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Structure of Puromycin Aminonucleoside

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Abstract. 3′-Amino-3′-deoxy-*N*,*N*-dimethyladenosine, $C_{12}H_{18}N_6O_3$, $M_r = 294{\cdot}3$, monoclinic, $P2_1$, $a = 4{\cdot}684$ (1), $b = 10{\cdot}252$ (1), $c = 14{\cdot}381$ (3) Å, $\beta = 91{\cdot}16$ (2)°, $V = 690{\cdot}49$ Å^3, $Z = 2$, $D_x = 1{\cdot}39$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 0{\cdot}84$ mm^{-1}, $F(000) = 312$, $T = 295$ K, $R = 0{\cdot}045$ for 986 observed reflections with $I > 1{\cdot}5\sigma(I)$. The adenine base is unprotonated at N(1) and is dimethylated at N(6). The nucleoside has a 3′-deoxy-3′-aminofuranosyl ribose sugar. The base is in the *anti* conformation ($\chi = 2{\cdot}3°$) with respect to the furanosyl ring, which shows a C(3′)-*endo*–C(2′)-*exo* pucker ($_2T^3$). O(5′) is disordered. The structure of the compound is similar to that of the nucleoside portion of the antibiotic puromycin.

Introduction. We report here the crystal structure of puromycin aminonucleoside, which forms the nucleoside portion of puromycin, a broad spectrum antibiotic and a structural analog of the 3′-aminoacyl adenosine moiety of charged tRNA. The present study was undertaken because of our interest in the conformational flexibility of modified nucleosides (Viswamitra & Gautham, 1984). Our analysis shows that the conformational features of the molecule are similar to those of the nucleoside moiety of puromycin dihydrochloride pentahydrate, the structure of which has previously been solved (Sundaralingam & Arora, 1972).

Experimental. Compound [6-dimethylamino-9-[(3′-amino-3′-deoxyribosyl)purine] purchased from Sigma Chemicals. Crystals were obtained by direct evaporation from aqueous solution of the compound. Cell parameters were refined by least squares using 20 reflections, $3 \le \theta \le 28°$, on a CAD-4 Enraf–Nonius diffractometer. Intensity data were collected up to $(\sin\theta)/\lambda = 0{\cdot}56$ Å^{-1}, with ω–2θ scan using Ni-filtered Cu $K\alpha$ radiation on a crystal of dimensions 0·2 × 0·04 × 0·03 mm. Three standard reflections monitored at regular intervals, crystal stable to X-rays. Analytical absorption correction (North, Phillips & Mathews, 1968) applied, transmission factor varied from 75·7 to 95·7%. Index range $-5 \le h \le 5$, $0 \le k \le 11$, $0 \le l \le 16$; of the 1181 unique reflections, 968 were considered observed [$I > 1{\cdot}5\sigma(I)$]. Structure solution by direct methods using *MULTAN*80 (Germain, Main & Woolfson, 1971). The terminal oxygen atom, O(5′), was found to be disordered. Of the 18 H atoms, 16 could be located from a difference electron density map. Number of parameters refined is 262. Full-matrix least-squares refinement on *F*'s using *SHELX*76 (Sheldrick, 1976), with non-H atoms refined anisotropically and H atoms refined isotropically, converged at $R = 0{\cdot}045$. Individual weights $w \propto 1/[\sigma^2(F) + 0{\cdot}001(F^2)]$, $wR = 0{\cdot}042$; maximum $\Delta/\sigma = 0{\cdot}12$; $\Delta\rho$ in the final difference map within +0·22 and −0·20 e Å^{-3}. The atomic scattering factors are as supplied in *SHELX*76. Structure solution using the Enraf–Nonius (1979) *SDP* on a PDP 11/44 computer.

Discussion. The final positional parameters along with equivalent isotropic temperature factors for the non-H atoms are given in Table 1.* Bond lengths and bond angles are listed in Table 2. Fig. 1 shows the conformation of the puromycin aminonucleoside molecule along with the atomic numbering scheme. The crystal packing viewed down the *a* axis is shown in Fig. 2.

