Ciprofloxacin salt and salt co-crystal with dihydroxybenzoic acids

Yuda Prasetya Nugraha,[a]* Haruki Sugiyama[b,c] and Hidehiro Uekusa[d]

[a]Department of Pharmaceutics, School of Pharmacy, Bandung Institute of Technology, Bandung 40132, Indonesia, [b]Research and Education Center for Natural Sciences, Keio University, Hiyoshi, 4-1-1, Kohoku, Yokohama 223-8521, Japan, [c]Department of Life and Coordination-Complex Molecular Science, Institute for Molecular Science, Myodaiji, Okazaki 444-8787, Japan, and [d]Department of Chemistry, Tokyo Institute of Technology, 2-12-1, Ookayama, Meguro, Tokyo 152-8551, Japan. *Correspondence e-mail: yudapn@itb.ac.id

The crystal structure of two multi-component crystals of ciprofloxacin [systematic name: 1-cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)quinoline-3-carboxylic acid], a fluoroquinolone antibiotic, namely, ciprofloxacin 2,6-dihydroxybenzoate salt, $C_{17}H_{19}FN_3O_3^+ \cdot C_7H_5O_4^-$, (I), and ciprofloxacin hydrochloride–3,5-dihydroxybenzoic–water (1/1/1), $C_{17}H_{19}FN_3O_3^+ \cdot Cl^- \cdot C_7H_6O_4 \cdot H_2O$, (II), were determined. In (I) and (II), the ciprofloxacin cations are connected *via* head-to-tail N—H⋯O hydrogen bonding. Both structures show an alternating layered arrangement between ciprofloxacin and dihydroxybenzoic acid.

1. Chemical context

The design and exploration of multi-component crystals of active pharmaceutical ingredients (APIs) have gained increasing interest over recent decades. The formation of multi-component crystals, *i.e.* salts and co-crystals through a crystal-engineering approach has been continuously demonstrated as a versatile tool to improve the physicochemical properties of APIs (Kavanagh *et al.*, 2019; Putra & Uekusa, 2020; Thakur & Thakuria, 2020). Recently, the co-crystallization of salt APIs or salt co-crystal formation has been increasingly studied. Salt co-crystallization has been utilized to suppress hydrate formation of salt APIs (Nugraha & Uekusa, 2018; Fujito *et al.*, 2021). As a part of our study of salt co-crystals of APIs, we investigated multi-component crystals of ciprofloxacin. Ciprofloxacin is a Biopharmaceutics Classification System (BCS) class IV fluoroquinolone antibiotic that is widely used therapeutically as the free base and the hydrochloride salt (Olivera *et al.*, 2011).

Ciprofloxacin · 2,6-dihydroxybenzoic acid · 3,5-dihydroxybenzoic acid

2. Structural commentary

Compound (I) was obtained as an anion-exchange product between ciprofloxacin hydrochloride and 2,6-dihydrobenzoic acid in solution. 2,6-Dihydroxybenzoic acid (2,6HBA) is a
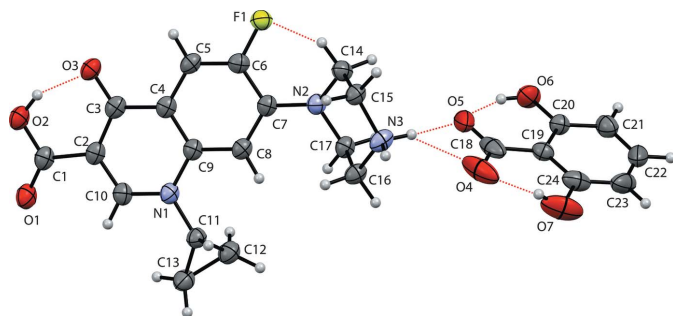
Figure 1
Displacement ellipsoid (50% probability level) drawing with the atomic labelling scheme for compound (I) showing the hydrogen bonds within the selected asymmetric unit.

Figure 3
Molecular overlay of ciprofloxacin cation in compounds (I) (red) and (II) (blue). Hydrogen atoms are omitted for clarity.

relatively strong carboxylic acid with a pK_a of 1.30 (Gdaniec *et al.*, 1994; Habibi-yangjeh *et al.*, 2005). Compound (I) crystallizes in the monoclinic space group $P2_1/c$. The asymmetric unit consists of one ciprofloxacin cation and one 2,6HBA anion (Fig. 1). The C—O distances of the ciprofloxacin carboxylic group *i.e.*, 1.218 (3) and 1.325 (3) Å indicate that it exists as the neutral carboxylic form. However, in 2,6HBA, the C–O distances are very similar *i.e.*, 1.263 (4) and 1.267 (3) Å due to resonance stabilization in the carboxylate anion (Childs *et al.*, 2007; Aakeröy *et al.*, 2006). As a result, the piperazinyl group of ciprofloxacin is protonated. Therefore, compound (I) is a salt. The formation of a salt is well-predicted by the pK_a rule (Cruz-Cabeza, 2012). The pK_a of ciprofloxacin are 6.18 and 8.73 for the carboxylic acid and the piperazinyl ring, respectively (Sun *et al.*, 2002). Therefore, salt formation is expected because the ΔpK_a between the piperazinyl ring of ciprofloxacin and the carboxylic acid of 2,6HBA is greater than 4. Similar behaviour is observed in the salicylate salt of ciprofloxacin (Surov *et al.*, 2019; Nugrahani *et al.*, 2020).

Compound (II) crystallizes in the non-centrosymmetric $P1$ space group despite the lack of a chiral centre. The asymmetric unit comprises one ciprofloxacin cation, one chloride anion and one 3,5HBA molecule, as shown in Fig. 2. In addition, one water molecule is incorporated into the crystal lattice. An anion-exchange reaction during crystallization did not occur in this system. Compared to 2,6HBA, the coformer is a weaker acid with a pK_a of 4.04 (Habibi-yangjeh *et al.*, 2005). Contrary to the previous structures, the coformer exists as a neutral molecule in the crystal. The carboxylic C18—O4 and C18—O5 distances of 2,6HBA are 1.320 (4) and 1.216 (4) Å, respec-
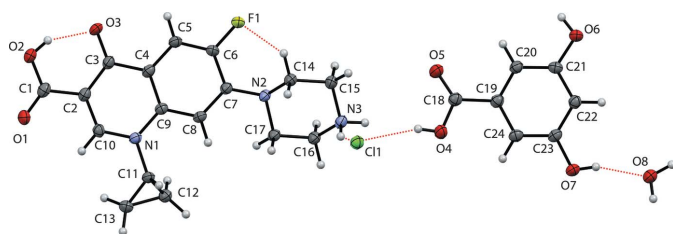
tively, confirming its neutral state. Additionally, the carboxylic C1—O1 and C1—O2 distances of ciprofloxacin, *i.e.* 1.227 (4) and 1.314 (4) Å, respectively, also confirm the neutral state of this moiety. On the other hand, the piperazinyl group is protonated. Hence, compound (II) is a salt co-crystal monohydrate of ciprofloxacin.

Compounds (I) and (II) exhibit similar conformations, as shown in Fig. 3. The molecular conformation of the ciprofloxacin molecule is governed by intramolecular O2—H2···O3 and C14—H14A···F1 hydrogen bonding (Tables 1 and 2). In both structures, the piperazinium ring exhibits a chair conformation. The main difference is the relative orientation between the piperazinium moiety and the quinolone ring. The C7—N2—C14—C15 torsion angles are 97.0 (2) and −167.8 (2)°, respectively, for compounds (I) and (II).

3. Supramolecular features

In compound (I), the carboxylate anion of 2,6HBA acts as a hydrogen-bond donor for intramolecular hydrogen bonds involving two hydroxyl groups, namely O6—H6···O5 and O7—H7···O4. The protonated nitrogen atom N3 of the piperazinyl ring is involved in the formation of trifurcated hydrogen bonds with O4, O5, and O6 of the coformer. These charge-assisted hydrogen bonds, *i.e.* N3—H3B···O4, N3—

Figure 4
Intermolecular hydrogen-bonding motifs in (I) showing infinite chains along the *a*-axis direction formed by ciprofloxacin and 2,6HBA (red). Hydrogen atoms are omitted for clarity.

