

6-Methyluracil: a redetermination of polymorph (II)

Gustavo Portalone*

Chemistry Department, "Sapienza" University of Rome, P.le A. Moro, 5, I-00185 Rome, Italy. *Correspondence e-mail: gustavo.portalone@uniroma1.it

Received 28 May 2019

Accepted 17 June 2019

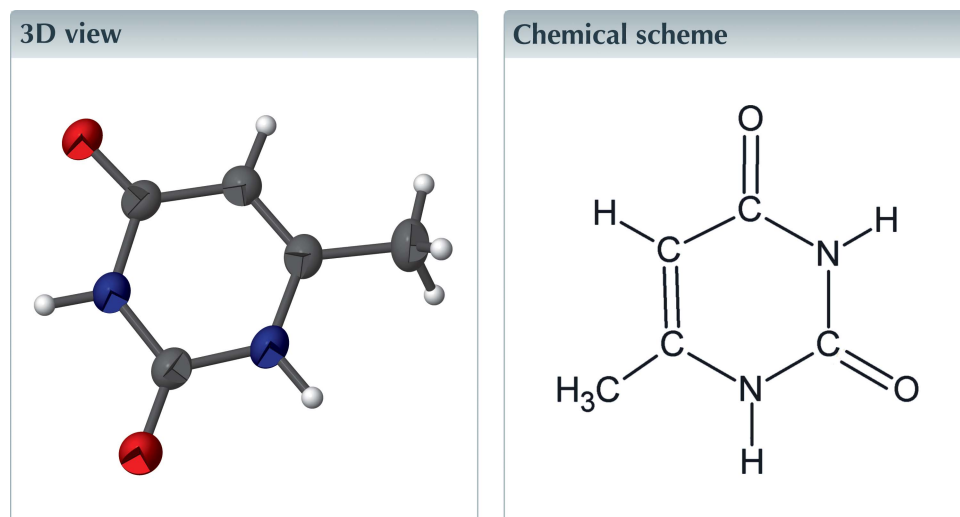
Edited by C. Rizzoli, Università degli Studi di Parma, Italy

Keywords: crystal structure; nucleobases.

CCDC reference: 1924198

Structural data: full structural data are available from iucrdata.iucr.org

6-Methyluracil, $C_5H_6N_2O_2$, exists in two crystalline phases: form (I), monoclinic, space group $P2_1/c$ [Reck *et al.* (1988). *Acta Cryst. A* **44**, 417–421] and form (II), monoclinic, space group $C2/c$ [Leonidov *et al.* (1993). *Russ. J. Phys. Chem.* **67**, 2220–2223]. The structure of polymorph (II) has been redetermined providing a significant increase in the precision of the derived geometric parameters. In the crystal, molecules form ribbons approximately running parallel to the *c*-axis direction through $N-H \cdots O$ hydrogen bonds. The radical differences observed between the crystal packing of the two polymorphs may be responsible in form (II) for an increase in the contribution of the polar canonical forms $C-(O^-)=N-H^+$ relative to the neutral canonical form $C(=O)-N-H$ induced by hydrogen-bonding interactions.



Structure description

As a result of the fundamental role of nucleic acids in genetic processes of living systems, much attention has been devoted to determining the structure of methylated derivatives of uracil, because methylation of DNA is probably involved in various genetic alterations and in the initiation of carcinogenic processes. In previous theoretical and experimental studies of uracil derivatives from this laboratory (Portalone *et al.*, 1999, 2002; Brunetti *et al.*, 2002; Portalone & Colapietro, 2004; Portalone, 2010), it has been shown that the hydrogen bonding can change the electronic properties of similar pyrimidine bases experiencing different crystal environments, *i.e.* showing different sites available for hydrogen-bond interactions.

