

Capecitabine from X-ray powder synchrotron data. Corrigendum

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In the paper by Rohlicek *et al.* [*Acta Cryst.* (2009), E65, o1325–o1326], one H atom was placed incorrectly.

Following our powder-diffraction study of capecitabine (Rohlicek *et al.*, 2009), Malińska *et al.* (2014) published the crystal structure of the same molecule based on single-crystal data. Although they modelled the wrong enantiomer [as was pointed out by Kratochvil *et al.* (2016)], the structures are very similar after inverting the single-crystal structure, including

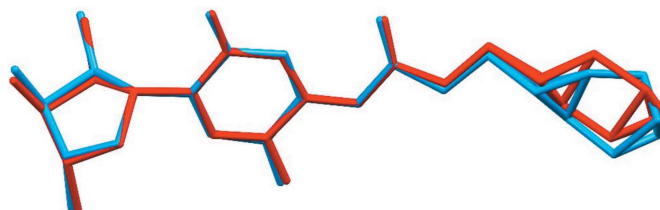


Figure 1
Overlay of the capecitabine molecular structures arising from powder diffraction (blue) and from single-crystal diffraction data (red). Only non-H atoms are shown for clarity.

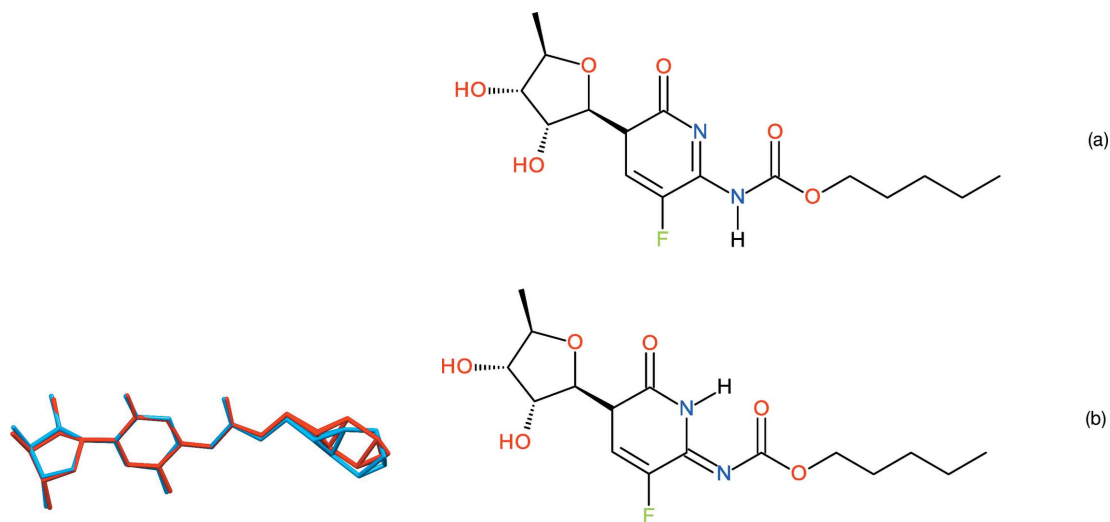


Figure 2
Schemes for the tautomeric forms of capecitabine (a) assumed in the powder-diffraction study and (b) established in the single-crystal study of Malińska *et al.* (2014).

the disordered part of the molecule (Fig. 1). Since single-crystal diffraction is more sensitive to H atoms than powder diffraction, Malinska *et al.* (2014) were able to locate the H atoms directly. This indicated a different tautomeric form of capecitabine to that assumed in our study, and as they pointed out, we had therefore placed one H atom wrongly.

In our defence, in the powder study, we placed the H atoms geometrically according to a reasonable chemical structure for capecitabine, which shows the tautomeric H atom attached to the N atom of the carbamate group and the plausible formation of an intermolecular N–H···O hydrogen bond. As shown by Malińska *et al.* (2014), the H atom is actually located on the N atom of the pyrimidine ring (Fig. 2), thereby forming an intramolecular N–H···O link.

With respect to the fact that structure solution from powder diffraction data is based on the proposed molecular structure, readers should beware of the incorrectly placed H atom in Rohlicek *et al.* (2009) and they should be also beware of the wrong enantiomer in a single-crystal study of Malińska *et al.* (2014).

