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Structure of a 1:1 Molecular Complex of 9-Methyladenine and 2-Thiohydantoin

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Abstract

The 1:1 molecular complex of 9-methyladenine and 2-thiohydantoin ($C_6H_7N_5 \cdot C_3H_4N_2OS$) is monoclinic, space group $C2/c$ with unit-cell parameters $a = 21.140(3)$, $b = 7.085(1)$, $c = 16.101 \text{ \AA}$ and $\beta = 103.27(2)^\circ$, with eight complexes per unit cell ($D_c = 1.499$, $D_o = 1.508 \text{ Mg m}^{-3}$). The intensity data were collected on an automated diffractometer using Nb-filtered $Mo K\alpha$ radiation, and the structure was solved using direct methods. The structure was refined in two blocks (non-hydrogen atoms anisotropic, hydrogens isotropic); the refinement converged to a final conventional $R(f)$ value of 3.5% (4.9% weighted) for the 2475 significant data. The structure consists of ribbons with alternating adenine and hydantoin moieties linked *via* (hydantoin)N—H...N(adenine) hydrogen bonds. The ribbons are held together *via* N—H...N hydrogen bonds involving the 9-methyladenine molecules. The sulfur and oxygen atoms of the 2-thiohydantoin molecules do not appear to act as acceptors in strong hydrogen bonds.

Introduction

There is considerable interest in the hydrogen-bonding characteristics in complexes of adenine derivatives with substituted hydantoins (Jones & Kemp, 1974) and

barbiturates (Hsu & Craven, 1974; Shieh & Voet, 1976*a,b*). This laboratory is currently investigating complexes of 9-methyladenine and various substituted hydantoins in an effort to characterize further these interactions. We were particularly interested in the role sulfur might play in hydrogen bonding.

Experimental

Crystals of the 1:1 complex of 9-methyladenine and 2-thiohydantoin were obtained in the form of yellow rectangular plates from hot water containing equimolar quantities of 9-methyladenine (Cyclo Chemical) and 2-thiohydantoin (Sigma Chemical). A crystal of the complex with dimensions $0.21 \times 0.15 \times 0.08 \text{ mm}$ was chosen for diffraction study. The crystal density (1.508 Mg m^{-3}), which was determined by flotation in a mixture of cyclohexane and dibromoethane, agrees with the calculated value (1.499 Mg m^{-3}), assuming eight molecules of each component in the unit cell. The space group and approximate cell dimensions were obtained from precession and Weissenberg photographs. Accurate cell dimensions (*Abstract*) were obtained by the least-squares refinement of the observed setting angles for fourteen $Mo K\alpha$ reflections in the range $28 < 2\theta < 44^\circ$, measured with an Oak Ridge computer-controlled diffractometer (Busing, Ellison, Levy, King & Rosenberry, 1968). Intensity data were collected on the diffractometer with Nb-filtered $Mo K\alpha$ radiation ($\lambda = 0.71073 \text{ \AA}$) using the θ - 2θ scan technique. Of the 2710 reflections with $2\theta \leq 55^\circ$, 2475

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were considered observed [$I > 3\sigma(I)$]. Each intensity was assigned a variance $\sigma^2(I)$ based on counting statistics plus a term $(0.04I)^2$, empirically derived during refinement. No absorption corrections were applied ($\mu = 2.634 \text{ cm}^{-1}$). No significant changes in two standard reflections were observed during the course of data collection.

The structure was readily solved using the direct-methods computer program *MULTAN 78* (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978). The largest figure of merit indicated the correct solution. Refinement of the scale factor, the non-hydrogen atomic positions and their anisotropic temperature factors converged at an $R(f)$ value of 0.065. A difference Fourier map at this point revealed the

positions of the eleven expected hydrogens. Further least-squares refinement during which the non-hydrogen atoms were refined anisotropically and the hydrogen atoms were refined isotropically reduced the $R(f)$ value to 0.035. The weighted R $\{[\sum w(F_o - F_c)^2 / \sum wF_o^2]\}$ and σ , the goodness of fit $\{[\sum w(F_o - F_c)^2 / (n - p)]^{1/2}$, where $n = 2475$ reflections and $p = 208$ variables}, were 0.049 and 1.82, respectively. The average shift in the final cycle of refinement was 7.2% of the corresponding standard deviation. The final difference map showed no features with heights greater than $0.2 \text{ e } \text{Å}^{-3}$. Scattering factors for the non-hydrogen atoms were taken from Cromer & Mann (1968) and for the hydrogen atoms from Stewart, Davidson & Simpson (1965). All refinement was done with the XRAY system (Stewart, Kruger, Ammon, Dickinson & Hall, 1972). The final atomic parameters, along with their standard deviations estimated from the inverse of the normal-equations matrix, are given in Table 1.*

Table 1. Atomic parameters

Positional parameters are given as fractions of lattice translations. The isotropic temperature factor is $\exp[-8\pi^2 U(\sin \theta/\lambda)^2]$; the values given are the arithmetic averages of the principal components of the anisotropic temperature factors. Standard deviations in units of the least significant digits are given in parentheses.

