Crystal structure of 5-fluoro-3-(thiophene-2-carbonyl)pyrimidine-2,4(1*H*,3*H*)-dione, $C_9H_5FN_2O_3S$

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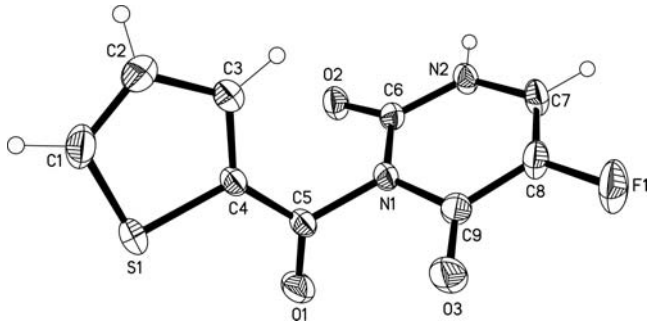

Abstract

$C_9H_5FN_2O_3S$, monoclinic, $P12_1/c1$ (no. 14), a = 5.574(4) Å, b = 19.77(2) Å, c = 8.866(7) Å, β = 100.49(1)°, V = 960.7 Å^3, Z = 4, $R_{gt}(F)$ = 0.052, $wR_{ref}(F^2)$ = 0.128, T = 298 K.

Source of material

The title compound was prepared by reacting 5-fluorouracil (5 mmol) with trithylamine (6 mmol) and thiophene-2-carbonyl chloride (5 mmol) in anhydrous acetonitrile stirred at 273 K for 2 hours. The mixture was then stirred at room temperature over 12 hours, followed by aqueous work-up and extraction. The purified product was dissolved in the mixture of methanol and acetone (v/v = 2/1). The resulting solution was left in air for a few days, yielding colorless column-shaped crystals.

Experimental details

All hydrogen atoms were positioned geometrically and allowed to ride on their parent atoms with d(C—H) = 0.93 Å, d(N—H) = 0.86 Å and U_{iso}(H) = 1.2 U_{eq}(C,N).

Discussion

5-Fluorouracil is one of the antitumor agents most frequently used for treating solid tumors, such as breast, colorectal, and gastric cancers, it has been increasingly employed alone or in combination with other drugs and hormones [1,2]. However, it exhibits strong side effects, such as gastrointestinal toxicity and delivery problems [3], therefore many derivatives of 5-fluorouracil have been developed to improve its topical delivery and reduce the side effects [4]. On the other hand, compounds containing thiophene aromatic ring are ubiquitous in nature. Thiophene oligomers and polymers have received great attention due to their potential anticancer and anti-inflammatory property [5]. In recent years, more and more attention has been focused on synthesis and properties of thiophene carboxylic acid derivatives, which not only play an important role in constructing coordination polymers with attractive topological structure but also found application in a large number of organic reactions and widely employed in organic synthesis [6-8]. The title thiophene derivative of 5-fluorouracil based on the concept of mutual prodrug was synthesized [9].

The bond lengths and angles in the title molecule are within normal ranges. The bond lengthes N1—C6, N1—C9, N2—C6 and N2—C7 (1.377(3) Å, 1.403(3) Å, 1.353(3) Å 1.360(3) Å) are shorter than N—C single bond of 1.44 Å, but longer than a typical N=C double bond of 1.27 Å. The bond lengthes C7—C8 and C8—C9 (1.318(4) Å, 1.435(4) Å, respectively) are both short than a typical C—C single bond (1.530 Å), but longer than a typical C=C double bond (1.330 Å). The bond lengthes C6—O2 and C9—O3 (1.22(1) Å, 1.202(9) Å) are shorter than a typical C—O single bond (1.439 Å), but longer than a typical C=O double bond (1.173 Å) [10-12]. The partial double-bond character of the molecule is presumed to be a result of the electron delocalization. The atoms in the heterocyclic ring (C6/C7/C8/C9/N1/N2) are slightly puckered, with r.m.s. deviation of 0.044(2) Å. The thiophene ring (C1/C2/C3/C4/S1) is essentially planar with r.m.s. deviations of 0.004(2) Å. The dihedral angle formed by the heterocyclic ring and thiophene ring is 75.23(7)°. It should be noted that the hydrogen bonding interactions play an important role in the crystal structure of the title compound. The adjacent molecules are linked by intermolecular hydrogen bond N2–H2···O2^i (symmetry code i: –x+1,–y+1,–z) to form dimers stabilizing the crystal structure.

