 1.065
1966 reflections
164 parameters
H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0586P)^2 + 0.2760P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.376 e Å^{-3}
$\Delta\rho_{min}$ = −0.188 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 3. *Selected geometric parameters (Å, °) for (II)*

N9—C1′	1.457 (3)		
C4—N9—C1′—O4′	111.5 (3)	O3′—C3′—C4′—C5′	145.4 (2)
N8—N9—C1′—O4′	−62.8 (3)	C2′—C1′—O4′—C4′	−8.2 (3)
O4′—C1′—C2′—C3′	25.8 (3)	C3′—C4′—O4′—C1′	−12.7 (3)
C1′—C2′—C3′—C4′	−32.5 (3)	O4′—C4′—C5′—O5′	−56.4 (3)
C2′—C3′—C4′—O4′	28.0 (3)	C3′—C4′—C5′—O5′	62.9 (3)

Table 4. *Hydrogen-bonding geometry (Å, °) for (II)*

D—H···A	D—H	H···A	D···A	D—H···A
N6—H61···O5′^{i}	0.84	2.33	3.077 (3)	149
N6—H62···O3′^{ii}	0.84	2.20	3.025 (3)	170
O3′—H3′O···N8	0.82	2.02	2.799 (3)	159
O5′—H5′O···N1^{iii}	0.82	2.08	2.896 (3)	176

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

All H atoms were found in difference Fourier syntheses but were constructed in geometrically reasonable positions and refined with a common isotropic displacement parameter. With the absence of suitable anomalous scatterers within the molecules, the determination of the absolute configuration was not possible from our X-ray data. However, comparison with the configuration of the parent molecules indicates that the proposed conformations are correct.

For both compounds, data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *SHELXTL* (Sheldrick, 1997*b*); program(s) used to solve structures: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structures: *SHELXL*97 (Sheldrick, 1997*a*); molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: KA1335). Services for accessing these data are described at the back of the journal.

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Acta Cryst. (1999). C**55**, 1950–1952

4-Phenyl-2,3,5,6,7,8-hexahydro-1*H*-pyrido-[1,2-*c*]pyrimidine-1,3-dione

IRENA WOLSKA[a] AND FRANCISZEK HEROLD[b]

[a]*Department of Crystallography, Faculty of Chemistry, Adam Mickiewicz University, Grunwaldzka 6, 60-780 Poznań, Poland, and* [b]*Department of Drug Technology, The Medical University of Warsaw, Banacha 1, 02-097 Warszawa, Poland. E-mail: iwolska@main.amu.edu.pl*

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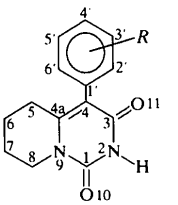
Abstract

In the structure of the title compound, $C_{14}H_{14}N_2O_2$, the saturated ring adopts a sofa conformation and the pyrimidine moiety is nearly planar. The mean planes of these fragments are close to coplanarity. The planar phenyl ring is twisted with respect to the pyrimidine-1,3-dione fragment. The molecules form centrosymmetric dimers *via* intermolecular N—H···O hydrogen bonds.

Comment

The syntheses of the 4-aryl-hexahydro-1*H*-pyrido[1,2-*c*]-pyrimidine-1,3-diones, (1)–(8), have been undertaken as a continuation of the search for new anxiolytic agents and studies on the relationship between structure and affinity to the 5-HT_{1A} receptor for those compounds. The compounds designed are structurally related to buspirone, a drug widely used in the treatment of mental diseases (Goa & Ward, 1986; Taylor & Moon, 1991; Faludi, 1994). Buspirone shows affinity to 5-HT_{1A}- and D_2-receptor types and is functionally a partial agonist of the 5-HT_{1A} receptors. Differences between the structures of buspirone and its new analogues are caused by a modification of the terminal imide moiety. It was noticed that as a result of this modification the lipophilicity of the molecule is higher and, consequently, the affinity to the 5-HT_{1A} receptor increases (Raghupathi *et al.*, 1991; Lopez-Rodriguez *et al.*, 1996; Lopez-Rodriguez, Morcillo *et al.*, 1997; Lopez-Rodriguez, Rosado *et al.*, 1997).



(1) *R* = H
(2) *R* = 2′-Me
(3) *R* = 3′-Me
(4) *R* = 4′-Me
(5) *R* = 4′-F
(6) *R* = 4′-OMe
(7) *R* = 2′-Cl
(8) *R* = 4′-Cl

The present structural work has been undertaken to obtain more detailed information about the bond