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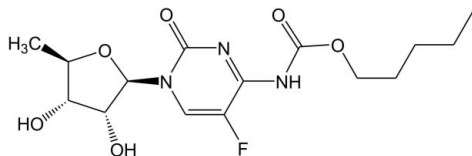
Received 3 April 2009; accepted 12 May 2009

Key indicators: powder synchrotron study; $T = 293$ K; mean $\sigma(C-C) = 0.004$ Å; disorder in main residue; R factor = 0.055; wR factor = 0.074; data-to-parameter ratio = 5.5.

In the title compound [systematic name 5-deoxy-5-fluoro-N-(pentylloxycarbonyl)cytidine], $C_{15}H_{22}FN_3O_6$, the pentyl chain is disordered over two positions with refined occupancies of 0.53 (5) and 0.47 (5). The furan ring assumes an envelope conformation. In the crystal, intermolecular $N-H \cdots O$ hydrogen bonds link the molecules into chains propagating along the b axis. The crystal packing exhibits electrostatic interactions between the 5-fluoropyrimidin-2(1*H*)-one fragments of neighbouring molecules as indicated by short $O \cdots C$ [2.875 (3) and 2.961 (3) Å] and $F \cdots C$ [2.886 (3) Å] contacts.

Related literature

Capecitabine is the first FDA-approved oral chemotherapy for the treatment for some types of cancer, including advanced bowel cancer or breast cancer, see: Wagstaff *et al.* (2003); Jones *et al.* (2004).



Experimental

Crystal data

$C_{15}H_{22}FN_3O_6$
 $M_r = 359.35$
Orthorhombic, $P2_12_12_1$
 $a = 5.20527$ (2) Å
 $b = 9.52235$ (4) Å
 $c = 34.77985$ (13) Å
 $V = 1723.91$ (1) Å³

$Z = 4$
Synchrotron radiation
 $\lambda = 0.79483$ (4) Å
 $\mu = 0.15$ mm⁻¹
 $T = 293$ K
Specimen shape: cylinder
40 × 1 × 1 mm

Specimen prepared at 101 kPa
Specimen prepared at 293 K

Particle morphology: no specific habit, white

Data collection

ID31 ESRF Grenoble diffractometer
Specimen mounting: 1.0 mm borosilicate glass capillary
Specimen mounted in transmission mode

Scan method: step
Absorption correction: none
 $2\theta_{\min} = 1.0$, $2\theta_{\max} = 35.0^\circ$
Increment in $2\theta = 0.003^\circ$

Refinement

$R_p = 0.055$
 $R_{wp} = 0.074$
 $R_{exp} = 0.036$
 $R_B = 0.102$
 $S = 2.11$
Wavelength of incident radiation: 0.79483(4) Å
Excluded region(s): no
Profile function: Pseudo-Voigt
profile coefficients as parameterized in Thompson *et al.*

(1987), asymmetry correction according to Finger *et al.* (1994)
499 reflections
91 parameters
77 restraints
H-atom parameters not refined
Preferred orientation correction: March–Dollase (Dollase, 1986); direction of preferred orientation 001, texture parameter $r = 1.03$ (1)

Table 1

Hydrogen-bond geometry (Å, °).

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
$N17-H171 \cdots O8^i$	0.860	1.956	2.797 (5)	170

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

Data collection: *ESRF SPEC package*; cell refinement: *GSAS* (Larson & Von Dreele, 1994); data reduction: *CRYSFIRE2004* (Shirley, 2000) and *MOPAC* (Dewar *et al.*, 1985); program(s) used to solve structure: *FOX* (Favre-Nicolin & Černý, 2002); program(s) used to refine structure: *GSAS*; molecular graphics: *Mercury* (Macrae *et al.*, 2006) and *PLATON* (Spek, 2009); software used to prepare material for publication: *enCIFer* (Allen *et al.*, 2004).

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: CV2544).

