

Acta Crystallographica Section E

Structure Reports

Online

ISSN 1600-5368

5-Fluoro-1-(3-methylbutanoyl)pyrimidine-2,4(1*H*,3*H*)-dione

 Hans-Joachim Lehmler^{a*} and Sean Parkin^b

^aThe University of Iowa, Department of Occupational and Environmental Health, 100 Oakdale Campus, 124 IREH, Iowa City, IA 52242-5000, USA, and ^bUniversity of Kentucky, Department of Chemistry, Lexington, KY 40506-0055, USA

Correspondence e-mail: hans-joachim-lehmler@uiowa.edu

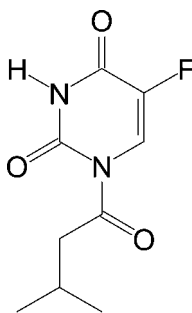
Received 28 February 2008; accepted 6 March 2008

 Key indicators: single-crystal X-ray study; $T = 90$ K; mean $\sigma(\text{C}-\text{C}) = 0.002$ Å; R factor = 0.049; wR factor = 0.112; data-to-parameter ratio = 15.5.

The 3-methylbutanoyl group and the 5-fluorouracil unit of the title compound, $\text{C}_9\text{H}_{11}\text{FN}_2\text{O}_3$, are essentially coplanar, with the carbonyl group oriented towards the ring CH group and away from the nearer ring carbonyl group. The 3-methylbutanoyl $(\text{C}=\text{C})\text{C}-\text{N}-\text{C}=\text{O}$ torsion angle of $9.6(2)^\circ$ is comparable to that in structurally related compounds. In the solid state, two inversion-related molecules form $\text{N}-\text{H}\cdots\text{O}$ hydrogen bonds to generate an intermolecular $R_2^2(8)$ ring. The crystal structure also displays intra- and intermolecular $\text{C}-\text{H}\cdots\text{O}$ interactions.

Related literature

For similar 5-fluoropyrimidine-2,4(1*H*,3*H*)-dione structures with N1-acyl substituents, see: Beall *et al.* (1993); Jiang *et al.* (1988); Lehmler & Parkin (2000); Lehmler & Parkin (2008). For related literature, see: Roberts & Sloan (1999).



Experimental

Crystal data

$\text{C}_9\text{H}_{11}\text{FN}_2\text{O}_3$	$\gamma = 104.085(3)^\circ$
$M_r = 214.20$	$V = 468.94(4) \text{ \AA}^3$
Triclinic, $P\bar{1}$	$Z = 2$
$a = 5.4879(3) \text{ \AA}$	Mo $K\alpha$ radiation
$b = 9.3702(5) \text{ \AA}$	$\mu = 0.13 \text{ mm}^{-1}$
$c = 9.9794(5) \text{ \AA}$	$T = 90.0(2) \text{ K}$
$\alpha = 103.470(2)^\circ$	$0.30 \times 0.20 \times 0.07 \text{ mm}$
$\beta = 100.204(3)^\circ$	

Data collection

Nonius KappaCCD diffractometer	4080 measured reflections
Absorption correction: multi-scan (SCALEPACK; Otwinowski & Minor, 1997)	2139 independent reflections
$T_{\min} = 0.963$, $T_{\max} = 0.991$	1629 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.031$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.049$	138 parameters
$wR(F^2) = 0.112$	H-atom parameters constrained
$S = 1.07$	$\Delta\rho_{\max} = 0.27 \text{ e \AA}^{-3}$
2139 reflections	$\Delta\rho_{\min} = -0.29 \text{ e \AA}^{-3}$

Table 1

Hydrogen-bond geometry (Å, °).

$D-\text{H}\cdots A$	$D-\text{H}$	$\text{H}\cdots A$	$D\cdots A$	$D-\text{H}\cdots A$
$\text{N3}-\text{H3}\cdots\text{O4}^i$	0.88	2.04	2.9091 (16)	171

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

Data collection: COLLECT (Nonius, 1998); cell refinement: SCALEPACK (Otwinowski & Minor, 1997); data reduction: DENZO-SMN (Otwinowski & Minor, 1997); program(s) used to solve structure: SHELXS97 (Sheldrick, 2008); program(s) used to refine structure: SHELXL97 (Sheldrick, 2008); molecular graphics: XP in SHELXTL (Sheldrick, 2008); software used to prepare material for publication: SHELXL97 and local procedures.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: OM2217).

