5-methyl isomer. The nine atoms of the phthalide ring system are close to coplanar (r.m.s.d. = 0·008 Å) and the six C—C lengths in the aromatic portion of the ring system average 1·390 Å (r.m.s.d. = 0·008 Å) compared with 1·397 ± 0·005 Å in benzene (Sutton, 1965). C(6)—C(7) [1·496 (6) Å] is not significantly different from the expected value (Bartell & Bonham, 1960) (1·505 Å) for a bond between sp^2- and sp^3-hybridized C atoms. Likewise, C(7)—O(1) can be considered normal. On the other side of the five-membered ring, the sp^2-hybridized state of C(8) causes the corresponding lengths, C(8)—C(1) and C(8)—O(1), to be significantly shorter.

The crystal structure (Fig. 2) contains stacks of anti-parallel, planar molecules extending along *c* and formed by centres of symmetry and *c* glides in alternating sequence.

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Conformation of an O(6)-Substituted Purine Derivative: Structure of 6-Methoxypurine Riboside

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Abstract. $C_{11}H_{14}N_4O_5.\frac{1}{2}H_2O$, orthorhombic, $P2_12_12_1$, $a = 26{\cdot}075$ (7), $b = 13{\cdot}125$ (4), $c = 7{\cdot}222$ (1) Å, $Z = 8$, $D_c = 1{\cdot}565$ Mg m^{-3}, μ(Cu $K\alpha$) = 0·99 mm^{-1}. R for the 1743 reflections with $I > \sigma(I)$ is 0·085. The two crystallographically independent molecules assume a conformation in which the methyl group is directed away from the imidazole moiety of the purine base.

Introduction. Various alkylating agents react with nucleic acids *in vivo* and *in vitro*. One of the major reaction sites is the O(6) position of guanine residues. The resulting O(6)-alkyl derivatives would be expected to display one of two favoured conformations about the C(6)—O(6) bond. In order to maintain the partial double-bond character of this bond, the substituent attached to O(6) should lie in or near the purine plane. However, the alkyl group could point either toward or away from the imidazole moiety of the purine. These two alternative conformations might affect the secondary structures of nucleic acids in different ways. For example, if the alkyl group is directed toward the imidazole ring, then the purine derivative might be expected to pair with uracil or thymine bases within double-helical nucleic acids, as postulated by Lawley (1972). On the other hand, if the alternative conformation is assumed, the bulky alkyl group would interfere with any type of Watson–Crick interactions at the reaction site. We determined the crystal structure of 6-methoxypurine riboside to obtain information about

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the conformations of O(6)-substituted purine derivatives.

Needle-shaped crystals were grown by slow evaporation of an aqueous solution of 6-methoxypurine riboside. Oscillation and Weissenberg photographs showed the crystals to be orthorhombic; the space group $P2_12_12_1$ is indicated by the systematic absence of reflections $h00$ with h odd, $0k0$ with k odd, and $00l$ with l odd. A crystal with approximate dimensions 0·40 × 0·05 × 0·05 mm was mounted on a Picker FACS-1 diffractometer with its c axis slightly inclined to the φ axis of the diffractometer. Intensity data were collected with the diffractometer by use of a scintillation counter, Ni-filtered Cu radiation, and a θ–2θ scanning technique. The 2θ scanning speed was 0·5° min^{-1}, and the background was counted for 20 s at each terminus of the scans. A base scan range of 1·25° was augmented to account for α_1–α_2 splitting. Measurements were made for each of the 2362 reflections with $2\theta \leq 127°$. Three strong, medium-angle reflections that were monitored periodically did not vary significantly during data collection.

There were 255 reflections with scan counts below background levels; these were given their calculated negative intensity values and were retained in all subsequent calculations. Intensities were assigned variances, $\sigma^2(I)$, according to counting statistics plus an additional term $(0{\cdot}03S)^2$, S being the scan count. The intensities and their variances were corrected for Lorentz and polarization factors, absorption corrections were applied by using the computer program *ORABS* (Wehe, Busing & Levy, 1962), and the data were scaled by means of a Wilson (1942) plot.

