Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

8-Aza-7-deaza-7-propynyladenosine methanol solvate

Wenqing Lin,[a] Kuiying Xu,[a] Henning Eickmeier[b] and Frank Seela[a]*

[a]Laboratorium für Organische und Bioorganische Chemie, Institut für Chemie, Universität Osnabrück, Barbarastraße 7, 49069 Osnabrück, Germany, and [b]Anorganische Chemie II, Institut für Chemie, Universität Osnabrück, Barbarastraße 7, 49069 Osnabrück, Germany
Correspondence e-mail: frank.seela@uni-osnabrueck.de

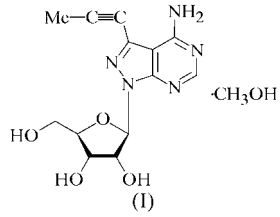
Received 12 November 2004
Accepted 19 January 2005
Online 11 March 2005

In the title compound, 4-amino-3-propynyl-1-(β-D-ribofuranosyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine methanol solvate, $C_{13}H_{15}N_5O_4{\cdot}CH_3OH$, the torsion angle of the N-glycosylic bond is between *anti* and high-*anti* [$\chi = -101.8\,(5)^\circ$]. The ribofuranose moiety adopts the C3′-*endo* ($^3T_2$) sugar conformation (N-type) and the conformation at the exocyclic C—C bond is +*sc* (*gauche*, *gauche*). The propynyl group is out of the plane of the nucleobase and is bent. The compound forms a three-dimensional network which is stabilized by several hydrogen bonds (O—H···O and O—H···N). The nucleobases are stacked head-to-tail. The methanol solvent molecule forms hydrogen bonds with both the nucleobase and the sugar moiety.

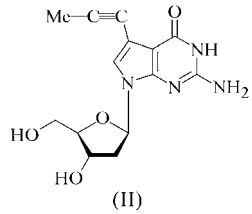
Comment

Among the various groups introduced into nucleosides to stabilize oligonucleotide duplexes, the propynyl group has attracted particular attention. This group has been introduced into the 5-position of pyrimidines or the 7-position of 7-deazapurine nucleosides (Froehler *et al.*, 1992; Sági *et al.*, 1993; Seela & Thomas, 1995; Seela & Zulauf, 1999; Barnes & Turner, 2001*a*,*b*; He & Seela, 2002*a*,*b*) (purine numbering is used throughout). Recently, the single-crystal X-ray structure of 7-deaza-2′-deoxy-7-propynylguanosine, (II), was published (Seela *et al.*, 2004). We now report the crystal structure of the related ribonucleoside 4-amino-3-propynyl-1-(β-D-ribofuranosyl)-1*H*-pyrazolo[3,4-*d*]pyrimidine methanol solvate (8-aza-7-deaza-7-propynyladenosine methanol solvate), (I). The synthesis of compound (I) is described in the *Experimental* and the structure is shown in Fig. 1. Selected geometric parameters are given in Table 1.

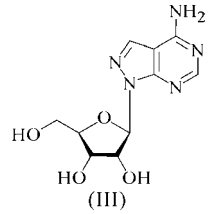
The N-glycosylic bond of compound (I) shows a conformation between *anti* and high-*anti*, with a C4—N9—C1′—O4′ torsion angle χ of $-101.8\,(5)^\circ$ (IUPAC–IUB Joint Commission on Biochemical Nomenclature, 1983). By comparison, 8-aza-7-deazaadenosine [8-azatubercidin, (III)], without the substitution of the propynyl group, exhibits the high-*anti* conformation ($\chi = -77.6^\circ$; Sprang *et al.*, 1978).



(I)



(II)



(III)

The ribofuranosyl ring in (I) adopts the C3′-*endo* ($^3T_2$) sugar puckering (N conformation), with the pseudorotation phase angle $P = 6.3\,(4)^\circ$ and the maximum amplitude of puckering $\tau_m = 36.5\,(2)^\circ$ (Rao *et al.*, 1981). This is in contrast with the ribofuranose moiety of compound (III), which exhibits an S-type pucker ($_1T^2$), with $P = 141.9^\circ$ and $\tau_m = -41.9^\circ$. The conformation at the C4′—C5′ bond in (I) is *syn* (+*sc*; *gauche*, *gauche*), with a C3′—C4′—C5′—O5′ torsion angle of $55.5\,(5)^\circ$, which is different from the *trans* conformation usually observed for 8-azapurine and purine nucleosides, such as in (III). In solution, the sugar moiety of (I) is in the N⇌S pseudorotational equilibrium, but it is also slightly biased to the N-conformation (54%), as calculated by the *PSEUROT* program (Van Wijk & Altona, 1993).