Figure 2
Displacement ellipsoid (50% probability level) drawing with the atomic labelling scheme for compound (II) showing the hydrogen bonds within the selected asymmetric unit.
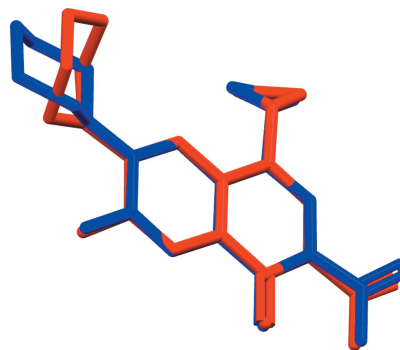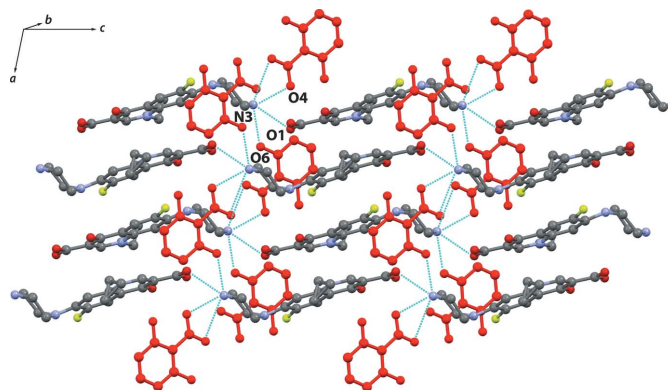
H3*B*···O5, and N3—H3*A*···O6, form an infinite chain structure along the *a*-axis direction (Table 1, Fig. 4). The chains are connected to the adjacent ciprofloxacin molecule through head-to-tail N3—H3*A*···O1 hydrogen bonding. The crystal packing of (I) is shown in Fig. 5. Along the *a*-axis, centrosymmetric pairs of ciprofloxacin molecules are stacked by π–π interactions. The distance between the centroids of symmetry-related C4–C9 rings is 3.4986 (11) Å. This arrangement leads to the formation of a columnar packing arrangement. Interestingly, a similar packing feature was observed in the 1.75

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2···O3	0.84	1.73	2.512 (2)	155
N3—H3*A*···O1[i]	0.91	2.38	2.977 (2)	123
N3—H3*A*···O6	0.91	2.09	2.890 (2)	146
N3—H3*B*···O4[ii]	0.91	2.18	2.897 (3)	136
N3—H3*B*···O5[ii]	0.91	2.24	3.090 (3)	155
C11—H11···O3[iii]	1.00	2.46	3.239 (3)	134
C12—H12*A*···O4[iv]	0.99	2.54	3.374 (3)	141
C13—H13*A*···O7[v]	0.99	2.51	3.193 (3)	126
C14—H14*A*···F1	0.99	2.13	2.831 (2)	126
C15—H15*B*···O1[iii]	0.99	2.33	3.282 (3)	161
C17—H17*A*···O5[ii]	0.99	2.60	3.408 (3)	139
O6—H6···O5	0.84	1.77	2.520 (3)	148
O7—H7···O4	0.84	1.85	2.508 (4)	134
C21—H21···O4[ii]	0.95	2.54	3.488 (3)	178

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

hydrate of ciprofloxacin salicylate (Nugrahani *et al.*, 2020). In addition, compound (I) shows a layered structure with alternating ciprofloxacin and 2,6HBA layers along the *b* axis.

The supramolecular features of compound (II) are similar to those observed in compound (I). Ciprofloxacin cations are interconnected through head-to-tail N3—H3*A*···O1 hydrogen bonds (Table 2), forming an infinite chain arrangement. The chloride ion and water molecule are involved in an extensive hydrogen-bond network bridging ciprofloxacin and 3,5HBA (Fig. 6*a*). Interestingly, compound (II) also shows a layered arrangement of ciprofloxacin and the coformer (Fig. 6*b*).

(a)

(b)

Figure 5
Packing motifs of (I) viewed along (*a*) the *a* axis and (*b*) the *c* axis highlighting the alternating layers of ciprofloxacin and the coformer.
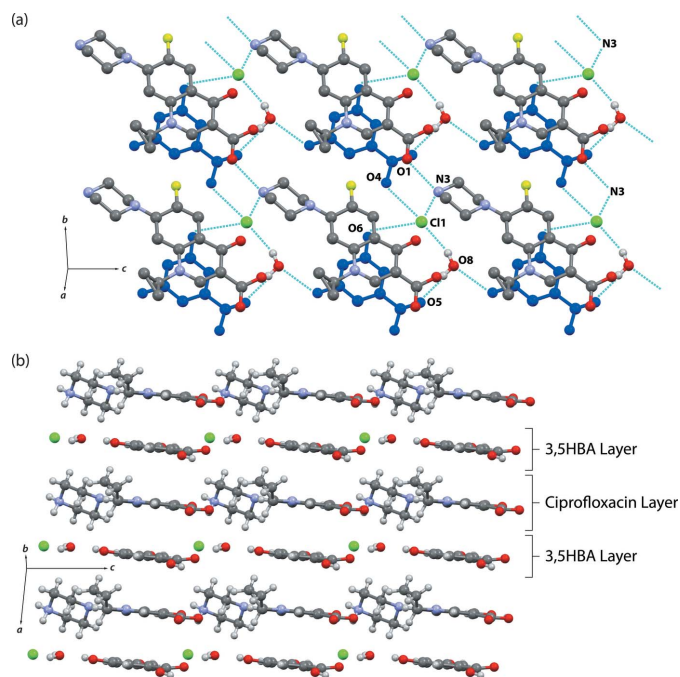

(a)

(b)

Figure 6
Intermolecular hydrogen-bonding motifs in (II) highlighting the role of the chloride ion and water molecule in bridging ciprofloxacin and 3,5HBA (blue). Hydrogen atoms are omitted for clarity. (*b*) The crystal packing of (II) showing the alternating layered arrangement.

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

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O2—H2$\cdots$O3	0.84	1.78	2.551 (3)	152
N3—H3A$\cdots$O1^i	0.91	1.75	2.652 (3)	172
N3—H3B$\cdots$Cl1	0.91	2.30	3.106 (3)	148
C10—H10$\cdots$F1^{ii}	0.95	2.46	3.158 (4)	130
C12—H12B$\cdots$O7^{iii}	0.99	2.47	3.435 (4)	166
C14—H14B$\cdots$F1	0.99	2.27	2.927 (3)	123
C16—H16B$\cdots$Cl1^{iv}	0.99	2.78	3.609 (3)	142
O4—H4$\cdots$Cl1	0.84	2.28	3.082 (2)	160
O6—H6$\cdots$Cl1^v	0.84	2.40	3.232 (2)	170
O7—H7$\cdots$O8	0.84	1.96	2.769 (3)	161
O8—H8A$\cdots$Cl1^i	0.88 (6)	2.51 (6)	3.362 (3)	164 (4)
O8—H8B$\cdots$O5^{vi}	0.82 (6)	2.05 (6)	2.865 (4)	170 (5)

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

4. Database survey

Several crystal structures of ciprofloxacin salts with benzoic acid derivatives have been reported, including salts with salicylic acid (Surov *et al.*, 2019; Nagalapalli & Yaga Bheem, 2014; CSD refcode family DOFWUT), 4-hydroxybenzoic acid (Surov *et al.*, 2020; CSD refcode PUNMUJ), 4-aminobenzoic acid (Surov *et al.*, 2020; CSD refcode PUNMIX) and gallic acid (Surov *et al.*, 2020; CSD refcode PUNMOD). A search for salt co-crystals of ciprofloxacin hydrochloride yielded one reported crystal structure, a co-crystal of ciprofloxacin hydrochloride with 4-hydroxybenzoic acid (Martínez-Alejo *et al.*, 2014; CSD refcode XOHTUL). Compound (II) was also disclosed in a patent without any structural information (Rojas *et al.*, 2016).

5. Synthesis and crystallization

Single crystals of (I) and (II) were obtained by preparing a saturated solution of equimolar ciprofloxacin hydrochloride and the respective coformer in methanol/water (1:1) at room temperature. The saturated solution was allowed to slowly evaporate at room temperature. A suitable single crystal was selected and measured for structure determination.

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 3. All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were refined using a riding model and their displacement parameters (U_{iso}) were fixed to $1.2U_{eq}$ of the parent carbon or nitrogen atom and $1.5U_{eq}$ for hydroxyl groups.

