6-에틸-5,6-디히드로우라실의 결정 및 분자구조

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The Crystal and Molecular Structure of 6-Ethyl-5,6-Dihydrouracil

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요 약. 6-ethyl-5,6-dihydrouracil($C_6H_{10}N_2O_2$)은 단사정계인 공간군 $P2_{1/c}$으로 $a=10.302(2)$, $b=10.419(3)$, $c=7.095(1)$ Å, $\beta=106.6(0)°$, $Z=4$, $V=729.7(3)$ Å^3, $D_c=1.29$ g/cm^3, λ(Mo Kα)=0.71073 Å, $\mu=0.010$ cm^{-1}, F(000)=304이며, $F>4.0$ $\sigma(F)$인 1070개의 관측된 회절점에 대한 R값은 0.054였다. 직접법에 의하여 구조를 풀었으며, 전행렬-최소자승법에 의하여 정밀화하였고, C-H 결합길이는 0.96 Å에 고정하였다. Hydrouracil 고리는 불규칙한 puckered 각을 가진 envelope conformation으로 되어 있고, 고리에 붙어 있는 에틸기는 axial 방향으로 향하고 있으며, 단위격자속에는 100평면에 거의 평행인 2차원의 결합망을 이룬, 두 개의 분자간 수소결합, N(1)-H---O(7)(1+x, 0.5−y, −0.5+z)와 N(3)-H---O(7)(1+x, 0.5−y, 0.5+z)가 있으며, 이웃 분자와의 최단거리는 C(4)---O(8)(−x, −y, 1−z)의 3.187 Å이다.

ABSTRACT. 6-ethyl-5,6-dihydrouracil($C_6H_{10}N_2O_2$) is monoclinic, space group $P2_{1/c}$ with $a=10.302(2)$, $b=10.419(3)$, $c=7.095(1)$ Å, $\beta=106.6(0)$, $Z=4$, $V=729.7(3)$ Å^3, $D_c=1.29$ g/cm^3, λ(Mo Kα)=0.71073 Å, $\mu=0.010$ cm^{-1}, F(000)=304, and $R=0.054$ for 1070 unique observed reflection with $F>4.0$ σ(F). The structure was solved by direct methods and refined by full-matrix least-squares refinement with the fixed C-H bond length at 0.96 Å. The hydrouracil molecule makes an envelope conformation with the ethyl substituent oriented to an axial position attainable to a varying degree of steric strain. There are two intermolecular hydrogen-bondings via N-H---O interactions, being nearly parallel to the 100 plane. The shortest distance between molecules is 3.187 Å of C(4) and O(8) (−x, −y, 1−z).

INTRODUCTION

The derivertives of 5,6-dihydrouracil were prepared[1] by the condensa-tion of α,β-unsaturated acid with urea or hydrogenation of their related-compounds[2~4] and the spectroscpic studies[5,6] have been widely done on their conformational charac-teristics.

Structural informations of hydrouracil have been known to have a half-chair conformation[5,6] and its C(6)-substitent equatorial seems to be more favo-rable than the one with the substituent axial.

However, Katritzky *et al.*[5] have extensively stu-died the NMR spectra of dihydrouracils and sug-gested the axial arrangement of C(6)-substituents in 5,6-dihydro-6-phenyluracil, orotic acid and its methyl ester. It is of interest to confirm the con-formation of the title compound by X-ray diffrac-tion method and to prove its structure clearly,
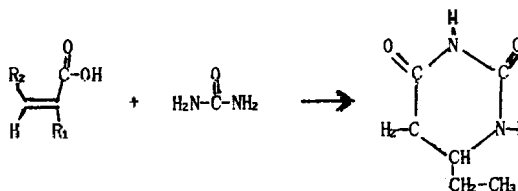
R: alkyl or H
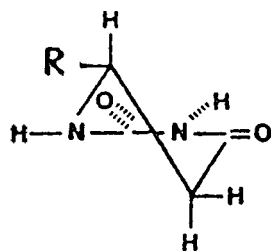
whose IR and NMR data were in sufficient to determine the detailed structure of the molecule. The existance of the hydrogen-bond might also give us some structural information.

