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Crystal structure and Hirshfeld surface analysis of anhydrous salt of levofloxacin and 4-methylbenzoic acid

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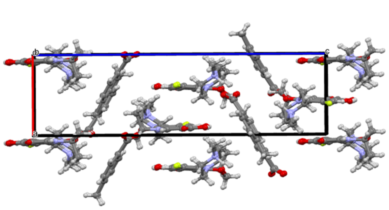
The anhydrous salt levofloxacinium 4-methylbenzoate, $C_{18}H_{21}FN_3O_4^+\cdot C_8H_7O_2^-$, has been synthesized and its crystal structure determined. In the crystal, the levofloxacinium ions interact with the 4-methylbenzoate anion *via* N—H$^+\cdots$O$^-$ and C—H$\cdots$O hydrogen bonds, forming a tape-like supramolecular structure. Hirshfeld surface analysis and the calculated two-dimensional finger plots of the various atom–atom contacts involving both the ions are described.

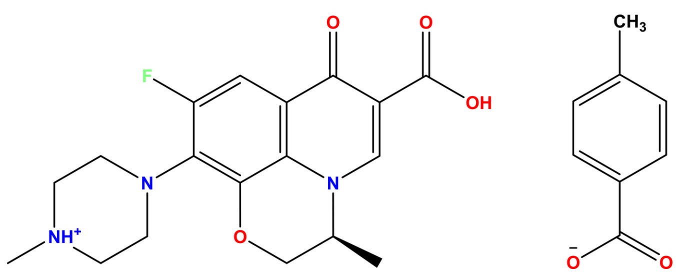
1. Chemical context

Small organic molecules and peptides have been known for decades for their aesthetic supramolecular architectures (Prabhakaran *et al.*, 2009; Upadhye *et al.*, 2009) and various applications including in the pharmaceutical industry (Shah *et al.*, 2023; Karmakar *et al.*, 2025; Gellman, 1998). Fluoroquinolones belonging to a class of broad-spectrum antibiotics having advantageous pharmacokinetic properties and are used in the treatment of various bacterial infections. Levofloxacin, (*levo* isomer of oflaxacin), systematic name: *S*-(−)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7*H*-pyridine[1,2,3-*de*]-1,4-benzoxazine-6-carboxylic acid, $C_{18}H_{20}FN_3O_4$, is a fluorinated third-generation fluoroquinolone antibiotic employed in the treatment of respiratory, urinary tract, cutaneous allergy and various other infections caused by Gram-positive and Gram-negative bacteria. A therapeutic review discussing the pharmacology, pharmacokinetics, *in vitro* activity, drug interactions, and adverse effects of levofloxacin has been published (Wimer *et al.*, 1998) and the use of levofloxacin in the treatment of community-acquired pneumonia was described (Noreddin *et al.*, 2010). A cohort analysis describing levofloxacin dosage to treat bone and joint infections was reported (Asseray *et al.*, 2016). A literature review of the levofloxacin in veterinary medicine was published recently wherein levofloxacin MIC values of animal microbial isolates are summarized (Sitovs *et al.*, 2021). A review on data summarizing the efficacy and the tolerability of levofloxacin in treating complicated urinary tract infections (UTIs) and pyelonephritis was described (Bientinesi *et al.*, 2020), as well as a review of levofloxacin for the treatment of bacterial infections (Noel, 2009) has also been published. Recently, a retrospective observational study of the efficacy and safety of levofloxacin in children with severe infections was conducted (Junqi *et al.*, 2024). Recently, levofloxacinium citrate salt hydrate (Nugrahani *et al.*, 2024) was reported, the crystal structure of which features O—H$\cdots$O, N—H$\cdots$O and



C—H···O interactions. Various solvates of levofloxacin and its citrate salt have also been reported (Nugrahani *et al.*, 2022) wherein improvement in the antibiotic potency and an antibiotic–antioxidant combination for drug dosage development was reported. A study involving salts of levofloxacin with 2,6- and 3,5-dihydroxybenzoic acid showed increased stability and antibiotic potency improvement (Nugrahani *et al.*, 2023). More recently, a drug–drug salt of levofloxacin flufenamic acid was reported along with its physicochemical properties, potency and anti-inflammation improvements that could be developed further into dosage formulations (Nugrahani *et al.*, 2025).

The preparation of anhydrous forms of levofloxacin, salts or co-crystals (Freitas *et al.*, 2018; Wei *et al.*, 2019) continues to be challenging as these anhydrous forms readily convert into hemihydrate/hydrate forms (Singh *et al.*, 2014). Continuing our research in the area of co-crystals (*e.g.* PrakashaReddy *et al.*, 2004), we herein report the synthesis of a new anhydrous levofloxacinium:4-methylbenzoate salt, (I). We have determined its molecular and crystal structures and conducted a Hirshfeld surface analysis to examine the intermolecular interactions.



