Acta Cryst E CRYSTALLOGRAPHIC COMMUNICATIONS

ISSN 2056-9890

Crystal structure of (*RS*)-4-(3-carboxy-1-ethyl-6,8-difluoro-4-oxo-1,4-dihydroquinolin-7-yl)-2-methylpiperazin-1-ium 3-carboxy-5-fluorobenzoate

Sheng Feng,[a] Gui-Liang Zhu,[a] Jia-Jia Sun,[a] Chen Chen[b] and Zhi-Hui Zhang[b]*

[a]School of Environmental and Safety Engineering, Changzhou University, Changzhou, 213164, People's Republic of China, and [b]Jiangsu Key Laboratory of Advanced Catalytic Materials and Technology, Changzhou, University, Changzhou 213164, People's Republic of China. *Correspondence e-mail: zhangzh@cczu.edu.cn

Received 29 October 2018
Accepted 29 November 2018

Edited by M. Weil, Vienna University of Technology, Austria

Keywords: crystal structure; proton transfer; lomefloxacin; hydrogen-bonded network.

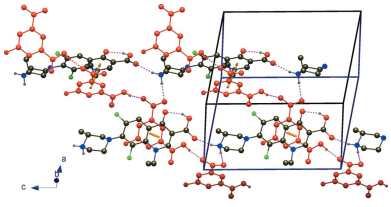
CCDC reference: 1025160

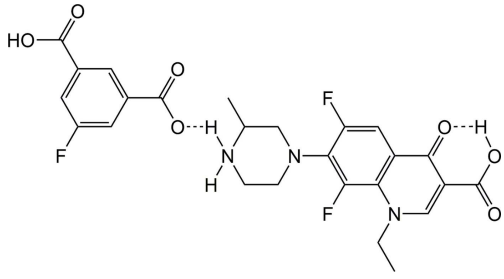
Supporting information: this article has supporting information at journals.iucr.org/e

In the title organic salt, $C_{17}H_{20}F_2N_3O_3^+\cdot C_8H_4FO_4^-$, proton transfer leads to one protonated lomefloxacin molecule (HLf^+) and one 3-carboxy-5-fluorobenzoate (5-F-Hip$^-$) anion in the asymmetric unit. The HLf^+ cation is bent, with a dihedral angle of 38.3 (1)° between the quinoline ring and the piperazinium moiety. In the crystal, two kinds of N—H···O and O—H···O hydrogen-bonded chains cross-link each other to produce a three-dimensional network structure that is additionally stabilized by weak C—H···O and C—H···F hydrogen bonds, as well as π–π interactions. The methyl group attached to the piperazinium ring is disordered over two sets of sites [refined ratio: 0.645 (5):0.335 (5)], indicating the presence of both enantiomers of the cation in the structure.

1. Chemical context

Lomefloxacin [Lf; systematic name: (*RS*)-4-(3-carboxy-1-ethyl-6,8-difluoro-4-oxo-1,4-dihydroquinolin-7-yl)-2-methylpiperazine] belongs to the fluoroquinolones that represent an important family of highly effective broad-spectrum antibacterial agents (Ross & Riley, 1990; Reddy *et al.*, 2011; Huang *et al.*, 2013). Lomefloxacin is very useful for the treatment of a variety of infections, although its therapeutic action as a drug is limited due to poor aqueous solubility (1.03 mg ml^{-1}, Ross & Riley, 1990). Using salts of lomefloxacin may overcome this problem. Several binary and ternary salts of lomefloxacin have been reported with supramolecular arrangements of the cationic and anionic moieties, such as the terephthalate (Zhou *et al.*, 2006), isophthalate (Zhang *et al.*, 2015), picrate (Jasinski *et al.*, 2011) or hydrochloride (Holstein *et al.*, 2012). However, the number of compounds related to solubility improvement is rather limited (Zhang *et al.*, 2015).





In this context, we have used 3-carboxy-5-fluorobenzoic acid (5-F-H$_2$ip) for a proton-transfer reaction, and report here synthesis and crystal structure of the produced salt $(HLf)^+\cdot$(5-F-Hip$^-$), (I).

OPEN ACCESS

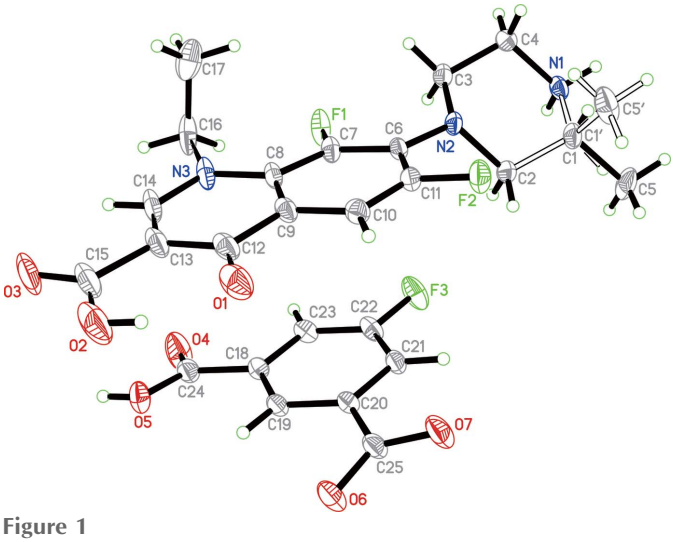


Figure 1
Molecular structures of the cation and anion in the title salt. Displacement ellipsoids are drawn at the 30% probability level.