Table 3
Experimental details.

	(I)	(II)
Crystal data		
Chemical formula	$C_{17}H_{19}FN_3O_3{}^+\cdot C_7H_5O_4{}^-$	$C_{17}H_{19}FN_3O_3{}^+\cdot C_7H_6O_4\cdot Cl^-\cdot H_2O$
M_r	485.46	539.93
Crystal system, space group	Monoclinic, $P2_1/c$	Triclinic, $P1$
Temperature (K)	93	93
a, b, c (Å)	7.9722 (5), 21.2705 (11), 13.0860 (7)	7.2165 (2), 8.8298 (4), 10.1184 (3)
α, β, γ (°)	90, 101.805 (6), 90	92.997 (3), 95.219 (2), 111.557 (4)
V (Å^3)	2172.1 (2)	594.60 (4)
Z	4	1
Radiation type	Cu $K\alpha$	Cu $K\alpha$
μ (mm^{-1})	0.98	2.00
Crystal size (mm)	$0.23 \times 0.05 \times 0.04$	$0.28 \times 0.2 \times 0.05$
Data collection		
Diffractometer	XtaLAB Synergy R, DW system, HyPix	XtaLAB Synergy R, DW system, HyPix
Absorption correction	Multi-scan (*CrysAlis PRO*; Rigaku OD, 2020)	Multi-scan (*CrysAlis PRO*; Rigaku OD, 2020)
T_{min}, T_{max}	0.919, 1.000	0.839, 1.000
No. of measured, independent and observed reflections	15936, 4378, 3601 (?)	16358, 4420, 4323 $[I > 2\sigma(I)]$
R_{int}	0.038	0.035
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.630	0.625
Refinement		
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.053, 0.139, 1.04	0.034, 0.094, 1.12
No. of reflections	4378	4420
No. of parameters	319	344
No. of restraints	0	3
H-atom treatment	H-atom parameters constrained	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}, \Delta\rho_{min}$ (e Å^{-3})	0.34, −0.41	0.25, −0.47
Absolute structure	–	Flack x determined using 1889 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter	–	0.011 (7)

Computer programs: *CrysAlis PRO* (Rigaku OD, 2020), *SHELXT2018/2* (Sheldrick, 2015a), *SHELXL2018/3* (Sheldrick, 2015b), *OLEX2* (Dolomanov *et al.*, 2009) and *Mercury* (Macrae *et al.*, 2020).

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Ciprofloxacin salt and salt co-crystal with dihydroxybenzoic acids

Yuda Prasetya Nugraha, Haruki Sugiyama and Hidehiro Uekusa

Computing details

For both structures, data collection: *CrysAlis PRO* (Rigaku OD, 2020); cell refinement: *CrysAlis PRO* (Rigaku OD, 2020); data reduction: *CrysAlis PRO* (Rigaku OD, 2020); program(s) used to solve structure: *SHELXT2018/2* (Sheldrick, 2015a); program(s) used to refine structure: *SHELXL2018/3* (Sheldrick, 2015b); molecular graphics: *OLEX2* (Dolomanov *et al.*, 2009); software used to prepare material for publication: *Mercury* (Macrae *et al.*, 2020).

4-(3-Carboxy-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinolin-7-yl)piperazin-1-ium 2,6-dihydroxybenzoate (I)

Crystal data

$C_{17}H_{19}FN_3O_3{}^+ \cdot C_7H_5O_4{}^-$	$F(000) = 1016$
$M_r = 485.46$	$D_x = 1.485$ Mg m^{-3}
Monoclinic, $P2_1/c$	Cu $K\alpha$ radiation, $\lambda = 1.54184$ Å
$a = 7.9722$ (5) Å	Cell parameters from 4777 reflections
$b = 21.2705$ (11) Å	$\theta = 4.0$–72.0°
$c = 13.0860$ (7) Å	$\mu = 0.98$ mm^{-1}
$\beta = 101.805$ (6)°	$T = 93$ K
$V = 2172.1$ (2) Å^3	Block, colourless
$Z = 4$	$0.23 \times 0.05 \times 0.04$ mm

Data collection

XtaLAB Synergy R, DW system, HyPix diffractometer	$T_{min} = 0.919$, $T_{max} = 1.000$
Radiation source: Rotating-anode X-ray tube, Rigaku XtaLAB Synergy-R	15936 measured reflections
	4378 independent reflections
Mirror monochromator	$R_{int} = 0.038$
Detector resolution: 10.0000 pixels mm^{-1}	$\theta_{max} = 76.3°$, $\theta_{min} = 4.0°$
ω scans	$h = -9 \rightarrow 9$
Absorption correction: multi-scan (CrysAlisPro; Rigaku OD, 2020)	$k = -17 \rightarrow 26$
	$l = -15 \rightarrow 16$

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	
$R[F^2 > 2\sigma(F^2)] = 0.053$	H-atom parameters constrained
$wR(F^2) = 0.139$	$w = 1/[\sigma^2(F_o^2) + (0.062P)^2 + 1.4432P]$
$S = 1.03$	where $P = (F_o^2 + 2F_c^2)/3$
4378 reflections	$(\Delta/\sigma)_{max} = 0.001$
319 parameters	$\Delta\rho_{max} = 0.34$ e Å^{-3}
0 restraints	$\Delta\rho_{min} = -0.41$ e Å^{-3}
Primary atom site location: dual	

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 ($Å^2$)

	x	*y*	*z*	U_{iso}*/U_{eq}
F1	0.05295 (16)	0.41493 (5)	0.67770 (9)	0.0377 (3)
O1	0.4436 (2)	0.54707 (8)	0.16888 (11)	0.0432 (4)
O2	0.3833 (2)	0.44645 (7)	0.18852 (11)	0.0402 (4)
H2	0.347742	0.424196	0.232696	0.060*
O3	0.28730 (19)	0.41034 (7)	0.35014 (11)	0.0362 (3)
N1	0.3471 (2)	0.59129 (8)	0.46044 (12)	0.0314 (4)
N2	0.0934 (2)	0.53783 (8)	0.75639 (13)	0.0328 (4)
N3	0.2572 (3)	0.58568 (8)	0.95730 (14)	0.0395 (4)
H3A	0.356800	0.595565	1.002153	0.047*
H3B	0.169225	0.594851	0.989447	0.047*
C1	0.4001 (3)	0.50538 (10)	0.22173 (15)	0.0354 (5)
C2	0.3602 (3)	0.51643 (10)	0.32635 (15)	0.0327 (4)
C3	0.3006 (2)	0.46647 (10)	0.38290 (15)	0.0326 (4)
C4	0.2566 (2)	0.48427 (10)	0.48093 (15)	0.0316 (4)
C5	0.1856 (3)	0.44006 (9)	0.54010 (15)	0.0327 (4)
H5	0.172151	0.397574	0.517532	0.039*
C6	0.1363 (3)	0.45781 (9)	0.62931 (15)	0.0321 (4)
C7	0.1580 (2)	0.51970 (9)	0.67053 (15)	0.0313 (4)
C8	0.2342 (2)	0.56281 (9)	0.61296 (15)	0.0314 (4)
H8	0.256130	0.604419	0.638611	0.038*
C9	0.2786 (2)	0.54598 (9)	0.51851 (15)	0.0303 (4)
C10	0.3838 (3)	0.57567 (10)	0.36771 (15)	0.0329 (4)
H10	0.428110	0.607231	0.329187	0.040*
C11	0.3814 (3)	0.65431 (9)	0.50290 (16)	0.0338 (4)
H11	0.471754	0.657418	0.568093	0.041*
C12	0.2333 (3)	0.69888 (10)	0.49555 (18)	0.0418 (5)
H12A	0.232822	0.727421	0.555245	0.050*
H12B	0.118861	0.684208	0.459028	0.050*
C13	0.3671 (3)	0.70946 (10)	0.43140 (17)	0.0407 (5)
H13A	0.334605	0.701423	0.355393	0.049*
H13B	0.448510	0.744615	0.451562	0.049*
C14	0.1041 (3)	0.49851 (10)	0.84970 (16)	0.0357 (5)
H14A	0.115360	0.453863	0.830791	0.043*
H14B	−0.002908	0.502959	0.876377	0.043*
C15	0.2556 (3)	0.51692 (9)	0.93462 (16)	0.0340 (4)
H15A	0.250824	0.493237	0.999094	0.041*
H15B	0.363113	0.505307	0.912586	0.041*
C16	0.2411 (3)	0.62529 (10)	0.86112 (16)	0.0364 (5)
H16A	0.344474	0.620481	0.830902	0.044*