EXPERIMENTAL

Title compound was synthesized by published procedure[7] and single crystals were grown by slow evaporation in water at room termperature. The crystals have the shape of a colorless laths and the 0.20×0.42×0.81 mm sizes of a crystal were used for data collection.

Accurate lattice parameters were obtained by least-squares refinement, setting for the 25 reflections in the ranges $3.5 < \theta < 11.8°$ measured with graphite-monochromatized Mo-Kα radiation ($\lambda =$ 0.71073 Å) on the Siemens P4 diffractometer with XSCANS software at 298 K. Intensities were recorded by the ω-2θ scan technique (scan range(ω)=

Fig. 1. A molecular conformation with the atomic labelling scheme of 6-ethyl-5,6-dihydrouracil.

1.34°) with variable scan speed from 10.0 to 60.0 °/min. in ω and 2θ_{max}=50.0° for the ranges $-12 \leq h \leq 12$, $-12 \leq k \leq 12$, $-1 \leq l \leq 8$.

The three standard reflections monitored every 97 reflections showed only 0.5% variations of intensity during the course of data collection.

In the 1289 independent reflections with Rint= 0.025 out of 3254 measured reflections, the 1070 unique observed reflections with $F > 4.0$ $\sigma(F)$ were used in structure determination. Corrections for Lorentz and polarization effects were applied to the intensity data, while no absorption or extinction correction was carried out.

The space group was obtained from sysmatic absences with: hkl; no condition, $h0l$; $l = 2n$, $0k0$; $k = 2n$, and the structure was solved by direct methods[8] and refined by full-matrix least-squares refinement,[8] with all non-hydrogen atoms by anisotropic thermal parameters and hydrogen atoms fixed at 0.96 Å by isotropic ones. The final R and wR values with 91 least-squares parameters were 0.054 and 0.063, where $w^{-1} = (\sigma^2(F_o^2) + (0.0737 \ P)^2 + 0.08 \ P)$, $P = (Max(F_o^2, \ 0) + 2F_c^2)/3$ and goodness of fit=1.12.

The $(\Delta/\sigma)_{max}$ of the final cycle was 0.002 and a difference Fourier map showed the highest peak 0.20 eÅ^{-3} and the lowest hole -0.26 eÅ^{-3}.

All atomic scattering factors were from the International Tables for X-ray Crystallography (1974)[9]
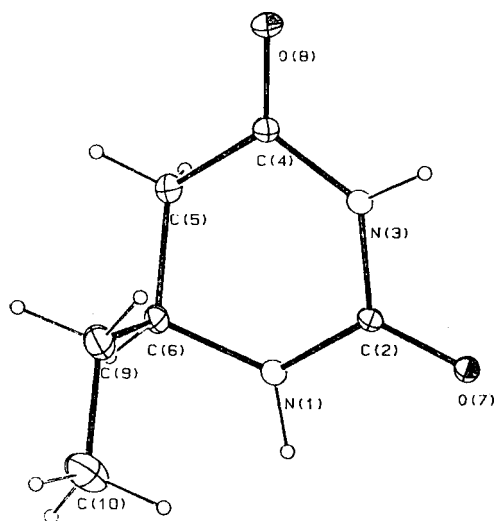
Table 1. Crystal data

Formula	$C_6H_{10}N_2O_2$
Formula weight	142.16
Crystal system	monoclinic
Space group	P2$_{1/c}$
Unit cell demensions	$a = 10.302(2)$ Å
	$b = 10.419(3)$
	$\beta = 106.6(0)°$
	$c = 7.095(1)$
Volume	729.7(3) Å^{-3}
Z	4
Density(cal.)	1.29 g/cm^3
Absorption coefficient	0.010 cm^{-1}
F(000)	304
Systematic absences	$h \ k \ l$; no condition
	$h \ 0 \ l$; $l = 2n$
	$0 \ k \ 0$; $k = 2n$

and calculations were performed using the SHE-LXL-93 programs.