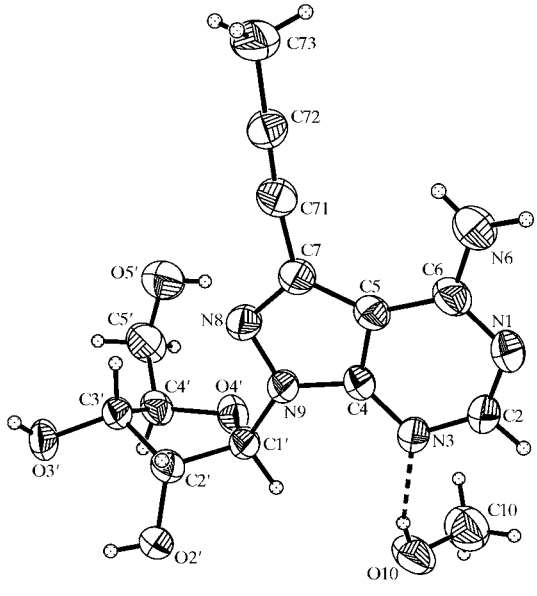


Figure 1
A perspective view of the molecule of (I), showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are represented as small spheres of an arbitrary size.

 DOI: 10.1107/S0108270105001927

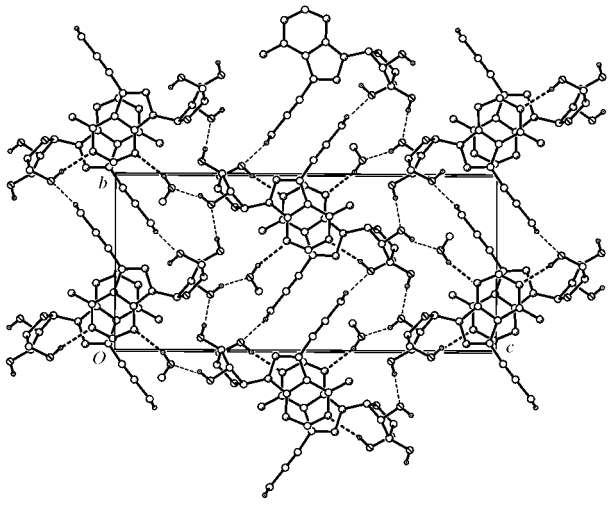


Figure 2
The crystal packing of (I), viewed down the *a* axis, showing the intermolecular hydrogen-bonded network.

In compound (I), the nucleobase ring and the exocyclic N6 (amino) and C1′ (sugar) atoms are nearly coplanar, the r.m.s. deviation of the least-squares plane being 0.0152 Å and the maximum deviation being −0.024 (4) Å for atom N1. Atom C71 of the propynyl group lies above the heterocyclic plane, with a deviation of 0.100 (7) Å. This group is slightly bent, with the C72—C71—C7 bond angle being 173.1 (5)°, and is inclined by nearly 4° to the 8-aza-7-deazapurine moiety. This inclination is larger than that observed in 1-(β-D-arabinofuranosyl)-5-propynyluracil (3.7°; Cygler *et al.*, 1984), but smaller than that in 7-deaza-7-propynyl-2′-deoxyguanosine, (II), in which we also found that the propynyl group is inclined by about 4.6° (Seela *et al.*, 2004). The triple-bond length of (I) is within the usual range (Cygler *et al.*, 1984), indicating that this bond is not in conjugation with the nucleobase.

The nucleoside forms a 1:1 complex with methanol *via* hydrogen bonds (Fig. 2 and Table 2). The nucleobases are aligned head-to-tail, with a plane-to-plane distance of 3.664 Å. This is close to the distance observed for the stacked nucleobases in B-DNA. Some other intermolecular hydrogen bonds are formed in the crystal structure of (I) (Table 2 and Fig. 2). The amino group does not participate in the hydrogen-bonding pattern, while a hydrogen bond is formed between the H atom of the methyl group of the propynyl side chain and the O atom of the O5′—H group of the sugar moiety (Table 2 and Fig. 2).