2. Structural commentary

The structures of the molecular entities of (I) are displayed in Fig. 1. Unlike other lomefloxacin salts (Zhang *et al.*, 2015), the title compound reveals no guest solvents residing in the crystal structure. In the asymmetric unit, there is one HLf^{+} cation and one 5-F-Hip^{-} anion, *i.e.* only one proton has been transferred from the free acid. Within the HLf^{+} moiety, a non-planar conformation of the molecule is formed with a dihedral angle of 38.3 (1)° between the aromatic ring plane and the piperazinium ring (the latter exhibits a chair conformation). An intramolecular *S*(6) hydrogen-bonding pattern (Etter *et al.*, 1990) is found between the carboxylic group and the carbonyl O atom (O2—H2···O1; Table 1). The 5-F-Hip^{-} anion is nearly planar (r.m.s. deviation = 0.132 Å), with the highest deviation of 0.2645 (13) Å for the carboxylate O6 atom.

Table 1
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O5—H5···O7^{i}	0.82	1.75	2.557 (2)	167
O2—H2···O1	0.82	1.78	2.535 (3)	153
N1—H1*B*···O7^{ii}	0.89	2.48	3.046 (2)	122
N1—H1*B*···O6^{ii}	0.89	1.91	2.790 (2)	170
N1—H1*A*···O3^{iii}	0.89	1.94	2.811 (2)	165
C21—H21···O4^{iv}	0.93	2.61	3.534 (3)	173
C17—H17*C*···F1	0.96	2.45	2.985 (3)	115
C17—H17*B*···F3^{v}	0.96	2.53	3.380 (3)	148
C16—H16*B*···F1^{v}	0.97	2.48	3.394 (3)	157
C16—H16*B*···F1	0.97	2.16	2.682 (2)	112
C16—H16*A*···O6^{vi}	0.97	2.35	3.287 (3)	162
C14—H14···O6^{vi}	0.93	2.59	3.448 (3)	154
C4—H4*A*···O4^{v}	0.97	2.60	3.274 (3)	127
C2—H2*B*···F2	0.97	2.30	2.883 (2)	118
C2—H2*A*···F3	0.97	2.57	3.078 (2)	113

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

3. Supramolecular features

In the crystal structure, N1—H1*A*···O3^{iii} interactions between the amino function of the piperazinium moiety and the non-protonated O atom of the carboxylic group of a neighboring HLf^{+} cation result in a head-to-tail chain motif with descriptor *C*(13). Adjacent 5-F-Hip^{-} moieties also form a head-to-tail chain, based on a *C*(8) pattern, involving O5—H5···O7^{i} bonds between the carboxylic acid function and the carboxylate function. The two kinds of chains interlink with each other through N1—H1*B*···O6^{ii} interactions between the second H atom of the amino group of the cation and one of the carboxylate O atoms of the anion to form a three-dimensional network structure. Within this array (Fig. 2), additional weak C—H···O and C—H···F interactions are present (Table 1) as additional stabilization forces, along with π–π interactions between fluoroquinolone benzene rings of the cations and and

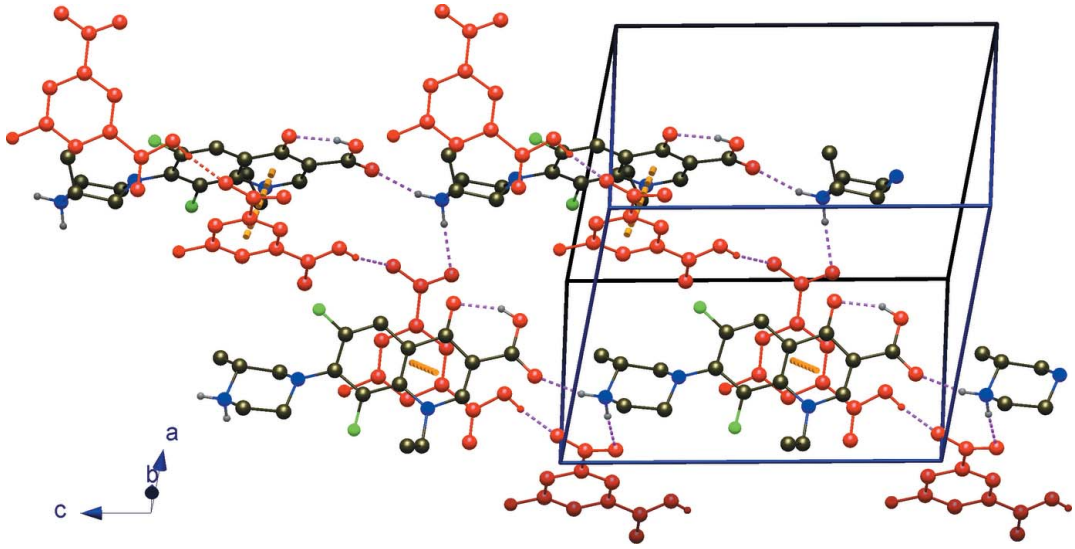


Figure 2
A perspective view of (I) showing the N—H···O and O—H···O hydrogen-bonding interactions (dotted lines) between the two kinds of chains. 'Acidic' chains, *i.e.* chains involving only the anion, are shown in red for clarity.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{17}H_{20}F_2N_3O_3^+\cdot C_8H_4FO_4^-$
M_r	535.47
Crystal system, space group	Monoclinic, $P2_1/n$
Temperature (K)	296
a, b, c (Å)	10.4324 (12), 16.5656 (19), 14.0448 (17)
β (°)	100.707 (3)
V (Å^3)	2384.9 (5)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.13
Crystal size (mm)	0.22 × 0.20 × 0.16
Data collection	
Diffractometer	Bruker APEXII CCD
Absorption correction	Multi-scan (*SADABS*; Bruker, 2010)
T_{min}, T_{max}	0.970, 0.980
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	16570, 6292, 4335
R_{int}	0.035
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.711
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.054, 0.161, 0.98
No. of reflections	6292
No. of parameters	358
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.29, −0.28