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> (Å ²)
(a) Non-hydrogen atom parameters ($\times 10^4$)				
(i) 9-Methyladenine				
N(1)	5591 (1)	1773 (2)	-1519 (1)	372 (6)
C(2)	6146 (1)	1081 (2)	-1036 (1)	367 (7)
N(3)	6321 (1)	897 (2)	-193 (1)	331 (6)
C(4)	5850 (1)	1509 (2)	178 (1)	278 (6)
C(5)	5257 (1)	2256 (2)	-235 (1)	276 (6)
C(6)	5129 (1)	2378 (2)	-1128 (1)	313 (6)
N(7)	4893 (1)	2715 (2)	349 (1)	328 (6)
C(8)	5268 (1)	2245 (2)	1088 (1)	344 (6)
N(9)	5851 (1)	1502 (2)	1028 (1)	310 (5)
N(10)	4576 (1)	3050 (2)	-1607 (1)	433 (7)
C(11)	6374 (1)	848 (3)	1720 (1)	408 (8)
(ii) 2-Thiohydantoin				
N(1)	2313 (1)	-46 (2)	-438 (1)	421 (7)
C(2)	1895 (1)	445 (2)	30 (1)	342 (7)
N(3)	1322 (1)	953 (2)	-519 (1)	362 (6)
C(4)	1357 (1)	843 (2)	-1355 (1)	366 (7)
C(5)	2037 (1)	151 (2)	-1340 (1)	423 (8)
O(4)	932 (1)	1237 (2)	-1970 (1)	500 (7)
S	2017 (1)	442 (1)	1090 (1)	448 (2)
(b) Hydrogen atom parameters ($\times 10^4$, $U \times 10^3$)				
(i) 9-Methyladenine				
H(2)	3552 (10)	-642 (28)	1364 (13)	54 (5)
H(8)	4843 (7)	-2364 (23)	-1602 (10)	33 (4)
H(10a)	4534 (11)	3083 (33)	-2186 (16)	72 (6)
H(10b)	4293 (11)	3510 (32)	-1378 (15)	64 (7)
H(11a)	3821 (12)	-681 (37)	-2197 (17)	82 (8)
H(11b)	3271 (11)	-1630 (34)	-1777 (14)	69 (7)
H(11c)	6553 (10)	-355 (34)	1547 (14)	67 (6)
(ii) 2-Thiohydantoin				
H(1)	2734 (12)	-367 (32)	-212 (15)	70 (7)
H(3)	-946 (12)	-1359 (33)	343 (15)	71 (6)
H(5a)	2020 (9)	-1042 (28)	-1603 (12)	46 (5)
H(5b)	2272 (9)	1123 (29)	-1590 (12)	54 (5)

Molecular structures

(i) 9-Methyladenine

The bond lengths and angles are shown in Fig. 1(a). These agree with a high-precision study by Kistenmacher & Rossi (1977). The largest difference in bond length is 0.008 Å and in bond angle is 1.1°, while the expected values of $3\sigma(\Delta)$ are 0.009 Å and 0.5°, respectively. The abnormal size of the angle at N(3) could possibly be related to the mode of hydrogen bonding.

The atoms of the purine nucleus are nearly coplanar with an r.m.s. (Δ) = 0.011 Å. The largest displacement from the least-squares plane through these atoms is

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36576 (14 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

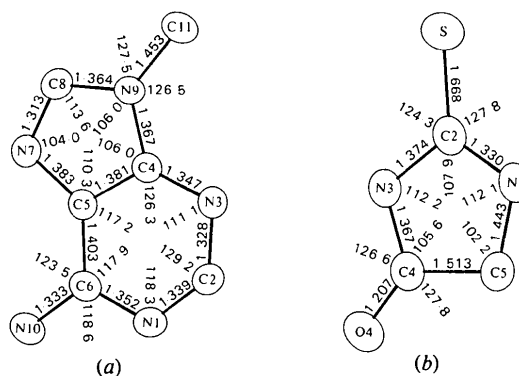


Fig. 1. Bond lengths (Å) and angles (°) for (a) 9-methyladenine and (b) 2-thiohydantoin. The boundary ellipsoids are drawn at the 50% probability level (ORTEP; Johnson, 1965).