2. Structural commentary

Reaction between levofloxacin and 4-methylbenzoic acid yielded the title salt, (I), which crystallizes in the orthorhombic $P2_12_12_1$ space group with one ion pair in the asymmetric unit. The molecular structure of the salt along with the atom-labelling is shown in Fig. 1. The quinoline ring along with the other attached carboxyl and fluorine atoms in the levofloxacinium are essentially planar (r.m.s. deviation = 0.0659 Å), as observed in another salt hydrate reported in the literature (Golovnev *et al.*, 2018). On the other hand, the carboxylate group in the 4-methylbenzoate is twisted notably from the planarity of methyl aromatic plane with a torsion angle of −18.1 (8)° for the chain of O5—C21—C22—C27 atoms. An intramolecular O2—H2···O3 hydrogen bond is observed between the hydroxy O atom of the –COOH group and the adjacent quinoline oxygen atom, forming an *S*(6) ring motif, as seen in other salts/co-crystals of levofloxacin reported in the literature (Nugrahani *et al.*, 2022).

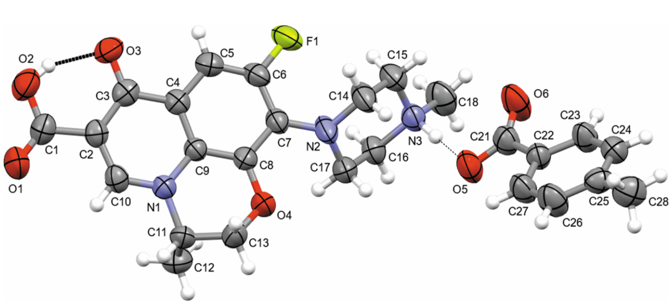


Figure 1
The molecular structure of the levofloxacinium:4-methylbenzoate salt, showing the atom labelling and displacement ellipsoids drawn at the 30% probability level. Intramolecular hydrogen bonds are drawn as thick dashed lines while intermolecular hydrogen bonds are drawn as thin dashed lines.

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2···O3	0.82	1.76	2.522 (6)	155
N3—H3···O5	0.98	1.63	2.610 (6)	175
N3—H3···O6	0.98	2.51	3.125 (6)	121
C11—H11···O6^{i}	0.98	2.28	3.147 (6)	147
C12—H12*C*···O3^{ii}	0.96	2.52	3.308 (8)	139
C13—H13*A*···O3^{iii}	0.97	2.40	3.302 (8)	154
C14—H14*B*···F1	0.97	2.30	2.785 (6)	110
C15—H15*B*···O1^{iv}	0.97	2.58	3.268 (7)	128
C16—H16*B*···O2^{ii}	0.97	2.55	3.277 (7)	131
C18—H18*C*···F1^{v}	0.96	2.54	3.279 (8)	134
C28—H28*B*···O2^{vi}	0.96	2.60	3.481 (7)	153

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

3. Supramolecular features

In the crystal, intermolecular hydrogen-bonding interactions are observed. Levofloxacinium and 4-methylbenzoate ions are connected through the N5—H6···O8 interaction (Table 1). Further, a hydrogen atom of the methyl group of 4-methylbenzoate interacts with the hydroxy group –COOH of the levofloxacinium cation through the C28—H28*B*···O2 hydrogen bond (Desiraju, *et al.*, 1999; Patel, *et al.*, 2024), forming a tape-like supramolecular structure as shown in Fig. 2. In addition, a number of other C—H···O interactions (C16—H16*B*···O2, C12—H12*C*···O3, C11—H11···O6, C15—H15*B*···O1, C10—H10···O6, C13—H13*A*···O3) between levofloxacinium ions and both levofloxacinium and 4-methylbenzoate are observed in the crystal structure as

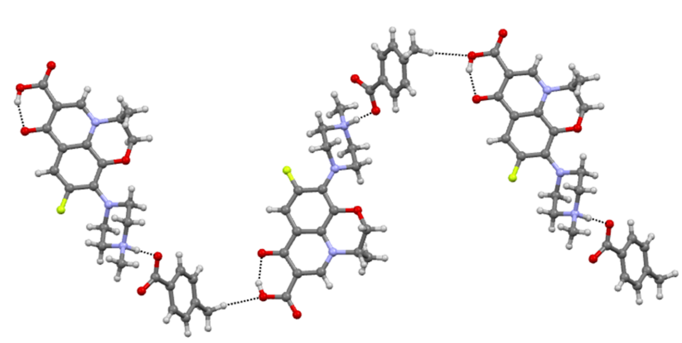


Figure 2
Formation of supramolecular tape-like structure through N—H^{+}···O^{-} and C—H···O interactions in the crystal.