Computer programs: *APEX2* and *SAINT* (Bruker, 2010), *SHELXS97* and *SHELXTL* (Sheldrick, 2008), *SHELXL2014* (Sheldrick, 2015) and *publCIF* (Westrip, 2010).

phenyl rings of the anions with a centroid-to-centroid separation of 3.7895 (12) Å.

4. Database survey

Two crystal structures (Zhang *et al.*, 2015) based on lomefloxacin and isophthalic acid have been reported in the CSD (Verson 5.39; Groom *et al.*, 2016) viz. CURKAD [4-(3-carboxy-1-ethyl-6,8-difluoro-4-oxo-1,4-dihydroquinolin-7-yl)-2-methylpiperazin-1-ium 3-carboxybenzoate hydrate] and CURKIL [4-(3-carboxy-1-ethyl-6,8-difluoro-4-oxo-1,4-dihydroquinolin-7-yl)-2-methylpiperazin-1-ium 2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate isophthalic acid methanol solvate monohydrate]. Both CURKAD and the title compound are proton-transfer compounds from isophthalic acids to the piperazine NH groups. In the structure of CURKIL, the isophthalic acid moiety remains protonated, and co-crystallized barbituric acid is the proton donor in this case. With respect to the supramolecular networks in these structures, the contribution of the extra fluorine atom in (I) leads to additional hydrogen bonds of the type C—H···F.

5. Synthesis and crystallization

A methanol solution (6 ml) of 5-fluoroisophthalic acid (5-F-H_2ip; 20 mg, 0.1 mmol) was mixed with a slurry of lomefloxacin (Lf) (35 mg, 0.1 mmol) in 5 ml water under stirring. The mixture was exposed to ultrasound for *ca* 20 min, and was then filtered and left to slowly evaporate. Colourless block-like single crystals suitable for X-ray analysis were obtained after several weeks. Yield: 65% (35 mg, based on Lf). Analysis calculated for $C_{25}H_{24}F_3N_3O_7$: C, 56.08; H, 4.52; N, 7.85%. Found: C, 56.06; H, 4.50; N, 7.82%. FT–IR (KBr pellet, cm^{-1}): 3431*b*, 3070 (*w*), 2475 (*w*), 1718 (*s*), 1620 (*vs*, 1539 (*m*), 1456 (*s*), 1371 (*m*), 1275 (*s*), 1090 (*m*), 959 (*m*), 901 (*w*), 766 (*m*), 689 (*m*), 521 (*w*).

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. H atoms bonded to C were placed geometrically and refined in a riding model: C—H = 0.96–0.98 Å; U_{iso}(H) = 1.2U_{eq}(C) or 1.5U_{eq}(C-methyl). All O-bound and N-bound H atoms were initially found in difference electron-density maps, and then refined using a riding model [O—H = 0.82 Å and N—H = 0.89 Å; U_{iso}(H) = 1.2U_{eq}(N) and 1.5U_{eq}(O)]. The methyl group bound to the piperazinium ring is disordered over two positions with occupancies of 0.645 (5) and 0.355 (5).

Funding information

We acknowledge financial support from Jiangsu Key Laboratory of Advanced Catalytic Materials and Technology (grant No. BM2012110).

References

Bruker (2010). *APEX2*, *SAINT* and *SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA.
Etter, M. C., MacDonald, J. C. & Bernstein, J. (1990). *Acta Cryst.* B**46**, 256–262.
Groom, C. R., Bruno, I. J., Lightfoot, M. P. & Ward, S. C. (2016). *Acta Cryst.* B**72**, 171–179.
Holstein, J. J., Hübschle, C. B. & Dittrich, B. (2012). *CrystEngComm*, **14**, 2520–2531.
Huang, X. F., Zhang, Z. H., Zhang, Q. Q., Wang, L. Z., He, M. Y., Chen, Q., Song, G. Q., Wei, L., Wang, F. & Du, M. (2013). *CrystEngComm*, **15**, 6090–6100.
Jasinski, J. P., Butcher, R. J., Siddegowda, M. S., Yathirajan, H. S. & Hakim Al-arique, Q. N. M. (2011). *Acta Cryst.* E**67**, o483–o484.
Reddy, J. S., Ganesh, S. V., Nagalapalli, R., Dandela, R., Solomon, K. A., Kumar, K. A., Goud, N. R. & Nangia, A. (2011). *J. Pharm. Sci.* **100**, 3160–3176.
Ross, D. L. & Riley, C. M. (1990). *Int. J. Pharm.* **63**, 237–250.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Sheldrick, G. M. (2015). *Acta Cryst.* C**71**, 3–8.
Westrip, S. P. (2010). *J. Appl. Cryst.* **43**, 920–925.
Zhang, Z.-H., Zhang, Q., Zhang, Q.-Q., Chen, C., He, M.-Y., Chen, Q., Song, G.-Q., Xuan, X.-P. & Huang, X.-F. (2015). *Acta Cryst.* B**71**, 437–446.
Zhou, T., Zhao, L. & Guo, J. X. (2006). *Z. Kristallogr. New Cryst. Struct.* **221**, 495–496.