In this context, 6-methyluracil (6Mura) is particularly attractive, as it exists in two crystalline forms characterized by completely different hydrogen-bonding schemes. A search for crystal structures of the title compound with the Cambridge Structural Database (CSD, version 5.40 updated to May 2019; Groom *et al.*, 2016) gave two hits, as crystalline polymorphs. Form (I), monoclinic space group $P2_1/c$, was determined by

Table 1
Hydrogen-bond geometry (Å, °).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$N1-H1\cdots O1^i$	0.91 (2)	1.95 (2)	2.8594 (17)	174.0 (16)
$N3-H3\cdots O2^{ii}$	0.93 (2)	1.90 (2)	2.8246 (18)	171.5 (18)

Symmetry codes: (i) $-x, -y + 1, -z$; (ii) $-x + \frac{1}{2}, -y + \frac{1}{2}, -z$.

XRPD at $R = 0.040$ (Reck *et al.*, 1988). Form (II), monoclinic space group $C2/c$, was determined by RT single-crystal diffraction performed on a Syntex P1 diffractometer at $R = 0.085$ (Leonidov *et al.*, 1993). Interestingly, Leonidov and coworkers analysed the differences in the molecular geometries of 6Mura in form (I) and (II), and came to the conclusion that the observed discrepancies in the corresponding bond distances and bond angles were insignificant. Therefore, to verify this assumption, it was considered worthwhile and of significant chemical interest to redetermine the crystal structure of form (II) to a better precision. The present determination ($R = 0.048$), although based on RT data collection, decreases the s.u.s on the bond distances and bond angles to about one third to one fourth of those in the original determination.

In the asymmetric unit, 6Mura is present as the diketo tautomer (Fig. 1). As previously mentioned, the crystal structures of the two polymorphs are radically different. In form (II), infinite ribbons approximately running parallel to the c -axis direction are connected by $N-H\cdots O$ hydrogen bonds (Fig. 2). Within a ribbon, each molecule is linked to two adjacent molecules *via* centrosymmetric, pairwise $N1-H1\cdots O1$ and $N3-H3\cdots O2$ hydrogen bonds (Table 1). In form (I), centrosymmetric dimers are formed by $N3\cdots O2$ hydrogen bonds. These dimers are then connected through $N1\cdots O2$ hydrogen bonds to form layers approximately parallel to the bc plane, leaving the $O1$ atom free from hydrogen-bonding interactions (Fig. 3).

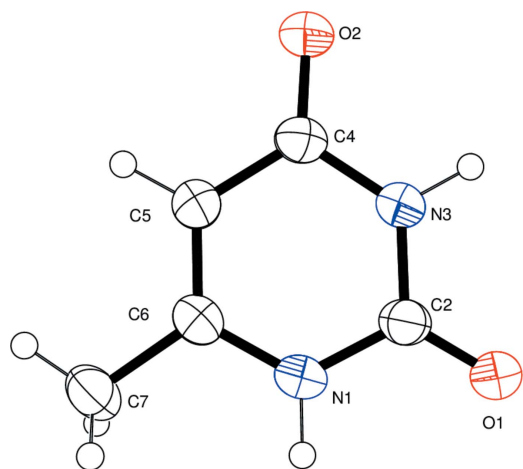


Figure 1
The asymmetric unit of 6Mura in form (II), showing the atom-labelling scheme. Displacements ellipsoids are at the 50% probability level. H atoms are shown as small spheres of arbitrary radii.

