

## The Crystal and Molecular Structure of 6-Oxadihydrouracil

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The crystal and molecular structure of 6-oxadihydrouracil ( $C_3H_4N_2O_3$ ) has been determined by single crystal x-ray diffraction techniques. The compound crystallizes in the space group  $P2_12_12_1$  with four molecules in a unit cell of dimensions:  $a = 5.106(1)\text{\AA}$ ,  $b = 12.461(2)\text{\AA}$  and  $c = 7.112(1)\text{\AA}$ . The structure was solved by direct methods and refined to a final value of  $R = 0.052$ . The oxauracil ring is non-planar with the C5 atom assuming tetrahedral geometry and the ring oxygen having oxazinal distances and angle ( $C-O = 1.43_2\text{\AA}$ ,  $N-O = 1.40_8\text{\AA}$ , and  $CON$  angle of  $109.0^\circ$ ). The usual hydrogen bonding patterns associated with the uracil ring are absent in this compound.

## Introduction.

Because of its fundamental importance in biological systems, particularly in the storage of genetic information, the structures of uracil and a varied assortment of its derivatives have been investigated. The structure of uracil itself was first reported in 1954 (1) and later redetermined in 1967 (2). The structure of the dihydro-uracil was reported in 1970 (3) followed by the determination of the structures of a series of substituted uracils (4), alkali metal derivatives (5) and various uracil complexes (6,7). Structure determinations on compounds in which a different hetero atom has been inserted into the uracil ring system are far less common. A previous report does exist for the 6-azauracil (8), for example. However, this is the first report on an oxadihydrouracil system.

## EXPERIMENTAL

Crystals of the compounds were furnished to us by K. Venkatasubramian. A suitable single crystal, essentially cylindrical in shape, with a length of 0.24 mm and other dimensions of 0.14 x 0.18 mm was chosen from the sample supplied and used for all subsequent experimental work. Extinctions along the three axial lines [(h00)-h odd, (0k0)-k odd, and (00l)-l odd] combined with the presence of perpendicular mirror planes identified the space group as  $P2_12_12_1$ . Eleven relatively large intensities were measured at  $2\theta$  values greater than  $70^\circ$ , where the  $\alpha_1, \alpha_2$  doublet is resolved and under fine conditions ( $1^\circ$  take-off angle and  $0.05^\circ$  slit). Lattice constants, determined by a least-squares fit of these twenty two values are:

$$\begin{aligned} a &= 5.106(1)\text{\AA} \\ b &= 12.461(2)\text{\AA} \\ c &= 7.112(1)\text{\AA} \end{aligned}$$

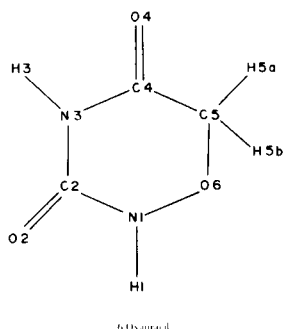


Figure 1

The calculated density of 1.71 g./cc, assuming four molecules per unit cell, was accepted as reasonable and subsequently confirmed by the completed structure determination.

Intensity data was then collected on a General Electric XRD-490 fully automated diffractometer system using  $Cu-K\alpha$  radiation; stationary-crystal, stationary counter methods; and balanced Ross filters. A total of 603 reflections were measured with 519 (86%) considered as observed by the criterion

$$[I_{(Ni)} - 2\sigma(I_{Ni})] - [I_{(Co)} + 2\sigma(I_{Co})] > 50 \text{ counts}$$

where  $\sigma$  was based entirely on counting statistics. After the standard Lorentz-polarization corrections, the intensities were corrected for  $K\alpha_1 - K\alpha_2$  splitting (9) and for absorption.

Absorption was corrected as a function of  $\phi$  with a maximum difference in intensity of  $\pm 7\%$  over the entire range of  $\phi$ .

Table I  
 Fractional Coordinates and Anisotropic Thermal Parameters (a) (b)  
 (Standard Deviations  $\times 10^4$  in parentheses)