Table 2. Fractional atomic coordinates ($\times 10^4$) and equivalent isotropic temperature factors ($\text{Å}^2 \times 10^3$)

Atom	x	y	z	U_{eq}
N(1)	8018(2)	4193(1)	−5(2)	.049
C(2)	7905(2)	3517(2)	1530(2)	.042
N(3)	8011(2)	4183(1)	3258(2)	.043
C(4)	8484(2)	5420(2)	3636(2)	.044
C(5)	8862(2)	6065(2)	1982(3)	.050
C(6)	8019(2)	5605(2)	−30(3)	.046
O(7)	7708(2)	2338(1)	1482(2)	.055
O(8)	8603(2)	5898(1)	5238(2)	.059
C(9)	6597(2)	6151(2)	−628(3)	.060
C(10)	5739(3)	5709(3)	−2627(4)	.088
H(1A)	790	368	−111	.065
H(3A)	785	370	419	.052
H(5A)	1000	592	225	.091
H(5B)	874	696	204	.061
H(6A)	855	585	−101	.056
H(9A)	678	710	−69	.074
H(9B)	608	601	42	.071
H(10A)	481	621	−305	.141
H(10B)	615	581	−360	.136
H(10C)	549	481	−259	.151

$^*U_{eq} = [1/3(1 - \cos^2\alpha - \cos^2\beta - \cos^2\gamma + 2\cos\alpha\cos\beta\cos\gamma]$
$(U_{11}\sin^2\alpha + U_{22}\sin^2\beta + U_{33}\sin^2\gamma + 2U_{12}\sin\alpha\sin\beta\cos\gamma + 2U_{13}\sin\alpha\sin\gamma\cos\beta + 2U_{23}\sin\beta\sin\gamma\cos\alpha)$.

RESULTS AND DISCUSSION

Fig. 1 depicts the plot of a molecular structure with the atomic numbering scheme and *Table* 1 gives crystal data. *Table* 2 lists the final atomic coordinates with the equivalent isotropic thermal parameters. *Table* 3 gives bond lengths and hydrogen-bonds, and *Table* 4 for bond angles and selected torsion angles.

The bond lengths and bond angles containing the nitrogen atom(N(3)) and diones in the uracil group, are appeared to be similar to those which were found in other uracil derivertives[10,11] or hete-

Table 3. Bond distances (Å) and hydrogen bonds with e.s.d.'s in parentheses

(a) bond lengths

N(1)-C(2)	1.330(2)	N(1)-C(6)	1.471(2)
C(2)-N(3)	1.386(2)	C(2)-O(7)	1.244(2)
N(3)-C(4)	1.377(2)	C(4)-C(5)	1.497(3)
C(4)-O(8)	1.215(2)	C(5)-C(6)	1.521(3)
C(6)-C(9)	1.515(3)	C(9)-C(10)	1.512(3)

(b) hydrogen-bonding geometry

	(a) N(1)-H(1a)---O(7)	(b) N(3)-H(3a)---O(7)
D-H	0.929(2) Å	0.881(2) Å
H---A	1.971(2)	1.995(2)
D-A	2.899(2)	2.872(2)
ang.D-H-A	176.8(2)°	173.1(2)°

*Symmetry code: (a) x, $0.5-y$, $-0.5+z$.
(b) x, $0.5-y$, $0.5+z$.