Table 2. *Least-squares planes through selected atoms*

The equations for the planes have the form $Lx + My + Nz = D$, where (L, M, N) are direction cosines of the plane normal with respect to the orthogonal axes a^* , b and c , and D is the distance of the plane from the crystallographic origin in Å. The average standard deviation associated with the displacement of atoms from the least-squares planes is 0.004 Å. The root-mean-square distance {r.m.s. (Δ)} of the individual atoms from the planes is defined as $\{\sum_{i=1}^N (\Delta_i^2)/N\}^{1/2}$.

(i) Plane equations

	<i>L</i>	<i>M</i>	<i>N</i>	<i>D</i>
(1)	0.3916	0.9140	0.1064	5.819
(2)	0.3028	0.9454	0.1205	1.525
(3)	0.3950	0.9137	0.0952	5.833

- (1) Plane through purine ring carbon and nitrogen atoms
 (2) Plane through hydantoin ring carbon and nitrogen atoms
 (3) Plane through purine ring carbon and nitrogen atoms at $(-x, y, \frac{1}{2} - z)$

(ii) Dihedral angles

$$\angle(1)(2) = 5.5(5)^\circ \quad \angle(1)(3) = -47.9(5)^\circ$$

(iii) Atomic displacements from planes (Å)

Plane (1). R.m.s. (Δ) = 0.011 (3) Å

N(1)	0.009	N(10)†	0.022
C(2)	0.011	C(11)†	-0.043
N(3)	0.003	H(2)†	0.037
C(4)	-0.003	H(8)†	0.015
C(5)	0.003	H(10a)†	0.026
C(6)	0.010	H(10b)†	-0.036
N(7)	0.004	H(11a)†	0.230
C(8)	-0.018	H(11b)†	-0.840
N(9)	-0.018	H(11c)†	0.132

Plane (2). R.m.s. (Δ) = 0.014 (3) Å

N(1)	-0.019	O(4)†	-0.051
C(2)	0.012	H(1)†	0.005
N(3)	0.001	H(3)†	-0.018
C(4)	-0.012	H(5a)†	-0.587
C(5)	0.017	H(5b)†	-0.804
S†	-0.145		

Plane (3). R.m.s. (Δ) = 0.013 (3) Å

N(1)	-0.027	N(7)	0.008
C(2)	-0.015	C(8)	0.006
N(3)	0.010	N(9)	0.011
C(4)	0.012	N(10)†	-0.038
C(5)	0.001	H(10a)†	-0.045
C(6)	-0.005	H(10b)†	0.034

† Atoms not included in the least-squares plane calculation.

0.018 (4) Å for N(9), associated with an out-of-plane distance of the attached methyl group C(11) of -0.043 (4) Å (Table 2).

(ii) 2-Thiohydantoin

The bond lengths and angles are shown in Fig. 1(b). These *do not* agree with the results of an earlier study

Table 3. *Torsion angles (°) of 2-thiohydantoin*

The positive sense of rotation is clockwise while looking along the B-C bond.

<i>A-B-C-D</i>	
N(1)-C(2)-N(3)-C(4)	-1.3 (3)
N(1)-C(5)-C(4)-N(3)	-0.1 (3)
N(1)-C(5)-C(4)-O(4)	179.2 (3)
C(2)-N(1)-C(5)-C(4)	-0.7 (3)
C(2)-N(3)-C(4)-C(5)	0.8 (3)
C(2)-N(3)-C(4)-O(4)	-178.5 (3)
N(3)-C(2)-N(1)-C(5)	1.2 (3)
C(4)-N(3)-C(2)-S	179.5 (3)
C(5)-N(1)-C(2)-S	-179.6 (3)

(Walker, Folting & Merritt, 1969). Owing to the higher degree of precision of our study and the consistency with previously obtained results (see above), we feel that our values are more reliable.

The atoms of the hydantoin nucleus are approximately coplanar (Table 2), and the largest displacement from the least-squares plane through these atoms is 0.145 (4) Å for the sulfur atom. A slight degree of pucker is reflected in the torsion angles presented in Table 3.

