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A second polymorph of 1-(carboxymethyl)-5-fluorouracil

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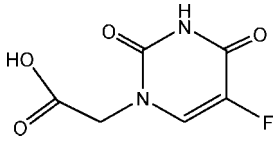
Key indicators: single-crystal X-ray study; T = 298 K; mean σ(C–C) = 0.010 Å; R factor = 0.067; wR factor = 0.203; data-to-parameter ratio = 8.8.

The molecular structure of the title compound (systematic name: 5-fluoro-2,4,-dioxo-1,2,3,4-tetrahydropyrimidine-1-acetic acid), $C_6H_5FN_2O_4$, is essentially identical to that in the previously reported polymorph [Zhang *et al.* (2006). *Z. Kristallogr. New Cryst. Struct.* **221**, 57–58]. The molecules are linked by O—H···O, N—H···O and weak C—H···O hydrogen bonds to form layers parallel to the (100) plane.

Related literature

For related literature, see: Akalin *et al.* (2007); Hulme *et al.* (2005); Maeda *et al.* (1997). For the first polymorph, see Zhang *et al.* (2006).



Experimental

Crystal data

$C_6H_5FN_2O_4$
M_r = 188.12
Monoclinic, Pc
a = 6.809 (4) Å
b = 4.840 (3) Å
c = 11.946 (7) Å
β = 92.218 (9)°
V = 393.4 (4) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.15 mm^{-1}
T = 298 (2) K
0.24 × 0.15 × 0.06 mm

Data collection

Bruker APEX area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2002)
T_{min} = 0.965, T_{max} = 0.984
1810 measured reflections
686 independent reflections
651 reflections with $I > 2\sigma(I)$
R_{int} = 0.050

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.067
$wR(F^2)$ = 0.203
S = 1.01
686 reflections
78 parameters
2 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.31 e Å^{-3}
$\Delta\rho_{min}$ = −0.25 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N2—H2···O3^{i}	0.86	1.96	2.815 (8)	175
O4—H4···O1^{ii}	0.82	2.12	2.938 (10)	174
C5—H5A···O3^{iii}	0.97	2.55	3.468 (7)	158
C4—H4A···O3^{iii}	0.93	2.53	3.367 (7)	149

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

Data collection: *SMART* (Bruker, 2002); cell refinement: *SAINT* (Bruker, 2002); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Bruker, 2002); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: CF2143).

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  doi:10.1107/S1600536807046454

supplementary materials

Acta Cryst. (2007). E**63**, o4214 [**doi:10.1107/S1600536807046454**]

A second polymorph of 1-(carboxymethyl)-5-fluorouracil

Q.-C. Zhang, Z. Shu, L. Shen, Q. Wang and Z.-M. Jin

Comment

Because of the poor tumor selectivity and high incidence of toxicity of 5-fluorouracil (5FU), which was frequently used as an antitumor agent, many derivatives of 5FU have been developed to improve its topical delivery and reduce the side effects (Akalin *et al.*, 2007; Hulme *et al.*, 2005; Maeda *et al.*, 1997). In this work, the title compound (I) was synthesized in our laboratory.

The structure of compound (I) was first determined by Zhang *et al.* (2006) [space group $P2_1/c$, cell constants a = 4.9363 (5), b = 17.056 (2), c = 9.4940 (8) Å and β = 114.466 (4)°]. Now we have discovered a new polymorph of (I), which crystallized in space group *Pc* and with different unit-cell parameters. The molecule of (I) is shown in Fig. 1. Most of the geometric parameters are similar in both polymorphs. The dihedral angle between the carboxyl group and uracil ring is 82.1 (8)°, which is essentially the same as that of the previous polymorph (Zhang *et al.*, 2006); these two planes are almost perpendicular.

The molecular packing in the present case is completely different from that of the first polymorph (Fig. 2). The molecules are linked by O—H···O and N—H···O hydrogen bonds to form a zigzag chain. These zigzag chains are cross-linked by C—H···O hydrogen bonds to form layers parallel to the (100) plane.

Experimental

The title compound was synthesized according to the method of Zhang *et al.* (2006) and single crystals were obtained by slow evaporation of an acetone solution.

Refinement

All of the H atoms were placed in calculated positions and allowed to ride on their parent atoms at distances of 0.82 (hydroxyl), 0.93 (aromatic) and 0.96Å (methyl), with U_{iso}(H) = 1.2–1.5U_{eq}(C,*O*). In the absence of significant anomalous scattering effects, Friedel pairs were merged.

Figures

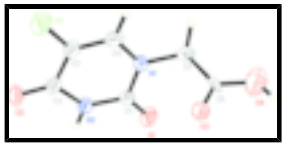

Fig. 1. The molecular structure of (I) with atom labels, showing 50% probability displacement ellipsoids.