References

- Beall, H. D., Pranker, R. J. & Sloan, K. B. (1993). *Drug Dev. Ind. Pharm.* **23**, 517–525.
- Jiang, A., Hu, S., Wang, Y. & Chen, Q. (1988). *Gaodeng Xuexiao Huaxue Xuebao*, **9**, 307–309.
- Lehmler, H.-J. & Parkin, S. (2000). *Acta Cryst.* **C56**, e518–519.
- Lehmler, H.-J. & Parkin, S. (2008). *Acta Cryst.* **E64**, o617.
- Nonius (1998). COLLECT. Nonius BV, Delft, The Netherlands.
- Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography, Part A*, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
- Roberts, W. J. & Sloan, K. B. (1999). *J. Pharm. Sci.* **88**, 515–522.
- Sheldrick, G. M. (2008). *Acta Cryst.* **A64**, 112–122.

supporting information

Acta Cryst. (2008). E64, o703 [doi:10.1107/S1600536808006296]

5-Fluoro-1-(3-methylbutanoyl)pyrimidine-2,4(1*H*,3*H*)-dione**Hans-Joachim Lehmler and Sean Parkin****S1. Comment**

Despite their potential pharmaceutical application, the crystal structures of only five 1-acyl-5-fluorouracil derivatives have been described in the literature (Beall *et al.*, 1993; Jiang *et al.*, 1988; Lehmler & Parkin, 2000; Lehmler & Parkin, 2008). We herein describe the crystal structure of a new 1-acyl-5-fluorouracil derivative, 5-fluoro-1-(1-oxo-3-methylbutyl)-2,4(1*H*,3*H*)-pyrimidinedione.

The molecular structures of 1-acyl-5-fluorouracil derivatives are similar. The 1-acyl group and the 5-fluorouracil moiety are essentially coplanar, with the C7=O7 carbonyl group oriented towards the C6—H group and away from the C2=O2 group. The C6—N1—C7—O7 dihedral angle of the title compound is 9.6 (2)°. The other 1-acyl-5-fluorouracil derivatives have comparable dihedral angles ranging from 1.6° to 17.3° (Beall *et al.*, 1993; Jiang *et al.*, 1988; Lehmler & Parkin, 2000; Lehmler & Parkin, 2008), which suggests that the carbonyl group of the 1-acyl group and the pyrimidine-2,4(1*H*,3*H*)-dione moiety are conjugated. The differences in the dihedral angles are most likely due to packing effects in the crystal.

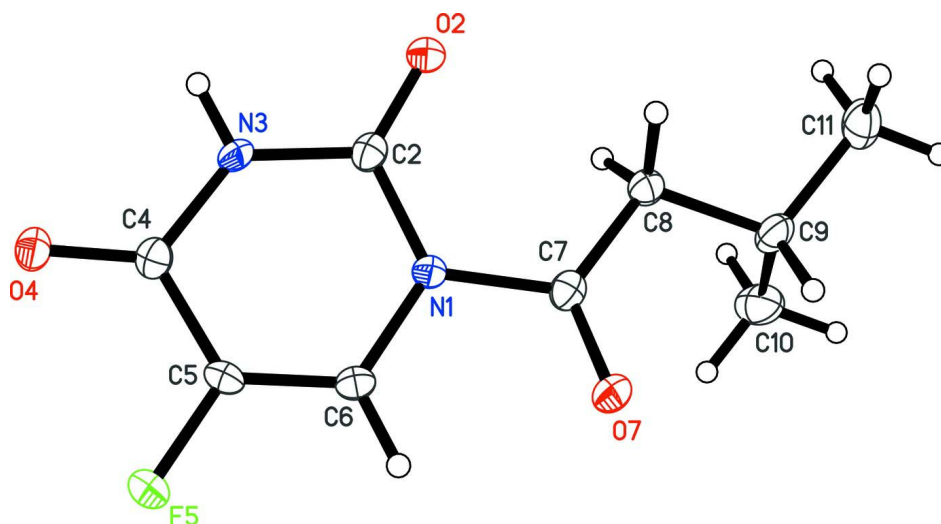
Similar to the crystal structure of other 1-acyl-5-fluorouracil derivatives (Beall *et al.*, 1993; Lehmler & Parkin, 2000; Lehmler & Parkin, 2008), the crystal structure of the title compound contains inversion related molecules that form dimers in which two N—H···O hydrogen bonds generate an intermolecular $R_2^2(8)$ ring. Furthermore, there are C—H···O type intra and intermolecular interactions.