Experimental

Compound (I) was synthesized by treatment of a degassed suspension of 7-iodo-8-aza-7-deazaadenosine (200 mg, 0.5 mmol) and CuI (9.6 mg, 0.05 mmol) in anhydrous dimethylformamide (3 ml) with $Pd(PPh_3)_4$ (29 mg, 0.025 mmol), triethylamine (0.14 ml, 1 mmol) and propyne gas at room temperature overnight. The reaction mixture was diluted with methanol (50 ml) and dichloromethane (50 ml), and Dowex 1X8 (100–200 mesh, 500 mg, bicarbonate form) was introduced. After stirring for 45 min, the mixture was filtered and the filtrate evaporated. Crystallization from methanol furnished compound (I) (80 mg, 47%, m.p. 463–464 K). R_F (methanol–dichloromethane, 1:9): 0.21; ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.15 (*m*, 3H, CH_3), 3.44, 3.54 (2*m*, 2H, C5′-H), 3.90 (*q*, 1H, C4′-H, *J* = 4.74 Hz), 4.19 (*q*, 1H, C3′-H, *J* = 4.84 Hz), 4.55 (*q*, 1H, C2′-H, *J* = 5.11 Hz), 4.84 (*d*, 1H, C5′-OH, *J* = 5.60 Hz), 5.14 (*d*, 1H, C3′-OH, *J* = 5.34 Hz), 5.39 (*d*, 1H, C2′-OH, *J* = 5.80 Hz), 6.07 (*d*, 1H, C1′-H, *J* = 4.59 Hz), 6.73, 7.98 (2*br*, 2H, NH_2), 8.22 (*s*, 1H, C2-H); ^{13}C NMR (62.5 MHz, DMSO-d_6): δ 4.40 (C73), 62.3 (C5′), 70.8 (C2′), 71.1 (C72), 73.0 (C3′), 85.2 (C4′), 88.3 (C1′), 93.1 (C71), 100.6 (C5), 127.6 (C7), 154.0 (C6), 156.6 (C2), 157.7 (C4); analysis calculated for $C_{13}H_{15}N_5O_4$: C 51.14, H 4.95, N 22.94%; found C 51.15, H 4.88, N 22.80%. For the diffraction experiment, a single crystal was fixed at the top of a Lindemann capillary with epoxy resin.

Crystal data

$C_{13}H_{15}N_5O_4{\cdot}CH_4O$
M_r = 337.34
Orthorhombic, $P2_12_12_1$
a = 7.3269 (11) Å
b = 10.0790 (16) Å
c = 21.813 (3) Å
V = 1610.8 (4) Å^3
Z = 4
D_x = 1.391 Mg m^{-3}
Mo *Kα* radiation
Cell parameters from 65 reflections
θ = 3.7–17.1°
μ = 0.11 mm^{-1}
T = 293 (2) K
Needle, colourless
0.56 × 0.20 × 0.15 mm

Data collection

Bruker *P*4 diffractometer
2θ/ω scans
2707 measured reflections
2032 independent reflections
1542 reflections with $I > 2\sigma(I)$
R_{int} = 0.030
θ_{max} = 27.0°
h = −9 → 1
k = −12 → 1
l = −1 → 27
3 standard reflections
every 97 reflections
intensity decay: 5%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.054
$wR(F^2)$ = 0.164
S = 1.10
2032 reflections
223 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.081P)^2 + 0.4152P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.36 e Å^{-3}
$\Delta\rho_{min}$ = −0.23 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N1—C2	1.327 (5)	N8—N9	1.371 (5)
N1—C6	1.349 (6)	O2′—C2′	1.432 (5)
C7—C71	1.445 (6)	C3′—C4′	1.521 (6)
C71—C72	1.175 (6)	C4′—C5′	1.482 (7)
C72—C73	1.479 (6)	O5′—C5′	1.379 (6)
O4′—C1′—N9	110.0 (3)	O3′—C3′—C2′	113.9 (3)
O4′—C1′—C2′	107.1 (3)	C1′—O4′—C4′	110.2 (3)
O2′—C2′—C1′	106.6 (3)	O4′—C4′—C3′	104.5 (3)
O2′—C2′—C3′	110.7 (3)	C5′—C4′—C3′	117.0 (4)
O3′—C3′—C4′	110.6 (3)	O5′—C5′—C4′	114.1 (4)
N9—C4—C5—C7	−0.7 (5)	N8—N9—C1′—C2′	−45.3 (5)
N3—C4—C5—C6	−1.9 (7)	O2′—C2′—C3′—O3′	42.7 (4)
C4—C5—C7—C71	−176.1 (4)	O3′—C3′—C4′—O4′	−154.1 (3)
N8—N9—C1′—O4′	74.3 (5)		