supporting information

Acta Cryst. (2019). E**75**, 68-70 [https://doi.org/10.1107/S2056989018016961]

Crystal structure of (*RS*)-4-(3-carboxy-1-ethyl-6,8-difluoro-4-oxo-1,4-dihydroquinolin-7-yl)-2-methylpiperazin-1-ium 3-carboxy-5-fluorobenzoate

Sheng Feng, Gui-Liang Zhu, Jia-Jia Sun, Chen Chen and Zhi-Hui Zhang

Computing details

Data collection: *APEX2* (Bruker, 2010); cell refinement: *SAINT* (Bruker, 2010); data reduction: *SAINT* (Bruker, 2010); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2015); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *publCIF* (Westrip, 2010).

(*RS*)-4-(3-Carboxy-1-ethyl-6,8-difluoro-4-oxo-1,4-dihydroquinolin-7-yl)-2-methylpiperazin-1-ium 3-carboxy-5-fluorobenzoate

Crystal data

$C_{17}H_{20}F_2N_3O_3^+\cdot C_8H_4FO_4^-$
$M_r = 535.47$
Monoclinic, $P2_1/n$
$a = 10.4324$ (12) Å
$b = 16.5656$ (19) Å
$c = 14.0448$ (17) Å
$\beta = 100.707$ (3)°
$V = 2384.9$ (5) Å^3
$Z = 4$
$F(000) = 1112$
$D_x = 1.491$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 5522 reflections
$\theta = 2.2$–$29.9°$
$\mu = 0.13$ mm^{-1}
$T = 296$ K
Block, colorless
0.22 × 0.20 × 0.16 mm

Data collection

Bruker APEXII CCD diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2010)
$T_{min} = 0.970$, $T_{max} = 0.980$
16570 measured reflections
6292 independent reflections
4335 reflections with $I > 2\sigma(I)$
$R_{int} = 0.035$
$\theta_{max} = 30.4°$, $\theta_{min} = 1.9°$
$h = -14\rightarrow14$
$k = -23\rightarrow21$
$l = -19\rightarrow13$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.054$
$wR(F^2) = 0.161$
$S = 0.98$
6292 reflections
358 parameters
0 restraints
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.085P)^2 + 0.686P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.29$ e Å^{-3}
$\Delta\rho_{min} = -0.28$ e Å^{-3}

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}	Occ. (<1)
C2	0.2703 (2)	0.12846 (10)	0.77391 (12)	0.0390 (4)	
H2A	0.1793	0.1429	0.7531	0.047*	
H2B	0.3232	0.1710	0.7536	0.047*	
C3	0.21645 (19)	−0.01366 (11)	0.75432 (12)	0.0385 (4)	
H3A	0.2383	−0.0636	0.7249	0.046*	
H3B	0.1251	−0.0021	0.7299	0.046*	
C4	0.23908 (19)	−0.02326 (11)	0.86352 (12)	0.0391 (4)	
H4A	0.1800	−0.0637	0.8804	0.047*	
H4B	0.3277	−0.0416	0.8868	0.047*	
C1	0.30073 (19)	0.12083 (11)	0.88315 (12)	0.0398 (4)	0.645 (5)
H1	0.3925	0.1055	0.9030	0.048*	0.645 (5)
C5	0.2784 (4)	0.1988 (2)	0.9320 (2)	0.0587 (11)	0.645 (5)
H5A	0.2890	0.1903	1.0006	0.088*	0.645 (5)
H5B	0.1915	0.2177	0.9074	0.088*	0.645 (5)
H5C	0.3403	0.2383	0.9191	0.088*	0.645 (5)
C1′	0.30073 (19)	0.12083 (11)	0.88315 (12)	0.0398 (4)	0.355 (5)
H1′	0.2728	0.1712	0.9098	0.048*	0.355 (5)
C5′	0.4401 (7)	0.1112 (5)	0.9223 (4)	0.064 (2)	0.355 (5)
H5′1	0.4858	0.1593	0.9101	0.096*	0.355 (5)
H5′2	0.4734	0.0660	0.8917	0.096*	0.355 (5)
H5′3	0.4525	0.1020	0.9909	0.096*	0.355 (5)
C6	0.32692 (16)	0.05742 (10)	0.63571 (11)	0.0314 (3)	
C7	0.25702 (16)	0.02250 (11)	0.55222 (12)	0.0348 (4)	
C8	0.29167 (16)	0.02851 (11)	0.46031 (11)	0.0360 (4)	
C9	0.39760 (17)	0.07840 (11)	0.45220 (12)	0.0375 (4)	
C10	0.46920 (18)	0.11506 (11)	0.53468 (13)	0.0378 (4)	
H10	0.5396	0.1481	0.5295	0.045*	
C11	0.43600 (17)	0.10242 (11)	0.62229 (12)	0.0354 (4)	
C12	0.4354 (2)	0.09342 (13)	0.35878 (13)	0.0468 (5)	
C13	0.3573 (2)	0.05467 (14)	0.27828 (13)	0.0511 (5)	
C14	0.2580 (2)	0.00583 (15)	0.29119 (13)	0.0533 (6)	
H14	0.2103	−0.0191	0.2366	0.064*	
C15	0.3820 (3)	0.06630 (18)	0.17808 (15)	0.0690 (8)	
C16	0.12118 (19)	−0.07161 (18)	0.37829 (15)	0.0621 (7)	
H16A	0.0763	−0.0816	0.3124	0.075*	
H16B	0.0576	−0.0514	0.4148	0.075*	
C17	0.1759 (2)	−0.14920 (18)	0.4221 (2)	0.0711 (8)	
H17A	0.2399	−0.1692	0.3869	0.107*	
H17B	0.1070	−0.1880	0.4192	0.107*	