(iii) *The molecular association*

The crystal structure consists of ribbons formed by alternating adenine and hydantoin moieties linked *via* $TN(1)-H \cdots AN(3)$ and $TN(3)-H \cdots AN(7)$ hydrogen bonds (where T represents 2-thiohydantoin and A represents 9-methyladenine, Fig. 2), parallel to (110) and alternately parallel to (1 $\bar{1}$ 0) (Fig. 3). The dihedral angle between the adenine and hydantoin least-squares planes along these ribbons is 5.5 (5)° (Table 2). The N...N distances (Table 4) compare well with those tabulated by Hsu & Craven (1974). Shieh & Voet (1976b) suggest that the N(3) atom of adenine is a

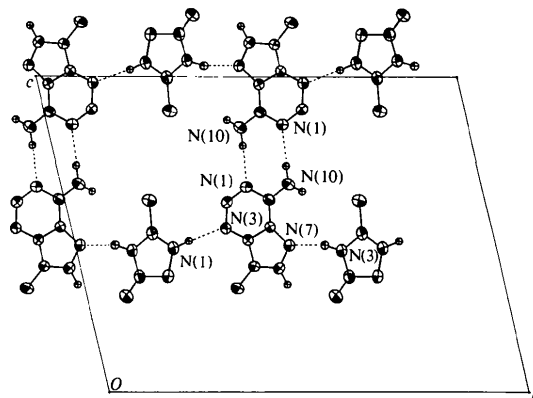


Fig. 2. Hydrogen bonding for the 9-methyladenine-2-thiohydantoin complex. The dashed lines represent hydrogen bonds (ORTEP; Johnson, 1965).

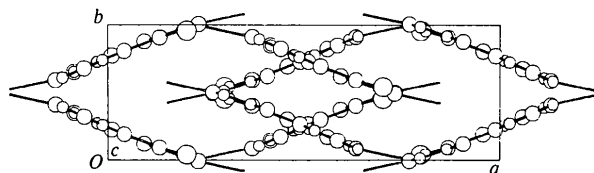


Fig. 3. Two adjacent ribbons of the complex. Note the alternating quality (*PLUTO*; Motherwell, 1978).

Table 4. *Hydrogen-bonding interactions*

The prefixes *A* and *T* refer to the 9-methyladenine and 2-thiohydantoin molecules, respectively.

Hydrogen bond <i>D</i> —H... <i>A</i>	Distance <i>D</i> ... <i>A</i> (Å)	Distance H... <i>A</i> (Å)	Angle <i>D</i> —H... <i>A</i> (°)
<i>TN</i> (1)—H... <i>AN</i> (3) ¹	2.896 (3)	1.988	174.3
<i>TN</i> (3)—H... <i>AN</i> (7) ²	2.807 (3)	1.893	163.0
<i>AN</i> (10)—H(10 <i>b</i>)... <i>AN</i> (1) ³	3.091 (3)	2.243	154.4

Superscripts refer to atoms related to those in Table 1 by the following symmetry operations: (1) $-x, -y, -z$; (2) $\frac{1}{2} - x, \frac{1}{2} - y, -z$; (3) $-x, y, \frac{1}{2} - z$.

weak hydrogen-bond acceptor, and this may be reflected in the longer *TN*(1)---*AN*(3) distance observed here.

The inter-ribbon association is between self-paired 9-methyladenine molecules. The N---N distance of 3.091 (3) Å is slightly longer than the 3.06 Å distance observed for adenine-adenine interactions (Hsu & Craven, 1974). This is apparently because the ribbons are not parallel (Fig. 3). The least-squares planes of the paired adenine ring nuclei form a dihedral angle of 47.9 (5)° (Table 2). This 'twisted pairing' phenomenon has been observed with 9-ethyladenine-parabanic acid (Shieh & Voet, 1976*b*) and 5'-methylthioadenosine (Borkakoti & Palmer, 1978), with adenine-adenine dihedral angles of 35.1° and 17.3°, respectively.

Although the relative orientation is favorable, the 3.299 (3) Å distance *AC*(8)---*TO*(4) is too long to be classified as a hydrogen bond. The maximum van der Waals contact distance for such an interaction is 2.6 Å (Pauling, 1960). The lack of hydrogen bonding by the carbonyl oxygen in crystal structures of oxopurines, pyrimidines and related cyclic amides has been observed in several structures, including alloxan (Bolton,

1964) and 9-ethyladenine-parabanic acid (Shieh & Voet, 1976*b*). The N(10)---S distance of 3.840 (4) Å is also too long to contribute to hydrogen bonding (Donohue, 1969).

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