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

D—H···A	D—H	H···A	D···A	D—H···A
O2′—H2′···O10^{i}	0.82	2.01	2.764 (4)	153
O3′—H3′···O2′^{i}	0.82	1.97	2.776 (4)	168
O5′—H5′···N1^{ii}	0.82	2.25	3.012 (5)	154
O10—H10···N3	0.82	2.10	2.891 (4)	162
C73—H73B···O5′^{iii}	0.96	2.29	3.173 (6)	153

Symmetry codes: (i) $-x+1, y+\frac{1}{2}, -z+\frac{1}{2}$; (ii) $x+\frac{1}{2}, -y+\frac{3}{2}, -z+1$; (iii) $x-\frac{1}{2}, -y+\frac{5}{2}, -z+1$.

In the absence of suitable anomalous scattering, Friedel equivalents could not be used to determine the absolute structure. Therefore, Friedel equivalents were merged before the final refinements. The known configuration of the parent molecule was used to define the enantiomer of the final model. All H atoms were initially 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 = 0.93–0.98 Å, O—H = 0.82 Å and N—H = 0.86 Å) and constrained to ride on their parent atoms, with U_{iso}(H) = 1.2U_{eq}(C,N) and 1.5U_{eq}(O).

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: FG1796). Services for accessing these data are described at the back of the journal.

References

Barnes, T. W. III & Turner, D. H. (2001*a*). *J. Am. Chem. Soc.* **123**, 4107–4118.
Barnes, T. W. III & Turner, D. H. (2001*b*). *J. Am. Chem. Soc.* **123**, 9186–9187.
Cygler, M., Anderson, W. F., Giziewicz, J. & Robins, M. J. (1984). *Can. J. Chem.* **62**, 147–152.
Froehler, B. C., Wadwani, S., Terhorst, T. J. & Gerrard, S. R. (1992). *Tetrahedron Lett.* **33**, 5307–5310.
He, J. & Seela, F. (2002*a*). *Nucleic Acids Res.* **30**, 5485–5496.
He, J. & Seela, F. (2002*b*). *Tetrahedron*, **58**, 4535–4542.
IUPAC–IUB Joint Commission on Biochemical Nomenclature (1983). *Eur. J. Biochem.* **131**, 9–15.
Rao, S. T., Westhof, E. & Sundaralingam, M. (1981). *Acta Cryst.* A**37**, 421–425.
Sági, J., Szemzö, A., Ébinger, K., Szabolcs, A., Sági, G., Ruff, E. & Ötvös, L. (1993). *Tetrahedron Lett.* **34**, 2191–2194.
Seela, F., Shaikh, K. & Eickmeier, H. (2004). *Acta Cryst.* C**60**, o489–o491.
Seela, F. & Thomas, H. (1995). *Helv. Chim. Acta*, **78**, 94–108.
Seela, F. & Zulauf, M. (1999). *J. Chem. Soc. Perkin Trans.* 1, pp. 479–488.
Sheldrick, G. M. (1997). *SHELXTL*. Release 5.10. Bruker AXS Inc., Madison, Wisconsin, USA.
Siemens (1996). *XSCANS*. Release 2.2. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Spek, A. L. (1999). *PLATON for Windows*. University of Utrecht, The Netherlands. (32-Bit Windows implentation by L. J. Farrugia, University of Glasgow, Scotland.)
Sprang, S., Scheller, R., Rohrer, D. & Sundaralingam, M. (1978). *J. Am. Chem. Soc.* **100**, 2867–2872.
Van Wijk, J. & Altona, C. (1993). *PSEUROT*. Version 6.3 of July 1993. University of Leiden, The Netherlands.