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supporting information

Acta Cryst. (2009). E65, o1325–o1326 [doi:10.1107/S1600536809017905]

Capecitabine from X-ray powder synchrotron data

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S1. Comment

Capecitabine is the first FDA-approved oral chemotherapy for the treatment for some types of cancer, including advanced bowel cancer or breast cancer (Wagstaff *et al.*, 2003; Jones *et al.*, 2004). Capecitabine is 5-deoxy-5-fluoro-*N*-[(pentyl-oxy)carbonyl]-cytidine and *in vivo* is enzymatically converted to the active drug 5-fluorouracil. Crystal structure determination of capecitabine was not reported yet. In this paper we report crystal structure determination of the title compound from the powder diffraction data by using synchrotron radiation.

The asymmetric unit consists of one molecule of capecitabine (Fig 1). The crystal packing is stabilized by intermolecular interactions - electrostatic interactions proved by short O \cdots C and F \cdots C contacts (Table 1) and N—H \cdots O hydrogen bonds (Table 2).

S2. Experimental

Samples of crystalline capecitabine were prepared by two methods, *a* and *b*, respectively. Method *a*: capecitabine (10 g) was dissolved in EtOH (80 g). The solution was concentrated under reduced pressure to a residual volume of 25 ml and kept under stirring overnight. The solid was filtered off and dried at room temperature furnishing capecitabine (6 g). Method *b*: capecitabine (18 g) was dissolved in DCM (200 g) and the solution was evaporated to dryness under reduced pressure. The residue was taken up with toluene (400 g) and about 150 g of solvent were distilled off. The solution was heated up to 50°C and then allowed to 3 spontaneously cool to 25°C. After cooling to 0°C, the solid was filtered off, washed with toluene and dried at 60°C under vacuum to constant weight furnishing capecitabine (16.5 g).

S3. Refinement

Both crystallization procedures lead to one polycrystalline form of capecitabine. It was confirmed by measuring on X-Ray powder diffractometer PANalytical Xpert Pro, Cu *K* α radiation ($\lambda = 1.541874$ Å). Attempts to determine the structure from these data were unsuccessful probably due to flexible molecule of capecitabine and low resolution of these data. The powder obtained by the first "a" procedure was used for structure determination. X-Ray diffraction data were collected on the high resolution diffractometer ID31 of the European Synchrotron Radiation Facility. The monochromatic wavelength was fixed at 0.79483 (4) Å. Si (111) crystal multi-analyser combined with Si (111) monochromator was used (beam offset angle $\alpha = 2^\circ$). A rotating 1-mm-diameter borosilicate glass capillary with capecitabine powder was used for the experiment. Data were measured from $1.002^\circ 2\theta$ to $34.998^\circ 2\theta$ at the room temperature, steps scans was set to $0.003^\circ 2\theta$.

First 20 peaks were used by CRYSFIRE 2004 package (Shirley, 2000) to get a list of possible lattice parameters. The most probable result was selected ($a = 5.21$ Å, $b = 9.52$ Å, $c = 34.79$ Å, $V = 1724$ Å³, FOM (20) = 330). If 15 Å³ are used as an atomic volume for C, N, O and F and 5 Å³ as a volume for hydrogen atom, the approximate molecular volume is

485 Å³. The found volume of 1724 Å³ suggests that there are four molecules in the unit cell ($Z = 4$). $P2_12_12_1$ space group was selected on the basis of peaks extinction and on the basis of agreement of the Le-bail fit. The structure was solved in program FOX (Favre-Nicolin & Černý, 2002) using parallel tempering algorithm. The initial model was generated by AM1 computing method implemented in program MOPAC (Dewar *et al.*, 1985). For the solution process hydrogen atoms were removed. This model was restrained with bonds and angles restraints, automatically generated by program FOX. The refinement was carried out in *GSAS* (Larson & Von Dreele, 1994). Hydrogen atoms were added in positions based on geometry and structure was restrained by bonds and angles restraints. Five planar restraints for sp^2 hybridization were used (O20/C18/O19/N17, N17/C13/N14/C12, C13/C12/F16/C11, N14/C10/O15/N9 and C4/N9/C10/C11). Due to relatively high U_{iso} thermal parameters of alkyl chain (C21—C25) the structure was refined with two disordered chains (C21—C25 and C21a—C25a) with occupancy factors 0.53 (5) and 0.47 (5). U_{iso} thermal parameters were constrained just for atoms in disordered chains by this way (C21/C21a, C22/C22a, C23/C23a, C24/C24a, C25/C25a). At the final stage atomic coordinates of non-hydrogen atoms were refined to the final agreement factors: $R_p=0.055$ and $R_{wp}=0.0743$. The diffraction profiles and the differences between the measured and calculated profiles are shown in Fig. 2.

