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1,3-Dimethyluracil: A Crystal Structure Without Hydrogen Bonds

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1,3-Dimethyluracil ($C_6H_8N_2O_2$) is monoclinic, space group $P2_1/c$, with $a = 4{\cdot}199(2)$, $b = 11{\cdot}309(4)$, $c = 14{\cdot}187(4)$ Å, $\beta = 101{\cdot}95(04)°$, $Z = 4$. The structure was solved by direct methods and refined to $R = 5{\cdot}6\%$ for 1033 diffractometer data. The planar molecules form dimers with short contacts of 3·3 Å between O(2) and the methyl group attached to N(1) and the dimers are arranged cross-wise in the crystal. Possible CH···O hydrogen bonds and dipole-induced dipole interactions between C(4)—O(4) carbonyl groups and adjacent pyrimidine rings are discussed as stabilizing forces for the structure.

Introduction

The structural characteristics of nucleic acids and oligonucleotides are associated with the stacking patterns and hydrogen-bonding schemes developed by their heterocyclic bases. Crystallographic studies of nucleosides and nucleobases and their derivatives are informative (Voet & Rich, 1970; Bugg, Thomas, Sundaralingam & Rao, 1971; Saenger & Suck, 1973) and can be used as a basis for the theoretical evaluation of their electronic structures by a quantum-mechanical approach (Jordan & Pullman, 1968; Pullman & Pullman, 1963).

1,3-Dimethyluracil was chosen for a detailed study by quantum-chemical, spectroscopic, thermal-diffusion and X-ray diffraction methods in order to give a more complete understanding of its physical behaviour than is usually obtained. It is of special interest to see how these molecules, which are unable to form hydrogen bonds, pack in the crystal, compared with other uracil derivatives unsubstituted at N(1) or N(3). In this contribution, the X-ray analysis of 1,3-dimethyluracil is reported.

Experimental

1,3-Dimethyluracil forms transparent needles (needle axis along **a**). The X-ray data were obtained from a crystal 0·30 × 0·25 × 0·15 mm. The space group $P2_1/c$ was derived from Weissenberg and precession photographs and the unit-cell parameters were determined by least-squares refinement of the 2θ angles of 15 reflexions measured on a Stoe four-circle diffractometer. Calculated and measured densities indicate that one molecule constitutes the asymmetric unit. The crystal data are given in Table 1.

1033 intensities were collected by the θ–2θ scan method with Ni-filtered Cu $K\alpha$ radiation to a maximum value of $2\theta = 124°$, with a scan rate in 2θ of 2° min^{-1}. Stationary background counts were taken for 10 s before and after each scan. Three reflexions monitored at intervals of 100 data showed no significant variation in intensity. The data were corrected for Lorentz and polarization effects but not for absorption. The data were placed on an absolute scale by Wilson's (1942) method. A Howells, Phillips & Rogers (1950) $N(z)$ cumulative probability distribution confirmed that the structure is centrosymmetric.

Structure determination and refinement

The structure was solved with *MULTAN* (Germain, Main & Woolfson, 1970, 1971) with 125 E values > 2·0. The Fourier distribution calculated with the most consistent of 32 computed phase sets produced 12 prominent peaks, of which 10 had chemically meaningful bond lengths and angles. An initial structure factor calculation with the coordinates of

Table 1. *Crystal data*

1,3-Dimethyluracil ($C_6H_8N_2O_2$)		M.W.	140
Monoclinic		M.p.	121–122 °C
a	4·199 (2) Å	$F(000)$	296
b	11·309 (4)	V	659·05 Å^3
c	14·187 (4)	Z	4
β	101·95 (04)°	μ(Cu $K\alpha$)	10·47 cm^{-1}
		ρ_o	1·40 g cm^{-3}
		ρ_c	1·41

Space group: $P2_1/c$ (systematic absences when l and k are odd in $h0l$ and $0k0$)

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these peaks and temperature factors assigned by the Wilson plot ($B = 3{\cdot}02$ Å) produced an R of 24%. Scattering factors were taken from *International Tables for X-ray Crystallography* (1968). Full-matrix least-squares refinement with anisotropic thermal parameters and H atoms located from difference syntheses reduced R to 5·6%. At this point all parameter shifts were $\frac{1}{3}$ or less of the standard deviations for H and $\frac{1}{10}$ for nonhydrogen atoms.