H17C	0.2161	−0.1403	0.4885	0.107*
C18	0.15025 (16)	0.22254 (10)	0.33449 (12)	0.0331 (4)
C19	0.25938 (16)	0.27147 (10)	0.33760 (12)	0.0331 (4)
H19	0.2883	0.2841	0.2806	0.040*
C20	0.32544 (16)	0.30154 (10)	0.42577 (11)	0.0325 (3)
C21	0.28309 (17)	0.28192 (11)	0.51078 (12)	0.0352 (4)
H21	0.3271	0.3008	0.5703	0.042*
C22	0.17472 (17)	0.23394 (12)	0.50507 (12)	0.0389 (4)
C23	0.10696 (17)	0.20350 (11)	0.41930 (12)	0.0374 (4)
H23	0.0340	0.1710	0.4182	0.045*
C24	0.07378 (18)	0.18979 (11)	0.24192 (13)	0.0398 (4)
C25	0.44349 (18)	0.35535 (11)	0.43029 (12)	0.0390 (4)
F1	0.14586 (10)	−0.01682 (8)	0.56051 (8)	0.0542 (3)
F2	0.51182 (11)	0.13417 (7)	0.70199 (8)	0.0502 (3)
F3	0.13353 (12)	0.21463 (9)	0.58853 (8)	0.0600 (4)
N1	0.21749 (14)	0.05481 (9)	0.91112 (10)	0.0366 (3)
H1A	0.2354	0.0485	0.9751	0.044*
H1B	0.1339	0.0688	0.8945	0.044*
N2	0.29693 (15)	0.05198 (8)	0.72827 (10)	0.0349 (3)
N3	0.22256 (15)	−0.00954 (12)	0.37700 (10)	0.0466 (4)
O1	0.52996 (17)	0.13801 (11)	0.35126 (11)	0.0634 (4)
O2	0.4753 (2)	0.11777 (15)	0.16934 (12)	0.0864 (6)
H2	0.5061	0.1367	0.2226	0.130*
O3	0.3194 (2)	0.03032 (14)	0.10876 (11)	0.0906 (7)
O4	−0.03217 (17)	0.16034 (13)	0.23770 (11)	0.0770 (6)
O5	0.13137 (13)	0.19749 (9)	0.16727 (9)	0.0483 (3)
H5	0.0852	0.1778	0.1192	0.073*
O6	0.46630 (13)	0.38375 (9)	0.35255 (9)	0.0500 (4)
O7	0.51218 (16)	0.36907 (10)	0.51142 (10)	0.0619 (4)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C2	0.0599 (11)	0.0327 (9)	0.0257 (8)	0.0003 (8)	0.0111 (8)	−0.0032 (7)
C3	0.0511 (10)	0.0366 (9)	0.0280 (8)	−0.0052 (8)	0.0074 (7)	−0.0045 (7)
C4	0.0526 (10)	0.0355 (9)	0.0297 (8)	0.0002 (8)	0.0089 (7)	0.0023 (7)
C1	0.0533 (10)	0.0421 (10)	0.0244 (8)	−0.0045 (8)	0.0079 (7)	−0.0076 (7)
C5	0.087 (3)	0.052 (2)	0.0429 (18)	−0.0161 (17)	0.0286 (17)	−0.0244 (15)
C1′	0.0533 (10)	0.0421 (10)	0.0244 (8)	−0.0045 (8)	0.0079 (7)	−0.0076 (7)
C5′	0.066 (4)	0.091 (5)	0.033 (3)	−0.029 (4)	0.006 (3)	0.000 (3)
C6	0.0390 (8)	0.0346 (8)	0.0204 (7)	0.0060 (7)	0.0047 (6)	−0.0019 (6)
C7	0.0321 (8)	0.0470 (10)	0.0252 (8)	0.0041 (7)	0.0050 (6)	−0.0063 (7)
C8	0.0358 (8)	0.0502 (10)	0.0201 (7)	0.0152 (7)	0.0005 (6)	−0.0052 (7)
C9	0.0411 (9)	0.0482 (10)	0.0240 (8)	0.0183 (8)	0.0084 (7)	0.0030 (7)
C10	0.0411 (9)	0.0401 (9)	0.0337 (9)	0.0066 (7)	0.0111 (7)	0.0017 (7)
C11	0.0418 (9)	0.0362 (9)	0.0262 (8)	0.0040 (7)	0.0011 (7)	−0.0031 (7)
C12	0.0539 (11)	0.0578 (12)	0.0312 (9)	0.0269 (10)	0.0143 (8)	0.0094 (8)
C13	0.0613 (12)	0.0703 (14)	0.0233 (8)	0.0313 (11)	0.0119 (8)	0.0059 (8)