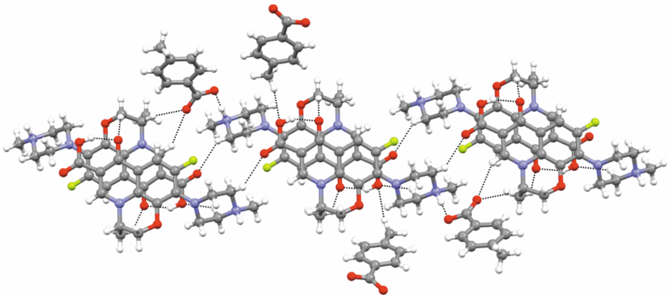


Figure 3
Various other C—H···O interactions observed in the crystal.

shown in Fig. 3. The three-dimensional projection along the crystallographic *b*-axis is shown in Fig. 4.

4. Hirshfeld surfaces and 2D fingerprint plots

A Hirshfeld surface analysis and corresponding fingerprint plots were generated using *CrystalExplorer* software (Spackman *et al.*, 2021; Spackman & Jayatilaka, 2009) to further investigate and determine the contributions of the several intermolecular interactions in the crystal. The Hirshfeld surface mapped over d_{norm} with the corresponding two-dimensional fingerprint plots (McKinnon *et al.*, 2007) for all intermolecular interactions and those delineated into specific contacts are shown in Fig. 5. The largest contribution comes from H···H contacts at 48.6% of the total, which is consistent with the significant hydrogen content of the molecule. The next most important contact is O···H/H···O at 24.5%, which primarily comes from the intramolecular O—H···O and intermolecular N—H···O as well as C—H···O interactions. The C···H/H···C interactions account for 12.1% while C···C contacts contribute 6.6%, followed by F···H/H···F contacts contributing 4.6%.

5. Synthesis and crystallization

Levofloxacin and 4-methylbenzoic acid were obtained from Aldrich, and HPLC grade methanol was used for reaction. Levofloxacin (100 mg, 0.277 mmol) was dissolved in methanol (10 ml) under constant stirring at 335 K for 40 min. Equimolar solution of 4-methylbenzoic acid (38 mg, 0.277 mmol) in methanol (10 ml) was added to the solution of levofloxacin and stirring was continued further for about 30 min at 335 K. The mixture was cooled to room temperature and the solution was filtered. X-ray quality single crystals of suitable dimension were obtained over a period of ten days by slow evaporation of the solvent.

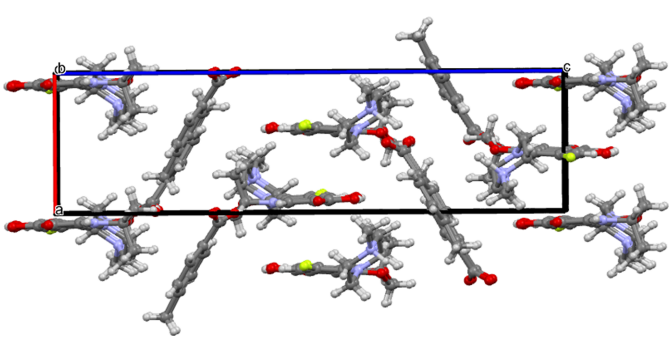


Figure 4
Three-dimensional packing viewed along the b-axis direction.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{18}H_{21}FN_3O_4^+ \cdot C_8H_7O_2^-$
M_r	497.51
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	120
a, *b*, *c* (Å)	7.1788 (10), 13.0274 (13), 25.979 (3)
V (Å^3)	2429.6 (5)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.10
Crystal size (mm)	0.39 × 0.29 × 0.23
Data collection	
Diffractometer	Bruker SMART APEXII CCD
Absorption correction	Analytical (*SADABS*; Krause *et al.*, 2015)
T_{min}, T_{max}	0.575, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	17036, 5409, 2456
R_{int}	0.116
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.644
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.060, 0.177, 1.00
No. of reflections	5409
No. of parameters	330
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.23, −0.17
Absolute structure	Flack x determined using 707 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter	0.02 (10)

Computer programs: *APEX2* (Bruker, 2005), *SAINT* (Bruker, 2017), *SHELXT2018/2* (Sheldrick, 2015*a*), *SHELXL2019/3* (Sheldrick, 2015*b*) and *OLEX2* (Dolomanov *et al.*, 2009).

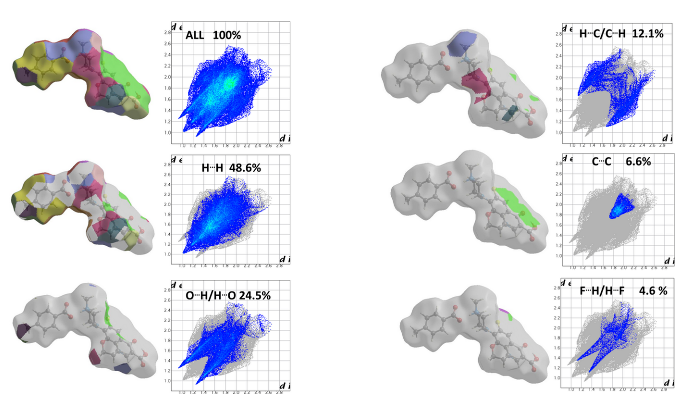


Figure 5
Hirshfeld surfaces of title compound mapped with d_{norm} (left image of each pair) and the corresponding two-dimensional fingerprint plots (right image of each pair) showing all contributions and then the major contributions of H···H followed by O···H/H···O, C···H/H···C, C···C and F···H/H···F contacts.

