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5-Fluorouracil-1-propionic acid

Jian-Qiang Qu,[a]* Xiao-Fei Jia,[a] Jian-Zhong Cui,[a] Hong Zhang[a] and Liu-Fang Wang[b]

[a]Department of Chemistry, Tianjin University, Tianjin 300072, People's Republic of China, and [b]State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, People's Republic of China

Correspondence e-mail: jqqu@tju.edu.cn

Key indicators

Single-crystal X-ray study
T = 294 K
Mean σ(C–C) = 0.004 Å
Disorder in main residue
R factor = 0.047
wR factor = 0.145
Data-to-parameter ratio = 12.8

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

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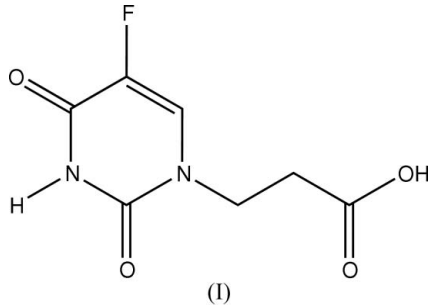
In the title compound, $C_7H_7FN_2O_4$, the propionic acid group is twisted out of the pyrimidine plane. In the crystal structure, molecules are connected by intermolecular N—H···O and O—H···O hydrogen bonds, forming columns.

Comment

5-Fluorouracil is a normal antitumor medicine which has been used in clinics for 40 years; it can be used to treat breast cancer, gastric carcinoma and bladder cancer (Duschinsky *et al.*, 1957; Heidelberger *et al.*, 1957; Correale *et al.*, 2005). However, the toxic side effects, such as marrow inhibition and a little harmful to liver, kidney and digestive system, limit its wider applicability (Wasterack & Bettina, 1987). Searching for compounds with high antitumor activity and low toxicity is an urgent task for scientists. In order to reduce the side effects, many derivatives of 5-fluorouracil have been synthesized and some of these compounds have better biological activity (Zhuo *et al.*, 1986). 5-Fluorouracil-1-propionic acid, (I), is a member of the family. Its rare earth metal complexes have been reported to have prooxidative and antitumor activity (Liu *et al.*, 2000).



(I)

The propionic acid group is twisted out of the pyrimidine plane [torsion angles C7—N1—C3—C2 and C4—N1—C3—C2 are −88.0 (3) and 94.4 (2)°, respectively] (Fig. 1). C—F, C—O and C—N bond distances are given in Table 1. Intermolecular N—H···O and O—H···O hydrogen bonds (Table 2) form columns along the *b* axis (Fig. 2).

Experimental

The title compound, (I), was prepared according to a modification of the literature method of Zhuo *et al.* (1986). A mixture of 5-fluorouracil (13 g), acrylonitrile (10 g), sodium hydrate (15 g) and water (100 ml) was refluxed at 343 K for 4 h and cooled to room temperature. After treatment with strong-acid styrene-series cation-exchange resin, the title compound was obtained (yield 63%, m.p. 457–458 K). Single crystals suitable for X-ray diffraction were

obtained by slow evaporation of an ethanol solution. IR (KBr, ν cm^{-1}): 3284, 1694, 1416; ^{1}H NMR (d_6-DMSO, δ, p.p.m.): 11.70 (*s*, 1H), 12.65 (*b*, 1H), 7.85 (*d*, 1H), 3.72 (*t*, 2H), 2.54 (*t*, 2H); analysis calculated for $C_7H_7FN_2O_4$: C 41.58, H 3.49, N 13.86%; found: C 41.50, H 3.62, N 13.77%.

Crystal data

$C_7H_7FN_2O_4$	D_x = 1.577 Mg m^{-3}
M_r = 202.15	Mo $K\alpha$ radiation
Monoclinic, $C2/c$	Cell parameters from 1663 reflections
a = 20.279 (6) Å	θ = 2.8–26.3°
b = 8.137 (2) Å	μ = 0.14 mm^{-1}
c = 13.222 (4) Å	T = 294 (2) K
β = 128.673 (4)°	Block, colourless
V = 1703.3 (8) Å^3	0.26 × 0.24 × 0.20 mm
Z = 8	

Data collection

Bruker SMART CCD area-detector diffractometer	1747 independent reflections
φ and ω scans	1245 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)	R_{int} = 0.035
T_{min} = 0.958, T_{max} = 0.972	θ_{max} = 26.5°
4556 measured reflections	$h = -20 \rightarrow 25$
	$k = -7 \rightarrow 10$
	$l = -16 \rightarrow 16$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0679P)^2 + 1.9948P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.047	$(\Delta/\sigma)_{max}$ = 0.002
$wR(F^2)$ = 0.145	$\Delta\rho_{max}$ = 0.30 e Å^{-3}
S = 1.05	$\Delta\rho_{min}$ = −0.41 e Å^{-3}
1747 reflections	
137 parameters	
H atoms treated by a mixture of independent and constrained refinement	

Table 1
Selected bond lengths (Å).