C14	0.0551 (12)	0.0824 (15)	0.0194 (8)	0.0299 (11)	−0.0009 (8)	−0.0088 (9)
C15	0.0890 (18)	0.0935 (19)	0.0263 (10)	0.0476 (16)	0.0155 (11)	0.0118 (11)
C16	0.0340 (10)	0.113 (2)	0.0366 (10)	0.0000 (11)	0.0000 (8)	−0.0361 (12)
C17	0.0545 (13)	0.0898 (19)	0.0727 (16)	−0.0240 (13)	0.0213 (12)	−0.0368 (15)
C18	0.0350 (8)	0.0344 (8)	0.0284 (8)	0.0011 (7)	0.0014 (7)	0.0012 (6)
C19	0.0377 (8)	0.0372 (9)	0.0236 (7)	0.0006 (7)	0.0036 (6)	0.0052 (6)
C20	0.0367 (8)	0.0331 (8)	0.0262 (8)	0.0031 (7)	0.0016 (6)	0.0046 (6)
C21	0.0406 (9)	0.0405 (9)	0.0225 (7)	0.0050 (7)	0.0010 (6)	0.0017 (6)
C22	0.0399 (9)	0.0517 (11)	0.0261 (8)	0.0057 (8)	0.0091 (7)	0.0082 (7)
C23	0.0345 (8)	0.0428 (10)	0.0344 (9)	0.0006 (7)	0.0054 (7)	0.0068 (7)
C24	0.0452 (10)	0.0417 (10)	0.0307 (8)	−0.0073 (8)	0.0023 (7)	0.0016 (7)
C25	0.0415 (9)	0.0446 (10)	0.0271 (8)	−0.0048 (8)	−0.0038 (7)	0.0082 (7)
F1	0.0424 (6)	0.0885 (9)	0.0324 (6)	−0.0148 (6)	0.0091 (5)	−0.0211 (6)
F2	0.0567 (7)	0.0588 (7)	0.0332 (6)	−0.0169 (5)	0.0034 (5)	−0.0103 (5)
F3	0.0566 (7)	0.0962 (10)	0.0305 (6)	−0.0063 (7)	0.0170 (5)	0.0108 (6)
N1	0.0432 (8)	0.0460 (8)	0.0210 (6)	0.0023 (6)	0.0072 (6)	−0.0016 (6)
N2	0.0506 (8)	0.0330 (7)	0.0219 (6)	−0.0036 (6)	0.0087 (6)	−0.0057 (5)
N3	0.0396 (8)	0.0754 (12)	0.0227 (7)	0.0143 (8)	0.0002 (6)	−0.0126 (7)
O1	0.0681 (10)	0.0823 (11)	0.0460 (8)	0.0089 (9)	0.0270 (8)	0.0126 (8)
O2	0.1021 (15)	0.1232 (18)	0.0419 (9)	0.0267 (13)	0.0340 (10)	0.0196 (10)
O3	0.1254 (16)	0.1244 (17)	0.0205 (7)	0.0381 (14)	0.0098 (9)	0.0027 (9)
O4	0.0699 (10)	0.1159 (15)	0.0427 (8)	−0.0525 (11)	0.0038 (8)	−0.0062 (9)
O5	0.0497 (8)	0.0640 (9)	0.0298 (6)	−0.0099 (6)	0.0036 (6)	−0.0103 (6)
O6	0.0497 (8)	0.0677 (9)	0.0292 (6)	−0.0176 (7)	−0.0014 (6)	0.0136 (6)
O7	0.0681 (9)	0.0778 (11)	0.0312 (7)	−0.0309 (8)	−0.0134 (7)	0.0147 (7)

Geometric parameters (Å, º)

C2—N2	1.469 (2)	C12—O1	1.252 (3)
C2—C1	1.513 (2)	C12—C13	1.419 (3)
C2—C1′	1.513 (2)	C13—C14	1.353 (3)
C2—H2A	0.9700	C13—C15	1.490 (3)
C2—H2B	0.9700	C14—N3	1.349 (2)
C3—N2	1.461 (2)	C14—H14	0.9300
C3—C4	1.516 (2)	C15—O3	1.222 (4)
C3—H3A	0.9700	C15—O2	1.317 (4)
C3—H3B	0.9700	C16—N3	1.478 (3)
C4—N1	1.492 (2)	C16—C17	1.492 (4)
C4—H4A	0.9700	C16—H16A	0.9700
C4—H4B	0.9700	C16—H16B	0.9700
C1—N1	1.494 (2)	C17—H17A	0.9600
C1—C5	1.501 (3)	C17—H17B	0.9600
C1—H1	0.9800	C17—H17C	0.9600
C5—H5A	0.9600	C18—C23	1.386 (2)
C5—H5B	0.9600	C18—C19	1.392 (2)
C5—H5C	0.9600	C18—C24	1.495 (2)
C1′—C5′	1.465 (7)	C19—C20	1.393 (2)
C1′—N1	1.494 (2)	C19—H19	0.9300

C1′—H1′	0.9800	C20—C21	1.386 (2)
C5′—H5′1	0.9600	C20—C25	1.512 (2)
C5′—H5′2	0.9600	C21—C22	1.372 (3)
C5′—H5′3	0.9600	C21—H21	0.9300
C6—C7	1.387 (2)	C22—F3	1.3594 (19)
C6—N2	1.395 (2)	C22—C23	1.374 (3)
C6—C11	1.402 (2)	C23—H23	0.9300
C7—F1	1.354 (2)	C24—O4	1.200 (2)
C7—C8	1.407 (2)	C24—O5	1.308 (2)
C8—C9	1.402 (3)	C25—O7	1.249 (2)
C8—N3	1.405 (2)	C25—O6	1.252 (2)
C9—C10	1.395 (3)	N1—H1A	0.8900
C9—C12	1.460 (2)	N1—H1B	0.8900
C10—C11	1.355 (2)	O2—H2	0.8200
C10—H10	0.9300	O5—H5	0.8200
C11—F2	1.351 (2)		