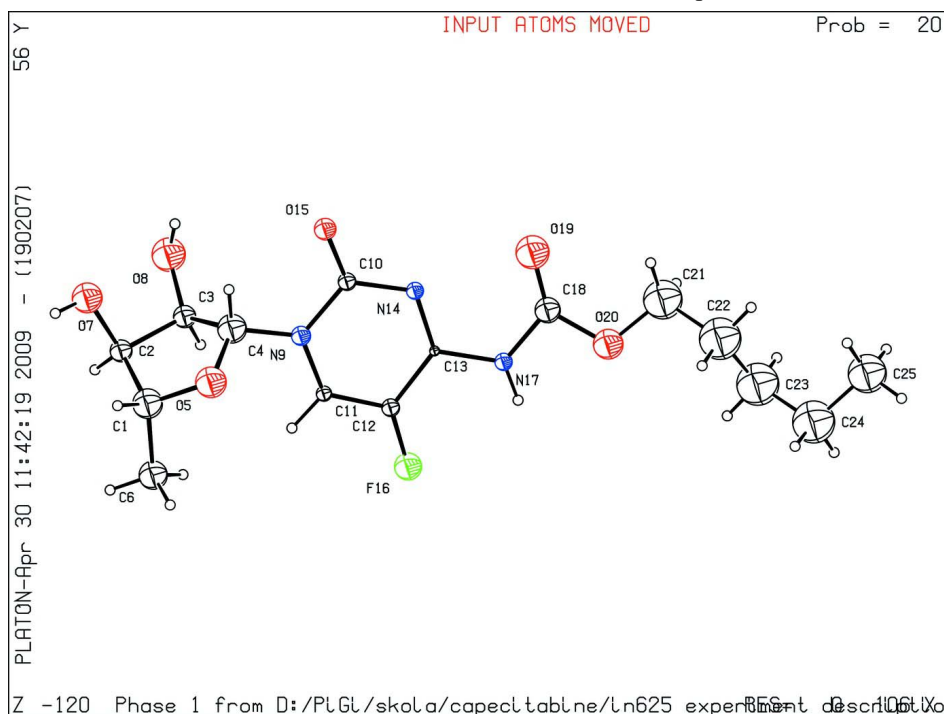
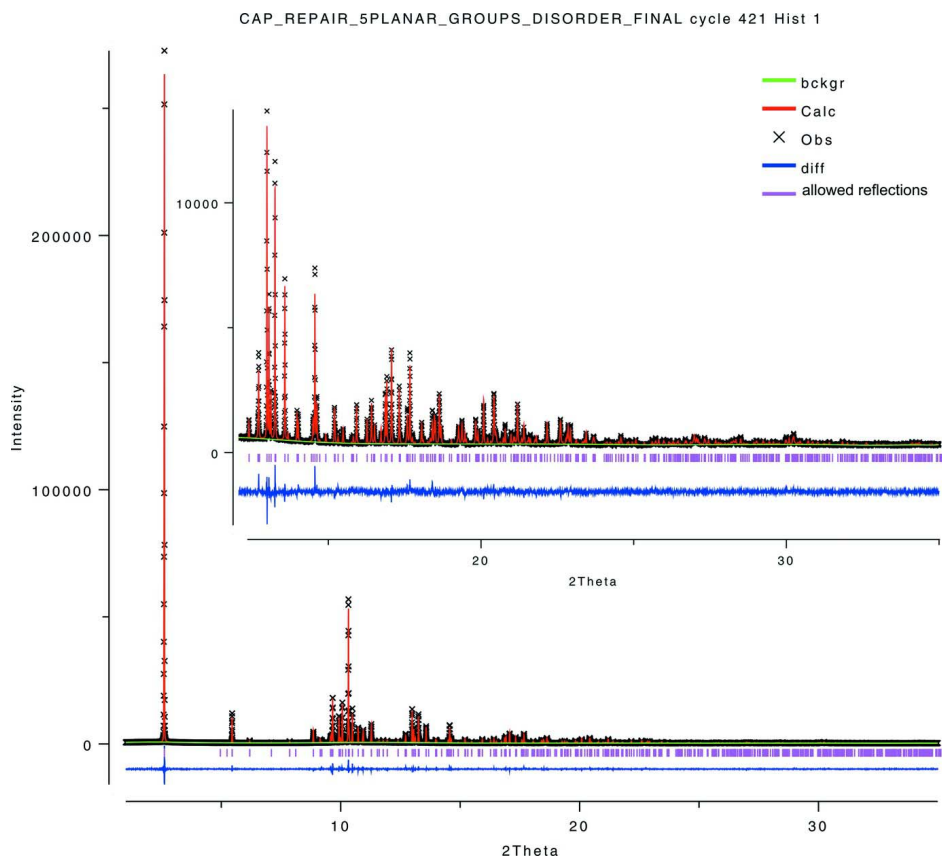