S2. Experimental

5-Fluoro-1-(1-oxo-3-methylbutyl)-2,4(1*H*,3*H*)-pyrimidinedione was synthesized by acylation of 5-fluorouracil with 3-methylbutanoyl chloride and recrystallized from diethylether at -20°C (Beall *et al.*, 1997; Lehmler & Parkin, 2000; Roberts & Sloan, 1999).

S3. Refinement

H atoms were found in difference Fourier maps and subsequently placed in idealized positions with constrained C—H distances of 0.98 Å (RCH₃), 0.99 Å (R₂CH₂), 0.95 Å (C_{Ar}H) and 0.88 Å (NH) with $U_{\text{iso}}(\text{H})$ values set to either 1.2 U_{eq} or 1.5 U_{eq} (RCH₃ only) of the attached atom.

**Figure 1**

View of the title compound showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.

5-Fluoro-1-(3-methylbutanoyl)pyrimidine-2,4(1H,3H)-dione

Crystal data

$C_9H_{11}FN_2O_3$

$M_r = 214.20$

Triclinic, $P\bar{1}$

Hall symbol: -P 1

$a = 5.4879$ (3) Å

$b = 9.3702$ (5) Å

$c = 9.9794$ (5) Å

$\alpha = 103.470$ (2)°

$\beta = 100.204$ (3)°

$\gamma = 104.085$ (3)°

$V = 468.94$ (4) Å³

$Z = 2$

$F(000) = 224$

$D_x = 1.517$ Mg m⁻³

Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å

Cell parameters from 4363 reflections

$\theta = 1.0$ – 27.5 °

$\mu = 0.13$ mm⁻¹

$T = 90$ K

Irregular block, colourless

$0.30 \times 0.20 \times 0.07$ mm

Data collection

Nonius KappaCCD

diffractometer

Radiation source: fine-focus sealed tube

Graphite monochromator

Detector resolution: 18 pixels mm⁻¹

ω scans at fixed $\chi = 55$ °

Absorption correction: multi-scan

(SCALEPACK; Otwinowski & Minor, 1997)

$T_{\min} = 0.963$, $T_{\max} = 0.991$

4080 measured reflections

2139 independent reflections

1629 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.031$

$\theta_{\max} = 27.5$ °, $\theta_{\min} = 2.2$ °

$h = -7 \rightarrow 7$

$k = -12 \rightarrow 12$

$l = -12 \rightarrow 12$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.049$

$wR(F^2) = 0.112$

$S = 1.07$

2139 reflections

138 parameters

0 restraints

Primary atom site location: structure-invariant

direct methods

Secondary atom site location: difference Fourier

map

Hydrogen site location: inferred from
neighbouring sites
H-atom parameters constrained