N2—C2—C1	110.44 (14)	O1—C12—C9	121.66 (19)
N2—C2—C1′	110.44 (14)	C13—C12—C9	115.34 (19)
N2—C2—H2A	109.6	C14—C13—C12	120.31 (17)
C1—C2—H2A	109.6	C14—C13—C15	118.4 (2)
N2—C2—H2B	109.6	C12—C13—C15	121.3 (2)
C1—C2—H2B	109.6	N3—C14—C13	125.18 (19)
H2A—C2—H2B	108.1	N3—C14—H14	117.4
N2—C3—C4	110.04 (14)	C13—C14—H14	117.4
N2—C3—H3A	109.7	O3—C15—O2	122.4 (2)
C4—C3—H3A	109.7	O3—C15—C13	122.0 (3)
N2—C3—H3B	109.7	O2—C15—C13	115.6 (2)
C4—C3—H3B	109.7	N3—C16—C17	112.61 (17)
H3A—C3—H3B	108.2	N3—C16—H16A	109.1
N1—C4—C3	110.75 (14)	C17—C16—H16A	109.1
N1—C4—H4A	109.5	N3—C16—H16B	109.1
C3—C4—H4A	109.5	C17—C16—H16B	109.1
N1—C4—H4B	109.5	H16A—C16—H16B	107.8
C3—C4—H4B	109.5	C16—C17—H17A	109.5
H4A—C4—H4B	108.1	C16—C17—H17B	109.5
N1—C1—C5	111.26 (18)	H17A—C17—H17B	109.5
N1—C1—C2	107.76 (14)	C16—C17—H17C	109.5
C5—C1—C2	111.7 (2)	H17A—C17—H17C	109.5
N1—C1—H1	108.7	H17B—C17—H17C	109.5
C5—C1—H1	108.7	C23—C18—C19	120.05 (15)
C2—C1—H1	108.7	C23—C18—C24	117.27 (15)
C1—C5—H5A	109.5	C19—C18—C24	122.67 (15)
C1—C5—H5B	109.5	C18—C19—C20	120.20 (15)
H5A—C5—H5B	109.5	C18—C19—H19	119.9
C1—C5—H5C	109.5	C20—C19—H19	119.9
H5A—C5—H5C	109.5	C21—C20—C19	119.84 (16)
H5B—C5—H5C	109.5	C21—C20—C25	119.31 (15)

C5′—C1′—N1	114.0 (3)	C19—C20—C25	120.85 (14)
C5′—C1′—C2	113.4 (3)	C22—C21—C20	118.46 (16)
N1—C1′—C2	107.76 (14)	C22—C21—H21	120.8
C5′—C1′—H1′	107.1	C20—C21—H21	120.8
N1—C1′—H1′	107.1	F3—C22—C21	118.36 (16)
C2—C1′—H1′	107.1	F3—C22—C23	118.42 (16)
C1′—C5′—H5′1	109.5	C21—C22—C23	123.22 (15)
C1′—C5′—H5′2	109.5	C22—C23—C18	118.23 (16)
H5′1—C5′—H5′2	109.5	C22—C23—H23	120.9
C1′—C5′—H5′3	109.5	C18—C23—H23	120.9
H5′1—C5′—H5′3	109.5	O4—C24—O5	123.81 (17)
H5′2—C5′—H5′3	109.5	O4—C24—C18	121.90 (17)
C7—C6—N2	125.94 (15)	O5—C24—C18	114.29 (15)
C7—C6—C11	114.87 (14)	O7—C25—O6	123.89 (17)
N2—C6—C11	119.18 (14)	O7—C25—C20	118.06 (15)
F1—C7—C6	116.89 (14)	O6—C25—C20	118.06 (15)
F1—C7—C8	118.88 (15)	C4—N1—C1′	111.92 (13)
C6—C7—C8	124.17 (16)	C4—N1—C1	111.92 (13)
C9—C8—N3	119.17 (15)	C4—N1—H1A	109.2
C9—C8—C7	117.20 (15)	C1—N1—H1A	109.2
N3—C8—C7	123.56 (17)	C4—N1—H1B	109.2
C10—C9—C8	119.86 (15)	C1—N1—H1B	109.2
C10—C9—C12	118.66 (18)	H1A—N1—H1B	107.9
C8—C9—C12	121.49 (17)	C6—N2—C3	121.34 (13)
C11—C10—C9	119.92 (17)	C6—N2—C2	116.36 (13)
C11—C10—H10	120.0	C3—N2—C2	111.61 (13)
C9—C10—H10	120.0	C14—N3—C8	118.45 (18)
F2—C11—C10	118.87 (16)	C14—N3—C16	117.24 (17)
F2—C11—C6	117.42 (14)	C8—N3—C16	124.05 (16)
C10—C11—C6	123.71 (16)	C15—O2—H2	109.5
O1—C12—C13	123.00 (18)	C24—O5—H5	109.5