Figure 1

The molecular structure of capecitabine showing the atomic numbering. Displacement spheres are drawn at the 20% probability level. Only major part of the disordered pentyl chain is shown.

**Figure 2**

The final Rietveld plot showing the measured data (black thin-plus), calculated data (red line) and difference curve (blue line). Calculated positions of the reflections are shown by vertical bars.

5-deoxy-5-fluoro-*N*-(pentylxycarbonyl)cytidine

Crystal data

$C_{15}H_{22}FN_3O_6$

$M_r = 359.35$

Orthorhombic, $P2_12_12_1$

$a = 5.20527(2) \text{ \AA}$

$b = 9.52235(4) \text{ \AA}$

$c = 34.77985(13) \text{ \AA}$

$V = 1723.91(1) \text{ \AA}^3$

$Z = 4$

$F(000) = 760$

Data collection

ID31 ESRF Grenoble
diffractometer

Radiation source: X-Ray

Si(111) monochromator

$D_x = 1.385 \text{ Mg m}^{-3}$

Synchrotron radiation, $\lambda = 0.79483(4) \text{ \AA}$

$\mu = 0.15 \text{ mm}^{-1}$

$T = 293 \text{ K}$

Particle morphology: no specific habit
white

cylinder, $40 \times 1 \text{ mm}$

Specimen preparation: Prepared at 293 K and
101 kPa

Specimen mounting: 1.0 mm borosilicate glass
capillary

Data collection mode: transmission

Scan method: step

$2\theta_{\min} = 1.000^\circ$, $2\theta_{\max} = 34.996^\circ$, $2\theta_{\text{step}} = 0.003^\circ$

Refinement

Least-squares matrix: full

$R_p = 0.055$

$R_{wp} = 0.074$

$R_{exp} = 0.036$

$R_{Bragg} = 0.102$

$\chi^2 = 4.452$

11333 data points

Excluded region(s): no

Profile function: Pseudo-Voigt profile

coefficients as parameterized in Thompson *et al.*

(1987), asymmetry correction according to

Finger *et al.* (1994)