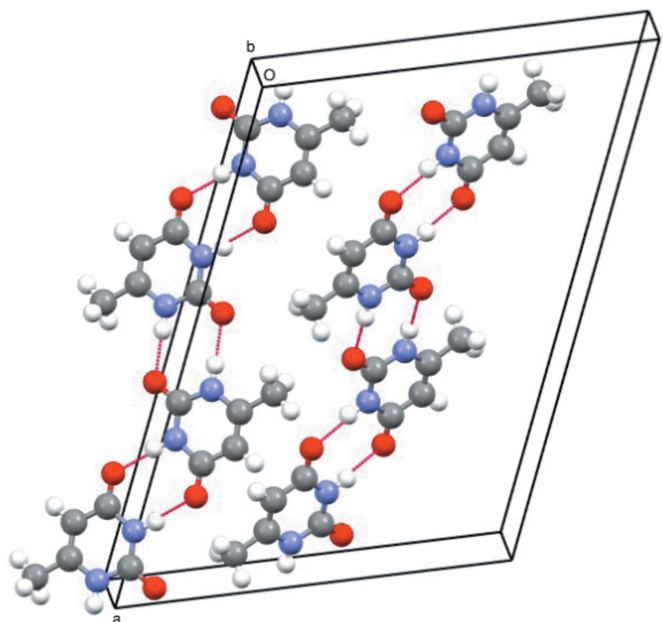


Figure 2
Crystal packing diagram for 6Mura in form (II), viewed approximately down b . All atoms are shown as small spheres of arbitrary radii. Hydrogen bonding is indicated by red dashed lines.

The effect of the different crystal environments on the molecular geometry of the two polymorphs can be appreciated in particular in the region involved in the hydrogen bonding, and mainly consists in a concerted distortion of the $C=O$ and $C-N$ bond distances. Indeed, by comparing the molecular

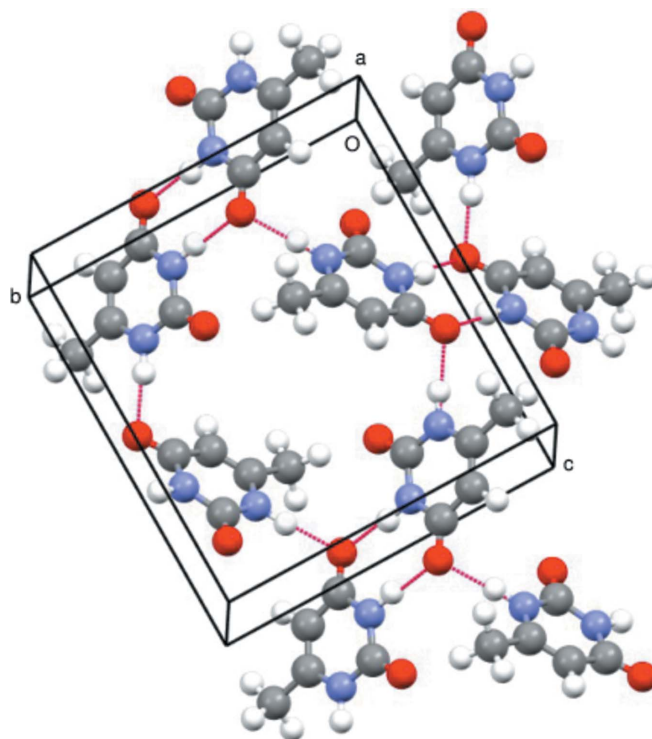


Figure 3
Crystal packing diagram for 6Mura in form (I), viewed approximately down a . All atoms are shown as small spheres of arbitrary radii. Hydrogen bonding is indicated by red dashed lines.

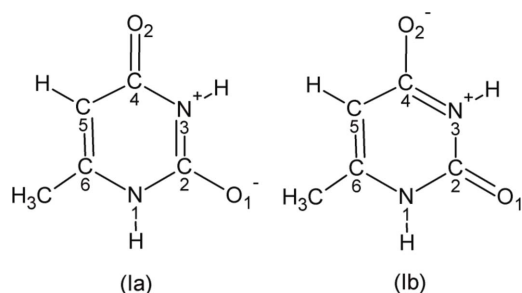


Figure 4
Polar canonical forms of 6Mura in form (II).

geometry of the almost planar O1=C2–N3–C4=O2 fragment in the two polymorphs, in passing from form (I) to form (II):

(i) the two carbonyl bond distances are longer by 0.008–0.035 (2) Å;

(ii) the N3–C2 and N3–C4 bond distances are shorter by 0.031–0.035 (2) Å.

Therefore, the observed structural changes in form (II) can be interpreted, in terms of VB theory, as an increase in the contribution of the polar canonical forms C–(O[−])=N⁺–H [(Ia) and (Ib) in Fig. 4], which are better proton donors and acceptors than the neutral canonical form C(=O)–N–H to form hydrogen-bonding interactions.