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. All hydrogen atoms were placed at idealized positions and refined using a riding model. The assignment of the absolute configuration is based on levofloxacin.

Acknowledgements

The authors are grateful to the Indrashil University and Central University of Gujarat, India, for research facilities. One of the authors (BCP) is indebted to the Knowledge Consortium of Gujarat (KCG), Department of Education, Government of Gujarat, India for a SHODH-Scheme fellowship. We thank an anonymous referee for constructive comments and suggestions.

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Computing details

4-{11-Carboxy-7-fluoro-2-methyl-10-oxo-4-oxa-1-azatricyclo[7.3.1.0^{5,13}]trideca-5,7,9(13),11-tetraen-6-yl}-1-methylpiperazin-1-ium 4-methylbenzoate

Crystal data

$C_{18}H_{21}FN_3O_4^+\cdot C_8H_7O_2^-$
M_r = 497.51
Orthorhombic, $P2_12_12_1$
a = 7.1788 (10) Å
b = 13.0274 (13) Å
c = 25.979 (3) Å
V = 2429.6 (5) Å^3
Z = 4
F(000) = 1048
D_x = 1.360 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 3952 reflections
θ = 2.5–27.5°
μ = 0.10 mm^{-1}
T = 120 K
Irregular, clear whiteish colourless
0.39 × 0.29 × 0.23 mm

Data collection

Bruker SMART APEXII CCD diffractometer
Radiation source: fine-focus sealed xray tube
ω scans
Absorption correction: analytical (SADABS; Krause *et al.*, 2015)
T_{min} = 0.575, T_{max} = 0.746
17036 measured reflections
5409 independent reflections
2456 reflections with $I > 2\sigma(I)$
R_{int} = 0.116
θ_{max} = 27.2°, θ_{min} = 1.8°
h = −9→9
k = −16→14
l = −33→33

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.060
$wR(F^2)$ = 0.177
S = 1.00
5409 reflections
330 parameters
0 restraints
Primary atom site location: dual
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0526P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.23 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}
Absolute structure: Flack x determined using 707 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter: 0.02 (10)

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}
F1	0.3846 (6)	0.4254 (2)	0.48601 (11)	0.0839 (13)
O4	0.4409 (7)	0.6279 (2)	0.63599 (12)	0.0654 (13)
O3	0.4055 (6)	0.7860 (3)	0.41864 (13)	0.0690 (12)
N1	0.4331 (7)	0.8049 (3)	0.57537 (14)	0.0507 (12)
O5	0.5049 (7)	0.1973 (2)	0.69163 (16)	0.0809 (14)
O2	0.4106 (8)	0.9794 (3)	0.41499 (15)	0.0817 (14)
H2	0.412608	0.918689	0.406726	0.123*
O6	0.5051 (8)	0.0488 (3)	0.65068 (18)	0.1007 (18)
N3	0.2677 (7)	0.2393 (3)	0.61849 (16)	0.0592 (14)
H3	0.351504	0.221625	0.646927	0.071*
N2	0.4162 (8)	0.4350 (3)	0.59214 (17)	0.0709 (16)
O1	0.4224 (8)	1.0696 (3)	0.48648 (15)	0.0909 (17)
C3	0.4150 (8)	0.7922 (4)	0.46730 (19)	0.0529 (14)
C2	0.4216 (8)	0.8873 (3)	0.49351 (19)	0.0510 (14)
C4	0.4170 (8)	0.7005 (3)	0.49911 (19)	0.0482 (13)
C7	0.4161 (9)	0.5228 (3)	0.5618 (2)	0.0530 (15)
C9	0.4225 (8)	0.7085 (3)	0.55283 (17)	0.0469 (13)
C8	0.4276 (8)	0.6204 (3)	0.58383 (17)	0.0505 (14)
C10	0.4327 (8)	0.8895 (4)	0.54619 (19)	0.0546 (15)
H10	0.440276	0.952924	0.562442	0.066*
C11	0.4308 (10)	0.8137 (3)	0.63186 (17)	0.0558 (16)
H11	0.502388	0.874645	0.641728	0.067*
C6	0.4047 (9)	0.5197 (4)	0.5082 (2)	0.0577 (16)
C16	0.1705 (9)	0.3364 (3)	0.6321 (2)	0.0596 (16)
H16A	0.101626	0.326800	0.663871	0.072*
H16B	0.082101	0.353582	0.605224	0.072*
C22	0.7367 (9)	0.0768 (4)	0.71312 (19)	0.0565 (16)
C5	0.4083 (9)	0.6029 (4)	0.4772 (2)	0.0574 (16)
H5	0.405122	0.595200	0.441643	0.069*
C1	0.4181 (10)	0.9871 (4)	0.4657 (2)	0.0651 (18)
C25	1.0649 (9)	0.0146 (4)	0.7643 (2)	0.0609 (16)
C23	0.7906 (10)	−0.0257 (4)	0.7157 (2)	0.0700 (19)
H23	0.717649	−0.075398	0.699742	0.084*
C21	0.5685 (10)	0.1086 (4)	0.6829 (2)	0.0678 (18)
C17	0.3068 (10)	0.4240 (4)	0.63871 (19)	0.0628 (17)
H17A	0.239637	0.487146	0.645588	0.075*
H17B	0.388308	0.410274	0.667678	0.075*
C13	0.5267 (10)	0.7203 (3)	0.65338 (19)	0.0639 (17)
H13A	0.656407	0.720735	0.642957	0.077*