Atomic parameters are listed in Table 2, and geometrical data in Fig. 1 and Tables 3, 4 and 5. A view of the molecule is shown in Fig. 2.*

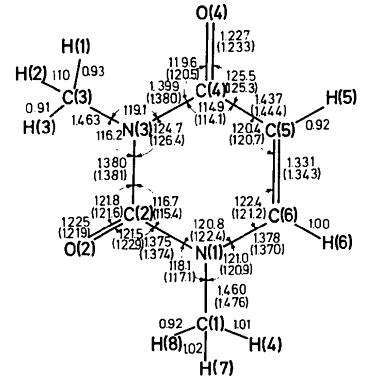

Fig. 1. A sketch of 1,3-dimethyluracil showing the atom designation and the bond lengths and angles. Averaged standard deviations derived from the least-squares correlation matrix are 0·003 Å and 0·2°. Data given in parentheses are those derived by Voet & Rich (1970) and subject to standard deviations of 0·03 Å and 2°.

Discussion

Bond angles and distances

Bond angles and distances in the essentially planar molecule (Table 4) are in overall agreement with the data averaged for a large number of uracil derivatives

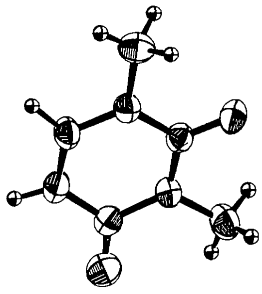

Fig. 2. View of an individual 1,3-dimethyluracil molecule drawn with 50% thermal ellipsoids (Johnson, 1970).

Table 3. *Bond lengths* (Å) *and angles* (°) *involving hydrogen atoms*

H(1)–C(3)	0·93	H(7)–C(1)	1·02
H(2)–C(3)	1·09	H(8)–C(1)	0·92
H(3)–C(3)	0·91	H(5)–C(5)	0·92
H(4)–C(1)	1·01	H(6)–C(6)	1·00
H(1)–C(3)–N(3)	112·2	H(6)–C(6)–N(1)	113·3
H(2)–C(3)–N(3)	104·1	H(6)–C(6)–C(5)	124·3
H(3)–C(3)–N(3)	112·3	H(1)–C(3)–H(2)	97·0
H(4)–C(1)–N(1)	111·8	H(1)–C(3)–H(3)	103·8
H(7)–C(1)–N(1)	109·9	H(2)–C(3)–H(3)	126·1
H(8)–C(1)–N(1)	110·0	H(4)–C(1)–H(7)	99·5
H(5)–C(5)–C(4)	123·4	H(4)–C(1)–H(8)	109·3
H(5)–C(5)–C(6)	116·2	H(7)–C(1)–H(8)	116·1