Table 1. Data collection and handling.

Crystal:	colorless column, size 0.14 × 0.20 × 0.38 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	3.44 cm^{-1}
Diffractometer, scan mode:	Bruker APEX CCD, φ/ω
$2\theta_{max}$:	50.04°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	4890, 1696
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 1501
$N(param)_{refined}$:	145
Programs:	SHELXS-97, SHELXL-97, SHELXTL [13]

Table 2. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{iso}
H(2A)	4*e*	0.4152	0.4502	0.0783	0.046
H(1)	4*e*	0.4401	0.8051	0.5041	0.071
H(2)	4*e*	0.6899	0.7067	0.5461	0.065
H(3)	4*e*	0.4943	0.6083	0.4079	0.054
H(7)	4*e*	0.2373	0.3731	0.2059	0.052

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Table 3. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
S(1)	4*e*	0.1284(2)	0.74958(3)	0.3376(1)	0.0552(5)	0.0274(4)	0.0862(6)	0.0064(3)	0.0093(4)	–0.0059(3)
F(1)	4*e*	–0.0868(4)	0.39426(9)	0.3615(2)	0.108(2)	0.039(1)	0.102(1)	–0.014(1)	0.067(1)	0.0025(9)
O(1)	4*e*	–0.1472(4)	0.6430(1)	0.1304(2)	0.047(1)	0.044(1)	0.070(1)	0.0108(9)	–0.011(1)	–0.005(1)
O(2)	4*e*	0.3464(3)	0.57222(9)	0.0491(2)	0.054(1)	0.031(1)	0.059(1)	–0.0003(8)	0.0267(9)	0.0027(8)
O(3)	4*e*	–0.1932(4)	0.5299(1)	0.3635(2)	0.057(1)	0.050(1)	0.071(1)	0.009(1)	0.035(1)	0.003(1)
N(1)	4*e*	0.0964(4)	0.55159(9)	0.2187(2)	0.035(1)	0.025(1)	0.041(1)	0.0011(8)	0.0108(8)	–0.0032(8)
N(2)	4*e*	0.3082(4)	0.4646(1)	0.1294(2)	0.044(1)	0.026(1)	0.049(1)	0.0019(9)	0.020(1)	–0.0042(9)
C(1)	4*e*	0.3954(6)	0.7635(2)	0.4590(4)	0.064(2)	0.041(2)	0.074(2)	–0.014(2)	0.019(2)	–0.017(2)
C(2)	4*e*	0.5366(6)	0.7077(2)	0.4836(3)	0.044(2)	0.053(2)	0.063(2)	–0.008(1)	0.003(1)	–0.009(1)
C(3)	4*e*	0.4241(5)	0.6511(1)	0.4034(3)	0.042(2)	0.034(2)	0.057(2)	0.005(1)	0.006(1)	–0.005(1)
C(4)	4*e*	0.1996(4)	0.6662(1)	0.3180(3)	0.036(1)	0.026(1)	0.046(1)	0.004(1)	0.013(1)	–0.001(1)
C(5)	4*e*	0.0328(4)	0.6245(1)	0.2153(3)	0.037(1)	0.027(1)	0.044(1)	0.005(1)	0.012(1)	–0.001(1)
C(6)	4*e*	0.2586(4)	0.5316(1)	0.1274(3)	0.034(1)	0.028(1)	0.040(1)	–0.002(1)	0.008(1)	–0.005(1)
C(7)	4*e*	0.1971(5)	0.4187(1)	0.2083(3)	0.059(2)	0.023(1)	0.050(2)	–0.002(1)	0.017(1)	–0.003(1)
C(8)	4*e*	0.0326(5)	0.4389(1)	0.2881(3)	0.058(2)	0.030(1)	0.052(2)	–0.009(1)	0.024(1)	–0.001(1)
C(9)	4*e*	–0.0375(5)	0.5084(1)	0.2977(3)	0.040(1)	0.037(1)	0.044(1)	–0.001(1)	0.014(1)	–0.003(1)

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