91 parameters

77 restraints

6 constraints

H-atom parameters not refined

Weighting scheme based on measured s.u.'s $w =$

$1/\sigma(Y_{obs})^2$

$(\Delta/\sigma)_{max} = 0.05$

Background function: Shifted Chebyshev

Preferred orientation correction: March–Dollase

(Dollase, 1986); direction of preferred

orientation 001, texture parameter $r = 1.03(1)$

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	U_{iso}^*/U_{eq}	Occ. (<1)
C1	−0.0205 (8)	0.8964 (3)	0.86415 (10)	0.087 (5)*	
C2	0.0063 (7)	0.7423 (4)	0.87424 (8)	0.048 (5)*	
C3	0.0924 (6)	0.6753 (3)	0.83655 (8)	0.049 (4)*	
C4	−0.0166 (5)	0.7766 (2)	0.80775 (7)	0.081 (5)*	
O5	−0.0717 (9)	0.9090 (3)	0.82416 (10)	0.093 (3)*	
C6	0.2118 (13)	0.9888 (6)	0.87530 (18)	0.079 (4)*	
O7	−0.2355 (9)	0.6775 (5)	0.88107 (14)	0.088 (3)*	
O8	0.0594 (11)	0.5279 (3)	0.83793 (13)	0.109 (3)*	
N9	0.1175 (4)	0.79531 (18)	0.77283 (7)	0.036 (4)*	
C10	0.0276 (4)	0.73076 (17)	0.73805 (7)	0.030 (4)*	
C11	0.3307 (5)	0.87392 (18)	0.77201 (7)	0.023 (4)*	
C12	0.4772 (3)	0.90315 (14)	0.73950 (6)	0.031 (4)*	
C13	0.3691 (3)	0.83732 (13)	0.70512 (6)	0.010 (4)*	
N14	0.1675 (4)	0.75150 (16)	0.70410 (6)	0.028 (4)*	
O15	−0.1690 (5)	0.6596 (2)	0.73930 (11)	0.046 (3)*	
F16	0.6861 (5)	0.98180 (17)	0.74183 (10)	0.072 (2)*	
N17	0.4922 (3)	0.86898 (14)	0.67035 (6)	0.030 (3)*	
C18	0.4009 (4)	0.8094 (2)	0.63692 (7)	0.063 (5)*	
O19	0.2448 (4)	0.7158 (3)	0.63482 (12)	0.108 (3)*	
O20	0.5359 (5)	0.8859 (3)	0.60977 (10)	0.087 (4)*	
C21	0.491 (4)	0.8346 (15)	0.57240 (14)	0.146 (6)*	0.53 (5)
C22	0.524 (3)	0.957 (2)	0.5449 (2)	0.169 (8)*	0.53 (5)
C23	0.801 (3)	0.9940 (19)	0.5361 (5)	0.174 (9)*	0.53 (5)
C24	0.817 (4)	1.1183 (13)	0.5087 (4)	0.174 (10)*	0.53 (5)
C25	0.700 (5)	1.082 (2)	0.4695 (5)	0.143 (9)*	0.53 (5)
C21a	0.518 (5)	0.8251 (19)	0.57299 (18)	0.146 (6)*	0.47 (5)
C22a	0.680 (3)	0.9142 (19)	0.54603 (17)	0.169 (8)*	0.47 (5)
C23a	0.560 (3)	0.939 (2)	0.5068 (4)	0.174 (9)*	0.47 (5)
C24a	0.764 (5)	0.9452 (15)	0.4756 (2)	0.174 (10)*	0.47 (5)
C25a	0.925 (4)	1.079 (2)	0.4786 (7)	0.143 (9)*	0.47 (5)
H251	0.7123	1.1617	0.453	0.25*	0.53 (5)
H252	0.5245	1.0576	0.4727	0.25*	0.53 (5)
H253	0.7906	1.0057	0.4585	0.25*	0.53 (5)

H241	0.7261	1.1953	0.5195	0.25*	0.53 (5)
H242	0.9921	1.1435	0.5053	0.25*	0.53 (5)
H231	0.8866	1.0173	0.5594	0.25*	0.53 (5)
H232	0.8831	0.9152	0.5246	0.25*	0.53 (5)
H221	0.4433	1.0371	0.5559	0.25*	0.53 (5)
H222	0.4406	0.9338	0.5214	0.25*	0.53 (5)
H211	0.3216	0.7981	0.5706	0.25*	0.53 (5)
H212	0.6111	0.7627	0.5664	0.25*	0.53 (5)
H61	0.1794	1.0833	0.868	0.1*	
H62	0.2378	0.9842	0.9023	0.1*	
H63	0.361	0.9557	0.8624	0.1*	
H21	0.1249	0.7267	0.8946	0.075*	
H31	0.273	0.6894	0.8356	0.075*	
H11	-0.166	0.9315	0.8775	0.12*	
H41	-0.1786	0.7386	0.8007	0.12*	
H111	0.3869	0.9132	0.7957	0.03*	
H171	0.6224	0.9246	0.6699	0.04*	
H82	-0.0753	0.5066	0.8272	0.1*	
H72	-0.216	0.592	0.883	0.12*	
H2511	1.0505	1.0802	0.4588	0.25*	0.47 (5)
H2512	1.008	1.082	0.5029	0.25*	0.47 (5)
H2513	0.8164	1.1589	0.476	0.25*	0.47 (5)
H2411	0.874	0.8661	0.478	0.25*	0.47 (5)
H2412	0.6824	0.943	0.4511	0.25*	0.47 (5)
H2311	0.4682	1.0252	0.5072	0.25*	0.47 (5)
H2312	0.4442	0.8643	0.5013	0.25*	0.47 (5)
H2211	0.7075	1.0029	0.5578	0.25*	0.47 (5)
H2212	0.8402	0.8684	0.5424	0.25*	0.47 (5)
H2111	0.5817	0.7316	0.5736	0.25*	0.47 (5)
H2112	0.3442	0.8245	0.5647	0.25*	0.47 (5)