F1—C6	1.352 (3)	N1—C3	1.473 (3)
O1—C1	1.229 (3)	N1—C4	1.380 (3)
O2—C1	1.324 (3)	N1—C7	1.370 (3)
O3—C4	1.217 (3)	N2—C4	1.377 (3)
O4—C5	1.222 (3)	N2—C5	1.376 (3)

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

D—H···A	D—H	H···A	D···A	D—H···A
N2—H2E···O1^{i}	0.81 (3)	2.00 (3)	2.797 (3)	171 (3)
O2—H2C···O4^{ii}	0.839 (10)	2.06 (2)	2.887 (3)	167 (8)
O2—H2D···O3^{iii}	0.839 (10)	2.154 (14)	2.990 (3)	174 (8)

Symmetry codes: (i) $x, y+1, z$; (ii) $-x, y-1, -z+\frac{1}{2}$; (iii) $-x+\frac{1}{2}, -y+\frac{3}{2}, -z+1$.

H atoms attached to O and N atoms were located in a difference map. The OH group is disordered over two positions with an occupancy ratio of 0.5:0.5 and the H atom was refined with a restraint of O—H = 0.82 (2) Å. The H atom of the NH group was refined freely. All other H atoms were placed in geometrically calculated positions (C—H = 0.93 or 0.97 Å) and refined as riding atoms [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*.

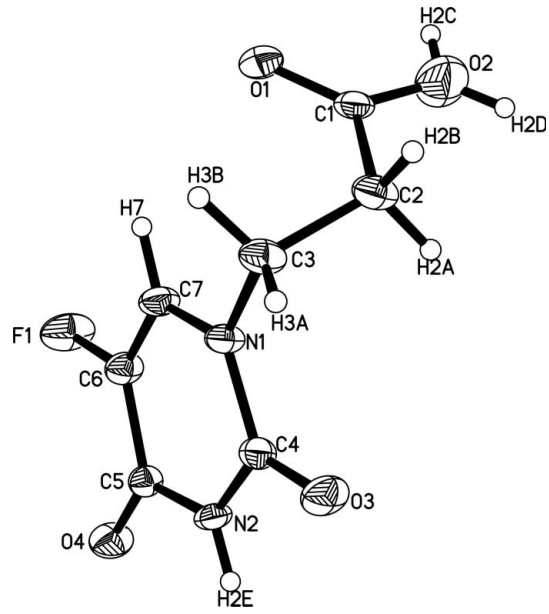


Figure 1
The molecular structure of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 35% probability level. Both disorder components of the OH group are shown.

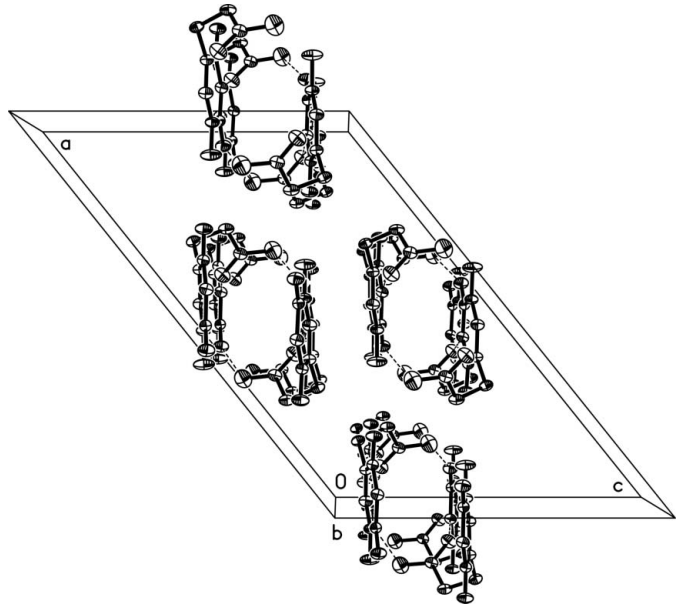


Figure 2
Packing of (I), viewed along the *b* axis.

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