Table 2. *Atomic coordinates and temperature factors*

The temperature factor is of the form $T=\exp[-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+2\beta_{12}hk+2\beta_{13}hl+2\beta_{23}kl)]$. Standard deviations given in parentheses were derived from the least-squares correlation matrix.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N(3)	0·4521 (4)	0·7034 (1)	0·0620 (1)	529 (11)	64 (1)	32 (1)	−4 (3)	23 (2)	−2 (1)
O(2)	0·6751 (4)	0·8415 (1)	−0·0217 (1)	778 (12)	87 (2)	35 (1)	−19 (3)	52 (2)	7 (1)
N(1)	0·7679 (4)	0·8591 (1)	0·1410 (1)	488 (10)	62 (1)	35 (1)	3 (3)	19 (2)	−1 (1)
C(4)	0·4053 (5)	0·6530 (2)	0·1481 (1)	676 (15)	61 (2)	43 (1)	14 (4)	60 (3)	5 (1)
C(2)	0·6343 (4)	0·8036 (2)	0·0558 (1)	462 (12)	62 (2)	34 (1)	27 (3)	27 (3)	3 (1)
C(3)	0·2990 (7)	0·6483 (2)	−0·0296 (2)	736 (17)	90 (2)	41 (1)	−32 (5)	17 (3)	−13 (1)
C(5)	0·5534 (6)	0·7164 (2)	0·2337 (1)	757 (15)	75 (2)	34 (1)	31 (4)	48 (3)	9 (1)
C(6)	0·7230 (5)	0·8146 (2)	0·2277 (1)	600 (13)	75 (2)	30 (1)	35 (4)	12 (3)	−2 (1)
C(4)	0·2396 (4)	0·5633 (1)	0·1457 (1)	1159 (16)	80 (2)	65 (1)	−105 (4)	107 (3)	−2 (1)
C(1)	0·9475 (6)	0·9688 (2)	0·1368 (2)	615 (15)	68 (2)	62 (1)	−30 (4)	35 (4)	−4 (1)
H(5)	0·4717 (64)	0·1955 (25)	0·2056 (22)	515 (0)	68 (0)	45 (0)	0 (0)	32 (0)	0 (0)
H(6)	0·1763 (63)	0·3651 (24)	0·2155 (19)	446 (0)	59 (0)	39 (0)	0 (0)	27 (0)	0 (0)
H(3)	−0·4473 (74)	0·3734 (27)	0·0650 (19)	724 (0)	83 (0)	39 (0)	−26 (0)	12 (0)	−13 (0)
H(2)	−0·1174 (74)	0·0944 (25)	0·5119 (19)	724 (0)	83 (0)	39 (0)	−26 (0)	12 (0)	−13 (0)
H(1)	−0·1627 (79)	0·3000 (28)	0·0696 (23)	724 (0)	83 (0)	39 (0)	−26 (0)	12 (0)	−13 (0)
H(4)	−0·1905 (72)	0·0305 (25)	0·0960 (21)	549 (0)	65 (0)	60 (0)	−29 (0)	34 (0)	−2 (0)
H(7)	−0·1201 (72)	0·4564 (24)	0·4034 (21)	549 (0)	65 (0)	60 (0)	−29 (0)	34 (0)	−2 (0)
H(8)	0·0206 (67)	−0·0018 (25)	0·1979 (24)	549 (0)	65 (0)	60 (0)	−29 (0)	34 (0)	−2 (0)

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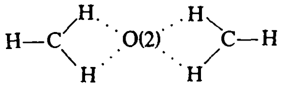
* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32024 (7 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

(Voet & Rich, 1970). Slight differences are evident in the elongated N(3)–C(4) and marginally shortened C(4)–O(4) bonds, probably as a result of the replacement of the (acidic) proton by the methyl group at N(3). The shortening of the C(5)–C(6) double bond relative to the averaged data cannot be explained on the basis of the electronic configuration of the molecule alone.

Conformation of the methyl groups

Because of the keto O atoms in the *ortho* position, the methyl groups are restricted in their rotation about the N–C bonds and assume locations with the O atom on the bisector of the H–C–H triangle:



Since both C(2)–N(3)–C(3) and C(1)–N(1)–C(2) are less than 120°, there appears to be no extraordinary steric strain between O(2) and the methyl groups.

Table 4. *Least-squares planes through (a) the molecule and (b) the interconnected bases (dimers)*

The plane equations are of the form $lx + my + nz + p = 0$, where x,y,z are along **a**, **b**, and **c***. Atoms which define the plane are marked by a dagger. The upper sign in the deviations of the dimer atoms is for the atom in one molecule, the lower for the corresponding atom in the molecule related by inversion. The angle between the two molecular planes in the dimer is 2·3°.

