Ciprofloxacin salt and salt co-crystal with dihydroxybenzoic acids

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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, C17H19FN3O3+·C7H5O4−·C7H5O4−·H2O, (I), and ciprofloxacin hydrochloride–3,5-dihydroxybenzoic–water (1/1/1), C17H19FN3O3+·Cl−·C7H5O4−·H2O·H2O, (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).

2. Structural commentary

Compound (I) was obtained as an anion-exchange product between ciprofloxacin hydrochloride and 2,6-dihydroxybenzoic acid in solution. 2,6-Dihydroxybenzoic acid (2,6HBA) is a
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; Aakerøy 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 $pK_a$ 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 mono-hydrate 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—H14⋯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 $167.8 (2)^\circ$, 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—H3⋯O4, N3—

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 2
Displacement ellipsoid (50% probability level) drawing with the atomic labelling scheme for compound (II) 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.

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.
H3B···O5, and N3—H3A···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—H3A···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 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—H3A···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. 6a). Interestingly, compound (II) also shows a layered arrangement of ciprofloxacin and the coformer (Fig. 6b).

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···H3A···O1i | 0.91 | 2.38  | 2.977 (2) | 123 |
| N3···H3A···O6 | 0.91 | 2.09  | 2.890 (2) | 146 |
| N3···H3B···O4ii | 0.91 | 2.18  | 2.897 (3) | 136 |
| N3···H3B···O5ii | 0.91 | 2.24  | 3.090 (3) | 155 |
| C11···H11···O3iii | 1.00 | 2.46  | 3.239 (3) | 134 |
| C12···H12A···O4iv | 0.99 | 2.54  | 3.374 (3) | 141 |
| C13···H13A···O7v | 0.99 | 2.51  | 3.193 (3) | 126 |
| C14···H14A···F1 | 0.99 | 2.13  | 2.831 (2) | 126 |
| C15···H15B···O1iii | 0.99 | 2.33  | 3.282 (3) | 161 |
| C17···H17A···O5iv | 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···O4v | 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, z − 1/2; (v) x, y, z − 1.

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.

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 · · · A     | D–H  | H · · · A  | D · · · A | D–H · · · A |
|----------------|-------|-----------|-----------|------------|
| C17–H17A · · · Cl1 | 1.99  | 0.00      | 2.90      | 161.8      |
| C17–H17B · · · Cl1 | 1.99  | 0.00      | 2.80      | 144.9      |
| C17–H17C · · · Cl1 | 1.99  | 0.00      | 2.66      | 133.6      |

Symmetry codes: (i) x, y, z; (ii) 1–x, 1–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 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 (Uiso) were fixed to 1.2Ueq of the parent carbon or nitrogen atom and 1.5Ueq for hydroxyl groups.

Table 3
Experimental details.

|                      | (I)                          | (II)                          |
|----------------------|------------------------------|-------------------------------|
| Crystal data         |                              |                               |
| Chemical formula     | C17H19FN3O3·C7H5O4·H2O       | C17H19FN3O3·C12H10O4Cl·H2O   |
| M_r                  | 539.93                       | Triclinic, P1                 |
| Crystal system, space group | Monoclinic, P21/c        |                               |
| 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 (Å3)               | 2172.1 (2)                  | 594.60 (4)                   |
| Z                    | 4                            | 1                            |
| Radiation type       | Cu Ka                       | Cu Ka                        |
| μ (mm−1)             | 0.98                         | 2.00                         |
| Crystal size (mm)    | 0.23 × 0.05 × 0.04          | 0.28 × 0.2 × 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_max, T_min         | 0.919, 1.000              | 0.839, 1.000                 |
| No. of measured, independent and observed reflections | 15936, 4378, 3601 (7) | 16358, 4420, 4323 (I > 2σ(I)) |
| D_min, (sinθ/λ)_max (Å−1) | 0.038                      | 0.035                        |
|                      | 0.630                     | 0.625                        |

Refinement

|                      |                          |                              |
|----------------------|--------------------------|------------------------------|
| R(F^2 > 2σ(F^2))     | 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 |
| Δρ_max, Δρ_min (e Å−3) | 0.34, −0.41              | 0.25, −0.47                  |
| Absolute structure   | Flack x determined using 1889 quotients [F] = [F] = [F] = [F] = [F] = [F] = [F] = [F] (Parsons et al., 2013) |
| Absolute structure parameter | 0.011 (7)                 |                               |

