Fig. 2. Projection of the structure along [010].
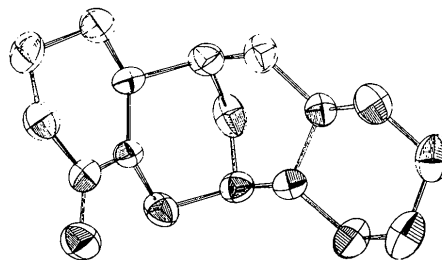

Fig. 3. ORTEP drawing of the cation with thermal ellipsoids at 50% probability.

limit of the O···O intermolecular-distance range (3·02–3·42 Å, Kitaigorodsky, 1976).

The molecular packing in the unit cell is shown in Fig. 2, and an ORTEP drawing at 50% probability is given in Fig. 3.

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2-Azaadenosine Hemihydrate

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Abstract. $C_9H_{12}N_6O_4.\frac{1}{2}H_2O$, orthorhombic, $C222_1$, $a = 7\cdot860$ (9), $b = 9\cdot445$ (10), $c = 31\cdot156$ (26) Å, $U = 2312\cdot9$ Å^3, $Z = 8$, $D_c = 1\cdot592$, D_m (flotation in benzene/carbon tetrachloride) $= 1\cdot56$ (1) Mg m^{-3}. The nucleoside adopts the anti conformation with a torsion angle, χ, of $13\cdot8°$. There is approximate 85/15 disorder around the exocyclic bond C(4')–C(5'), the major component exhibiting the gauche–gauche (gg) confor-

mation while the minor component is gauche–trans (gt).

Introduction. The nucleoside was generously donated by Dr J. A. Montgomery (Southern Research Institute). Crystals of relatively poor quality were obtained by slow evaporation of an aqueous solution. The crystal used for data collection, like all other crystals examined, was twinned [the twinning plane being (001)] and had approximate dimensions 0·72 ×

0.40×0.20 mm. Precession and Weissenberg photography showed that the crystals are orthorhombic; the observed systematic absences of hkl with $h + k$ odd and $00l$ with l odd indicate the space group $C222_1$. The intensity data were collected using Mo $K\alpha$ radiation on a four-circle Picker automatic diffractometer equipped with a graphite monochromator. The cell constants were obtained by least-squares procedures from the diffractometer settings of twelve reflections; it was assumed that the wavelength $\lambda(\text{Mo } K\alpha_1) = 0.7093$ Å. The intensities were collected by the $\theta/2\theta$ scan method at a scan rate of $0.5°$ (2θ) min^{-1} out to 2θ (Mo) $= 63°$. Stationary-crystal–stationary-counter background counts of 20 s were measured on each side of the peak. To allow for the presence of both $K\alpha_1$ and $K\alpha_2$ radiations, the peaks were scanned from $0.6°$ in 2θ below the calculated $K\alpha_1$ peak position to $0.6°$ in 2θ above the calculated $K\alpha_2$ peak position. Visual examination of the peaks recorded on a chart recorder showed no evidence of overlapping reflections despite the poor quality of the crystal. The data were processed in the manner described by Corfield, Doedens & Ibers (1967) and corrected for Lorentz–polarization effects (Goldfield & Raymond, 1971). The computer programs used in this analysis have been described elsewhere (Singh & Hodgson, 1977a).