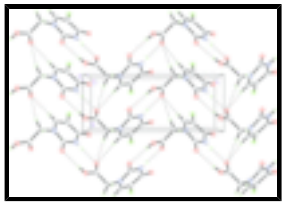

Fig. 2. A packing diagram viewed along the *a* axis. Hydrogen bonds are shown as dashed lines.

5-fluoro-2,4,-dioxo-1,2,3,4-tetrahydropyrimidine-1-acetic acid

Crystal data

$C_6H_5FN_2O_4$	F_{000} = 192
M_r = 188.12	D_x = 1.588 Mg m^{-3}
Monoclinic, *Pc*	Mo *K*α radiation λ = 0.71073 Å
Hall symbol: P -2yc	Cell parameters from 792 reflections
a = 6.809 (4) Å	θ = 3.0–24.9º
b = 4.840 (3) Å	μ = 0.15 mm^{-1}
c = 11.946 (7) Å	*T* = 298 (2) K
β = 92.218 (9)º	Prism, colorless
V = 393.4 (4) Å^3	0.24 × 0.15 × 0.06 mm
Z = 2	

Data collection

Bruker APEX area-detector diffractometer	686 independent reflections
Radiation source: fine-focus sealed tube	651 reflections with $I > 2\sigma(I)$
Monochromator: graphite	R_{int} = 0.050
T = 298(2) K	θ_{max} = 25.0º
φ and ω scans	θ_{min} = 3.0º
Absorption correction: multi-scan (SADABS; Bruker, 2002)	*h* = −8→8
T_{min} = 0.965, T_{max} = 0.984	*k* = −5→5
1810 measured reflections	*l* = −14→10

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)]$ = 0.067	$w = 1/[\sigma^2(F_o^2) + (0.1506P)^2 + 0.4386P]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2)$ = 0.203	$(\Delta/\sigma)_{max} < 0.001$
S = 1.01	$\Delta\rho_{max}$ = 0.31 e Å^{-3}
686 reflections	$\Delta\rho_{min}$ = −0.25 e Å^{-3}
78 parameters	Extinction correction: none

2 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map

Special details

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

Refinement. Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

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

	x	*y*	*z*	U_{iso}*/U_{eq}
F1	−0.0373 (7)	−0.2785 (12)	0.8215 (5)	0.0534 (15)
O1	0.5896 (8)	0.3756 (13)	0.8203 (5)	0.0409 (15)
O2	0.0272 (8)	0.1213 (12)	0.9853 (4)	0.0406 (15)
O3	0.3896 (7)	0.3555 (11)	0.5663 (4)	0.0336 (14)
O4	0.6827 (13)	0.2288 (18)	0.5011 (8)	0.076 (2)
H4	0.6498	0.3303	0.4488	0.114*
N1	0.4205 (8)	0.0178 (12)	0.7466 (5)	0.0251 (14)
N2	0.3075 (8)	0.2427 (15)	0.9007 (5)	0.0272 (14)
H2	0.3254	0.3686	0.9508	0.033*
C1	0.4518 (11)	0.2258 (15)	0.8224 (6)	0.0277 (17)
C2	0.1388 (10)	0.0870 (15)	0.9099 (6)	0.0300 (18)
C3	0.1195 (10)	−0.1137 (16)	0.8207 (5)	0.0286 (17)
C4	0.2555 (12)	−0.1477 (16)	0.7452 (6)	0.0350 (19)
H4A	0.2393	−0.2841	0.6908	0.042*
C5	0.5662 (11)	−0.0101 (16)	0.6602 (6)	0.0324 (19)
H5A	0.5543	−0.1913	0.6259	0.039*
H5B	0.6973	0.0056	0.6945	0.039*
C6	0.5375 (10)	0.2102 (15)	0.5711 (5)	0.0240 (16)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
F1	0.048 (3)	0.054 (3)	0.060 (3)	−0.027 (3)	0.017 (2)	−0.020 (3)
O1	0.040 (3)	0.039 (3)	0.044 (3)	−0.018 (3)	0.010 (3)	−0.007 (3)
O2	0.038 (3)	0.045 (3)	0.041 (3)	−0.012 (3)	0.021 (3)	−0.012 (3)
O3	0.033 (3)	0.031 (3)	0.037 (3)	0.010 (3)	0.011 (2)	0.009 (2)
O4	0.089 (6)	0.071 (5)	0.072 (5)	0.012 (5)	0.033 (4)	0.023 (4)
N1	0.027 (3)	0.026 (3)	0.024 (3)	0.000 (3)	0.005 (2)	−0.001 (3)
N2	0.034 (3)	0.027 (3)	0.022 (3)	−0.009 (3)	0.007 (2)	−0.006 (2)

