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(*E*)-4,4′-Ethylenedipyridinium bis{[(5-fluoro-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-4-yl)-acetamido]acetate} dihydrate

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Key indicators

Single-crystal X-ray study
T = 298 K
Mean σ(C–C) = 0.006 Å
R factor = 0.091
wR factor = 0.171
Data-to-parameter ratio = 12.1

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

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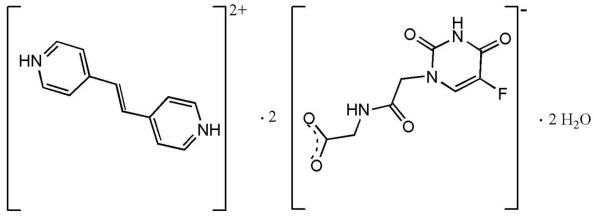
The asymmetric unit of the title compound, $C_{10}H_9N_2^{2+}\cdot 2C_6H_4FN_2O_4^-\cdot 2H_2O$, consists of one half of the (*E*)-4,4′-ethylenedipyridinium cation, one [(5-fluoro-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-4-yl)acetamido]acetate anion and one water molecule, the complete formula unit being generated by a crystallographic inversion centre at the mid-point of the central C═C bond of the (*E*)-4,4′-ethylenedipyridinium cation. In the crystal structure, a three-dimensional network is formed *via* N—H···O and O—H···O hydrogen bonds.

Comment

5-Fluorouracil (5FU) is an antimetabolite with a broad spectrum of activity against solid tumours. It is also known to be an effective antitumour compound against breast, colorectal and gastric cancers (Nichifor *et al.*, 1997; Beall & Sloan, 2002). However, it causes toxic side effects and disorders of the bone marrow or of the epithelium of the gastrointestinal tract. Thus, many derivatives of 5FU have been developed to minimize toxic side effects and delivery problems (Nichifor & Schacht, 1997; Saniger *et al.*, 2003). In our laboratory, we have synthesized a dipeptide derivative of 5FU, [(5-fluoro-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-4-yl)acetamido]acetic acid (FAA), and as a continuation of our research, we report here the crystal structure of the title compound, (*E*)-4,4′-ethylenedipyridinium bis{[(5-fluoro-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-4-yl)acetamido]acetate} dihydrate, (I).



(I)

In the structure of (I) (Fig. 1), the formula unit comprises one (*E*)-4,4′-ethylenedipyridinium cation (which resides on a crystallographic inversion centre), two [(5-fluoro-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-4-yl)acetamido]acetate (FAD) anions and two water molecules. In the unique FAD anion, the N1—C3 bond distance (Table 1) is shorter than the typical C—N bond length [*ca* 1.473 (13) Å], but longer than the typical double C═N bond (*ca* 1.279 Å; Allen *et al.*, 1987), indicating electron delocalization over atoms O3, C3 and N1.

The (*E*)-4,4′-ethylenedipyridinium cation acts as a proton receptor in the title charge-transfer complex. The conjugation

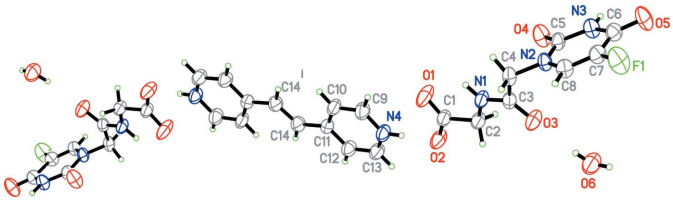


Figure 1
A view of (I), showing 30% probability displacement ellipsoids and the atom-numbering scheme. [Symmetry code: (i) $-x+2, -y, -z+1$.]

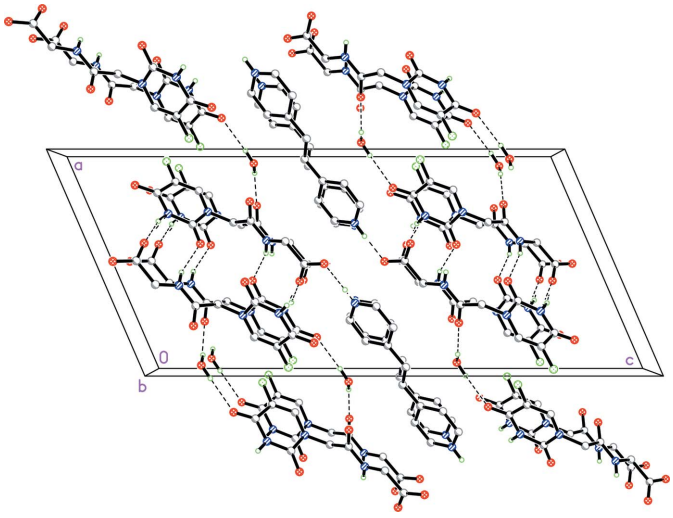


Figure 2
The crystal packing of (I), viewed down the *b* axis. Hydrogen bonds are shown as dashed lines.

in the cation is confirmed by the distances of N4—C9, C9—C10, C10—C11, C11—C12, C12—C13 and C13—N4, which are intermediate between single and double bonds (Zhu *et al.*, 2003). In the crystal structure, intermolecular N—H···O and O—H···O hydrogen bonds connect cations, anions and water molecules into a three-dimensional network (Table 2 and Fig. 2).