Synthesis and crystallization

6-Methyluracil (Sigma Aldrich, 97%) was subjected to further purification by successive sublimation under reduced pressure. 1 mmol was dissolved in DMF (3 ml) and stirred for 8 h at 50°C. The solution was then cooled to room temperature and allowed to slowly evaporate to give, after two weeks, colourless crystals of polymorph (II) suitable for X-ray analysis. Several trials of data collection at LT using a crystal of polymorph (II) mounted under paraffin oil in a nylon loop failed, as the sample cracked when slowly cooled in liquid nitrogen.

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2.

References

Agilent (2014). *CrysAlis PRO*. Agilent Technologies Ltd, Yarnton, England.

Table 2
Experimental details.

Crystal data	
Chemical formula	C ₅ H ₆ N ₂ O ₂
<i>M_r</i>	126.12
Crystal system, space group	Monoclinic, C2/c
Temperature (K)	298
<i>a</i> , <i>b</i> , <i>c</i> (Å)	20.572 (3), 3.9052 (5), 14.811 (3)
β (°)	110.95 (2)
<i>V</i> (Å ³)	1111.2 (4)
<i>Z</i>	8
Radiation type	Mo <i>K</i> α
μ (mm ^{−1})	0.12
Crystal size (mm)	0.14 × 0.11 × 0.08
Data collection	
Diffractometer	Agilent Xcalibur Sapphire3
Absorption correction	Multi-scan (<i>CrysAlis PRO</i> ; Agilent, 2014)
<i>T_{min}</i> , <i>T_{max}</i>	0.770, 1.000
No. of measured, independent and observed [<i>I</i> > 2 σ (<i>I</i>)] reflections	8110, 1400, 1154
<i>R_{int}</i>	0.044
(<i>sin</i> θ / λ) _{max} (Å ^{−1})	0.671
Refinement	
<i>R</i> [<i>F</i> ² > 2 σ (<i>F</i> ²)], <i>wR</i> (<i>F</i> ²), <i>S</i>	0.048, 0.133, 1.11
No. of reflections	1400
No. of parameters	91
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{\max}$, $\Delta\rho_{\min}$ (e Å ^{−3})	0.27, −0.17

Computer programs: *CrysAlis PRO* (Agilent, 2014), *SIR2004* (Burla *et al.*, 2005), *SHELXL2014* (Sheldrick, 2015) and *WinGX* (Farrugia, 2012).

- Brunetti, B., Portalone, G. & Piacente, V. (2002). *J. Chem. Eng. Data*, **47**, 17–19.
- Burla, M. C., Caliandro, R., Camalli, M., Carrozzini, B., Cascarano, G. L., De Caro, L., Giacovazzo, C., Polidori, G. & Spagna, R. (2005). *J. Appl. Cryst.* **38**, 381–388.
- Farrugia, L. J. (2012). *J. Appl. Cryst.* **45**, 849–854.
- Groom, C. R., Bruno, I. J., Lightfoot, M. P. & Ward, S. C. (2016). *Acta Cryst.* **B72**, 171–179.
- Leonidov, N. B., Zorkij, P. M., Masunov, A. E., Gladkikh, O. P., Bel'skii, V. K., Dzyabchenko, A. V. & Ivanov, S. A. (1993). *Russ. J. Phys. Chem.* **67**, 2220–2223.
- Portalone, G. (2010). *Acta Cryst.* **C66**, o295–o301.
- Portalone, G., Ballirano, P. & Maras, A. (2002). *J. Mol. Struct.* **608**, 35–39.
- Portalone, G., Bencivenni, L., Colapietro, M., Pieretti, A. & Ramondo, F. (1999). *Acta Chem. Scand.* **53**, 57–68.
- Portalone, G. & Colapietro, M. (2004). *J. Chem. Crystallogr.* **34**, 609–612.
- Reck, G., Kretschmer, R.-G., Kutschabsky, L. & Pritzkow, W. (1988). *Acta Cryst.* **A44**, 417–421.
- Sheldrick, G. M. (2015). *Acta Cryst.* **C71**, 3–8.