H13B	0.522493	0.722761	0.690684	0.077*
C24	0.9502 (10)	−0.0553 (4)	0.7415 (2)	0.0657 (18)
H24	0.980162	−0.124614	0.743378	0.079*
C15	0.3828 (10)	0.2534 (4)	0.5714 (2)	0.073 (2)
H15A	0.302064	0.266210	0.542151	0.088*
H15B	0.452586	0.191077	0.564583	0.088*
C27	0.8484 (11)	0.1468 (4)	0.7376 (2)	0.074 (2)
H27	0.815831	0.215889	0.737288	0.089*
C26	1.0093 (12)	0.1159 (4)	0.7628 (2)	0.085 (2)
H26	1.081991	0.165116	0.779177	0.102*
C14	0.5154 (10)	0.3417 (4)	0.5778 (2)	0.076 (2)
H14A	0.606069	0.325097	0.604224	0.091*
H14B	0.581967	0.352980	0.545812	0.091*
C12	0.2334 (11)	0.8264 (4)	0.6508 (2)	0.080 (2)
H12A	0.178361	0.885510	0.634783	0.120*
H12B	0.233870	0.835415	0.687461	0.120*
H12C	0.162330	0.766401	0.642152	0.120*
C28	1.2434 (10)	−0.0176 (5)	0.7894 (2)	0.083 (2)
H28A	1.255020	−0.090935	0.787757	0.125*
H28B	1.243211	0.003861	0.824784	0.125*
H28C	1.346502	0.013623	0.771844	0.125*
C18	0.1332 (11)	0.1541 (4)	0.6121 (3)	0.086 (2)
H18A	0.071686	0.141200	0.644297	0.129*
H18B	0.198158	0.093334	0.601357	0.129*
H18C	0.042429	0.172378	0.586578	0.129*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
F1	0.124 (4)	0.0551 (17)	0.072 (2)	−0.009 (2)	0.020 (2)	−0.0210 (15)
O4	0.098 (4)	0.0453 (17)	0.053 (2)	0.002 (2)	−0.007 (2)	−0.0014 (15)
O3	0.079 (3)	0.079 (2)	0.048 (2)	−0.001 (3)	0.003 (2)	0.0036 (18)
N1	0.060 (4)	0.044 (2)	0.049 (2)	0.000 (2)	−0.004 (2)	−0.0011 (17)
O5	0.096 (4)	0.050 (2)	0.097 (3)	0.015 (2)	−0.025 (3)	−0.0044 (19)
O2	0.102 (4)	0.077 (2)	0.066 (3)	−0.015 (3)	−0.006 (3)	0.020 (2)
O6	0.119 (5)	0.057 (2)	0.127 (4)	0.012 (2)	−0.065 (4)	−0.019 (2)
N3	0.068 (4)	0.044 (2)	0.066 (3)	0.001 (2)	−0.011 (3)	−0.0008 (19)
N2	0.097 (5)	0.042 (2)	0.074 (3)	0.013 (3)	0.031 (3)	0.005 (2)
O1	0.138 (5)	0.052 (2)	0.083 (3)	0.000 (3)	−0.006 (3)	0.009 (2)
C3	0.039 (4)	0.065 (3)	0.055 (3)	0.001 (3)	−0.001 (3)	0.003 (2)
C2	0.044 (4)	0.049 (3)	0.060 (3)	0.001 (3)	−0.003 (3)	0.004 (2)
C4	0.041 (4)	0.050 (3)	0.054 (3)	0.000 (3)	0.001 (3)	−0.002 (2)
C7	0.058 (4)	0.041 (2)	0.060 (3)	0.004 (3)	0.008 (3)	0.000 (2)
C9	0.050 (4)	0.043 (2)	0.048 (3)	0.002 (3)	−0.002 (3)	−0.002 (2)
C8	0.056 (4)	0.048 (2)	0.047 (3)	0.006 (3)	0.003 (3)	−0.001 (2)
C10	0.052 (4)	0.046 (3)	0.065 (3)	0.003 (3)	−0.008 (3)	0.002 (2)
C11	0.074 (5)	0.048 (3)	0.045 (3)	−0.003 (3)	−0.005 (3)	−0.006 (2)
C6	0.065 (5)	0.049 (3)	0.060 (4)	−0.001 (3)	0.008 (3)	−0.014 (3)