Computer programs: CrysAlis PRO (Rigaku OD, 2020), SHELXTL2018/2 (Sheldrick, 2015a), SHELXL2018/3 (Sheldrick, 2015b), OLEX2 (Dolomanov et al., 2009) and Mercury (Macrae et al., 2020).
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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
\[\text{C}_{37}\text{H}_{19}\text{FN}_{3}\text{O}_{3}^{+}\cdot\text{C}_{7}\text{H}_{5}\text{O}_{4}^{-}\]
Mr = 485.46
Monoclinic, \(P2_1/c\)
\(a = 7.9722\) (5) Å
\(b = 21.2705\) (11) Å
\(c = 13.0860\) (7) Å
\(\beta = 101.805\) (6)°
\(V = 2172.1\) (2) Å\(^3\)
\(Z = 4\)

\(F(000) = 1016\)
\(D_x = 1.485\) Mg m\(^{-3}\)
Cu \(K\alpha\) radiation, \(\lambda = 1.54184\) Å
Cell parameters from 4777 reflections
\(\theta = 4.0\text{–}72.0^\circ\)
\(\mu = 0.98\) mm\(^{-1}\)
\(T = 93\) K
Block, colourless
0.23 × 0.05 × 0.04 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\(^{-1}\)
\(\omega\) scans
Absorption correction: multi-scan
(CrysAlisPro; Rigaku OD, 2020)

\(T_{\text{min}} = 0.919, T_{\text{max}} = 1.000\)
15936 measured reflections
4378 independent reflections
\(R_{\text{int}} = 0.038\)
\(\theta_{\text{max}} = 76.3^\circ, \theta_{\text{min}} = 4.0^\circ\)
\(h = -9\rightarrow9\)
\(k = -17\rightarrow26\)
\(l = -15\rightarrow16\)

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

| Atom | x      | y      | z      | Uiso/Usq |
|------|--------|--------|--------|----------|
| 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  | 0.169225    | 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   | 0.3060(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) |
| 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 0.812703 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) 1.10688 (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) 0.044 (5)
H21 0.434867 0.712831 1.218955 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)

|      | U¹¹ | U²² | U³³ | U¹² | U¹³ | U²³ |
|------|-----|-----|-----|-----|-----|-----|
| 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) | 0.0238 (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 (9) | 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) |
| Atom | U11 | U22 | U33 | U12 | U13 | U23 |
|------|-----|-----|-----|-----|-----|-----|
| 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, °)**

| Atoms | Bond Length/Angle |
|-------|-------------------|
| 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) |
| Bond | Angle (deg) | Bond | Angle (deg) |
|------|------------|------|------------|
| 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) | C14—C16—H16A | 110.0 |
| C5—C4—C3 | 120.65 (18) | C14—C16—H16B | 110.0 |
| C9—C4—C3 | 121.38 (19) | N2—C17—C16 | 111.57 (16) |
| C9—C4—C5 | 117.95 (18) | N2—C17—H17A | 109.3 |
| C4—C5—H5 | 119.8 | N2—C17—H17B | 109.3 |
| C6—C5—C4 | 120.40 (19) | C16—C17—H17A | 109.3 |
| C6—C5—H5 | 119.8 | C16—C17—H17B | 109.3 |
| F1—C6—C5 | 117.95 (18) | H17A—C17—H17B | 108.0 |
| F1—C6—C7 | 118.58 (18) | C20—O6—H6 | 109.5 |
| C5—C6—C7 | 123.34 (19) | C20—O7—H7 | 109.5 |
| N2—C7—C6 | 122.04 (18) | C24—O7—H7 | 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) |
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—H3d···O1i| 0.91 | 2.38  | 2.977 (2) | 123     |
| N3—H3d···O6 | 0.91 | 2.09  | 2.890 (2) | 146     |

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Supporting information

N3—H3B···O4\textsuperscript{ii} 0.91 2.18 2.897 (3) 136
N3—H3B···O5\textsuperscript{ii} 0.91 2.24 3.090 (3) 155
C11—H11···O3\textsuperscript{iii} 1.00 2.46 3.239 (3) 134
C12—H12\textsuperscript{A}···O4\textsuperscript{iv} 0.99 2.54 3.374 (3) 141
C13—H13\textsuperscript{A}···O7\textsuperscript{v} 0.99 2.51 3.193 (3) 126
C14—H14\textsuperscript{A}···F1 0.99 2.13 2.831 (2) 126
C15—H15\textsuperscript{B}···O1\textsuperscript{iii} 0.99 2.33 3.282 (3) 161
C17—H17\textsuperscript{A}···O5\textsuperscript{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\textsuperscript{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+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\textsubscript{17}H\textsubscript{19}FN\textsubscript{3}O\textsubscript{3}\textsuperscript{+}·C\textsubscript{7}H\textsubscript{6}O\textsubscript{4}·Cl\textsuperscript{−}·H\textsubscript{2}O