H16B	0.229875	0.670139	0.878811	0.044*
C17	0.0831 (3)	0.60408 (10)	0.78271 (15)	0.0327 (4)
H17A	−0.020076	0.611142	0.812303	0.039*
H17B	0.071566	0.629659	0.718442	0.039*
O4	1.1188 (2)	0.66620 (11)	1.0984 (2)	0.0830 (8)
O5	0.8981 (3)	0.62083 (8)	0.99400 (18)	0.0683 (6)
O6	0.5971 (2)	0.63810 (8)	1.02051 (13)	0.0476 (4)
H6	0.675991	0.625422	0.991803	0.071*
O7	1.0721 (3)	0.74339 (12)	1.23479 (19)	0.0809 (8)
H7	1.128472	0.712831	1.218955	0.121*
C18	0.9592 (3)	0.65706 (12)	1.0688 (2)	0.0531 (7)
C19	0.8411 (3)	0.68834 (9)	1.12632 (16)	0.0336 (4)
C20	0.6639 (3)	0.67641 (10)	1.10169 (16)	0.0332 (4)
C21	0.5540 (3)	0.70341 (11)	1.1582 (2)	0.0447 (5)
H21	0.434867	0.694228	1.142088	0.054*
C22	0.6208 (4)	0.74400 (12)	1.2386 (2)	0.0593 (8)
H22	0.545515	0.763145	1.277098	0.071*
C23	0.7929 (5)	0.75756 (13)	1.2647 (2)	0.0625 (8)
H23	0.835717	0.785656	1.320376	0.075*
C24	0.9025 (3)	0.72996 (12)	1.20927 (18)	0.0475 (6)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
F1	0.0444 (7)	0.0350 (6)	0.0334 (6)	−0.0065 (5)	0.0070 (5)	−0.0004 (5)
O1	0.0555 (10)	0.0466 (9)	0.0264 (7)	0.0049 (7)	0.0058 (7)	0.0000 (7)
O2	0.0470 (9)	0.0437 (9)	0.0280 (7)	0.0011 (7)	0.0030 (6)	−0.0068 (6)
O3	0.0384 (8)	0.0360 (8)	0.0312 (7)	0.0019 (6)	0.0003 (6)	−0.0065 (6)
N1	0.0347 (9)	0.0338 (9)	0.0239 (8)	0.0014 (7)	0.0017 (7)	0.0003 (6)
N2	0.0370 (9)	0.0345 (9)	0.0254 (8)	−0.0019 (7)	0.0030 (7)	−0.0007 (7)
N3	0.0477 (10)	0.0353 (9)	0.0290 (9)	0.0021 (8)	−0.0074 (8)	−0.0025 (7)
C1	0.0360 (11)	0.0418 (11)	0.0255 (10)	0.0036 (9)	−0.0008 (8)	−0.0026 (9)
C2	0.0300 (10)	0.0390 (11)	0.0260 (9)	0.0034 (8)	−0.0014 (8)	−0.0031 (8)
C3	0.0288 (9)	0.0364 (10)	0.0288 (10)	0.0040 (8)	−0.0033 (8)	−0.0031 (8)
C4	0.0290 (9)	0.0370 (10)	0.0254 (9)	0.0016 (8)	−0.0022 (7)	−0.0011 (8)
C5	0.0331 (10)	0.0313 (10)	0.0298 (10)	0.0020 (8)	−0.0024 (8)	−0.0035 (8)
C6	0.0304 (10)	0.0340 (10)	0.0293 (10)	−0.0024 (8)	−0.0001 (8)	0.0016 (8)
C7	0.0300 (9)	0.0360 (10)	0.0253 (9)	0.0006 (8)	−0.0002 (7)	−0.0010 (8)
C8	0.0308 (10)	0.0337 (10)	0.0265 (9)	0.0011 (8)	−0.0017 (7)	−0.0016 (8)
C9	0.0297 (10)	0.0345 (10)	0.0242 (9)	0.0027 (8)	−0.0001 (7)	0.0005 (8)
C10	0.0332 (10)	0.0387 (11)	0.0249 (9)	0.0031 (8)	0.0014 (8)	0.0011 (8)
C11	0.0398 (11)	0.0325 (10)	0.0282 (10)	−0.0005 (8)	0.0053 (8)	−0.0009 (8)
C12	0.0457 (12)	0.0372 (11)	0.0420 (12)	0.0049 (9)	0.0074 (10)	−0.0010 (9)
C13	0.0538 (13)	0.0345 (11)	0.0328 (11)	0.0025 (9)	0.0067 (9)	0.0015 (9)
C14	0.0406 (11)	0.0380 (11)	0.0275 (10)	−0.0058 (9)	0.0047 (8)	0.0008 (8)
C15	0.0385 (11)	0.0330 (10)	0.0283 (10)	0.0013 (8)	0.0018 (8)	−0.0005 (8)
C16	0.0410 (11)	0.0326 (10)	0.0321 (10)	0.0006 (8)	−0.0011 (9)	−0.0021 (8)
C17	0.0335 (10)	0.0359 (10)	0.0269 (9)	0.0020 (8)	0.0017 (8)	−0.0010 (8)

O4	0.0390 (10)	0.0790 (14)	0.140 (2)	0.0173 (9)	0.0391 (12)	0.0559 (15)
O5	0.1042 (17)	0.0351 (9)	0.0862 (15)	0.0002 (10)	0.0675 (13)	−0.0015 (10)
O6	0.0513 (10)	0.0531 (10)	0.0356 (8)	−0.0164 (8)	0.0027 (7)	−0.0101 (7)
O7	0.0613 (12)	0.0922 (16)	0.0708 (14)	−0.0414 (11)	−0.0296 (11)	0.0281 (13)
C18	0.0488 (14)	0.0374 (13)	0.082 (2)	0.0124 (10)	0.0340 (14)	0.0259 (13)
C19	0.0320 (10)	0.0335 (10)	0.0344 (10)	−0.0010 (8)	0.0048 (8)	0.0063 (8)
C20	0.0342 (10)	0.0347 (10)	0.0296 (10)	−0.0019 (8)	0.0036 (8)	0.0007 (8)
C21	0.0394 (12)	0.0431 (12)	0.0547 (14)	0.0024 (10)	0.0172 (10)	0.0040 (11)
C22	0.096 (2)	0.0364 (13)	0.0590 (16)	−0.0030 (13)	0.0477 (16)	−0.0036 (11)
C23	0.108 (2)	0.0474 (14)	0.0343 (12)	−0.0330 (15)	0.0198 (14)	−0.0087 (11)
C24	0.0525 (14)	0.0496 (13)	0.0341 (11)	−0.0194 (11)	−0.0056 (10)	0.0104 (10)

Geometric parameters (Å, º)

F1—C6	1.359 (2)	C12—H12A	0.9900
O1—C1	1.218 (3)	C12—H12B	0.9900
O2—H2	0.8400	C12—C13	1.503 (3)
O2—C1	1.325 (3)	C13—H13A	0.9900
O3—C3	1.265 (2)	C13—H13B	0.9900
N1—C9	1.405 (3)	C14—H14A	0.9900
N1—C10	1.347 (3)	C14—H14B	0.9900
N1—C11	1.455 (3)	C14—C15	1.516 (3)
N2—C7	1.383 (3)	C15—H15A	0.9900
N2—C14	1.468 (3)	C15—H15B	0.9900
N2—C17	1.457 (3)	C16—H16A	0.9900
N3—H3A	0.9100	C16—H16B	0.9900
N3—H3B	0.9100	C16—C17	1.521 (3)
N3—C15	1.492 (3)	C17—H17A	0.9900
N3—C16	1.498 (3)	C17—H17B	0.9900
C1—C2	1.486 (3)	O4—C18	1.267 (3)
C2—C3	1.431 (3)	O5—C18	1.263 (4)
C2—C10	1.369 (3)	O6—H6	0.8400
C3—C4	1.448 (3)	O6—C20	1.358 (3)
C4—C5	1.408 (3)	O7—H7	0.8400
C4—C9	1.400 (3)	O7—C24	1.355 (3)
C5—H5	0.9500	C18—C19	1.479 (3)
C5—C6	1.359 (3)	C19—C20	1.406 (3)
C6—C7	1.420 (3)	C19—C24	1.409 (3)
C7—C8	1.402 (3)	C20—C21	1.382 (3)
C8—H8	0.9500	C21—H21	0.9500
C8—C9	1.400 (3)	C21—C22	1.381 (4)
C10—H10	0.9500	C22—H22	0.9500
C11—H11	1.0000	C22—C23	1.375 (5)
C11—C12	1.501 (3)	C23—H23	0.9500
C11—C13	1.490 (3)	C23—C24	1.376 (4)
C1—O2—H2	109.5	C13—C12—H12B	117.8
C9—N1—C11	119.24 (16)	C11—C13—C12	60.21 (15)