Geometric parameters (Å, °)

C1—C2	1.515 (5)	O20—C21	1.408 (2)
C1—O5	1.421 (5)	O20—C21a	1.407 (2)
C1—C6	1.545 (7)	C21—C22	1.518 (2)
C1—H11	0.950	C21—H211	0.949 (16)
C2—C3	1.525 (4)	C21—H212	0.95 (2)
C2—O7	1.422 (6)	C22—C23	1.520 (2)
C2—H21	0.950	C22—H221	0.95 (2)
C3—C4	1.502 (4)	C22—H222	0.950 (9)
C3—O8	1.413 (4)	C23—C24	1.522 (2)
C3—H31	0.950	C23—H231	0.950 (19)
C4—O5	1.413 (4)	C23—H232	0.95 (2)
C4—N9	1.4123 (19)	C24—H241	0.949 (19)
C4—H41	0.950	C24—H242	0.95 (2)
C6—H61	0.950	C25—C24	1.530 (2)
C6—H62	0.950	C25—H251	0.951 (19)

C6—H63	0.950	C25—H252	0.95 (3)
O7—H72	0.820	C25—H253	0.95 (2)
O8—H82	0.820	C21a—C22a	1.519 (2)
N9—C10	1.4352 (18)	C21a—H2111	0.95 (3)
N9—C11	1.3389 (19)	C21a—H2112	0.95 (3)
C10—N14	1.4015 (19)	C22a—C23a	1.520 (2)
C10—O15	1.2282 (19)	C22a—H2211	0.950 (15)
C11—C12	1.3919 (19)	C22a—H2212	0.95 (2)
C11—H111	0.950	C23a—C24a	1.523 (2)
C12—C13	1.4625 (19)	C23a—H2311	0.95 (2)
C12—F16	1.3228 (19)	C23a—H2312	0.950 (18)
C13—N14	1.3305 (18)	C24a—C25a	1.530 (2)
C13—N17	1.4013 (19)	C24a—H2411	0.95 (2)
N17—C18	1.3783 (19)	C24a—H2412	0.952 (18)
N17—H171	0.860	C25a—H2511	0.950 (19)
C18—O19	1.208 (2)	C25a—H2512	0.95 (3)
C18—O20	1.384 (2)	C25a—H2513	0.95 (3)
O15...C12 ⁱ	2.961 (3)	O15...C11 ⁱⁱⁱ	2.875 (3)
F16...C10 ⁱⁱ	2.886 (3)		
C2—C1—O5	109.0 (3)	O20—C21—H212	110.1 (17)
C2—C1—C6	114.9 (2)	C22—C21—H211	110.1 (16)
C2—C1—H11	107.52	C22—C21—H212	109.9 (6)
O5—C1—C6	110.2 (2)	H211—C21—H212	109.4 (9)
O5—C1—H11	107.4	C21—C22—C23	114.3 (2)
C6—C1—H11	107.5	C21—C22—H221	108.2 (6)
C1—C2—C3	103.46 (14)	C21—C22—H222	108.2 (14)
C1—C2—O7	112.16 (19)	C23—C22—H221	108.3 (14)
C1—C2—H21	112.53	C23—C22—H222	108.3 (12)
C3—C2—O7	102.85 (18)	H221—C22—H222	109.5 (16)
C3—C2—H21	112.59	C22—C23—C24	110.9 (2)
O7—C2—H21	112.5	C22—C23—H231	109.1 (13)
C2—C3—C4	101.19 (13)	C22—C23—H232	109.1 (15)
C2—C3—O8	110.48 (18)	C24—C23—H231	109.1 (15)
C2—C3—H31	105.17	C24—C23—H232	109.1 (12)
C4—C3—O8	127.86 (19)	H231—C23—H232	109.5 (16)
C4—C3—H31	105.07	C23—C24—C25	111.3 (2)
O8—C3—H31	105.13	C23—C24—H241	109.1 (12)
C3—C4—O5	112.34 (14)	C23—C24—H242	109.0 (16)
C3—C4—N9	117.90 (12)	C25—C24—H241	109 (2)
C3—C4—H41	105.26	C25—C24—H242	109.0 (17)
O5—C4—N9	109.57 (17)	H241—C24—H242	109.4 (11)
O5—C4—H41	105.29	C24—C25—H251	110 (2)
N9—C4—H41	105.37	C24—C25—H252	110 (2)
C1—O5—C4	106.4 (3)	C24—C25—H253	109.6 (17)
C1—C6—H61	109.5	H251—C25—H252	109.3 (19)
C1—C6—H62	109.5	H251—C25—H253	110 (2)