The structure was solved by direct methods using the program MULTAN (Main, Woolfson & Germain, 1971). The H atoms were located in difference Fourier maps. It was apparent at an early stage that there was some disorder around the C(4')–C(5') bond, since the thermal parameters for O(5') were significantly larger than those for other atoms and since a difference Fourier map indicated the presence of a large peak within bonding distance of C(5') but which could not be attributed to a H atom. A disordered model was used in which the occupancy factor of O(5') was assigned as α and that of another atom O(5')A was assigned as $(1 - \alpha)$; the value of α was then refined, with the proper constraints being imposed on the other parameters. The value of α refined to 0.855, i.e. there is approximate 85/15 disorder. The only H atoms on C(5') which could be located were those of the major conformer; similarly, no terminal H atom was observed on O(5')A. The parameters of one of the H atoms on C(5') and those on O(5') and the water oxygen atom O(W) were not varied. Other H atoms were refined isotropically, while non-hydrogen atoms were refined anisotropically. The water O atom is constrained to lie on a crystallographic twofold axis. Least-squares refinements were carried out on F, the function minimized being $\sum w(|F_o| - |F_c|)^2$ where the weighting factor w was taken as $4F_o^2/\sigma^2(F_o^2)$. No correction for secondary extinction was necessary, and none was applied. The scattering factors used for C, N, and O were from International Tables for X-ray Crystallography (1962) while those for H were from Stewart,

Davidson & Simpson (1965). The final agreement factors $R_1 = \sum(||F_o| - |F_c||)/\sum F_o$ and $R_2 = [\sum w(|F_o| - |F_c|)^2/\sum w(F_o)^2]^{1/2}$ were 0.054 and 0.072, respectively, based on 1766 observations with $I \geq 3.0\sigma(I)$ and 212 variables. The positional parameters, along with their standard deviations as estimated from the inverse matrix, are listed in Table 1.* A final difference Fourier map was featureless.

Discussion. The azapurine nucleosides differ from the natural nucleosides in the substitution of CH by N in the purine ring. The most studied such class are the 8-azapurine nucleosides, many of which have been shown to exhibit antineoplastic activity (Montgomery, Elliott & Thomas, 1975), and we have previously reported the crystal structure of 8-azaadenosine (Singh & Hodgson, 1974a, 1977b). Similarly, we and others have examined

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Table 1. *Positional parameters in 2-azaadenosine.-*
$\frac{1}{2}H_2O$

	x	y	z
N(1)	0.2932 (3)	0.6217 (3)	0.0381 (1)
N(2)	0.3388 (3)	0.5214 (3)	0.0656 (1)
N(3)	0.2263 (3)	0.4440 (3)	0.0878 (1)
C(4)	0.0630 (3)	0.4761 (3)	0.0800 (1)
C(5)	0.0040 (3)	0.5789 (3)	0.0525 (1)
C(6)	0.1278 (3)	0.6569 (3)	0.0303 (1)
N(6)	0.0980 (3)	0.7593 (4)	0.0025 (1)
N(7)	−0.1721 (3)	0.5827 (3)	0.0518 (1)
C(8)	−0.2150 (4)	0.4818 (4)	0.0790 (1)
N(9)	−0.0804 (3)	0.4145 (3)	0.0974 (1)
C(1')	−0.0837 (4)	0.2996 (3)	0.1291 (1)
C(2')	−0.0362 (4)	0.3527 (3)	0.1741 (1)
O(2')	0.0526 (3)	0.2438 (3)	0.1959 (1)
C(3')	−0.2113 (4)	0.3767 (4)	0.1930 (1)
O(3')	−0.2110 (3)	0.3769 (4)	0.2384 (1)
C(4')	−0.3141 (4)	0.2551 (4)	0.1732 (1)
O(4')	−0.2493 (3)	0.2460 (3)	0.1305 (1)
C(5')	−0.5027 (5)	0.2707 (6)	0.1717 (1)
O(5')	−0.5453 (4)	0.4069 (3)	0.1595 (1)
O(5')A	−0.6374 (25)	0.2569 (23)	0.1558 (7)
O(W)	0.0	0.0199 (4)	0.2500
H(OW)	0.0	0.091	0.226
H(N6)	−0.027 (6)	0.806 (4)	−0.002 (2)
H2(N6)	0.179 (4)	0.817 (3)	−0.010 (1)
H(C8)	−0.305 (8)	0.470 (6)	0.089 (2)
H(C1')	−0.040	0.219	0.120
H(C2')	0.041 (4)	0.441 (3)	0.173 (1)
H(O2')	0.088	0.282	0.216
H(C3')	−0.250 (4)	0.459 (3)	0.183 (1)
H(O3')	−0.237 (5)	0.455 (3)	0.237 (1)
H(C4')	−0.239 (6)	0.158 (5)	0.192 (1)
H(5')	−0.545	0.215	0.148
H(5'')	−0.525 (5)	0.247 (3)	0.202 (1)
H(O5')	−0.615	0.386	0.138