The trial structure was obtained with the computer program package *MULTAN* 78 (Main, Hull, Lessinger, Germain, Declercq, & Woolfson, 1978). 48 phase sets were generated for 320 normalized structure factors ($|E| > 1{\cdot}43$), based on a starting set of six reflections. 3500 triples were utilized in the phase-determining process. The E map computed from the phase set with the highest combined figure-of-merit revealed 35 of the 41 nonhydrogen atoms. A Fourier synthesis phased with these atoms revealed the remaining nonhydrogen atoms. The structure was

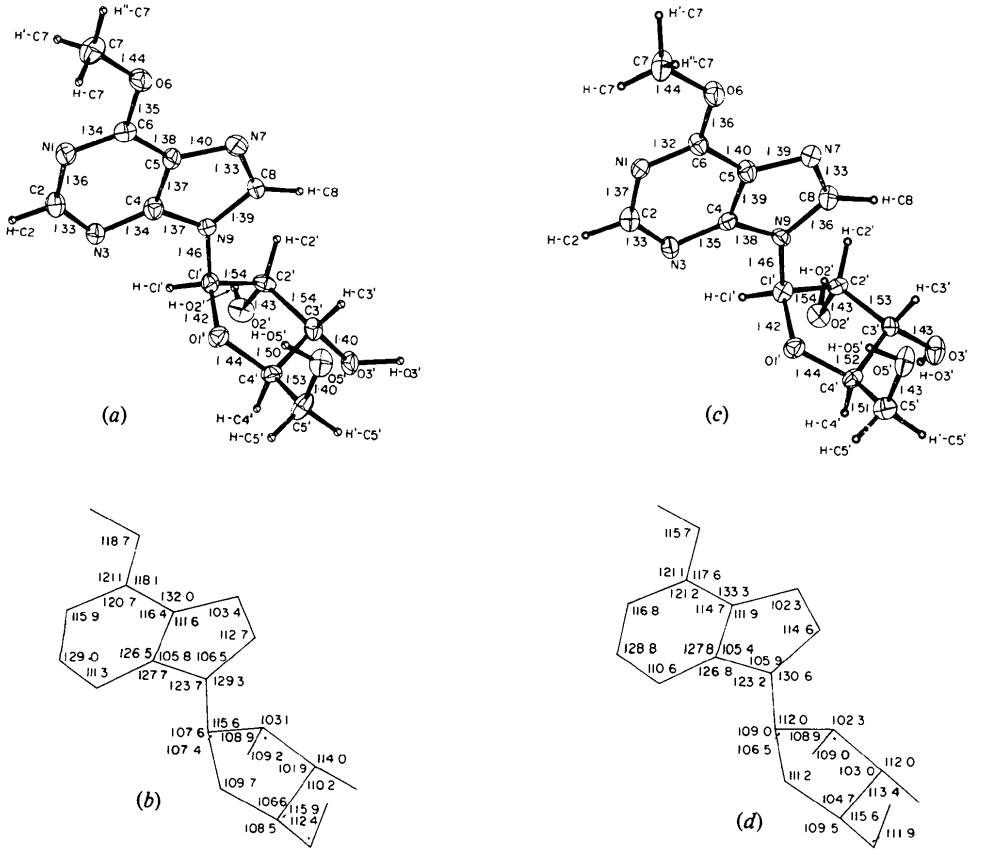

Fig. 1. Conformation of 6-methoxypurine riboside (*a*) nucleoside *A*, (*c*) nucleoside *B*. Nonhydrogen atoms are represented by thermal ellipsoids defined by the principal axes of thermal vibration and scaled to include 30% probability. H atoms are represented by spheres of 0·07 Å radius. Estimated standard deviations are about 0·01 Å for bond lengths (*a*,*c*) and 0·5° for bond angles (*b*,*d*). This drawing and Fig. 2 were prepared by using the computer program *ORTEP* (Johnson, 1965).

refined by use of a modified version of the least-squares program *ORFLS* (Busing, Martin & Levy, 1962; Busing, 1971). The quantity minimized was $\sum w(F_o^2 - F_c^2/k^2)^2$, where k is a scale factor and the weight w is equal to $1/\sigma^2(F_o^2)$. Scattering factors and anomalous-dispersion corrections were from *International Tables for X-ray Crystallography* (1974). H atoms were located in difference Fourier maps during the latter stages of refinement. They were assigned the isotropic temperature factors of the atoms to which they are bonded and were included in the calculation of structure factors, but not in the least-squares refinement. The final R index $(\sum||F_o| - |F_c||/\sum|F_o|)$ for all data is 0·107, and the goodness-of-fit $\{[\sum w(F_o^2 - F_c^2)^2/(m - s)]^{1/2}$, where m is the number of reflections used and s the number of parameters refined $\}$ is 1·20. The R index using the 1743 reflections for which $I > \sigma(I)$ is 0·085. All parameter shifts during the last cycle of refinement were less than $0{\cdot}3\sigma$. A final difference Fourier map showed a hole of $-0{\cdot}7$ e Å^{-3} that was near O(6) of nucleoside *A*; the map showed no other peaks or troughs that exceeded 0·5 e Å^{-3} in magnitude.