The nucleoside has an adenine base, which is unprotonated at N(1) and dimethylated at N(6), and a 3′-amino-3′-deoxyfuranosyl ribose sugar. The bond lengths and bond angles are in good agreement with the average values found in crystal structures containing unprotonated adenine bases (Taylor & Kennard, 1982). The dimethylation of the base at N(6) is found to have little or no effect on the bond distances as was also seen in the structure of puromycin (Sundaralingam & Arora, 1972).

The nucleoside shows *anti* conformation with χ [C(8)–N(9)–C(1′)–O(4′)] = 2·3 (8)° compared with 18° found in the puromycin structure. An earlier proton magnetic resonance (PMR) study of the compound has shown that it probably has a 50:50 population of *syn* and *anti* conformers in solution (Narula & Dhingra, 1984).

The least-squares plane for the adenine base shows that it is essentially planar. The substituent atoms N(6)

* Lists of structure factors, anisotropic thermal parameters, torsion angles and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51201 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Table 1. *Final fractional coordinates and temperature factors of the non-hydrogen atoms, with e.s.d.'s in parentheses*

$$U_{eq} = \tfrac{1}{3}\sum_i\sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}(Å^2)
N(1)	−0·5644 (9)	0·4268 (6)	0·7686 (3)	0·0408 (14)
C(2)	−0·4084 (13)	0·4444 (7)	0·6927 (4)	0·0459 (20)
N(3)	−0·2398 (9)	0·5418 (6)	0·6706 (3)	0·0396 (14)
C(4)	−0·2333 (10)	0·6313 (6)	0·7389 (3)	0·0341 (15)
C(5)	−0·3804 (11)	0·6286 (6)	0·8213 (3)	0·0363 (15)
C(6)	−0·5573 (11)	0·5179 (6)	0·8358 (3)	0·0365 (16)
N(7)	−0·3174 (11)	0·7390 (6)	0·8732 (3)	0·0509 (16)
C(8)	−0·1364 (14)	0·8040 (7)	0·8228 (4)	0·0510 (20)
N(9)	−0·0802 (9)	0·7450 (6)	0·7400 (3)	0·0378 (13)
N(6)	−0·7187 (10)	0·4981 (6)	0·9099 (3)	0·0480 (16)
C(9)	−0·7049 (23)	0·5798 (9)	0·9925 (5)	0·0725 (29)
C(10)	−0·8993 (16)	0·3830 (8)	0·9163 (5)	0·0583 (24)
O(4′)	0·2497 (7)	0·9042 (5)	0·6971 (2)	0·0423 (11)
C(1′)	0·1123 (13)	0·7884 (6)	0·6673 (4)	0·0392 (17)
C(2′)	−0·0405 (12)	0·8181 (6)	0·5757 (3)	0·0376 (16)
O(2′)	0·1526 (9)	0·8105 (0)	0·5029 (3)	0·0507 (14)
C(3′)	−0·1178 (11)	0·9623 (6)	0·5911 (4)	0·0343 (15)
N(3′)	−0·1872 (12)	1·0362 (6)	0·5077 (3)	0·0407 (15)
C(4′)	0·1384 (11)	1·0139 (6)	0·6440 (4)	0·0383 (16)
C(5′)	0·0872 (14)	1·1252 (7)	0·7093 (4)	0·0327 (20)
O(5′)*	0·3434 (14)	1·1608 (7)	0·7536 (5)	0·0664 (24)
O(5)*	−0·0997 (28)	1·0999 (13)	0·7789 (7)	0·0547 (40)

* Atom O(5′) has s.o.f. of 0·66, O(5) of 0·34.