full crystallographic data

IUCrData (2019). 4, x190861 [https://doi.org/10.1107/S2414314619008617]

6-Methyluracil: a redetermination of polymorph (II)

Gustavo Portalone

6-Methyluracil

Crystal data

$C_5H_6N_2O_2$	$F(000) = 528$
$M_r = 126.12$	$D_x = 1.508 \text{ Mg m}^{-3}$
Monoclinic, $C2/c$	Mo $K\alpha$ radiation, $\lambda = 0.710689 \text{ \AA}$
$a = 20.572 (3) \text{ \AA}$	Cell parameters from 2315 reflections
$b = 3.9052 (5) \text{ \AA}$	$\theta = 2.9\text{--}30.6^\circ$
$c = 14.811 (3) \text{ \AA}$	$\mu = 0.12 \text{ mm}^{-1}$
$\beta = 110.95 (2)^\circ$	$T = 298 \text{ K}$
$V = 1111.2 (4) \text{ \AA}^3$	Tablets, colourless
$Z = 8$	$0.14 \times 0.11 \times 0.08 \text{ mm}$

Data collection

Agilent Xcalibur Sapphire3 diffractometer	$T_{\min} = 0.770, T_{\max} = 1.000$
Radiation source: fine-focus sealed X-ray tube, Enhance (Mo) X-ray Source	8110 measured reflections
Graphite monochromator	1400 independent reflections
Detector resolution: $16.0696 \text{ pixels mm}^{-1}$	1154 reflections with $I > 2\sigma(I)$
ω and ϕ scans	$R_{\text{int}} = 0.044$
Absorption correction: multi-scan (CrysAlis PRO; Agilent, 2014)	$\theta_{\max} = 28.5^\circ, \theta_{\min} = 3.0^\circ$
	$h = -27 \rightarrow 27$
	$k = -5 \rightarrow 5$
	$l = -19 \rightarrow 19$

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: mixed
$R[F^2 > 2\sigma(F^2)] = 0.048$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.133$	$w = 1/[\sigma^2(F_o^2) + (0.0609P)^2 + 0.4161P]$
$S = 1.11$	where $P = (F_o^2 + 2F_c^2)/3$
1400 reflections	$(\Delta/\sigma)_{\max} < 0.001$
91 parameters	$\Delta\rho_{\max} = 0.27 \text{ e \AA}^{-3}$
0 restraints	$\Delta\rho_{\min} = -0.17 \text{ e \AA}^{-3}$
Primary atom site location: structure-invariant direct methods	

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Refinement. The N-bound H atoms were located in a difference Fourier map and refined freely. All other H atoms were placed geometrically and refined using a riding atom approximation, with C–H = 0.97 Å, and with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ or $1.5U_{\text{eq}}(\text{C})$ for methyl H atoms. A rotating model was used for the methyl groups.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	0.06097 (6)	0.5147 (3)	−0.06247 (9)	0.0486 (4)
O2	0.26885 (6)	0.0108 (3)	0.10454 (9)	0.0468 (3)
N1	0.07366 (7)	0.2401 (3)	0.07840 (9)	0.0380 (3)
H1	0.0293 (10)	0.304 (5)	0.0715 (13)	0.049 (5)*
C2	0.09750 (8)	0.3466 (4)	0.00759 (11)	0.0366 (4)
N3	0.16426 (6)	0.2545 (3)	0.02038 (9)	0.0361 (3)
H3	0.1820 (10)	0.333 (5)	−0.0258 (15)	0.057 (5)*
C4	0.20846 (7)	0.0710 (4)	0.09840 (11)	0.0357 (4)
C5	0.17907 (7)	−0.0298 (4)	0.16844 (11)	0.0372 (4)
H5	0.2066	−0.1641	0.2240	0.045*
C6	0.11357 (8)	0.0595 (4)	0.15811 (11)	0.0359 (4)
C7	0.08038 (9)	−0.0227 (5)	0.23014 (13)	0.0488 (5)
H7A	0.1100	−0.1790	0.2783	0.073*
H7B	0.0354	−0.1289	0.1975	0.073*
H7C	0.0742	0.1864	0.2615	0.073*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0372 (6)	0.0662 (8)	0.0451 (7)	0.0128 (5)	0.0178 (5)	0.0152 (5)
O2	0.0319 (6)	0.0639 (8)	0.0475 (7)	0.0091 (5)	0.0178 (5)	0.0105 (5)
N1	0.0300 (7)	0.0451 (7)	0.0423 (7)	0.0023 (5)	0.0171 (5)	0.0025 (6)
C2	0.0312 (7)	0.0414 (8)	0.0387 (8)	0.0008 (6)	0.0142 (6)	−0.0007 (6)
N3	0.0308 (6)	0.0435 (7)	0.0365 (7)	0.0021 (5)	0.0150 (5)	0.0031 (5)
C4	0.0304 (7)	0.0389 (7)	0.0383 (8)	−0.0006 (6)	0.0130 (6)	−0.0022 (6)
C5	0.0344 (8)	0.0416 (8)	0.0359 (8)	0.0005 (6)	0.0129 (6)	0.0038 (6)
C6	0.0369 (8)	0.0356 (7)	0.0385 (8)	−0.0035 (6)	0.0174 (6)	−0.0016 (6)
C7	0.0496 (10)	0.0552 (10)	0.0519 (11)	−0.0006 (7)	0.0308 (8)	0.0042 (7)