C16	0.064 (5)	0.049 (3)	0.066 (3)	0.010 (3)	−0.001 (3)	0.001 (3)
C22	0.064 (5)	0.047 (3)	0.058 (3)	0.001 (3)	−0.011 (3)	0.000 (2)
C5	0.060 (5)	0.059 (3)	0.053 (3)	0.002 (3)	0.003 (3)	−0.008 (2)
C1	0.066 (5)	0.063 (3)	0.066 (4)	−0.002 (4)	−0.006 (4)	0.015 (3)
C25	0.059 (5)	0.070 (3)	0.054 (3)	0.003 (3)	−0.007 (3)	−0.004 (3)
C23	0.082 (6)	0.048 (3)	0.080 (4)	0.000 (3)	−0.029 (4)	−0.007 (3)
C21	0.079 (6)	0.051 (3)	0.073 (4)	−0.008 (4)	−0.012 (4)	0.000 (3)
C17	0.084 (5)	0.047 (3)	0.057 (3)	0.005 (3)	0.004 (3)	0.001 (3)
C13	0.087 (5)	0.054 (3)	0.050 (3)	−0.001 (3)	−0.012 (3)	0.003 (2)
C24	0.078 (6)	0.055 (3)	0.064 (3)	0.006 (3)	−0.002 (4)	−0.004 (3)
C15	0.093 (6)	0.052 (3)	0.076 (4)	0.009 (3)	0.010 (4)	−0.008 (3)
C27	0.090 (6)	0.051 (3)	0.083 (4)	0.002 (4)	−0.018 (4)	−0.010 (3)
C26	0.091 (6)	0.063 (3)	0.102 (5)	−0.004 (4)	−0.029 (5)	−0.015 (3)
C14	0.091 (6)	0.045 (3)	0.092 (4)	0.010 (3)	0.025 (4)	−0.002 (3)
C12	0.100 (7)	0.081 (4)	0.060 (4)	0.014 (4)	0.011 (4)	−0.004 (3)
C28	0.069 (6)	0.097 (4)	0.083 (4)	0.009 (4)	−0.019 (4)	−0.011 (3)
C18	0.089 (6)	0.063 (3)	0.108 (5)	−0.015 (4)	−0.019 (4)	−0.010 (3)

Geometric parameters (Å, º)

F1—C6	1.365 (5)	C16—H16B	0.9700
O4—C8	1.362 (5)	C16—C17	1.512 (8)
O4—C13	1.426 (6)	C22—C23	1.392 (7)
O3—C3	1.269 (6)	C22—C21	1.498 (8)
N1—C9	1.388 (6)	C22—C27	1.371 (8)
N1—C10	1.337 (6)	C5—H5	0.9300
N1—C11	1.472 (6)	C25—C24	1.363 (7)
O5—C21	1.264 (6)	C25—C26	1.379 (8)
O2—H2	0.8200	C25—C28	1.498 (8)
O2—C1	1.323 (6)	C23—H23	0.9300
O6—C21	1.231 (6)	C23—C24	1.382 (9)
N3—H3	0.9800	C17—H17A	0.9700
N3—C16	1.488 (6)	C17—H17B	0.9700
N3—C15	1.488 (7)	C13—H13A	0.9700
N3—C18	1.481 (7)	C13—H13B	0.9700
N2—C7	1.389 (6)	C24—H24	0.9300
N2—C17	1.449 (7)	C15—H15A	0.9700
N2—C14	1.458 (6)	C15—H15B	0.9700
O1—C1	1.202 (6)	C15—C14	1.503 (8)
C3—C2	1.415 (6)	C27—H27	0.9300
C3—C4	1.453 (6)	C27—C26	1.387 (9)
C2—C10	1.371 (6)	C26—H26	0.9300
C2—C1	1.487 (7)	C14—H14A	0.9700
C4—C9	1.400 (7)	C14—H14B	0.9700
C4—C5	1.394 (6)	C12—H12A	0.9600
C7—C8	1.396 (6)	C12—H12B	0.9600
C7—C6	1.396 (7)	C12—H12C	0.9600
C9—C8	1.402 (6)	C28—H28A	0.9600