the structures of the antibiotics formycin (Prusiner, Brennan & Sundaralingam, 1973), formycin B (Singh & Hodgson, 1975; Hodgson & Singh, 1976; Koyama, Nakamura, Umezawa & Iitaka, 1976), and their cations (Koyama, Umezawa & Iitaka, 1974; Singh & Hodgson, 1977a); these antibiotics are analogs of the 8-azapurine nucleosides. For the 8-azapurine nucleosides, and for the analogous 6-azapyrimidine nucleosides (Schwalbe & Saenger, 1973; Saenger & Suck, 1973; Singh & Hodgson, 1974b,c) the preferred conformation is in the high-anti region with the torsion angle $\chi[O(4')-C(1')-N(9)-N(8)]$ near 100°, and we have ascribed this feature to the absence of a steric constraint brought about (in the natural nucleosides) by the proton on C(8) [or C(6) for the pyrimidine nucleosides] (Hodgson & Singh, 1976).

The report of the synthesis (Montgomery & Thomas, 1969) of 2-azaadenosine provided us with an opportunity to test this steric hypothesis, since we would anticipate that the glycosyl conformation of 2-azaadenosine should be similar to that of the natural nucleosides and unlike that of the 8-azapurine nucleosides. A view of the molecule is shown in Fig. 1, and it is apparent that the conformation is anti; the value of χ is 13·8°, which is comparable to values of 9·9° in adenosine (Lai & Marsh, 1972) and 4·5° in 3-deazaadenosine (Singh, May, Townsend & Hodgson, 1976) but quite different from that of 103·7° in 8-azaadenosine (Singh & Hodgson, 1977b).

The bond lengths and angles in the azapurine moiety are similar to those in other nucleoside structures (Ringertz, 1972), except in the region near N(2). The N(1)—N(2) bond of 1·329 (4) Å is shorter than the normal N(1)—C(2) bond, and the N(1)—N(2)—N(3) bond angle of 122·9 (3)° is considerably smaller than the value of approximately 129° normally associated with the N(1)—C(2)—N(3) angle. These changes, of

course, lead to other minor adjustments in the six-membered ring. The N(9)—C(1') glycosyl bond of 1·470 (4) Å is similar to those in adenosine (Lai & Marsh, 1972) and other nucleosides (Sundaralingam, 1973) but is longer than that of 1·447 (3) Å in 8-azaadenosine. The bond lengths in the structure are shown in Fig. 1. The nine-membered azapurine can be viewed as an approximately planar unit (maximum deviation 0·014 Å) or as consisting of a planar six-membered ring (maximum deviation 0·006 Å) and a planar five-membered ring (maximum deviation 0·005 Å) which are inclined at a dihedral angle of 1·2°.

As is the case in adenosine (Lai & Marsh, 1972), the five-membered ribose ring adopts the C(3')-endo envelope (^3E) conformation with C(3') displaced by 0·600 Å in the same direction as C(5') from the least-squares plane through C(1'), C(2'), C(4') and O(4'); the maximum deviation of any of these four atoms from the least-squares plane is 0·011 Å. This is in contrast to the C(2')-endo conformation found in the 8-azapurine nucleosides and their analogs. The conformation around the exocyclic C(4')—C(5') is the normal gauche–gauche (gg) in the major (85%) conformer (shown in Fig. 1) and is gauche–trans (gt) in the minor conformer.