C10—N1—C9	119.88 (17)	C11—C13—H13A	117.8
C10—N1—C11	120.86 (17)	C11—C13—H13B	117.8
C7—N2—C14	123.30 (17)	C12—C13—H13A	117.8
C7—N2—C17	120.67 (17)	C12—C13—H13B	117.8
C17—N2—C14	110.55 (16)	H13A—C13—H13B	114.9
H3A—N3—H3B	107.8	N2—C14—H14A	109.4
C15—N3—H3A	109.0	N2—C14—H14B	109.4
C15—N3—H3B	109.0	N2—C14—C15	111.36 (17)
C15—N3—C16	112.86 (16)	H14A—C14—H14B	108.0
C16—N3—H3A	109.0	C15—C14—H14A	109.4
C16—N3—H3B	109.0	C15—C14—H14B	109.4
O1—C1—O2	121.63 (19)	N3—C15—C14	111.86 (17)
O1—C1—C2	123.19 (19)	N3—C15—H15A	109.2
O2—C1—C2	115.18 (19)	N3—C15—H15B	109.2
C3—C2—C1	121.03 (18)	C14—C15—H15A	109.2
C10—C2—C1	118.14 (19)	C14—C15—H15B	109.2
C10—C2—C3	120.83 (19)	H15A—C15—H15B	107.9
O3—C3—C2	122.61 (19)	N3—C16—H16A	110.0
O3—C3—C4	121.90 (19)	N3—C16—H16B	110.0
C2—C3—C4	115.48 (18)	N3—C16—C17	108.50 (17)
C5—C4—C3	120.65 (18)	H16A—C16—H16B	108.4
C9—C4—C3	121.38 (19)	C17—C16—H16A	110.0
C9—C4—C5	117.95 (18)	C17—C16—H16B	110.0
C4—C5—H5	119.8	N2—C17—C16	111.57 (16)
C6—C5—C4	120.40 (19)	N2—C17—H17A	109.3
C6—C5—H5	119.8	N2—C17—H17B	109.3
F1—C6—C5	117.95 (18)	C16—C17—H17A	109.3
F1—C6—C7	118.58 (18)	C16—C17—H17B	109.3
C5—C6—C7	123.34 (19)	H17A—C17—H17B	108.0
N2—C7—C6	122.04 (18)	C20—O6—H6	109.5
N2—C7—C8	121.89 (18)	C24—O7—H7	109.5
C8—C7—C6	115.79 (18)	O4—C18—C19	118.7 (3)
C7—C8—H8	119.2	O5—C18—O4	122.3 (3)
C9—C8—C7	121.53 (19)	O5—C18—C19	119.0 (2)
C9—C8—H8	119.2	C20—C19—C18	121.1 (2)
C4—C9—N1	119.20 (18)	C20—C19—C24	117.7 (2)
C4—C9—C8	120.89 (19)	C24—C19—C18	121.2 (2)
C8—C9—N1	119.91 (18)	O6—C20—C19	120.12 (19)
N1—C10—C2	123.07 (19)	O6—C20—C21	118.6 (2)
N1—C10—H10	118.5	C21—C20—C19	121.3 (2)
C2—C10—H10	118.5	C20—C21—H21	120.7
N1—C11—H11	115.6	C22—C21—C20	118.7 (2)
N1—C11—C12	118.27 (18)	C22—C21—H21	120.7
N1—C11—C13	120.07 (17)	C21—C22—H22	119.0
C12—C11—H11	115.6	C23—C22—C21	122.0 (2)
C13—C11—H11	115.6	C23—C22—H22	119.0
C13—C11—C12	60.32 (15)	C22—C23—H23	120.4
C11—C12—H12A	117.8	C22—C23—C24	119.3 (2)

C11—C12—H12B	117.8	C24—C23—H23	120.4
C11—C12—C13	59.47 (14)	O7—C24—C19	119.6 (3)
H12A—C12—H12B	115.0	O7—C24—C23	119.3 (3)
C13—C12—H12A	117.8	C23—C24—C19	121.1 (2)
F1—C6—C7—N2	−1.6 (3)	C9—C4—C5—C6	1.8 (3)
F1—C6—C7—C8	−175.68 (16)	C10—N1—C9—C4	2.8 (3)
O1—C1—C2—C3	176.50 (19)	C10—N1—C9—C8	−177.48 (18)
O1—C1—C2—C10	−4.2 (3)	C10—N1—C11—C12	102.8 (2)
O2—C1—C2—C3	−2.7 (3)	C10—N1—C11—C13	32.6 (3)
O2—C1—C2—C10	176.59 (18)	C10—C2—C3—O3	−175.52 (18)
O3—C3—C4—C5	−4.5 (3)	C10—C2—C3—C4	4.3 (3)
O3—C3—C4—C9	177.25 (17)	C11—N1—C9—C4	−175.72 (17)
N1—C11—C12—C13	−110.4 (2)	C11—N1—C9—C8	4.0 (3)
N1—C11—C13—C12	107.5 (2)	C11—N1—C10—C2	177.41 (18)
N2—C7—C8—C9	−171.43 (18)	C14—N2—C7—C6	42.6 (3)
N2—C14—C15—N3	52.0 (2)	C14—N2—C7—C8	−143.72 (19)
N3—C16—C17—N2	−58.5 (2)	C14—N2—C17—C16	61.2 (2)
C1—C2—C3—O3	3.8 (3)	C15—N3—C16—C17	53.4 (2)
C1—C2—C3—C4	−176.44 (17)	C16—N3—C15—C14	−51.4 (2)
C1—C2—C10—N1	178.08 (18)	C17—N2—C7—C6	−166.08 (18)
C2—C3—C4—C5	175.74 (17)	C17—N2—C7—C8	7.6 (3)
C2—C3—C4—C9	−2.5 (3)	C17—N2—C14—C15	−56.9 (2)
C3—C2—C10—N1	−2.6 (3)	O4—C18—C19—C20	−175.4 (2)
C3—C4—C5—C6	−176.56 (18)	O4—C18—C19—C24	3.0 (3)
C3—C4—C9—N1	−0.9 (3)	O5—C18—C19—C20	2.6 (3)
C3—C4—C9—C8	179.39 (18)	O5—C18—C19—C24	−179.0 (2)
C4—C5—C6—F1	173.48 (16)	O6—C20—C21—C22	−177.9 (2)
C4—C5—C6—C7	−2.5 (3)	C18—C19—C20—O6	−3.4 (3)
C5—C4—C9—N1	−179.21 (17)	C18—C19—C20—C21	177.1 (2)
C5—C4—C9—C8	1.1 (3)	C18—C19—C24—O7	2.3 (3)
C5—C6—C7—N2	174.32 (18)	C18—C19—C24—C23	−178.0 (2)
C5—C6—C7—C8	0.2 (3)	C19—C20—C21—C22	1.6 (3)
C6—C7—C8—C9	2.7 (3)	C20—C19—C24—O7	−179.2 (2)
C7—N2—C14—C15	97.0 (2)	C20—C19—C24—C23	0.5 (3)
C7—N2—C17—C16	−93.5 (2)	C20—C21—C22—C23	−0.9 (4)
C7—C8—C9—N1	176.92 (17)	C21—C22—C23—C24	0.0 (4)
C7—C8—C9—C4	−3.4 (3)	C22—C23—C24—O7	179.9 (2)
C9—N1—C10—C2	−1.1 (3)	C22—C23—C24—C19	0.2 (4)
C9—N1—C11—C12	−78.7 (2)	C24—C19—C20—O6	178.08 (19)
C9—N1—C11—C13	−148.89 (19)	C24—C19—C20—C21	−1.4 (3)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2···O3	0.84	1.73	2.512 (2)	155
N3—H3*A*···O1ⁱ	0.91	2.38	2.977 (2)	123
N3—H3*A*···O6	0.91	2.09	2.890 (2)	146