Moiety	Plane coefficients	Atoms	Deviations (Å)
(*a*) Heterocycle	$l = 0{\cdot}8315$	N(3)†	0·012
	$m = 0{\cdot}5513$	O(2)	−0·030
	$n = 0{\cdot}0689$	N(1)†	−0·004
	$p = 2{\cdot}5169$	C(4)†	−0·006
		C(2)†	−0·007
		C(3)	0·073
		C(5)†	−0·004
		C(6)†	0·009
		C(4)	0·004
		C(1)	0·053
(*b*) Dimer	$l = 0{\cdot}8134$	N(3)†	±0·014
	$m = 0{\cdot}5752$	O(2)†	±0·052
	$n = 0{\cdot}0867$	N(1)†	±0·041
	$p = -2{\cdot}6600$	C(4)†	∓0·047
		C(2)†	±0·038
		C(3)†	±0·076
		C(5)†	∓0·043
		C(6)†	±0·012
		O(4)†	∓0·074
		C(1)†	±0·142

Packing of the molecules; intermolecular interactions

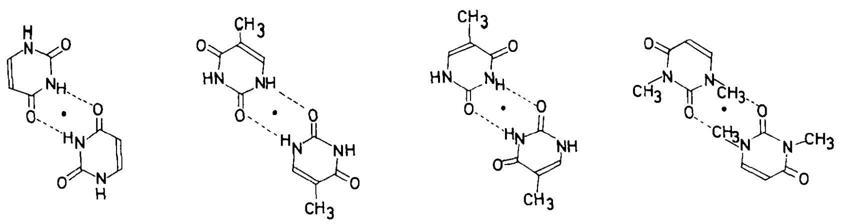
Voet & Rich (1970) have reviewed the crystal structures of nucleic-acid bases and found that uracil derivatives, whether they are substituted at C(5), C(6) or N(1) or whether they bear keto, thioketo or selenoketo groups, form essentially three types of paired, hydrogen-bonded structures with N(3)···O(4) or N(1)···O(2) or N(3)···O(2) interactions (Fig. 3). The crystallization of such dimers is not surprising since solution studies have demonstrated that nucleo bases complex with themselves (Kyogoku, Lord & Rich, 1967). The packing of these dimers in the crystal does not follow a general pattern: in all cases, however, a more or less coplanar arrangement of the dimers is observed, the dimers sometimes being further hydrogen bonded with other dimers to yield linear sheet structures as, for example, in 5-ethyl-6-methyluracil (Reeke & Marsh, 1966).

1,3-Dimethyluracil is not able to form hydrogen bonds. Therefore, it is most surprising to find that dimers exist in this crystal structure also (Figs. 3, 4), the dimers being related by centres of symmetry and held

Table 5. *Conformation of the methyl group of the structure*

The torsion angles *A–B–C–D* are defined as zero when, looking along the central *B–C* bond, the bonds *A–B* and *C–D* are *cis*-planar. They are counted positive if the far bond rotates clockwise.

	Dihedral angle (°)
C(2)–N(1)–C(1)–H(4)	59·5 *gauche* (+)
C(2)–N(1)–C(1)–H(7)	−168·6 *trans*
C(2)–N(1)–C(1)–H(8)	−46·5 *gauche* (−)
C(2)–N(3)–C(3)–H(1)	−56·9 *gauche* (−)
C(2)–N(3)–C(3)–H(2)	51·4 *gauche* (+)
C(2)–N(3)–C(3)–H(3)	−168·8 *trans*



(*a*) (*b*) (*c*) (*d*)

Fig. 3. The three types of hydrogen-bonded dimers found in uracil derivatives with free NH groups. (*a*) Uracil. (*b*) and (*c*) Thymine monohydrate. (*d*) The dimer structure of 1,3-dimethyluracil.

