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5-Fluorouracil-1-acetic acid

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Key indicators

Single-crystal X-ray study
T = 294 K
Mean σ(C–C) = 0.003 Å
R factor = 0.041
wR factor = 0.121
Data-to-parameter ratio = 12.0

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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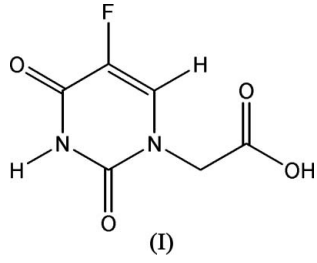
In the title compound, $C_6H_5FN_2O_4$, the acetic acid group lies out of the pyrimidine plane. In the crystal structure, molecules are connected by intermolecular N—H···O, O—H···O and C—H···O hydrogen bonds, forming a three-dimensional network.

Comment

The cycle-specific schedule-dependent antimetabolite 5-fluorouracil has been used in clinics for 40 years and has evolved as an important agent in the treatment of a large spectrum of tumours, including breast cancer, gastric carcinoma and bladder cancer (Duschinsky *et al.*, 1957; Heidelberger *et al.*, 1957; Correale *et al.*, 2005). However, its slight harmfulness to the liver, kidney and digestive system limits its wider applicability (Wasterack & Bettina, 1987). For these reasons, many derivatives of 5-fluorouracil have been synthesized and some compounds have better biological activity. 5-Fluorouracil-1-acetic acid, (I), is a member of the family (Tada, 1975). Its metal complexes have been reported to have biological activity (Wang *et al.*, 1993; Qu *et al.*, 2001; Huang *et al.*, 2005).



(I)

The acetic acid group lies out of the pyrimidine plane (Fig. 1). The C—F, C—O and C—N bond distances are given in Table 1. In (I), there are intermolecular N—H···O, O—H···O and C—H···O hydrogen bonds (Table 2), forming a three-dimensional network (Fig. 2).

Experimental

The title compound, (I), was prepared according to the literature method of Tada (1975). A mixture of 5-fluorouracil (5.2 g), chloroacetic acid (3.8 g), potassium hydroxide (4.48 g) and water (100 ml) was refluxed at 353 K for 2 h and cooled to room temperature. After the pH of the mixture was adjusted to 2 with hydrochloric acid, the title compound was obtained (yield 71%; m.p. 548–549 K). Single crystals suitable for X-ray diffraction were obtained by slow evaporation of an ethanol solution.

Crystal data

$C_6H_5FN_2O_4$
M_r = 188.12
Monoclinic, $P2_1/n$
a = 4.9730 (10) Å
b = 17.093 (3) Å
c = 8.7485 (17) Å
β = 97.424 (3)°
V = 737.4 (2) Å^3
Z = 4
D_x = 1.694 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1757 reflections
θ = 2.6–26.2°
μ = 0.16 mm^{-1}
T = 294 (2) K
Block, colourless
0.24 × 0.20 × 0.18 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.963, T_{max} = 0.972
4104 measured reflections
1507 independent reflections
1139 reflections with $I > 2\sigma(I)$
R_{int} = 0.023
θ_{max} = 26.4°
$h = -6 \rightarrow 6$
$k = -11 \rightarrow 21$
$l = -10 \rightarrow 10$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.121
S = 1.03
1507 reflections
126 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0616P)^2 + 0.3397P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.38 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}

Table 1
Selected bond lengths (Å).

F1—C3	1.422 (2)	N1—C2	1.370 (3)
O1—C2	1.232 (2)	N1—C1	1.385 (3)
O2—C1	1.213 (2)	N2—C1	1.374 (2)
O3—C6	1.200 (2)	N2—C4	1.376 (3)
O4—C6	1.322 (2)	N2—C5	1.461 (2)

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O4—H4···O1^{i}	0.98 (3)	1.81 (3)	2.696 (2)	148 (3)
N1—H1···O1^{ii}	0.91 (3)	2.00 (3)	2.904 (2)	171 (2)
C4—H4*A*···O2^{iii}	0.93	2.53	3.284 (3)	139
C5—H5*A*···O3^{iv}	0.97	2.56	3.368 (2)	141
C5—H5*B*···O3^{v}	0.97	2.50	3.459 (3)	172

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

The H atoms attached to O and N atoms were located in a difference map and refined freely. Other H atoms were placed in geometrically calculated positions, with C—H = 0.93 or 0.97 Å, and refined as riding atoms, with $U_{iso}(H) = 1.2U_{eq}(C)$.

Data collection: *SMART* (Bruker, 1997); cell refinement: *SAINT* (Bruker, 1997); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1997); software used to prepare material for publication: *SHELXTL*.

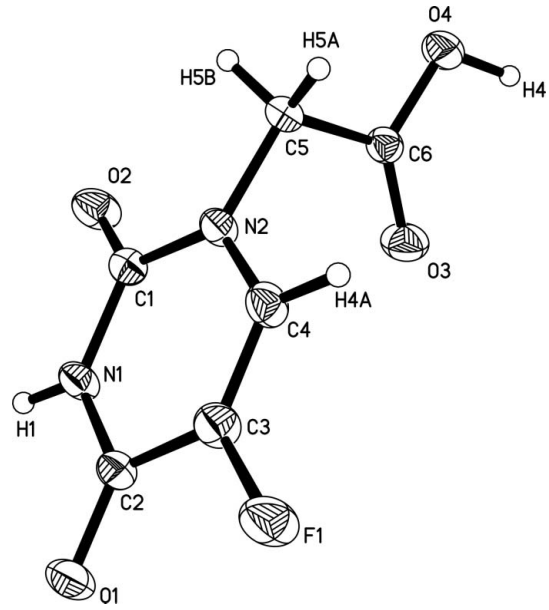


Figure 1
The molecular structure of (I), showing the atom-labelling scheme. Displacement ellipsolids are drawn at the 30% probability level.

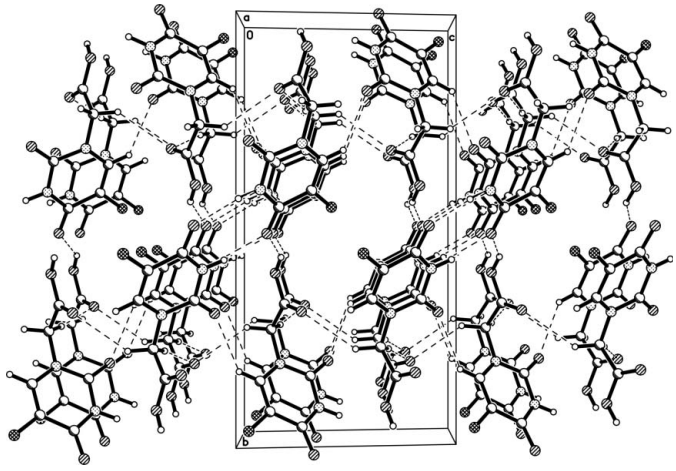


Figure 2
The packing of (I), viewed along the *a* axis. Dashed lines indicate hydrogen bonds.

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