Table 4. (a) Bond angles (°) and (b) selected torsion angles (°) with e.s.d.'s in parentheses

(a) bond angles			
N(3)-C(2)-N(1)	117.1(2)	C(4)-N(3)-C(2)	125.1(2)
C(5)-C(4)-N(3)	115.1(1)	C(5)-C(6)-N(1)	107.8(2)
C(6)-N(1)-C(2)	122.7(2)	C(6)-C(5)-C(4)	112.8(2)
O(7)-C(2)-N(1)	123.5(1)	O(7)-C(2)-N(3)	119.3(1)
O(8)-C(4)-N(3)	120.1(2)	O(8)-C(4)-C(5)	124.8(2)
C(9)-C(6)-N(1)	112.0(2)	C(9)-C(6)-C(5)	113.0(2)
C(10)-C(9)-C(6)	114.0(2)		
(b) selected torsion angles			
C(6)-N(1)-C(2)-N(3)	−10.4(2)	C(6)-N(1)-C(2)-O(7)	169.3(3)
C(2)-N(1)-C(6)-C(5)	40.8(2)	C(2)-N(1)-C(6)-C(9)	−84.2(2)
N(1)-C(2)-N(3)-C(4)	−13.6(2)	O(7)-C(2)-N(3)-C(4)	166.6(3)
C(2)-N(3)-C(4)-C(5)	1.8(2)	C(2)-N(3)-C(4)-O(8)	−176.2(3)
N(3)-C(4)-C(5)-C(6)	30.7(2)	O(8)-C(4)-C(5)-C(6)	−151.3(3)
C(4)-C(5)-C(6)-N(1)	−48.8(2)	C(4)-C(5)-C(6)-C(9)	75.6(2)
N(1)-C(6)-C(9)-C(10)	−58.0(2)	C(5)-C(6)-C(9)-C(10)	179.9(3)

Table 5. Comparisons of fluctuations of bond lengths and bond angles in non-diones part of a uracil group: ADT, ADN and AFD

(a) bond lengths (Å)

	C(4)-C(5)	C(5)-C(6)	C(6)-N(1)
title compound:	1.497(3)	1.521(3)	1.471(2)
ADT: molecule A:	1.400(1)	1.38(1)	1.381(9)
ADT: molecule B:	1.40(1)	1.37(1)	1.368(9)
ADN:	1.452(4)	1.431(5)	1.361(4)
AFD:	1.438(8)	1.382(8)	1.365(7)

(b) bond angles (°)

	C(4)-C(5)-C(6)	C(5)-C(6)-N(1)
title compound:	112.8(2)	107.8(2)
ADT: molecule A:	121.7(6)	118.6(6)
ADT: molecule B:	122.7(6)	118.3(7)
ADN:	120.4(3)	118.5(3)
AFD:	121.3(6)	119.8(6)

rocyclic dione-derivertives.[12~15] Other bond lengths and angles in the group, however, show some fluctuations, due to the linking branched-group on the C(5) and C(6) atoms. These comparisons with 6-amino-1,3-dimethyl-5-(dimethylamino)-1,2,3,4-tetrazol-1-yl)uracil hemihydrate(ADT),[10] 6-amino-1,3-dimethyl-5-nitrosouracil monohydrate(ADN)[11] and 6-amino-5-formyl-1,3-dimethyluracil monohydrate(AFD)[11] are given in *Table* 5.

The least-squares planes of the hydrouracil ring are given *Table* 6. The plane through five atoms, N(1), C(2), N(3), C(4) and C(5), is puckered but almost planar with the maximum deviation from its best plane of $-0.099(2)$ Å for the C(2) atom, and the C(6) atom with the ethyl-substituent is displaced by 0.564(2) Å upwards from its plane.