Discussion. The nonhydrogen atom positional parameters and their estimated standard deviations are listed in Table 1.* The estimated errors in positional coordinates are about 0·007 Å. The conformations of the two crystallographically independent nucleosides, together with bond lengths and angles involving nonhydrogen atoms, are shown in Fig. 1. The purine rings are almost planar; none of the nine ring atoms deviates from the least-squares planes by more than 0·022 Å in molecule *A* and 0·033 Å in molecule *B*. In molecule *A*, atoms O(6) and C(7) are displaced from the purine plane by 0·079 and 0·087 Å, respectively; in molecule *B*, these two atoms are displaced by 0·049 and 0·156 Å, respectively. Both molecules display a conformation in which the methyl group is directed away from the imidazole moiety of the base [the O(6)—C(7) bond is *trans* to the C(5)—C(6) bond]. There are no significant differences between corresponding bond lengths and angles in the two molecules.

The ribose moieties assume a C(3′)-*endo* conformation. Atom C(3′) in molecule *A* is displaced 0·514 Å from the least-squares plane through atoms C(1′), O(1′), C(2′), and C(4′); none of the other atoms deviate more than 0·018 Å from this plane. In molecule *B*, C(3′) is displaced by 0·538 Å from the plane through the other four atoms of the ribose ring; none of the other ring atoms deviate more than 0·009 Å from this plane. The conformation about the glycosidic linkage is *anti* (Donohue & Trueblood, 1960; Sundaralingam, 1969); the torsion angle O(1′)—C(1′)—N(9)—C(8) is equal to 90° for molecule *A* and 91° for molecule *B*. The conformation about the C(4′)—C(5′) bond is *gauche-gauche* (Shefter & Trueblood, 1965), with the torsion angles φ_{OO}[O(5′)—C(5′)—C(4′)—O(1′)] equal to −57 and −64° for molecules *A* and *B*, respectively, and φ_{OC}[O(5′)—C(5′)—C(4′)—C(3′)] equal to 63 and 54°.

The crystal-packing and hydrogen-bonding schemes are shown in Fig. 2. Hydrogen-bond distances and

Table 1. *Positional parameters* (×10⁴) *and isotropic thermal parameters* (×10³) *for nonhydrogen atoms*

$U_{eq} = \frac{1}{3}(U_{11} + U_{22} + U_{33} + 2U_{23}\cos\alpha + 2U_{13}\cos\beta + 2U_{12}\cos\gamma)$.