Z = 1

Mr = 539.93

Triclinic, \( P1 \)

\( a = 7.2165 (2) \text{ Å} \)
\( b = 8.8298 (4) \text{ Å} \)
\( c = 10.1184 (3) \text{ Å} \)

\( \alpha = 92.997 (3)^{\circ} \)
\( \beta = 95.219 (2)^{\circ} \)
\( \gamma = 111.557 (4)^{\circ} \)

\( V = 594.60 (4) \text{ Å}^3 \)

\( F(000) = 282 \)

\( D_\text{c} = 1.508 \text{ Mg m}^{-3} \)

\( \lambda = 1.54184 \text{ Å} \)

Cell parameters from 10041 reflections

\( \theta = 4.4–75.8^\circ \)

\( \mu = 2.00 \text{ mm}^{-1} \)

\( T = 93 \text{ K} \)

Block, colourless

\( 0.28 \times 0.2 \times 0.05 \text{ mm} \)

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\(^{-1}\)

\( \omega \) scans

Absorption correction: multi-scan

\( T \) min = 0.839, \( T \) max = 1.000

16358 measured reflections

4420 independent reflections

4323 reflections with \( I > 2\sigma(I) \)

Refinement

Refinement on \( F^2 \)

\( R[F^2 > 2\sigma(F^2)] = 0.034 \)

\( wR(F^2) = 0.094 \)

\( S = 1.12 \)

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

\( w = 1/[\sigma^2(F^2) + (0.0589P)^2 + 0.0709P] \)

where \( P = (F^2 + 2F_c^2)/3 \)

\( \Delta(\sigma)_{\text{max}} < 0.001 \)

\( \Delta \rho_{\text{max}} = 0.25 \text{ e Å}^{-3} \)

\( \Delta \rho_{\text{min}} = -0.47 \text{ e Å}^{-3} \)

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     | Uiso* / Ueq |
|----|-------|-------|-------|-------------|
| C11| 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)   |
### Atomic displacement parameters ($\AA^2$)

|     | $U^{11}$  | $U^{22}$  | $U^{33}$  | $U^{12}$  | $U^{13}$  | $U^{23}$  |
|-----|-----------|-----------|-----------|-----------|-----------|-----------|
| 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)
O8 0.0438 (13) 0.0286 (13) 0.0212 (11) 0.0146 (10) 0.0044 (9) 0.0017 (9)

Geometric parameters (Å, °)

| Bond          | Length/Angle | Bond          | Length/Angle |
|---------------|--------------|---------------|--------------|
| 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       |
| Bond          | Length (Å) | Bond          | Length (Å) | Bond          | Length (Å) |
|--------------|------------|--------------|------------|--------------|------------|
| 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  C21—C22—H22 121.6 (3)
C11—C12—H12B 117.8  C23—C22—H22 120.2
C13—C12—H12A 117.8  H8A—O8—H8B 112 (5)
C13—C12—H12B 117.8  F1—C6—C7—N2 −2.4 (4)
F1—C6—C7—C8 −178.8 (3)  C9—N1—C11—C13 −140.3 (3)
O1—C1—C2—C3 −173.3 (3)  C9—C4—C5—C6 0.7 (4)
O1—C1—C2—C10 4.3 (4)  C10—N1—C9—C4 −3.6 (4)
O2—C1—C2—C3 5.9 (4)  C10—N1—C9—C8 175.5 (3)
O2—C1—C2—C10 −176.5 (3)  C10—N1—C11—C12 117.4 (3)
O3—C3—C4—C5 2.6 (4)  C10—N1—C11—C13 47.5 (4)
O3—C3—C4—C9 −179.1 (3)  C11—N1—C10—C2 175.1 (3)
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—C22—C21 −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—C19—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)
### 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—H3A⋯O1\(^i\) | 0.91 | 1.75| 2.652 (3) | 172    |
| N3—H3B⋯Cl1   | 0.91 | 2.30| 3.106 (3) | 148    |
| C10—H10⋯F1\(^ii\) | 0.95 | 2.46| 3.158 (4) | 130    |
| C12—H12B⋯O7\(^iii\) | 0.99 | 2.47| 3.435 (4) | 166    |
| C14—H14B⋯F1  | 0.99 | 2.27| 2.927 (3) | 123    |
| C16—H16B⋯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—H8A⋯Cl1\(^i\) | 0.88 (6) | 2.51 (6) | 3.362 (3) | 164 (4) |
| O8—H8B⋯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.