C1—C6—H63	109.4	H252—C25—H253	109 (2)
H61—C6—H62	109.4	O20—C21a—C22a	107.2 (2)
H61—C6—H63	109.4	O20—C21a—H2111	110.1 (16)
H62—C6—H63	109.6	O20—C21a—H2112	109.9 (18)
C2—O7—H72	109.5	C22a—C21a—H2111	110.2 (17)
C3—O8—H82	109.47	C22a—C21a—H2112	110.1 (13)
C4—N9—C10	120.62 (14)	H2111—C21a—H2112	109.4 (6)
C4—N9—C11	119.91 (14)	C21a—C22a—C23a	114.4 (2)
C10—N9—C11	119.47 (12)	C21a—C22a—H2211	108.3 (6)
N9—C10—N14	118.71 (13)	C21a—C22a—H2212	108.2 (15)
N9—C10—O15	118.59 (15)	C23a—C22a—H2211	108.2 (19)
N14—C10—O15	122.71 (15)	C23a—C22a—H2212	108.3 (10)
N9—C11—C12	125.65 (14)	H2211—C22a—H2212	109.4 (10)
N9—C11—H111	117.16	C22a—C23a—C24a	111.0 (2)
C12—C11—H111	117.19	C22a—C23a—H2311	109 (2)
C11—C12—C13	111.59 (12)	C22a—C23a—H2312	109.0 (11)
C11—C12—F16	120.89 (15)	C24a—C23a—H2311	109.1 (12)
C13—C12—F16	127.52 (14)	C24a—C23a—H2312	109.2 (19)
C12—C13—N14	126.04 (12)	H2311—C23a—H2312	109.5 (16)
C12—C13—N17	115.94 (14)	C23a—C24a—C25a	111.4 (2)
N14—C13—N17	118.02 (18)	C23a—C24a—H2411	109.0 (10)
C10—N14—C13	118.29 (13)	C23a—C24a—H2412	109 (2)
C13—N17—C18	118.81 (13)	C25a—C24a—H2411	109 (3)
C13—N17—H171	120.56	C25a—C24a—H2412	109.0 (16)
C18—N17—H171	120.63	H2411—C24a—H2412	109.4 (11)
N17—C18—O19	125.88 (16)	C24a—C25a—H2511	110 (2)
N17—C18—O20	100.60 (15)	C24a—C25a—H2512	110 (2)
O19—C18—O20	133.52 (16)	C24a—C25a—H2513	109.6 (17)
C18—O20—C21	111.3 (2)	H2511—C25a—H2512	109 (2)
C18—O20—C21a	111.7 (2)	H2511—C25a—H2513	109 (2)
O20—C21—C22	107.3 (2)	H2512—C25a—H2513	110 (2)
O20—C21—H211	110.0 (9)		

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

Hydrogen-bond geometry ($\text{\AA}, ^\circ$)

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
N17—H171 \cdots O8 ⁱⁱ	0.860	1.956	2.797 (5)	170

Symmetry code: (ii) $-x+1, y+1/2, -z+3/2$.