N2—C3—C4—N1	54.3 (2)	C18—C19—C20—C25	−179.48 (16)
N2—C2—C1—N1	−59.2 (2)	C19—C20—C21—C22	−1.1 (3)
N2—C2—C1—C5	178.3 (2)	C25—C20—C21—C22	179.11 (16)
N2—C2—C1′—C5′	67.9 (4)	C20—C21—C22—F3	179.86 (15)
N2—C2—C1′—N1	−59.2 (2)	C20—C21—C22—C23	0.8 (3)
N2—C6—C7—F1	3.7 (3)	F3—C22—C23—C18	−179.23 (16)
C11—C6—C7—F1	−175.55 (15)	C21—C22—C23—C18	−0.2 (3)
N2—C6—C7—C8	−179.07 (16)	C19—C18—C23—C22	−0.2 (3)
C11—C6—C7—C8	1.7 (3)	C24—C18—C23—C22	−179.07 (16)
F1—C7—C8—C9	171.85 (15)	C23—C18—C24—O4	12.6 (3)
C6—C7—C8—C9	−5.3 (3)	C19—C18—C24—O4	−166.2 (2)
F1—C7—C8—N3	−5.2 (3)	C23—C18—C24—O5	−168.50 (16)
C6—C7—C8—N3	177.68 (16)	C19—C18—C24—O5	12.6 (3)
N3—C8—C9—C10	−178.45 (15)	C21—C20—C25—O7	12.1 (3)
C7—C8—C9—C10	4.4 (2)	C19—C20—C25—O7	−167.74 (18)
N3—C8—C9—C12	1.7 (2)	C21—C20—C25—O6	−167.64 (17)

C7—C8—C9—C12	−175.47 (15)	C19—C20—C25—O6	12.5 (3)
C8—C9—C10—C11	−0.1 (3)	C3—C4—N1—C1′	−55.9 (2)
C12—C9—C10—C11	179.77 (16)	C3—C4—N1—C1	−55.9 (2)
C9—C10—C11—F2	175.67 (15)	C5′—C1′—N1—C4	−69.3 (3)
C9—C10—C11—C6	−3.9 (3)	C2—C1′—N1—C4	57.47 (19)
C7—C6—C11—F2	−176.49 (15)	C5—C1—N1—C4	−179.7 (2)
N2—C6—C11—F2	4.2 (2)	C2—C1—N1—C4	57.47 (19)
C7—C6—C11—C10	3.1 (3)	C7—C6—N2—C3	22.2 (3)
N2—C6—C11—C10	−176.24 (16)	C11—C6—N2—C3	−158.57 (16)
C10—C9—C12—O1	0.1 (3)	C7—C6—N2—C2	−119.34 (19)
C8—C9—C12—O1	179.95 (17)	C11—C6—N2—C2	59.9 (2)
C10—C9—C12—C13	−179.44 (16)	C4—C3—N2—C6	159.44 (15)
C8—C9—C12—C13	0.4 (2)	C4—C3—N2—C2	−57.40 (19)
O1—C12—C13—C14	178.65 (19)	C1—C2—N2—C6	−153.88 (15)
C9—C12—C13—C14	−1.8 (3)	C1′—C2—N2—C6	−153.88 (15)
O1—C12—C13—C15	−1.3 (3)	C1—C2—N2—C3	61.0 (2)
C9—C12—C13—C15	178.26 (17)	C1′—C2—N2—C3	61.0 (2)
C12—C13—C14—N3	1.2 (3)	C13—C14—N3—C8	1.0 (3)
C15—C13—C14—N3	−178.91 (19)	C13—C14—N3—C16	−173.3 (2)
C14—C13—C15—O3	−3.4 (3)	C9—C8—N3—C14	−2.4 (2)
C12—C13—C15—O3	176.5 (2)	C7—C8—N3—C14	174.54 (17)
C14—C13—C15—O2	176.5 (2)	C9—C8—N3—C16	171.48 (18)
C12—C13—C15—O2	−3.6 (3)	C7—C8—N3—C16	−11.6 (3)
C23—C18—C19—C20	−0.1 (3)	C17—C16—N3—C14	104.7 (2)
C24—C18—C19—C20	178.77 (16)	C17—C16—N3—C8	−69.3 (2)
C18—C19—C20—C21	0.7 (3)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O5—H5···O7^{i}	0.82	1.75	2.557 (2)	167
O2—H2···O1	0.82	1.78	2.535 (3)	153
N1—H1*B*···O7^{ii}	0.89	2.48	3.046 (2)	122
N1—H1*B*···O6^{ii}	0.89	1.91	2.790 (2)	170
N1—H1*A*···O3^{iii}	0.89	1.94	2.811 (2)	165
C21—H21···O4^{iv}	0.93	2.61	3.534 (3)	173
C17—H17*C*···F1	0.96	2.45	2.985 (3)	115
C17—H17*B*···F3^{v}	0.96	2.53	3.380 (3)	148
C16—H16*B*···F1^{v}	0.97	2.48	3.394 (3)	157
C16—H16*B*···F1	0.97	2.16	2.682 (2)	112
C16—H16*A*···O6^{vi}	0.97	2.35	3.287 (3)	162
C14—H14···O6^{vi}	0.93	2.59	3.448 (3)	154
C4—H4*A*···O4^{v}	0.97	2.60	3.274 (3)	127
C2—H2*B*···F2	0.97	2.30	2.883 (2)	118
C2—H2*A*···F3	0.97	2.57	3.078 (2)	113

Symmetry codes: (i) *x*−1/2, −*y*+1/2, *z*−1/2; (ii) *x*−1/2, −*y*+1/2, *z*+1/2; (iii) *x*, *y*, *z*+1; (iv) *x*+1/2, −*y*+1/2, *z*+1/2; (v) −*x*, −*y*, −*z*+1; (vi) −*x*+1/2, *y*−1/2, −*z*+1/2.