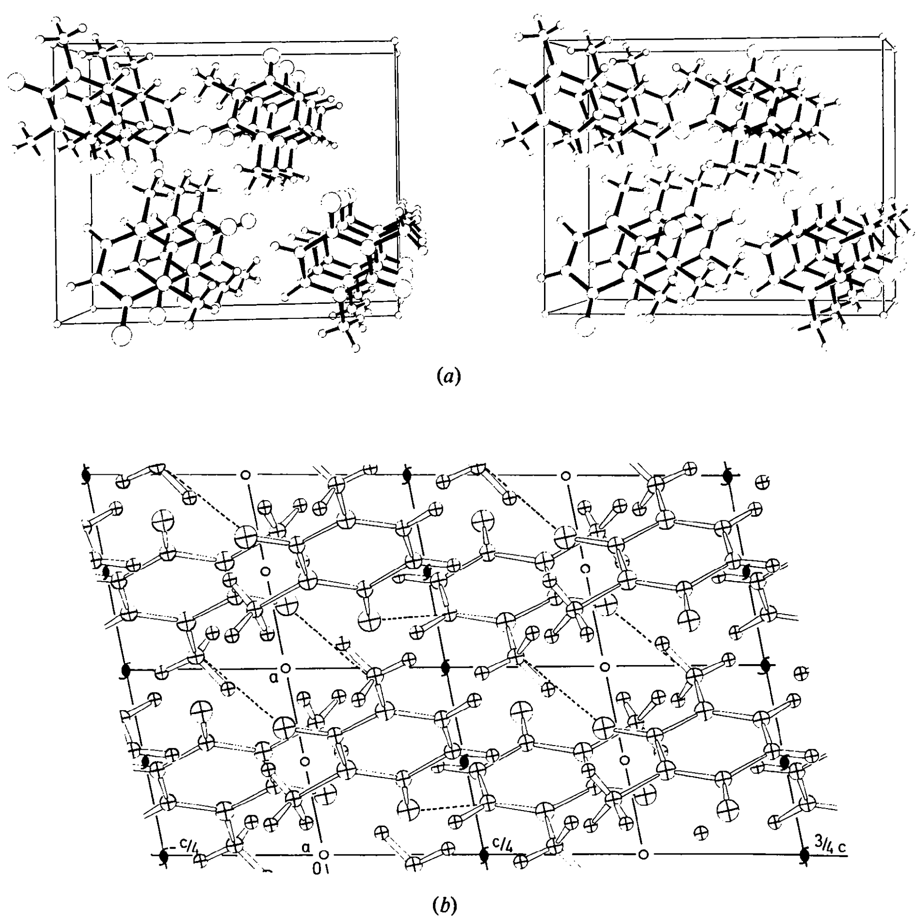


Fig. 4. (*a*) A stereographic projection of the crystal structure along **a**. (*b*) Projection of the structure along **b**. Note dimer formation across inversion centres marked O.

together by C(1)···O(2) contacts of 3·29 Å. This is significantly shorter than the expected van der Waals distance of 3·4 Å between methyl groups and O atoms and could be due to C–H···O hydrogen bonding (Sutor, 1963). The differences in intermolecular forces in crystals of 1,3-dimethyluracil and other uracil derivatives are also evident from the respective melting points: 121 for 1,3-dimethyluracil, 174 for 1-methyluracil and 338°C for uracil. In this context it is surprising that the calculated heats of sublimation for uracil (20 kcal mol^{-1}) and 1,3-dimethyluracil (22 kcal mol^{-1}) are in the reverse order (Clark, Perschel & Tinoco, 1965).