$$w = 1/[\sigma^2(F_o^2) + (0.0498P)^2 + 0.0466P]$$

where $P = (F_o^2 + 2F_c^2)/3$

$$(\Delta/\sigma)_{\max} = 0.001$$

$$\Delta\rho_{\max} = 0.27 \text{ e } \text{\AA}^{-3}$$

$$\Delta\rho_{\min} = -0.29 \text{ e } \text{\AA}^{-3}$$

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 $F^2 > 2\sigma(F^2)$ 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 (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
N1	0.0774 (2)	0.62396 (13)	0.89316 (12)	0.0141 (3)
O2	-0.2469 (2)	0.74248 (12)	0.89048 (11)	0.0206 (3)
C2	-0.1490 (3)	0.65330 (17)	0.82969 (16)	0.0152 (3)
N3	-0.2565 (2)	0.56922 (13)	0.68799 (12)	0.0153 (3)
H3	-0.3906	0.5911	0.6444	0.018*
O4	-0.2928 (2)	0.38819 (11)	0.48195 (10)	0.0189 (3)
C4	-0.1798 (3)	0.45604 (16)	0.60712 (15)	0.0157 (4)
F5	0.13171 (17)	0.31908 (10)	0.61287 (9)	0.0218 (3)
C5	0.0440 (3)	0.42855 (17)	0.68495 (16)	0.0155 (3)
C6	0.1651 (3)	0.50812 (16)	0.81867 (15)	0.0152 (3)
H6	0.3130	0.4864	0.8646	0.018*
O7	0.3841 (2)	0.64683 (11)	1.08882 (11)	0.0195 (3)
C7	0.2244 (3)	0.70161 (17)	1.03933 (15)	0.0157 (4)
C8	0.1692 (3)	0.84157 (17)	1.12009 (15)	0.0168 (4)
H8A	0.0015	0.8099	1.1450	0.020*
H8B	0.1534	0.9094	1.0584	0.020*
C9	0.3816 (3)	0.93148 (18)	1.25622 (16)	0.0210 (4)
H9	0.4364	0.8564	1.3022	0.025*
C10	0.6162 (3)	1.02656 (19)	1.22141 (19)	0.0308 (4)
H10A	0.5657	1.1010	1.1765	0.046*
H10B	0.6817	0.9586	1.1561	0.046*
H10C	0.7522	1.0813	1.3092	0.046*
C11	0.2765 (3)	1.03360 (19)	1.35944 (16)	0.0255 (4)
H11A	0.4155	1.0936	1.4447	0.038*
H11B	0.1349	0.9693	1.3864	0.038*
H11C	0.2115	1.1034	1.3136	0.038*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0142 (7)	0.0140 (6)	0.0140 (7)	0.0062 (5)	0.0024 (5)	0.0027 (5)

O2	0.0191 (6)	0.0240 (6)	0.0184 (6)	0.0123 (5)	0.0021 (5)	0.0017 (5)
C2	0.0138 (8)	0.0165 (8)	0.0143 (8)	0.0023 (6)	0.0027 (6)	0.0055 (6)
N3	0.0128 (7)	0.0175 (7)	0.0154 (7)	0.0073 (6)	-0.0001 (5)	0.0043 (5)
O4	0.0185 (6)	0.0183 (6)	0.0160 (6)	0.0043 (5)	0.0004 (5)	0.0019 (5)
C4	0.0162 (9)	0.0131 (8)	0.0162 (8)	0.0023 (6)	0.0028 (6)	0.0045 (6)
F5	0.0236 (6)	0.0210 (5)	0.0199 (5)	0.0121 (4)	0.0036 (4)	-0.0002 (4)
C5	0.0170 (8)	0.0136 (7)	0.0181 (8)	0.0076 (6)	0.0066 (6)	0.0036 (6)
C6	0.0148 (8)	0.0154 (8)	0.0174 (8)	0.0069 (6)	0.0036 (6)	0.0062 (6)
O7	0.0201 (6)	0.0225 (6)	0.0169 (6)	0.0108 (5)	0.0010 (5)	0.0059 (5)
C7	0.0148 (9)	0.0172 (8)	0.0146 (8)	0.0027 (7)	0.0030 (6)	0.0064 (6)
C8	0.0180 (9)	0.0174 (8)	0.0159 (8)	0.0075 (7)	0.0027 (6)	0.0049 (6)
C9	0.0219 (9)	0.0193 (8)	0.0197 (9)	0.0101 (7)	-0.0027 (7)	0.0032 (7)
C10	0.0203 (10)	0.0263 (10)	0.0366 (11)	0.0061 (8)	0.0008 (8)	-0.0029 (8)
C11	0.0306 (10)	0.0217 (9)	0.0194 (9)	0.0073 (8)	0.0002 (7)	0.0018 (7)