C1	0.035 (4)	0.023 (4)	0.026 (4)	−0.001 (4)	0.004 (3)	−0.001 (3)
C2	0.024 (4)	0.031 (4)	0.036 (4)	−0.004 (4)	0.005 (3)	0.006 (3)
C3	0.034 (4)	0.030 (4)	0.021 (3)	−0.008 (3)	0.003 (3)	−0.002 (3)
C4	0.055 (5)	0.022 (4)	0.028 (4)	−0.007 (4)	0.000 (4)	−0.001 (3)
C5	0.044 (5)	0.020 (4)	0.034 (4)	0.002 (3)	0.005 (3)	0.003 (3)
C6	0.028 (4)	0.025 (3)	0.020 (3)	0.006 (4)	0.009 (3)	−0.007 (3)

Geometric parameters (Å, °)

F1—C3	1.333 (9)	N2—C2	1.382 (10)
O1—C1	1.187 (9)	N2—C1	1.385 (10)
O2—C2	1.212 (9)	N2—H2	0.860
O3—C6	1.227 (8)	C2—C3	1.445 (10)
O4—C6	1.322 (11)	C3—C4	1.328 (11)
O4—H4	0.820	C4—H4A	0.930
N1—C1	1.365 (10)	C5—C6	1.515 (10)
N1—C4	1.379 (10)	C5—H5A	0.970
N1—C5	1.465 (8)	C5—H5B	0.970
C6—O4—H4	109.5	C4—C3—C2	122.6 (7)
C1—N1—C4	122.9 (6)	F1—C3—C2	116.5 (6)
C1—N1—C5	116.3 (6)	C3—C4—N1	120.6 (7)
C4—N1—C5	120.7 (6)	C3—C4—H4A	119.7
C2—N2—C1	129.5 (7)	N1—C4—H4A	119.7
C2—N2—H2	115.3	N1—C5—C6	111.0 (6)
C1—N2—H2	115.3	N1—C5—H5A	109.4
O1—C1—N1	122.7 (7)	C6—C5—H5A	109.4
O1—C1—N2	124.1 (7)	N1—C5—H5B	109.4
N1—C1—N2	113.2 (6)	C6—C5—H5B	109.4
O2—C2—N2	122.1 (7)	H5A—C5—H5B	108.0
O2—C2—C3	126.8 (6)	O3—C6—O4	124.3 (7)
N2—C2—C3	111.1 (6)	O3—C6—C5	121.3 (6)
C4—C3—F1	120.7 (6)	O4—C6—C5	114.4 (7)

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2···O3^{i}	0.86	1.96	2.815 (8)	175
O4—H4···O1^{ii}	0.82	2.12	2.938 (10)	174
C5—H5A···O3^{iii}	0.97	2.55	3.468 (7)	158
C4—H4A···O3^{iii}	0.93	2.53	3.367 (7)	149

Symmetry codes: (i) *x*, −*y*+1, *z*+1/2; (ii) *x*, −*y*+1, *z*−1/2; (iii) *x*, *y*−1, *z*.

Fig. 1

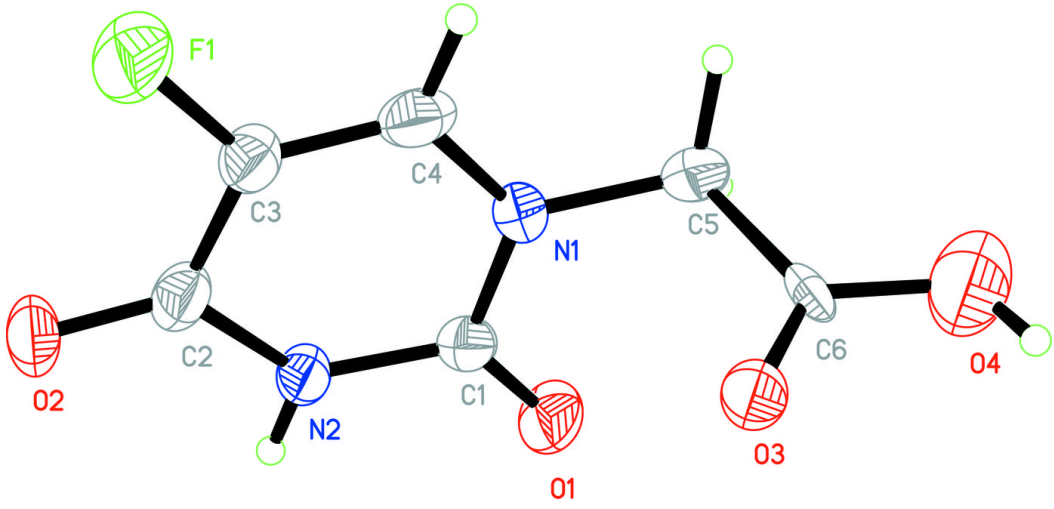

Fig. 2