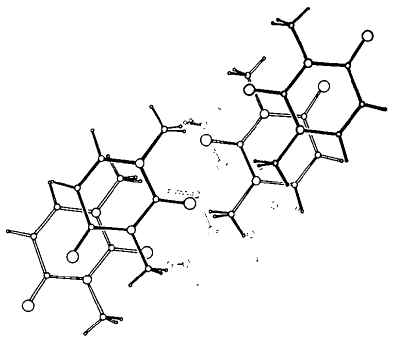


Fig. 5. A view perpendicular to the plane of a dimer, showing overlap of adjacent molecules. The polar keto groups are either oriented antiparallel [C(2)–O(2)] or located above the heterocycle of the next molecule [C(4)–O(4)].

The two 1,3-dimethyluracil molecules in the dimer are almost coplanar, with a slight twist of 2·3° between the individual planes. As shown in Fig. 4, the dimers are largely tilted towards *b* and adjacent molecules show the overlap pattern also recognized in a great number of other nucleo bases: the polar C(4)–O(4) keto group of one base is located 3·5 Å above the aromatic ring of the next neighbour (Fig. 5) (Bugg *et al.*, 1971; Saenger & Suck, 1973).

Fig. 6 shows crystal structures of derivatives which, in contrast to 1,3-dimethyluracil, are able to form at least one NH···O hydrogen bond. It is apparent that the peculiar base stacking of 1,3-dimethyluracil differs from the other patterns: in uracil (Stewart, 1967) and thymine (Gerdil, 1961) [Fig. 6(*a*) and (*b*)], N(3) of one molecule is situated above the adjacent heterocycle; in 1-methylthymine (Hoogsteen, 1963) the C(5)—CH_3 groups are in contact with pyrimidine rings [Fig. 6(*c*)]; in 5-ethyl-6-methyluracil (Reeke & Marsh, 1966) almost no overlap is observed, and only the exocyclic C(2)—O(2) carbonyl groups, as well as the H atoms attached to C(6), interact [Fig. 6(*f*)].

In contrast to the crystal structures with NH···O hydrogen bonding, 1,3-dimethyluracil displays a distinct overlap between C(4)—O(4) carbonyl groups and adjacent heterocycles which must be attributed to dipole-induced dipole forces. We may conclude that, in crystal structures of simple, disc-like molecules, where steric interactions can be neglected, the packing of the molecules is mainly determined by hydrogen-bonding forces if hydrogen bonds can form. In this case, van der Waals interactions are of minor importance. If, however, no hydrogen bonds can form, only van der Waals forces can be utilized, yielding a more realistic picture of intermolecular interactions.

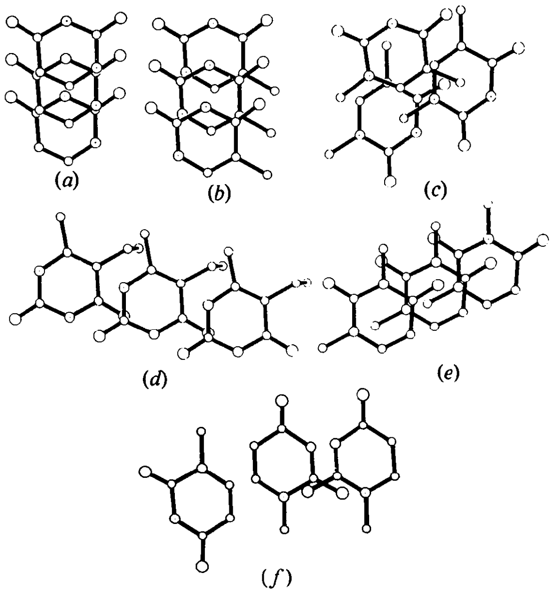


Fig. 6. Comparative view of the overlapping molecules in several uracil crystal structures. Interplanar distances are given in parentheses. (*a*) Uracil (3·31 Å). (*b*) Thymine monohydrate (3·51 Å). (*c*) 1-Methylthymine (3·86 Å). (*d*) 5-Ethyl-6-methyluracil (3·31 Å). (*e*) 1,3-Dimethyluracil (3·50 Å). (*f*) *N*-Methyluracil (3·14 Å).

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