Experimental

The starting material, 5-fluorouracil-1-acetic acid, was prepared from 5-fluoruracil and bromoacetic acid following the method of Liu *et al.* (2002), and the key intermediate, methyl 2-(5-fluorouracil-1-aceto)aminoacetate, was synthesized from 5-fluorouracil-1-acetic acid, dicyclohexyl carbodiimide (DCC) and 1-hydroxybenzotriazole (HOBT). An *N*,*N*-dimethylformamide (DMF) solution (25 ml) of DCC (0.024 mol, 4.94 g) was added dropwise to a DMF solution (75 ml) of 5-fluorouracil-1-acetic acid (0.02 mol, 3.76 g) and HOBT (0.02 mol, 2.70 g) at 273 K. After 5 h reaction at room temperature, methyl glycinate (0.02 mol, 2.51 g) and triethylamine (0.02 mol, 2.02 g) were added to the above mixture. After 4 h, a white solid, methyl 2-(5-fluorouracil-1-aceto)aminoacetate, was obtained after filtration, reduced-pressure distillation of DMF and column-chromatographic separation. 2-(5-Fluorouracil-1-aceto)aminoacetic acid was then obtained by hydrolysis with sodium hydroxide solution (1 mol l^{-1}). An ethanol solution (10 ml) of 4,4′-bipyridine (0.4 mmol, 0.31 g) was added dropwise to a stirred aqueous solution (10 ml) of 2-(5-fluorouracil-1-aceto)aminoacetic acid (0.2 mmol, 0.07 g) at 253 K. The reaction mixture was filtered and the filtrate was allowed to stand for approximately four weeks until colourless single crystals were formed.

Crystal data

$C_{12}H_{12}N_2^{2+}\cdot 2C_8H_7FN_3O_5^-\cdot 2H_2O$
$M_r = 708.60$
Monoclinic, $P2_1/c$
$a = 12.6887\ (14)$ Å
$b = 5.1050\ (6)$ Å
$c = 26.598\ (3)$ Å
$\beta = 113.496\ (2)^\circ$
$V = 1580.1\ (3)$ Å^3
$Z = 2$
$D_x = 1.489$ Mg m^{-3}
Mo $K\alpha$ radiation
$\mu = 0.13$ mm^{-1}
$T = 298\ (2)$ K
Rod, colourless
0.30 × 0.08 × 0.06 mm

Data collection

Bruker APEX area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2002)
$T_{min} = 0.963$, $T_{max} = 0.989$
7879 measured reflections
2814 independent reflections
2234 reflections with $I > 2\sigma(I)$
$R_{int} = 0.044$
$\theta_{max} = 25.2^\circ$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.091$
$wR(F^2) = 0.171$
$S = 1.25$
2814 reflections
232 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.037P)^2 + 1.4841P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.19$ e Å^{-3}
$\Delta\rho_{min} = -0.23$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N4—C13	1.321 (5)	C12—C13	1.374 (5)
N4—C9	1.325 (5)	C14—C14^{i}	1.325 (7)
C9—C10	1.361 (5)	O3—C3	1.227 (4)
C10—C11	1.387 (5)	N1—C3	1.325 (4)
C11—C12	1.380 (5)	N1—C2	1.443 (5)
C13—N4—C9	120.8 (4)	C13—C12—C11	119.9 (4)
N4—C9—C10	121.1 (4)	N4—C13—C12	120.8 (4)
C9—C10—C11	120.0 (4)	O1—C1—O2	125.3 (4)
C12—C11—C10	117.4 (4)	O3—C3—N1	122.7 (4)

Symmetry code: (i) $-x+2, -y, -z+1$.

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

D—H···A	D—H	H···A	D···A	D—H···A
N4—H4···O2	0.86	1.70	2.563 (4)	177
N1—H1···O4^{ii}	0.86	2.14	2.967 (4)	162
N3—H3···O1^{iii}	0.86	1.92	2.757 (4)	165
O6—H6A···O3	0.83 (4)	2.08 (2)	2.875 (4)	160 (4)
O6—H6B···O5^{iv}	0.82 (4)	2.14 (4)	2.941 (4)	164 (4)

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

H atoms attached to O atoms were located in a difference Fourier map and refined, with O—H distances restrained to 0.82 (1) Å and with U_{iso}(H) = 1.2U_{eq}(parent atom). The other H atoms were posi-

tioned geometrically and allowed to ride on their parent atoms at distances of Csp^2—H = 0.93 Å with U_{iso}(H) = 1.2U_{eq}(parent atom), Csp^3—H = 0.97 Å with U_{iso}(H) = 1.2U_{eq}(parent atom) and N—H = 0.86 Å with U_{iso}(H) = 1.2U_{eq}(parent atom).

Data collection: *SMART* (Bruker, 2002); cell refinement: *SAINT* (Bruker, 2002); 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, 2002); software used to prepare material for publication: *SHELXL97*.

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