Atom	X	Y	Z	$\beta_{11}$	$\beta_{22}$	$\beta_{33}$	$\beta_{12}$	$\beta_{13}$	$\beta_{23}$
C1	0.7053(5)	0.2088(2)	0.2725(3)	205(10)	36(2)	89(5)	19(4)	17(7)	14(3)
C2	0.7605(5)	0.1517(2)	0.0875(3)	181 (9)	31(1)	96(5)	8(4)	8(6)	2(3)
N3	0.9489(4)	0.0723(2)	0.1022(3)	222 (8)	36(1)	54(4)	40(3)	-47(5)	-10(2)
C4	1.0928(4)	0.0524(2)	0.2601(3)	174 (9)	27(1)	71(5)	-2(3)	-5(7)	-2(3)
N5	1.0144(4)	0.1019(2)	0.4189(3)	177 (7)	46(1)	74(4)	30(3)	-11(6)	-9(2)
O6	0.7514(4)	0.1357(1)	0.4245(2)	213 (6)	39(1)	86(3)	15(3)	32(5)	11(2)
O7	0.6568(4)	0.1730(2)	-0.0591(2)	309 (8)	67(1)	92(4)	58(3)	-67(6)	12(2)
O8	1.2949(3)	-0.0034(1)	0.2560(2)	212 (7)	50(1)	79(3)	35(3)	-25(5)	0(2)
H1	0.5187(0)	0.2326(0)	0.2763(0)	4.0(0)					
H1'	0.8234(0)	0.2720(0)	0.2862(0)	4.0(0)					
H3	0.9825(0)	0.0262(0)	-0.0102(0)	4.0(0)					
H5	1.1382(0)	0.1161(0)	0.5251(0)	4.0(0)					

(a) The temperature factors cited for the hydrogen atoms are the fixed isotropic values of  $4.0 \text{ c}/\text{\AA}^2$ . The coordinates given for the hydrogen atoms are those obtained by refining the initial positions while holding the temperature factors of the hydrogens fixed. (b) Anisotropic temperature factors for the non-hydrogens are of the form:  $\exp[-\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl]$ .

#### Structure Determination.

After calculating properly scaled (10) and normalized structure magnitudes (E-values), the structure was solved using the direct methods program, MULTAN, with 2 permutations and a probability of 99.99%. The E-map from the permutation with the highest figure of merit (1.12) contained only twelve peaks corresponding to the 3 oxygens, 2 nitrogens, 3 carbons and 4 hydrogens. From the peak heights, in addition to the obvious chemical choices, each peak could be assigned its respective scattering factor. Initially, two least squares runs (11) were performed as follows:

(a) Correct scattering factor curves assigned; initial isotropic temperature factors of  $4 \text{ \AA}^2$  for all atoms were assumed; hydrogen temperature factors were held fixed; and the unit weights were used. In four cycles, the structure refined to a value of  $R = .10_3$ .

(b) Identical to run (a) except that  $1/\sigma^2$  weights were used. In four cycles, the structure refined to a value of  $R = .09_8$ . Hence,  $1/\sigma^2$  weights were used in all subsequent refinements.

The non-hydrogen atoms were then converted to anisotropic temperature factors and additional least squares cycles run with only the isotropic temperature factors of the hydrogen atoms fixed. The data refined to a value of  $R = 0.05_3$  with all shifts less than one-tenth the magnitude of the estimated standard deviations of their respective parameter. As a further check, another series of least squares cycles were run in which the

isotropic temperature factors of the hydrogens was allowed to vary. The value of R remained essentially constant (0.05<sub>2</sub>). The positional parameters were identical but the hydrogen temperature factors varied from 2.8 to  $7.6 \text{ \AA}^2$ . Finally, a difference map was run in which the highest regions found were less than  $0.2 \text{ e}^2/\text{\AA}^3$ . Thus, the structure refinement was considered as complete.

#### Results.

The final least squares coordinates and temperature

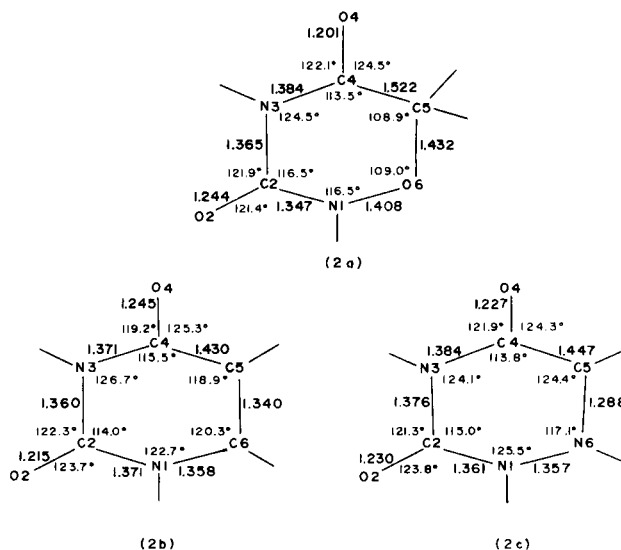


Figure 2. Bond distances in the 6-oxadihydrouracil (2a), uracil (2b), and 6-azauracil (2c) molecules.

factors for all atoms are listed in Table I. The estimated standard deviations (ESD's) are less than .002 Å and 0.2° for non-hydrogen distances and angles, respectively. The calculated ESD's for bonds and angles involving hydrogen atoms are less than .004 Å and 0.4°, respectively.