C10—H10	0.9300	C28—H28B	0.9600
C11—H11	0.9800	C28—H28C	0.9600
C11—C13	1.505 (7)	C18—H18A	0.9600
C11—C12	1.509 (9)	C18—H18B	0.9600
C6—C5	1.350 (7)	C18—H18C	0.9600
C16—H16A	0.9700		

C8—O4—C13	114.0 (4)	C24—C25—C28	121.2 (5)
C9—N1—C11	119.3 (4)	C26—C25—C28	121.9 (6)
C10—N1—C9	120.4 (4)	C22—C23—H23	119.3
C10—N1—C11	120.1 (4)	C24—C23—C22	121.4 (5)
C1—O2—H2	109.5	C24—C23—H23	119.3
C16—N3—H3	108.0	O5—C21—C22	116.8 (5)
C15—N3—H3	108.0	O6—C21—O5	124.5 (6)
C15—N3—C16	110.6 (4)	O6—C21—C22	118.7 (5)
C18—N3—H3	108.0	N2—C17—C16	109.3 (4)
C18—N3—C16	111.0 (5)	N2—C17—H17A	109.8
C18—N3—C15	111.3 (4)	N2—C17—H17B	109.8
C7—N2—C17	123.7 (4)	C16—C17—H17A	109.8
C7—N2—C14	122.8 (4)	C16—C17—H17B	109.8
C17—N2—C14	113.3 (4)	H17A—C17—H17B	108.3
O3—C3—C2	122.5 (4)	O4—C13—C11	111.5 (4)
O3—C3—C4	121.0 (4)	O4—C13—H13A	109.3
C2—C3—C4	116.5 (4)	O4—C13—H13B	109.3
C3—C2—C1	122.1 (5)	C11—C13—H13A	109.3
C10—C2—C3	120.0 (4)	C11—C13—H13B	109.3
C10—C2—C1	117.9 (4)	H13A—C13—H13B	108.0
C9—C4—C3	120.4 (4)	C25—C24—C23	121.7 (5)
C5—C4—C3	121.2 (5)	C25—C24—H24	119.1
C5—C4—C9	118.4 (4)	C23—C24—H24	119.1
N2—C7—C8	121.1 (4)	N3—C15—H15A	109.5
N2—C7—C6	122.9 (4)	N3—C15—H15B	109.5
C6—C7—C8	116.0 (4)	N3—C15—C14	110.8 (4)
N1—C9—C4	119.3 (4)	H15A—C15—H15B	108.1
N1—C9—C8	119.8 (4)	C14—C15—H15A	109.5
C4—C9—C8	120.8 (4)	C14—C15—H15B	109.5
O4—C8—C7	118.5 (4)	C22—C27—H27	119.6
O4—C8—C9	121.0 (4)	C22—C27—C26	120.8 (5)
C7—C8—C9	120.5 (4)	C26—C27—H27	119.6
N1—C10—C2	123.3 (4)	C25—C26—C27	122.2 (6)
N1—C10—H10	118.3	C25—C26—H26	118.9
C2—C10—H10	118.3	C27—C26—H26	118.9
N1—C11—H11	108.5	N2—C14—C15	110.9 (5)
N1—C11—C13	107.6 (4)	N2—C14—H14A	109.5
N1—C11—C12	110.1 (5)	N2—C14—H14B	109.5
C13—C11—H11	108.5	C15—C14—H14A	109.5
C13—C11—C12	113.4 (5)	C15—C14—H14B	109.5
C12—C11—H11	108.5	H14A—C14—H14B	108.0

F1—C6—C7	116.9 (4)	C11—C12—H12A	109.5
C5—C6—F1	118.3 (4)	C11—C12—H12B	109.5
C5—C6—C7	124.8 (4)	C11—C12—H12C	109.5
N3—C16—H16A	109.3	H12A—C12—H12B	109.5
N3—C16—H16B	109.3	H12A—C12—H12C	109.5
N3—C16—C17	111.4 (5)	H12B—C12—H12C	109.5
H16A—C16—H16B	108.0	C25—C28—H28A	109.5
C17—C16—H16A	109.3	C25—C28—H28B	109.5
C17—C16—H16B	109.3	C25—C28—H28C	109.5
C23—C22—C21	121.0 (5)	H28A—C28—H28B	109.5
C27—C22—C23	117.0 (6)	H28A—C28—H28C	109.5
C27—C22—C21	122.0 (5)	H28B—C28—H28C	109.5
C4—C5—H5	120.3	N3—C18—H18A	109.5
C6—C5—C4	119.3 (5)	N3—C18—H18B	109.5
C6—C5—H5	120.3	N3—C18—H18C	109.5
O2—C1—C2	114.7 (5)	H18A—C18—H18B	109.5
O1—C1—O2	121.0 (5)	H18A—C18—H18C	109.5
O1—C1—C2	124.3 (5)	H18B—C18—H18C	109.5
C24—C25—C26	116.8 (6)		