N3—H3*B*···O4ⁱⁱ	0.91	2.18	2.897 (3)	136
N3—H3*B*···O5ⁱⁱ	0.91	2.24	3.090 (3)	155
C11—H11···O3ⁱⁱⁱ	1.00	2.46	3.239 (3)	134
C12—H12*A*···O4ⁱᵛ	0.99	2.54	3.374 (3)	141
C13—H13*A*···O7ᵛ	0.99	2.51	3.193 (3)	126
C14—H14*A*···F1	0.99	2.13	2.831 (2)	126
C15—H15*B*···O1ⁱⁱⁱ	0.99	2.33	3.282 (3)	161
C17—H17*A*···O5ⁱⁱ	0.99	2.60	3.408 (3)	139
O6—H6···O5	0.84	1.77	2.520 (3)	148
O7—H7···O4	0.84	1.85	2.508 (4)	134
C21—H21···O4ⁱⁱ	0.95	2.54	3.488 (3)	178

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

4-(3-Carboxy-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinolin-7-yl)piperazin-1-ium chloride–3,5-hydroxybenzoic acid–water (1/1/1) (II)

Crystal data

$C_{17}H_{19}FN_3O_3^+ \cdot C_7H_6O_4 \cdot Cl^- \cdot H_2O$
$M_r = 539.93$
Triclinic, $P1$
$a = 7.2165\ (2)$ Å
$b = 8.8298\ (4)$ Å
$c = 10.1184\ (3)$ Å
$\alpha = 92.997\ (3)°$
$\beta = 95.219\ (2)°$
$\gamma = 111.557\ (4)°$
$V = 594.60\ (4)$ Å³

$Z = 1$
$F(000) = 282$
$D_x = 1.508$ Mg m⁻³
Cu $K\alpha$ radiation, $\lambda = 1.54184$ Å
Cell parameters from 10041 reflections
$\theta = 4.4$–75.8°
$\mu = 2.00$ mm⁻¹
$T = 93$ K
Block, colourless
$0.28 \times 0.2 \times 0.05$ mm

Data collection

XtaLAB Synergy R, DW system, HyPix
   diffractometer
Radiation source: Rotating-anode X-ray tube,
   Rigaku XtaLAB Synergy-R
Mirror monochromator
Detector resolution: 10.0000 pixels mm⁻¹
ω scans
Absorption correction: multi-scan
   (CrysAlisPro; Rigaku OD, 2020)

$T_{min} = 0.839$, $T_{max} = 1.000$
16358 measured reflections
4420 independent reflections
4323 reflections with $I > 2\sigma(I)$
$R_{int} = 0.035$
$\theta_{max} = 74.5°$, $\theta_{min} = 4.4°$
$h = -9 \rightarrow 9$
$k = -10 \rightarrow 11$
$l = -12 \rightarrow 12$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.034$
$wR(F^2) = 0.094$
$S = 1.12$
4420 reflections
344 parameters
3 restraints
Primary atom site location: dual
Hydrogen site location: mixed

H atoms treated by a mixture of independent
   and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0589P)^2 + 0.0709P]$
   where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.25$ e Å⁻³
$\Delta\rho_{min} = -0.47$ e Å⁻³
Absolute structure: Flack x determined using
   1889 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter: 0.011 (7)

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}
Cl1	0.85144 (9)	0.46863 (8)	0.40663 (7)	0.02533 (17)
F1	0.4599 (3)	0.5185 (2)	0.98137 (17)	0.0273 (4)
O1	0.3224 (3)	−0.3703 (3)	1.2978 (2)	0.0284 (5)
O2	0.3642 (4)	−0.1499 (3)	1.4315 (2)	0.0294 (5)
H2	0.379572	−0.051835	1.423817	0.044*
O3	0.3972 (3)	0.1143 (3)	1.3272 (2)	0.0280 (5)
N1	0.2840 (4)	−0.1445 (3)	0.9603 (2)	0.0213 (5)
N2	0.3796 (4)	0.3457 (3)	0.7334 (2)	0.0210 (5)
N3	0.4407 (4)	0.4661 (3)	0.4778 (2)	0.0233 (5)
H3A	0.412202	0.525266	0.413562	0.028*
H3B	0.528778	0.423848	0.448534	0.028*
C1	0.3370 (4)	−0.2274 (4)	1.3126 (3)	0.0249 (6)
C2	0.3276 (4)	−0.1342 (4)	1.1970 (3)	0.0222 (6)
C3	0.3655 (4)	0.0366 (4)	1.2138 (3)	0.0226 (6)
C4	0.3687 (4)	0.1155 (4)	1.0907 (3)	0.0220 (6)
C5	0.4158 (4)	0.2850 (4)	1.0937 (3)	0.0227 (6)
H5	0.444144	0.349621	1.176480	0.027*
C6	0.4203 (4)	0.3556 (4)	0.9773 (3)	0.0214 (6)
C7	0.3828 (4)	0.2667 (4)	0.8503 (3)	0.0202 (6)
C8	0.3389 (4)	0.1003 (4)	0.8483 (3)	0.0212 (6)
H8	0.314618	0.036841	0.765286	0.025*
C9	0.3297 (4)	0.0241 (4)	0.9661 (3)	0.0204 (6)
C10	0.2882 (4)	−0.2168 (4)	1.0730 (3)	0.0218 (6)
H10	0.262685	−0.330555	1.066643	0.026*
C11	0.2568 (4)	−0.2397 (4)	0.8324 (3)	0.0219 (6)
H11	0.381927	−0.228926	0.791979	0.026*
C12	0.0740 (5)	−0.2667 (4)	0.7366 (3)	0.0257 (6)
H12A	0.087678	−0.270948	0.640183	0.031*
H12B	−0.021768	−0.217677	0.763308	0.031*
C13	0.0926 (5)	−0.4047 (4)	0.8124 (3)	0.0259 (6)
H13A	0.007825	−0.440061	0.885206	0.031*
H13B	0.117236	−0.493315	0.762121	0.031*
C14	0.5686 (4)	0.4771 (4)	0.7139 (3)	0.0231 (6)
H14A	0.667670	0.429259	0.691921	0.028*
H14B	0.623427	0.549862	0.797431	0.028*
C15	0.5351 (5)	0.5757 (4)	0.6022 (3)	0.0253 (6)
H15A	0.447094	0.632955	0.628102	0.030*
H15B	0.665144	0.659131	0.586453	0.030*
C16	0.2536 (5)	0.3306 (4)	0.5001 (3)	0.0240 (6)