Figure 2 compares the structural details for this 6-oxadihydrouracil system to those obtained for uracil itself (2) and to the 6-azauracil system (8,12).

The 6-azauracil system (2c) coincides quite closely to that of the uracil itself (2b) since the substitution of nitrogen at position 6 leaves the geometry essentially unchanged. The double-bond character of the 5-6 bond in both of these is evident in the lengths (1.34<sub>0</sub> Å for C = C in uracil, 1.28<sub>8</sub> Å for C = N in the 6-azauracil); and in the bond angles about each of these positions (ranging from 117.1° to 124.4°). The planarity of both ring systems further corroborates their similarity.

On the other hand, in the 6-oxadihydrouracil the 5-6 bond has a carbon-oxygen distance of 1.43<sub>3</sub> Å, with internal angles at the C-5 position (108.9°) and the O-6 position (109.0°). Hence the planarity of the ring is destroyed by the tetrahedral arrangement about C5 and by the oxazinyl O-6 (compare its bond distance to N-1, 1.40<sub>8</sub> Å with that of a typical oxazine (13) distance of 1.39<sub>5</sub> Å). This non-planarity of the oxadihydrouracil ring shown in Figure 3.

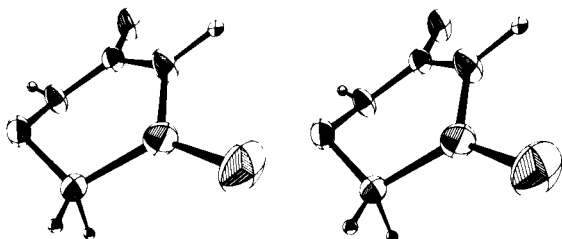


Figure 3. ORTEP drawing of molecule using thermal displacement ellipsoids.

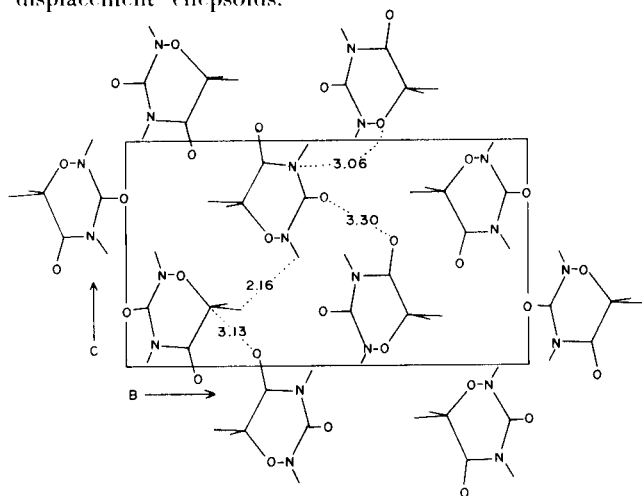


Figure 4. Unit-cell contents projected down the a-axis. Close contacts  $\leq 3.30$  Å indicated.

The usual hydrogen bonding patterns found in uracils are destroyed by the non-planarity of this compound. The only intermolecular hydrogen contact distance less than 2.4 Å is the 2.16 Å distance between one of the hydrogens on the C-5 of one molecule to the hydrogen on the N-1 of another molecule. The crystal packing itself is not very compact with only three distances (3.06, 3.13, 3.30 Å) less than the anticipated minimal Van der Waal separation. The unit cell projected down the a-axis with all of these close contacts indicated is given in Figure 4.

Acknowledgments.

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$$R = \frac{\sum w |kF_o| - |F_c|}{\sum w |kF_o|}$$

is cited throughout the paper. Scattering factors for carbon, nitrogen, oxygen and copper are taken from the paper by D. Cromer and J. Waber, *Acta Cryst.*, **18**, 104 (1965), while that for hydrogen is from "International Tables for X-ray Crystallography," Vol. III, Kynoch Press, Birmingham, England, 1968.

(12) The complete structural details are not presented in Ref. 8 which concerns itself primarily with a spectroscopic study involving the degeneracy of the 260  $\mu$  band in uracils. Although the fractional coordinates are given in that paper, this represents the first discussion of the structural details of the 6-azauracil system.

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