	x	*y*	*z*	U_{eq} (Å²)
Nucleoside *A*				
N(1)	8627 (3)	10609 (5)	−520 (10)	37
C(2)	8277 (3)	9881 (7)	−68 (13)	36
N(3)	8356 (2)	8928 (5)	487 (10)	37
C(4)	8859 (3)	8722 (6)	629 (13)	35
C(5)	9255 (3)	9379 (6)	265 (13)	33
C(6)	9121 (3)	10344 (6)	−332 (12)	33
O(6)	9502 (2)	10996 (4)	−802 (9)	41
C(7)	9369 (4)	12001 (6)	−1436 (14)	50
N(7)	9731 (2)	8926 (5)	608 (11)	38
C(8)	9608 (3)	7995 (7)	1177 (13)	34
N(9)	9083 (2)	7829 (5)	1195 (10)	28
C(1′)	8796 (3)	6956 (7)	1902 (12)	31
O(1′)	8679 (2)	7153 (4)	3786 (8)	36
C(2′)	9077 (3)	5926 (6)	1821 (13)	30
O(2′)	8717 (2)	5149 (4)	1332 (9)	39
C(3′)	9252 (3)	5763 (6)	3843 (13)	32
O(3′)	9277 (2)	4739 (4)	4376 (9)	36
C(4′)	8838 (3)	6304 (6)	4907 (12)	33
C(5′)	8990 (4)	6703 (7)	6813 (13)	45
O(5′)	9373 (2)	7444 (4)	6718 (9)	46
Nucleoside *B*				
N(1)	5981 (2)	10596 (5)	10368 (11)	34
C(2)	6504 (3)	10507 (6)	10346 (12)	38
N(3)	6788 (2)	9710 (5)	9868 (10)	33
C(4)	6490 (3)	8936 (6)	9294 (13)	29
C(5)	5960 (3)	8915 (6)	9166 (13)	34
C(6)	5715 (3)	9791 (6)	9815 (13)	32
O(6)	5195 (2)	9809 (4)	9773 (9)	43
C(7)	4959 (3)	10712 (6)	10506 (15)	55
N(7)	5782 (3)	7985 (5)	8522 (12)	40
C(8)	6216 (4)	7463 (6)	8284 (13)	38
N(9)	6650 (2)	7987 (5)	8723 (9)	29
C(1′)	7190 (3)	7713 (6)	8496 (12)	30
O(1′)	7364 (2)	8073 (4)	6747 (8)	35
C(2′)	7271 (3)	6549 (6)	8493 (12)	30
O(2′)	7762 (2)	6326 (4)	9282 (8)	34
C(3′)	7285 (3)	6305 (6)	6426 (12)	31
O(3′)	7561 (2)	5383 (3)	6048 (9)	43
C(4′)	7535 (3)	7248 (6)	5599 (11)	30
C(5′)	7401 (4)	7469 (7)	3602 (13)	45
O(5′)	6858 (2)	7515 (4)	3318 (8)	48
W	6421 (2)	5639 (4)	2597 (8)	56

* Lists of structure factors, anisotropic thermal parameters for the nonhydrogen atoms, and positional and thermal parameters for H atoms, and Table 2 have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35302 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

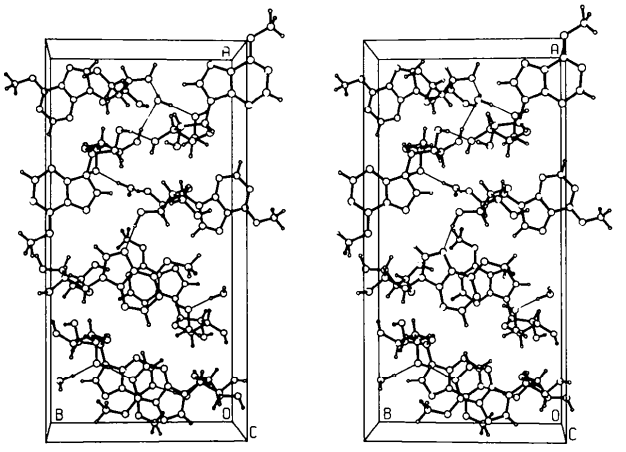

Fig. 2. Stereodrawing of the crystal packing and hydrogen-bonding scheme as viewed down the *c* axis. Heavy lines represent covalent bonds, and narrow lines represent hydrogen bonds.

angles are listed in Table 2.* The bases form planar ribbons that run in the **b** direction and lie nearly parallel to the *ab* plane. The ribbons of bases are stacked in the **c** direction; the stacking pattern can be seen in Fig. 2.

Our results suggest that the preferred conformation of O(6)-substituted purine derivatives is the one in which the substituent is directed away from the imidazole moiety of the purine ring. This finding is not unexpected since a variety of N(6)-substituted adenine derivatives and S-substituted 6-mercaptopurine derivatives all display this general conformation (Bugg & Sternglanz, 1974). The preference for this conformation is also somewhat predictable from examination of CPK space-filling molecular models of purine derivatives that have alkyl groups at the O(6) position; the alternative conformation, with the alkyl group directed toward the imidazole ring, produces close contacts between atoms of the alkyl group and atom N(7) of the imidazole moiety. We feel that O(6)-alkylated purine derivatives within polynucleotides would be expected to assume conformations similar to that found in this crystal structure. Since this conformation would interfere with base pairing within double-helical nucleic acids, it might account for the finding that poly(6-methylguanylic acid) and poly(6-ethylguanylic acid) fail to form stable complexes with either polycytidylic acid or polyuridylic acid (Mehta & Ludlum, 1976).

* See previous footnote.

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