Geometric parameters (\AA , $^\circ$)

O1—C2	1.2308 (19)	C4—C5	1.430 (2)
O2—C4	1.2352 (18)	C5—C6	1.347 (2)
N1—C6	1.368 (2)	C5—H5	0.9700
N1—C2	1.372 (2)	C6—C7	1.493 (2)
N1—H1	0.91 (2)	C7—H7A	0.9701
C2—N3	1.3657 (19)	C7—H7B	0.9701
N3—C4	1.3872 (19)	C7—H7C	0.9701
N3—H3	0.93 (2)		
C6—N1—C2	123.21 (13)	C6—C5—C4	120.79 (14)

C6—N1—H1	120.2 (12)	C6—C5—H5	119.6
C2—N1—H1	116.6 (12)	C5—C6—N1	119.92 (14)
O1—C2—N3	122.54 (14)	C5—C6—C7	123.91 (15)
O1—C2—N1	121.93 (14)	N1—C6—C7	116.16 (13)
N3—C2—N1	115.53 (14)	C6—C7—H7A	109.5
C2—N3—C4	125.36 (13)	C6—C7—H7B	109.5
C2—N3—H3	116.6 (12)	H7A—C7—H7B	109.5
C4—N3—H3	117.9 (12)	C6—C7—H7C	109.5
O2—C4—N3	120.14 (14)	H7A—C7—H7C	109.5
O2—C4—C5	124.69 (14)	H7B—C7—H7C	109.5
N3—C4—C5	115.16 (13)		
C6—N1—C2—O1	-178.53 (14)	O2—C4—C5—C6	177.08 (14)
C6—N1—C2—N3	1.3 (2)	N3—C4—C5—C6	-1.6 (2)
O1—C2—N3—C4	178.78 (14)	C4—C5—C6—N1	1.9 (2)
N1—C2—N3—C4	-1.0 (2)	C4—C5—C6—C7	-177.22 (14)
C2—N3—C4—O2	-177.57 (14)	C2—N1—C6—C5	-1.8 (2)
C2—N3—C4—C5	1.2 (2)	C2—N1—C6—C7	177.42 (14)

Hydrogen-bond geometry (Å, °)

<i>D—H...A</i>	<i>D—H</i>	<i>H...A</i>	<i>D...A</i>	<i>D—H...A</i>
N1—H1...O1 ⁱ	0.91 (2)	1.95 (2)	2.8594 (17)	174.0 (16)
N3—H3...O2 ⁱⁱ	0.93 (2)	1.90 (2)	2.8246 (18)	171.5 (18)

Symmetry codes: (i) $-x, -y+1, -z$; (ii) $-x+1/2, -y+1/2, -z$.