Table 6. Least-squares planes with displacement (Å) from the best plane. Equation is expressed in the form of $Ax+By+Cz=D$, where x, y, and z are in Å

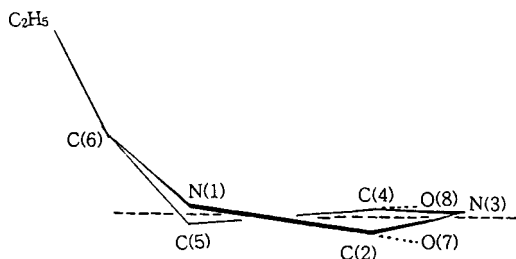| A. least-squares planes related to the dihydrouracil and the ethyl groups							
Atom in plane	Shifts	Atoms out of plane	Shifts	Constants			
				A	B	C	D
N(1)	.055(2)			−.8950	.3464	−.2811	−5.9339
C(2)	−.099(2)						
N(3)	.027(2)						
C(4)	.034(2)						
C(5)	−.067(2)						
		C(6)	.564(2)				
		O(7)	−.343(2)				
		O(8)	.082(2)				
		C(9)	2.077(2)				
		C(10)	2.728(3)				
		H(1A)	−.009(2)				
		H(3A)	−.009(2)				
		H(5A)	−1.169(2)				
		H(5B)	.371(2)				
		H(6A)	.173(2)				
N(1)	−.081(2)			−.9400	−.2745	−.2027	−6.4845
C(2)	−.084(2)						
N(3)	.096(2)						
C(4)	.012(2)						
C(5)	−.258(2)						
C(6)	.320(2)						
		O(7)	−.233(2)				
		O(8)	.118(2)				
		C(9)	1.822(2)				
		C(10)	2.420(3)				

Fig. 2. A molecular scheme of the envelope conformation of 6-ethyl-5,6-dihydrouracil.
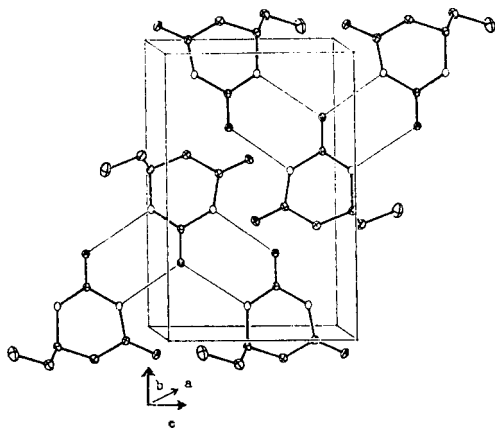

Fig. 3. The unit cell packing diagram of molecules. The hydrogen bonds have been designated with thin lines.

The resulting angle between two planes (the plane through five atoms and the triangular plane through N(1), C(5) and C(6) atoms) appeared to be of 139.7°, indicating that the apex C(6) atom took an axial position rather than equatorial, and seemed to be exhibited an envelope conformation as shown in *Fig.* 2. Consequently, the orientations of the C(9) and H(6a) atoms are axial, upwards and downwards with a tetrahedral geometry with respect to the C(6) atom as shown in *Table* 5, and of two hydrogen atoms of the C(5), one H(5A) atom took an axial position with the deviation of $-1.169(2)$ Å, the other H(5B) atom equatorial with the deviation of 0.371(2) Å. Thus, the axial position of the ethyl group connected to the C(6) atom is considered to be reduced its steric strain.

The molecules have two intermolecular hydrogen-bondings, N-H---O. One N(1) links the O(7)

$(x, 0.5-y, -0.5+z)$ by the distance of 2.899(2) Å and the other N(3) does the O(7) $(x, 0.5-y, 0.5+z)$ of 2.872(2) Å, respectively. These bondings are nearly parallel to the 100 plane as shown in *Fig.* 3, and the hydrouracil rings are stacked along the 010 and 020 planes with the shortest distance of 3.187 Å between the C(4) and O(8) $(-x, -y, 1-z)$ atoms in molecules. The axial orientation of the ethyl group considered as the result of the van der Waals contacts holding the molecules together.

The X-ray results above mentioned prove more detailed structure of compound rather than in use of insufficient IR and NMR data, already reported by the conformational analysis of 5,6-dihydrouracils.[7]

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