F1—C6—C5—C4	176.0 (5)	C10—N1—C11—C12	84.3 (6)
O3—C3—C2—C10	−179.7 (6)	C10—C2—C1—O2	178.9 (6)
O3—C3—C2—C1	0.0 (10)	C10—C2—C1—O1	−0.8 (10)
O3—C3—C4—C9	−178.3 (6)	C11—N1—C9—C4	177.4 (5)
O3—C3—C4—C5	−0.1 (9)	C11—N1—C9—C8	−6.0 (9)
N1—C9—C8—O4	0.7 (9)	C11—N1—C10—C2	−175.3 (6)
N1—C9—C8—C7	179.7 (6)	C6—C7—C8—O4	−179.4 (5)
N1—C11—C13—O4	−56.6 (6)	C6—C7—C8—C9	1.6 (9)
N3—C16—C17—N2	56.2 (6)	C16—N3—C15—C14	54.8 (6)
N3—C15—C14—N2	−54.6 (6)	C22—C23—C24—C25	−1.9 (10)
N2—C7—C8—O4	0.7 (9)	C22—C27—C26—C25	0.3 (10)
N2—C7—C8—C9	−178.3 (6)	C5—C4—C9—N1	179.4 (5)
N2—C7—C6—F1	2.9 (10)	C5—C4—C9—C8	2.8 (9)
N2—C7—C6—C5	−178.5 (6)	C1—C2—C10—N1	178.6 (6)
C3—C2—C10—N1	−1.7 (10)	C23—C22—C21—O5	164.6 (6)
C3—C2—C1—O2	−0.8 (9)	C23—C22—C21—O6	−17.5 (9)
C3—C2—C1—O1	179.6 (7)	C23—C22—C27—C26	1.2 (9)
C3—C4—C9—N1	−2.4 (9)	C21—C22—C23—C24	177.0 (6)
C3—C4—C9—C8	−179.0 (5)	C21—C22—C27—C26	−176.2 (6)
C3—C4—C5—C6	−177.9 (6)	C17—N2—C7—C8	44.6 (9)
C2—C3—C4—C9	0.9 (9)	C17—N2—C7—C6	−135.3 (6)
C2—C3—C4—C5	179.1 (6)	C17—N2—C14—C15	57.0 (7)
C4—C3—C2—C10	1.1 (9)	C13—O4—C8—C7	155.4 (5)
C4—C3—C2—C1	−179.2 (6)	C13—O4—C8—C9	−25.6 (8)
C4—C9—C8—O4	177.2 (5)	C24—C25—C26—C27	−2.5 (10)
C4—C9—C8—C7	−3.8 (9)	C15—N3—C16—C17	−56.0 (6)
C7—N2—C17—C16	118.4 (6)	C27—C22—C23—C24	−0.4 (9)
C7—N2—C14—C15	−118.4 (6)	C27—C22—C21—O5	−18.1 (8)

C7—C6—C5—C4	−2.6 (10)	C27—C22—C21—O6	159.9 (6)
C9—N1—C10—C2	0.2 (9)	C26—C25—C24—C23	3.3 (9)
C9—N1—C11—C13	32.8 (8)	C14—N2—C7—C8	−140.5 (6)
C9—N1—C11—C12	−91.2 (6)	C14—N2—C7—C6	39.6 (10)
C9—C4—C5—C6	0.3 (9)	C14—N2—C17—C16	−57.0 (7)
C8—O4—C13—C11	54.5 (6)	C12—C11—C13—O4	65.4 (6)
C8—C7—C6—F1	−177.0 (5)	C28—C25—C24—C23	−176.2 (6)
C8—C7—C6—C5	1.6 (10)	C28—C25—C26—C27	177.0 (6)
C10—N1—C9—C4	1.9 (9)	C18—N3—C16—C17	180.0 (4)
C10—N1—C9—C8	178.5 (5)	C18—N3—C15—C14	178.6 (5)
C10—N1—C11—C13	−151.6 (5)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2···O3	0.82	1.76	2.522 (6)	155
N3—H3···O5	0.98	1.63	2.610 (6)	175
N3—H3···O6	0.98	2.51	3.125 (6)	121
C11—H11···O6^{i}	0.98	2.28	3.147 (6)	147
C12—H12*C*···O3^{ii}	0.96	2.52	3.308 (8)	139
C13—H13*A*···O3^{iii}	0.97	2.40	3.302 (8)	154
C14—H14*B*···F1	0.97	2.30	2.785 (6)	110
C15—H15*B*···O1^{iv}	0.97	2.58	3.268 (7)	128
C16—H16*B*···O2^{ii}	0.97	2.55	3.277 (7)	131
C18—H18*C*···F1^{v}	0.96	2.54	3.279 (8)	134
C28—H28*B*···O2^{vi}	0.96	2.60	3.481 (7)	153

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