Table 2. *Bond lengths* (Å) *and bond angles* (°) *involving the non*-H *atoms*

N(1)–C(2)	1·338 (7)	N(6)–C(10)	1·456 (10)
C(2)–N(3)	1·316 (9)	O(4′)–C(1′)	1·413 (8)
N(3)–C(4)	1·344 (7)	C(1′)–C(2′)	1·517 (8)
C(4)–C(5)	1·383 (6)	C(2′)–C(3′)	1·539 (9)
C(5)–C(6)	1·423 (8)	C(3′)–C(4′)	1·504 (8)
C(6)–N(1)	1·344 (8)	C(4′)–C(5′)	1·500 (9)
C(5)–N(7)	1·384 (8)	C(4′)–O(4′)	1·450 (7)
N(7)–C(8)	1·309 (8)	C(5′)–O(5′)	1·396 (9)
C(8)–N(9)	1·366 (8)	C(2′)–O(2′)	1·400 (7)
N(9)–C(4)	1·369 (8)	C(3′)–N(3′)	1·450 (8)
C(6)–N(6)	1·335 (7)	C(1′)–N(9)	1·464 (7)
N(6)–C(9)	1·454 (9)	C(5′)–O(5)	1·368 (13)
C(6)–N(1)–C(2)	119·1 (5)	O(4′)–C(1′)–C(2′)	107·4 (5)
N(1)–C(2)–N(3)	129·8 (6)	C(1′)–C(2′)–C(3′)	100·1 (4)
C(2)–N(3)–C(4)	110·3 (5)	C(2′)–C(3′)–C(4′)	102·9 (4)
N(3)–C(4)–C(5)	127·5 (5)	C(3′)–C(4′)–O(4′)	105·6 (4)
C(4)–C(5)–C(6)	116·3 (5)	O(4′)–C(1′)–N(9)	108·8 (5)
C(4)–C(5)–N(7)	109·9 (5)	C(2′)–C(1′)–N(9)	113·2 (5)
C(5)–N(7)–C(8)	104·5 (5)	C(1′)–C(2′)–O(2′)	109·7 (4)
N(7)–C(8)–N(9)	113·3 (6)	C(3′)–C(2′)–O(2′)	108·6 (4)
C(8)–N(9)–C(4)	106·1 (5)	C(2′)–C(3′)–N(3′)	115·6 (5)
N(1)–C(6)–N(6)	117·5 (5)	C(4′)–C(3′)–N(3′)	113·4 (5)
C(5)–C(6)–N(6)	125·4 (5)	C(3′)–C(4′)–C(5′)	116·6 (5)
C(9)–N(6)–C(10)	115·6 (6)	C(4′)–C(5′)–O(5′)	109·7 (6)
C(5)–C(6)–N(1)	117·1 (5)	O(4′)–C(4′)–C(5′)	108·7 (5)
C(5)–C(4)–N(9)	106·1 (5)	C(1′)–N(9)–C(4)	125·5 (5)
C(6)–N(6)–C(9)	123·2 (6)	C(1′)–N(9)–C(8)	128·4 (5)
C(6)–N(6)–C(10)	120·9 (5)	O(5′)–C(5′)–O(5)	105·8 (7)
C(6)–C(5)–N(7)	133·7 (5)	C(4′)–C(5′)–O(5)	115·3 (7)
N(3)–C(4)–N(9)	126·4 (5)		

and C(1′) are displaced on opposite sides of the plane by +0·028 (5) and −0·023 (6) Å respectively, unlike the puromycin structure, where they are on the same side of the base plane, displaced by 0·198 and 0·056 Å respectively.

The ribose is in C(3′)-*endo*–C(2′)-*exo* conformation ($_2T^3$), with the atoms C(3′) and C(2′) displaced by −0·261 (5) and 0·359 (5) Å respectively from the three-atom plane defined by C(1′), C(4′) and O(4′). The ribose exhibits a similar pucker in puromycin. The pseudorotation parameters of the furanose ring in the present structure are $P = -2{\cdot}9$ and 38·1° (Altona & Sundaralingam, 1972).

The O(5′) atom is disordered between *gauche–trans* (O5′) and *gauche–gauche* (O5) conformations about the bond C(4′)–C(5′) with 2:1 occupancy ratio for the two sites. The PMR study (Narula & Dhingra, 1984) estimated 80% of the nucleoside molecules to be in *gauche–gauche* conformation about the C(4′)–C(5′) bond, a conformation also seen in puromycin.

The present study thus shows that the conformation of molecules is similar to that of the nucleoside portion in puromycin. The conformational flexibility of puromycin seems to lie mainly in its amino-acid segment, as suggested by theoretical studies (Yathindra & Sundaralingam, 1973) and the PMR solution study on puromycin and its related compounds (Narula & Dhingra, 1984).