H16A	0.198514	0.256713	0.417103	0.029*
H16B	0.152583	0.375766	0.523119	0.029*
C17	0.2940 (4)	0.2351 (4)	0.6112 (3)	0.0221 (6)
H17A	0.167365	0.147006	0.626540	0.027*
H17B	0.388812	0.184215	0.586309	0.027*
O4	0.8307 (4)	0.7243 (3)	0.2157 (2)	0.0292 (5)
H4	0.845149	0.674900	0.282288	0.044*
O5	0.8281 (4)	0.9108 (3)	0.3721 (2)	0.0338 (5)
O6	0.9253 (4)	1.4048 (3)	0.1019 (2)	0.0282 (5)
H6	0.922943	1.426566	0.183393	0.042*
O7	0.7685 (4)	0.9471 (3)	−0.2173 (2)	0.0282 (5)
H7	0.769716	1.019031	−0.268691	0.042*
C18	0.8310 (5)	0.8689 (4)	0.2561 (3)	0.0245 (6)
C19	0.8373 (4)	0.9759 (4)	0.1448 (3)	0.0233 (6)
C20	0.8753 (4)	1.1395 (4)	0.1782 (3)	0.0230 (6)
H20	0.894255	1.180995	0.269053	0.028*
C21	0.8855 (4)	1.2429 (4)	0.0771 (3)	0.0230 (6)
C22	0.8531 (4)	1.1805 (4)	−0.0565 (3)	0.0229 (6)
H22	0.860643	1.250739	−0.125512	0.028*
C23	0.8099 (4)	1.0150 (4)	−0.0877 (3)	0.0231 (6)
C24	0.8048 (4)	0.9107 (4)	0.0123 (3)	0.0243 (6)
H24	0.779908	0.798399	−0.009350	0.029*
O8	0.7775 (4)	1.1327 (3)	−0.4306 (2)	0.0309 (5)
H8A	0.799 (7)	1.230 (7)	−0.457 (5)	0.046*
H8B	0.779 (7)	1.068 (7)	−0.492 (5)	0.046*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0315 (3)	0.0267 (3)	0.0219 (3)	0.0151 (3)	0.0052 (2)	0.0029 (2)
F1	0.0445 (10)	0.0200 (9)	0.0203 (8)	0.0152 (8)	0.0057 (7)	−0.0001 (7)
O1	0.0376 (12)	0.0253 (12)	0.0242 (11)	0.0142 (9)	0.0011 (9)	0.0058 (9)
O2	0.0419 (13)	0.0289 (12)	0.0176 (10)	0.0132 (10)	0.0032 (9)	0.0048 (8)
O3	0.0426 (13)	0.0294 (12)	0.0144 (9)	0.0160 (10)	0.0048 (9)	0.0003 (8)
N1	0.0270 (12)	0.0220 (13)	0.0168 (12)	0.0117 (10)	0.0024 (9)	−0.0002 (9)
N2	0.0255 (12)	0.0232 (13)	0.0144 (11)	0.0097 (10)	0.0009 (9)	0.0008 (9)
N3	0.0303 (12)	0.0286 (13)	0.0173 (11)	0.0174 (10)	0.0047 (9)	0.0046 (10)
C1	0.0243 (14)	0.0325 (18)	0.0202 (14)	0.0131 (12)	0.0027 (11)	0.0050 (12)
C2	0.0238 (13)	0.0266 (15)	0.0179 (13)	0.0108 (11)	0.0036 (10)	0.0041 (12)
C3	0.0262 (14)	0.0272 (15)	0.0175 (14)	0.0131 (12)	0.0044 (11)	0.0038 (11)
C4	0.0234 (13)	0.0268 (15)	0.0177 (13)	0.0117 (11)	0.0035 (10)	0.0007 (11)
C5	0.0282 (14)	0.0232 (15)	0.0182 (13)	0.0117 (12)	0.0036 (10)	−0.0011 (11)
C6	0.0267 (14)	0.0176 (13)	0.0206 (14)	0.0094 (11)	0.0032 (11)	−0.0006 (11)
C7	0.0222 (13)	0.0228 (15)	0.0171 (13)	0.0105 (11)	0.0018 (10)	0.0016 (11)
C8	0.0239 (13)	0.0230 (15)	0.0167 (13)	0.0095 (11)	0.0021 (10)	−0.0023 (11)
C9	0.0210 (13)	0.0217 (14)	0.0188 (14)	0.0084 (10)	0.0030 (10)	0.0005 (11)
C10	0.0242 (13)	0.0215 (15)	0.0225 (14)	0.0112 (11)	0.0033 (11)	0.0050 (11)
C11	0.0291 (14)	0.0213 (14)	0.0173 (13)	0.0121 (12)	0.0024 (11)	−0.0009 (11)

C12	0.0317 (15)	0.0243 (15)	0.0213 (13)	0.0117 (12)	−0.0005 (12)	0.0006 (11)
C13	0.0329 (15)	0.0211 (15)	0.0242 (14)	0.0110 (12)	0.0038 (11)	−0.0004 (11)
C14	0.0281 (14)	0.0233 (15)	0.0183 (13)	0.0103 (12)	0.0021 (11)	0.0011 (11)
C15	0.0335 (15)	0.0240 (15)	0.0198 (14)	0.0116 (12)	0.0050 (11)	0.0040 (11)
C16	0.0291 (15)	0.0241 (15)	0.0192 (13)	0.0111 (12)	0.0006 (11)	0.0012 (11)
C17	0.0264 (14)	0.0242 (16)	0.0174 (13)	0.0121 (11)	0.0006 (10)	0.0006 (11)
O4	0.0432 (13)	0.0270 (12)	0.0240 (11)	0.0194 (10)	0.0077 (9)	0.0056 (9)
O5	0.0540 (14)	0.0318 (13)	0.0216 (11)	0.0224 (11)	0.0074 (10)	0.0025 (9)
O6	0.0423 (12)	0.0214 (11)	0.0220 (10)	0.0133 (9)	0.0046 (9)	−0.0007 (8)
O7	0.0408 (12)	0.0264 (12)	0.0186 (10)	0.0140 (10)	0.0046 (9)	−0.0003 (9)
C18	0.0269 (14)	0.0271 (16)	0.0230 (14)	0.0137 (12)	0.0048 (11)	0.0025 (12)
C19	0.0240 (13)	0.0265 (16)	0.0216 (14)	0.0116 (11)	0.0039 (11)	0.0017 (12)
C20	0.0254 (13)	0.0255 (15)	0.0196 (13)	0.0117 (11)	0.0029 (11)	−0.0003 (11)
C21	0.0244 (13)	0.0205 (14)	0.0243 (14)	0.0092 (11)	0.0023 (11)	−0.0019 (11)
C22	0.0249 (14)	0.0247 (15)	0.0215 (14)	0.0115 (11)	0.0045 (11)	0.0035 (12)
C23	0.0240 (13)	0.0281 (16)	0.0187 (14)	0.0119 (12)	0.0023 (11)	−0.0010 (12)
C24	0.0261 (14)	0.0259 (15)	0.0232 (15)	0.0122 (12)	0.0058 (11)	−0.0007 (12)
O8	0.0438 (13)	0.0286 (13)	0.0212 (11)	0.0146 (10)	0.0044 (9)	0.0017 (9)

Geometric parameters (Å, º)

F1—C6	1.357 (4)	C12—C13	1.513 (4)
O1—C1	1.227 (4)	C13—H13A	0.9900
O2—H2	0.8400	C13—H13B	0.9900
O2—C1	1.314 (4)	C14—H14A	0.9900
O3—C3	1.263 (4)	C14—H14B	0.9900
N1—C9	1.397 (4)	C14—C15	1.517 (4)
N1—C10	1.339 (4)	C15—H15A	0.9900
N1—C11	1.463 (4)	C15—H15B	0.9900
N2—C7	1.407 (4)	C16—H16A	0.9900
N2—C14	1.468 (4)	C16—H16B	0.9900
N2—C17	1.467 (4)	C16—C17	1.510 (4)
N3—H3A	0.9100	C17—H17A	0.9900
N3—H3B	0.9100	C17—H17B	0.9900
N3—C15	1.489 (4)	O4—H4	0.8400
N3—C16	1.484 (4)	O4—C18	1.320 (4)
C1—C2	1.475 (4)	O5—C18	1.216 (4)
C2—C3	1.428 (4)	O6—H6	0.8400
C2—C10	1.369 (4)	O6—C21	1.356 (4)
C3—C4	1.457 (4)	O7—H7	0.8400
C4—C5	1.406 (4)	O7—C23	1.372 (4)
C4—C9	1.407 (4)	C18—C19	1.501 (4)
C5—H5	0.9500	C19—C20	1.385 (4)
C5—C6	1.358 (4)	C19—C24	1.395 (4)
C6—C7	1.419 (4)	C20—H20	0.9500
C7—C8	1.384 (4)	C20—C21	1.395 (4)
C8—H8	0.9500	C21—C22	1.399 (4)
C8—C9	1.394 (4)	C22—H22	0.9500