There is extensive hydrogen bonding in the crystals. Base pairs, depicted in Fig. 2, are formed between molecules related by the 2_1 screw along a; these base pairs are formed by N(6)—H···N(7') and N(6')—H···N(1) hydrogen bonds of length 2·891 (4) and 2·931 (4) Å, respectively, with associated N—H···N angles of 162 and 154° respectively. This base-pairing configuration, which is reminiscent of both the Watson–Crick and Hoogsteen models for adenine–thymine base pairs, has been observed in several other neutral adenine derivatives including 9-methyladenine (Stewart & Jensen, 1964), deoxyadenosine (Watson, Sutor & Tollin, 1965), and 2'-O-methyladenosine
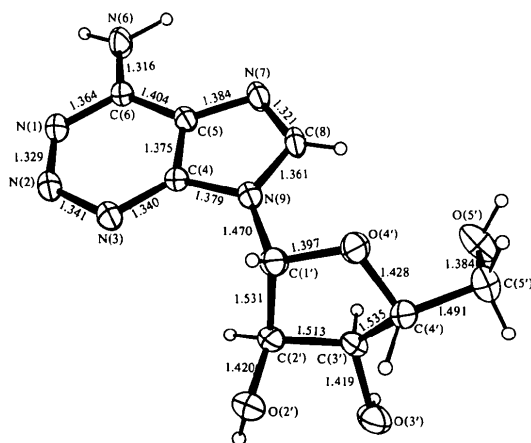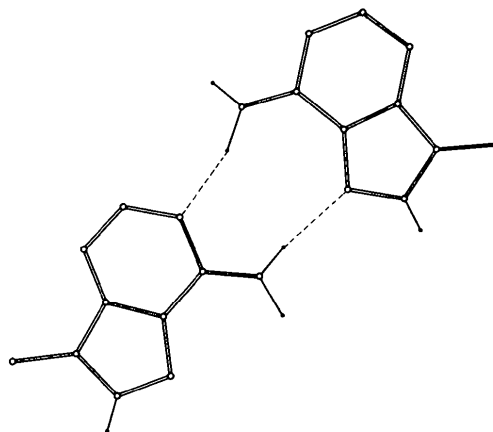

Fig. 1. View of the 2-azaadenosine molecule, showing the principal bond lengths (Å); e.s.d.'s are 0·004 Å for all bonds. Thermal ellipsoids are drawn at the 50% probability level; H atoms are shown as small circles of arbitrary size.

Fig. 2. View of the hydrogen-bonded base pairing in 2-azaadenosine. The two molecules are related by the 2_1 axis along a.
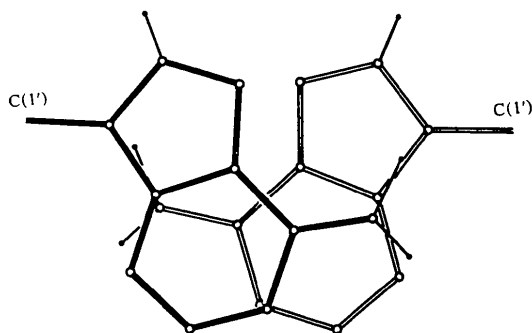
Fig. 3. View of the base stacking in 2-azaadenosine. The top molecule is related to the bottom molecule by the twofold axis along a.

(Prusiner & Sundaralingam, 1976). The N(6')—H···N(1) separation in the present complex is within the range of 2·88 to 3·00 Å observed in these other structures, but the N(6)—H···N(7') distance of 2·891 (4) Å is significantly shorter than those of 3·00 to 3·06 Å previously observed. In addition to this base-pairing interaction, the terminal hydroxyl groups O(2')H, O(3')H, and O(5')H form hydrogen bonds of lengths 2·707 (4), 2·669 (4), and 2·888 (5) Å to O(3'), the water molecule, and N(3) in related molecules. The water molecule also forms an apparent donor hydrogen bond to O(2'), with an O···O hydrogen-bond length of 2·73 (4) Å and O—H···O angle of 160°. As in most nucleoside structures (Bugg, 1972), there is some base stacking in the crystals. The stacking arrangement here, which is shown in Fig. 3, involves C(6) of one nucleoside lying above the plane of the six-membered ring of the next nucleoside; the average interplanar separation between adjacent planes is 3·38 (5) Å.

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