Geometric parameters (Å, °)

N1—C6	1.4026 (18)	C7—C8	1.499 (2)
N1—C2	1.4102 (19)	C8—C9	1.530 (2)
N1—C7	1.4529 (18)	C8—H8A	0.9900
O2—C2	1.2053 (17)	C8—H8B	0.9900
C2—N3	1.3884 (18)	C9—C10	1.522 (2)
N3—C4	1.3755 (19)	C9—C11	1.526 (2)
N3—H3	0.8800	C9—H9	1.0000
O4—C4	1.2300 (17)	C10—H10A	0.9800
C4—C5	1.445 (2)	C10—H10B	0.9800
F5—C5	1.3493 (16)	C10—H10C	0.9800
C5—C6	1.326 (2)	C11—H11A	0.9800
C6—H6	0.9500	C11—H11B	0.9800
O7—C7	1.2079 (17)	C11—H11C	0.9800
C6—N1—C2	120.64 (12)	C9—C8—H8A	109.1
C6—N1—C7	115.63 (12)	C7—C8—H8B	109.1
C2—N1—C7	123.62 (12)	C9—C8—H8B	109.1
O2—C2—N3	121.20 (14)	H8A—C8—H8B	107.9
O2—C2—N1	124.36 (13)	C10—C9—C11	110.92 (13)
N3—C2—N1	114.44 (13)	C10—C9—C8	110.36 (13)
C4—N3—C2	128.19 (13)	C11—C9—C8	110.06 (13)
C4—N3—H3	115.9	C10—C9—H9	108.5
C2—N3—H3	115.9	C11—C9—H9	108.5
O4—C4—N3	122.26 (14)	C8—C9—H9	108.5
O4—C4—C5	125.01 (14)	C9—C10—H10A	109.5
N3—C4—C5	112.73 (13)	C9—C10—H10B	109.5
C6—C5—F5	120.63 (13)	H10A—C10—H10B	109.5
C6—C5—C4	122.96 (14)	C9—C10—H10C	109.5
F5—C5—C4	116.38 (12)	H10A—C10—H10C	109.5
C5—C6—N1	120.82 (14)	H10B—C10—H10C	109.5
C5—C6—H6	119.6	C9—C11—H11A	109.5

N1—C6—H6	119.6	C9—C11—H11B	109.5
O7—C7—N1	116.87 (13)	H11A—C11—H11B	109.5
O7—C7—C8	123.93 (13)	C9—C11—H11C	109.5
N1—C7—C8	119.20 (12)	H11A—C11—H11C	109.5
C7—C8—C9	112.30 (13)	H11B—C11—H11C	109.5
C7—C8—H8A	109.1		
C6—N1—C2—O2	174.10 (14)	F5—C5—C6—N1	178.82 (12)
C7—N1—C2—O2	-1.8 (2)	C4—C5—C6—N1	0.9 (2)
C6—N1—C2—N3	-5.5 (2)	C2—N1—C6—C5	3.1 (2)
C7—N1—C2—N3	178.58 (12)	C7—N1—C6—C5	179.32 (13)
O2—C2—N3—C4	-174.94 (14)	C6—N1—C7—O7	-9.6 (2)
N1—C2—N3—C4	4.7 (2)	C2—N1—C7—O7	166.53 (13)
C2—N3—C4—O4	179.30 (13)	C6—N1—C7—C8	171.17 (12)
C2—N3—C4—C5	-1.1 (2)	C2—N1—C7—C8	-12.7 (2)
O4—C4—C5—C6	177.69 (15)	O7—C7—C8—C9	15.1 (2)
N3—C4—C5—C6	-1.9 (2)	N1—C7—C8—C9	-165.67 (13)
O4—C4—C5—F5	-0.3 (2)	C7—C8—C9—C10	78.01 (16)
N3—C4—C5—F5	-179.92 (12)	C7—C8—C9—C11	-159.23 (13)

Hydrogen-bond geometry (Å, °)

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
N3—H3...O4 ⁱ	0.88	2.04	2.9091 (16)	171

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