C10—H10	0.9500	C22—C23	1.389 (5)
C11—H11	1.0000	C23—C24	1.398 (4)
C11—C12	1.499 (4)	C24—H24	0.9500
C11—C13	1.492 (4)	O8—H8A	0.88 (6)
C12—H12A	0.9900	O8—H8B	0.82 (6)
C12—H12B	0.9900		
C1—O2—H2	109.5	C11—C13—C12	59.9 (2)
C9—N1—C11	120.6 (2)	C11—C13—H13A	117.8
C10—N1—C9	119.9 (3)	C11—C13—H13B	117.8
C10—N1—C11	119.0 (3)	C12—C13—H13A	117.8
C7—N2—C14	115.7 (2)	C12—C13—H13B	117.8
C7—N2—C17	114.7 (2)	H13A—C13—H13B	114.9
C17—N2—C14	111.0 (2)	N2—C14—H14A	109.5
H3A—N3—H3B	108.0	N2—C14—H14B	109.5
C15—N3—H3A	109.3	N2—C14—C15	110.6 (2)
C15—N3—H3B	109.3	H14A—C14—H14B	108.1
C16—N3—H3A	109.3	C15—C14—H14A	109.5
C16—N3—H3B	109.3	C15—C14—H14B	109.5
C16—N3—C15	111.4 (2)	N3—C15—C14	110.2 (2)
O1—C1—O2	121.8 (3)	N3—C15—H15A	109.6
O1—C1—C2	121.2 (3)	N3—C15—H15B	109.6
O2—C1—C2	117.0 (3)	C14—C15—H15A	109.6
C3—C2—C1	121.3 (3)	C14—C15—H15B	109.6
C10—C2—C1	117.3 (3)	H15A—C15—H15B	108.1
C10—C2—C3	121.4 (3)	N3—C16—H16A	109.5
O3—C3—C2	122.5 (3)	N3—C16—H16B	109.5
O3—C3—C4	122.3 (3)	N3—C16—C17	110.7 (2)
C2—C3—C4	115.2 (3)	H16A—C16—H16B	108.1
C5—C4—C3	120.8 (3)	C17—C16—H16A	109.5
C5—C4—C9	118.6 (3)	C17—C16—H16B	109.5
C9—C4—C3	120.6 (3)	N2—C17—C16	109.4 (2)
C4—C5—H5	120.3	N2—C17—H17A	109.8
C6—C5—C4	119.5 (3)	N2—C17—H17B	109.8
C6—C5—H5	120.3	C16—C17—H17A	109.8
F1—C6—C5	119.0 (3)	C16—C17—H17B	109.8
F1—C6—C7	117.8 (2)	H17A—C17—H17B	108.2
C5—C6—C7	123.2 (3)	C18—O4—H4	109.5
N2—C7—C6	120.4 (3)	C21—O6—H6	109.5
C8—C7—N2	122.6 (3)	C23—O7—H7	109.5
C8—C7—C6	116.9 (3)	O4—C18—C19	113.1 (3)
C7—C8—H8	119.4	O5—C18—O4	123.1 (3)
C7—C8—C9	121.1 (3)	O5—C18—C19	123.8 (3)
C9—C8—H8	119.4	C20—C19—C18	117.9 (3)
N1—C9—C4	119.8 (2)	C20—C19—C24	121.7 (3)
C8—C9—N1	119.6 (3)	C24—C19—C18	120.4 (3)
C8—C9—C4	120.7 (3)	C19—C20—H20	120.3
N1—C10—C2	123.0 (3)	C19—C20—C21	119.3 (3)

N1—C10—H10	118.5	C21—C20—H20	120.3
C2—C10—H10	118.5	O6—C21—C20	122.8 (3)
N1—C11—H11	116.2	O6—C21—C22	117.1 (3)
N1—C11—C12	118.9 (3)	C20—C21—C22	120.1 (3)
N1—C11—C13	117.2 (2)	C21—C22—H22	120.2
C12—C11—H11	116.2	C23—C22—C21	119.6 (3)
C13—C11—H11	116.2	C23—C22—H22	120.2
C13—C11—C12	60.8 (2)	O7—C23—C22	121.6 (3)
C11—C12—H12A	117.8	O7—C23—C24	117.3 (3)
C11—C12—H12B	117.8	C22—C23—C24	121.1 (3)
C11—C12—C13	59.4 (2)	C19—C24—C23	118.2 (3)
H12A—C12—H12B	115.0	C19—C24—H24	120.9
C13—C12—H12A	117.8	C23—C24—H24	120.9
C13—C12—H12B	117.8	H8A—O8—H8B	112 (5)
F1—C6—C7—N2	−2.4 (4)	C9—N1—C11—C13	−140.3 (3)
F1—C6—C7—C8	−178.8 (3)	C9—C4—C5—C6	0.7 (4)
O1—C1—C2—C3	−173.3 (3)	C10—N1—C9—C4	−3.6 (4)
O1—C1—C2—C10	4.3 (4)	C10—N1—C9—C8	175.5 (3)
O2—C1—C2—C3	5.9 (4)	C10—N1—C11—C12	117.4 (3)
O2—C1—C2—C10	−176.5 (3)	C10—N1—C11—C13	47.5 (4)
O3—C3—C4—C5	2.6 (4)	C10—C2—C3—O3	178.2 (3)
O3—C3—C4—C9	−179.1 (3)	C10—C2—C3—C4	−2.9 (4)
N1—C11—C12—C13	−106.9 (3)	C11—N1—C9—C4	−175.7 (2)
N1—C11—C13—C12	109.5 (3)	C11—N1—C9—C8	3.4 (4)
N2—C7—C8—C9	−175.5 (3)	C11—N1—C10—C2	175.1 (3)
N2—C14—C15—N3	−55.7 (3)	C14—N2—C7—C6	62.4 (4)
N3—C16—C17—N2	58.0 (3)	C14—N2—C7—C8	−121.4 (3)
C1—C2—C3—O3	−4.2 (4)	C14—N2—C17—C16	−59.9 (3)
C1—C2—C3—C4	174.7 (3)	C15—N3—C16—C17	−56.1 (3)
C1—C2—C10—N1	−177.1 (3)	C16—N3—C15—C14	54.5 (3)
C2—C3—C4—C5	−176.4 (3)	C17—N2—C7—C6	−166.4 (3)
C2—C3—C4—C9	2.0 (4)	C17—N2—C7—C8	9.8 (4)
C3—C2—C10—N1	0.5 (4)	C17—N2—C14—C15	59.2 (3)
C3—C4—C5—C6	179.1 (3)	O4—C18—C19—C20	−168.3 (3)
C3—C4—C9—N1	1.1 (4)	O4—C18—C19—C24	11.9 (4)
C3—C4—C9—C8	−178.0 (3)	O5—C18—C19—C20	11.1 (5)
C4—C5—C6—F1	178.0 (3)	O5—C18—C19—C24	−168.6 (3)
C4—C5—C6—C7	−1.1 (5)	O6—C21—C22—C23	−179.4 (3)
C5—C4—C9—N1	179.5 (3)	O7—C23—C24—C19	−177.1 (3)
C5—C4—C9—C8	0.4 (4)	C18—C19—C20—C21	178.9 (3)
C5—C6—C7—N2	176.7 (3)	C18—C19—C24—C23	179.2 (3)
C5—C6—C7—C8	0.3 (4)	C19—C20—C21—O6	−178.9 (3)
C6—C7—C8—C9	0.8 (4)	C19—C20—C21—C22	1.4 (4)
C7—N2—C14—C15	−167.8 (2)	C20—C19—C24—C23	−0.5 (4)
C7—N2—C17—C16	166.7 (2)	C20—C21—C22—C23	0.3 (4)
C7—C8—C9—N1	179.7 (3)	C21—C22—C23—O7	177.1 (3)
C7—C8—C9—C4	−1.2 (4)	C21—C22—C23—C24	−2.2 (4)

C9—N1—C10—C2	2.9 (4)	C22—C23—C24—C19	2.3 (4)	
C9—N1—C11—C12	−70.4 (4)	C24—C19—C20—C21	−1.3 (4)	

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2···O3	0.84	1.78	2.551 (3)	152
N3—H3*A*···O1[i]	0.91	1.75	2.652 (3)	172
N3—H3*B*···Cl1	0.91	2.30	3.106 (3)	148
C10—H10···F1[ii]	0.95	2.46	3.158 (4)	130
C12—H12*B*···O7[iii]	0.99	2.47	3.435 (4)	166
C14—H14*B*···F1	0.99	2.27	2.927 (3)	123
C16—H16*B*···Cl1[iv]	0.99	2.78	3.609 (3)	142
O4—H4···Cl1	0.84	2.28	3.082 (2)	160
O6—H6···Cl1[v]	0.84	2.40	3.232 (2)	170
O7—H7···O8	0.84	1.96	2.769 (3)	161
O8—H8*A*···Cl1[i]	0.88 (6)	2.51 (6)	3.362 (3)	164 (4)
O8—H8*B*···O5[vi]	0.82 (6)	2.05 (6)	2.865 (4)	170 (5)

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