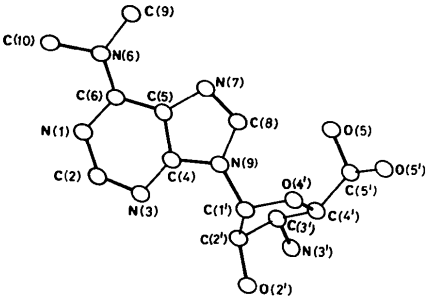

Fig. 1. Atomic numbering scheme for the puromycin aminonucleoside molecule.

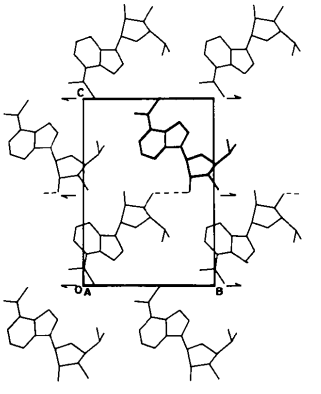

Fig. 2. The crystal packing viewed down the *a* axis.

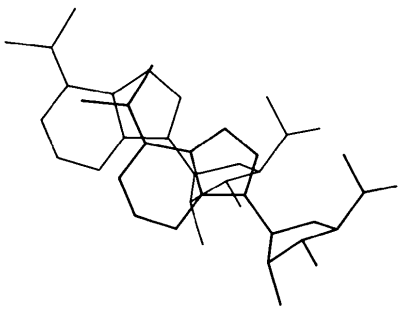

Fig. 3. A view perpendicular to the adenine base plane, indicating stacking interactions.

Molecular packing

The crystal structure is stabilized by the intermolecular hydrogen bond O(2′)–H···N(3′) [2·821 (6) Å and 172·4°]. There are no stacking interactions due to ring overlap of bases. However, the exocyclic atoms N(6) and C(10) of the base stack on top (≃3·54 Å) of the adenine base of the molecule related by the *a*-cell translation, as shown in Fig. 3.

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Dimerization Products of Substituted 1,2-Benzoquinones

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Abstract. 1,4,4a,8a-Tetrahydro-2,8-dimethyl-1,4-ethanonaphthalene-5,6,9,10-tetrone (1), $C_{14}H_{12}O_4$, M_r = 244·25, orthorhombic, *F*2*dd*, a = 7·505 (1), b = 14·180 (2), c = 44·548 (5) Å, V = 4741 (1) Å^3, Z = 16, D_x = 1·369 g cm^{-3}, λ(Mo $K\alpha$) = 0·71073 Å, μ = 0·94 cm^{-1}, F(000) = 2048, T = 293 K, R = 0·0496, 933 reflections. 1,4,4a,8a-Tetrahydro-9,9-dihydroxy-2,-8-dimethyl-1,4-ethanonaphthalene-5,6,10-trione (2), $C_{14}H_{14}O_5$, M_r = 262·27, monoclinic, *Cc*, a = 9·174 (1), b = 10·799 (2), c = 12·557 (2) Å, β = 103·40 (2)°, V = 1210·2 (5) Å^3, Z = 4, D_x = 1·439 g cm^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, μ = 8·76 cm^{-1}, F(000) = 552, T = 295 K, R = 0·0320, 819 reflections. 1,4,4a,8a-Tetrahydro-2,8-di-*tert*-butyl-1,4-ethanonaphthalene-5,6,9,-10-tetrone (3), $C_{20}H_{24}O_4$, M_r = 328·41, triclinic, $P\bar{1}$, a = 8·786 (1), b = 9·112 (1), c = 12·387 (1) Å, α = 101·24 (1), β = 92·40 (1), γ = 114·73 (1)°, V = 875·0 (2) Å^3, Z = 2, D_x = 1·247 g cm^{-3}, λ(Mo $K\alpha$) = 0·71073 Å, μ = 0·80 cm^{-1}, F(000) = 352, T = 292 K, R = 0·0499, 1598 reflections. The bridged portions of the three molecules exhibit similar conformations although the keto function in (2) is replaced by a dihydroxy substituent. The cyclohexenedione ring in (1) is more flattened than that in (2) and (3). Bond C(1)–C(8*a*) = 1·572 (5) is significantly longer than the C(4)–C(4*a*) distance of 1·554 (1). It is suggested that this difference is inherent in the ring system and does not arise from steric factors.

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