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Crystal structure and Hirshfeld surface analysis of [(*R*,*S*)-2,8-bis(trifluoromethyl)quinolin-4-yl]-(piperidin-2-yl)methanol methanol monosolvate

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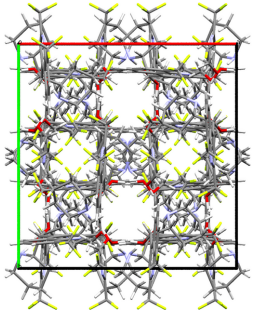
The title compound, $C_{17}H_{16}F_6N_2O{\cdot}CH_3OH$, is composed of a quinolinyl group and a piperidinyl group connected *via* a hydroxymethine (–CHOH) functionality. The compound, which is monosolvated by methanol, was crystallized *via* slow evaporation of a methanol solution, yielding colorless prism-like crystals. The hydroxymethine center of the compound is in the absolute *R* configuration, whereas the chiral center of the piperidinyl ring is in the *S* configuration. The conformation of the piperidinyl ring is a chair. The supramolecular architecture of the crystal is sustained by a set of hydrogen bonds: O—H···O, N—H···O and C—H···F. The intermolecular forces are further analyzed and confirmed by a Hirshfeld surface analysis. DFT structural data computed with the *ORCA* quantum chemistry program package using the B3LYP/def2-TZVPP basis set compare quite well with the experimental X-ray crystal structural data.

1. Chemical context

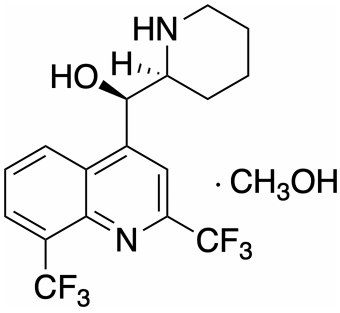
Quinoline derivatives such as quinine, mefloquine and chloroquine are biologically relevant compounds that have a range of applications (Matada *et al.*, 2021). For example, when they serve as antimalarials, these compounds target heme during the hemozoin formation process in the blood stage level of the life cycle of the *Plasmodium* parasite (Gorka *et al.*, 2013 and references therein). These quinoline-based drugs are believed to interact directly with heme to generate a heme–drug adduct, thus inhibiting hemozoin (Gorka *et al.*, 2013). We have shown in previous work that quinine coordinates to the ruthenium center of a heme model compound, (OEP)Ru(CO) (OEP = 2,3,7,8,12,13,17,18-octaethylporphyrinato; Awasabisah *et al.*, 2024). In that report, we obtained the crystal structure of a quinoline–ruthenium porphyrin complex, (OEP)Ru(CO)(Qnl), which confirmed the coordination of the quinoline nitrogen atom to the ruthenium center. In a follow-up to that investigation, we aimed to study the reactions of other quinoline-based compounds with synthetic heme model complexes. During these studies we obtained a crystal structure of mefloquine, a synthetic analogue of quinine. The compound crystallized as the absolute (−)mefloquine isomer (*i.e.* *R*,*S*-mefloquine).



2. Structural commentary

The title compound crystallizes in the tetragonal $I4_1/acd$ space group with one mefloquine and one methanol molecule in the asymmetric unit and *Z* being 32. Previously reported structures for *rac*-mefloquine with no methanol solvate (Skórska, *et*

al., 2006) and the structures of chiral (−)mefloquine and (+) mefloquine crystallized in contrast in centrosymmetric monoclinic ($P2_1/n$) and non-centrosymmetric orthorhombic ($P2_12_12_1$) space groups (Dassonville-Klimpt *et al.*, 2013). The molecular structure of the title compound is shown in Fig. 1.



The quinolinyl ring and the piperidinyl ring in mefloquine are linked *via* a hydroxymethine moiety. The hydroxymethine carbon center and the nitrogen center of the piperidinyl group are in the absolute *R* and absolute *S* configurations, respectively. As expected, the quinolinyl group is planar, whereas the piperidinyl ring exhibits a chair conformation. The nitrogen atom of the latter, N2, is pyramidalized with the sum of the three angles being 328.4°. The torsional angles involving the two rings, *i.e.* C8—C12—C13—N2 and C8—C12—C13—C14, are 179.7 (1) and −55.7 (1)°, respectively. The geometry at the hydroxymethine center, as expected, is tetrahedral with the C8—C12—C13 bond angle of 111.62 (10)° being the largest, and the O1—C12—C13 bond angle, 107.89 (10)°, being the smallest.

The title compound was also subjected to DFT computations. The structure was geometrically optimized with the *ORCA* program using the B3LYP/def2-TZVPP basis set (Neese, 2012, 2022; Neese *et al.*, 2020). The coordinates obtained by X-ray diffraction were used as an input file. The methanol solvate, however, was not included in the calculation. The experimentally determined bond lengths obtained by X-ray crystallography are well in agreement with those obtained from the optimized structure (see supporting information). For example, the quinolinyl C—N bond lengths obtained by X-ray crystallography are 1.3575 (17) and 1.3070 (17) Å, and their respective values determined by DFT calculations are 1.352 and 1.306 Å, which constitutes an excellent agreement. The piperidinyl C—N bond lengths determined by X-ray crystallography are 1.4719 (16) and 1.4740 (17) Å, and their DFT values are slightly shorter at 1.465 and 1.464 Å, respectively. The quinolinyl and piperidinyl C—N—C bond angles are 116.43 (11) and 112.43 (11)°, respectively. Their corresponding DFT values are 118.23 and 113.08°. DFT calculations (B3LYP/def2-TZVPP) of the frontier molecular orbitals revealed the HOMO to be located largely on the piperidinyl ring, while the LUMO resides on the quinolinyl moiety (Fig. 2).

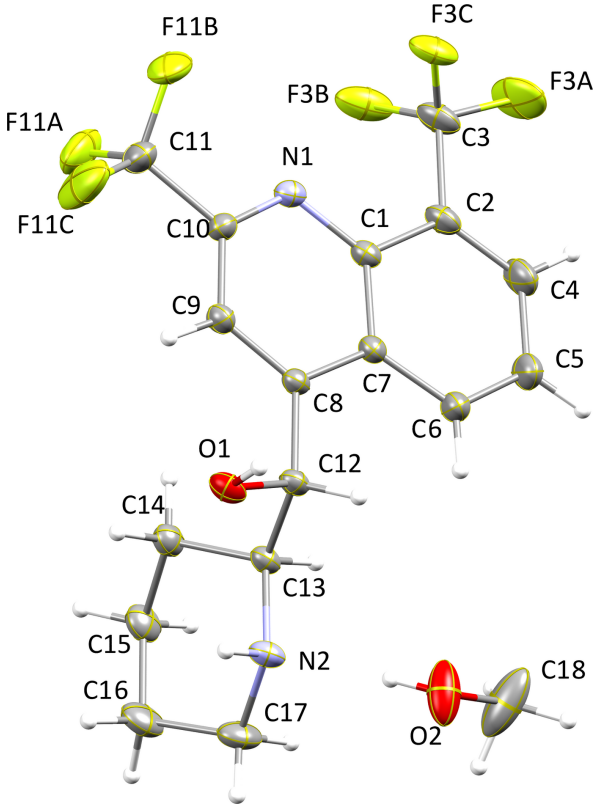


Figure 1
Molecular structure of the title compound. Displacement ellipsoids are drawn at the 50% probability level.

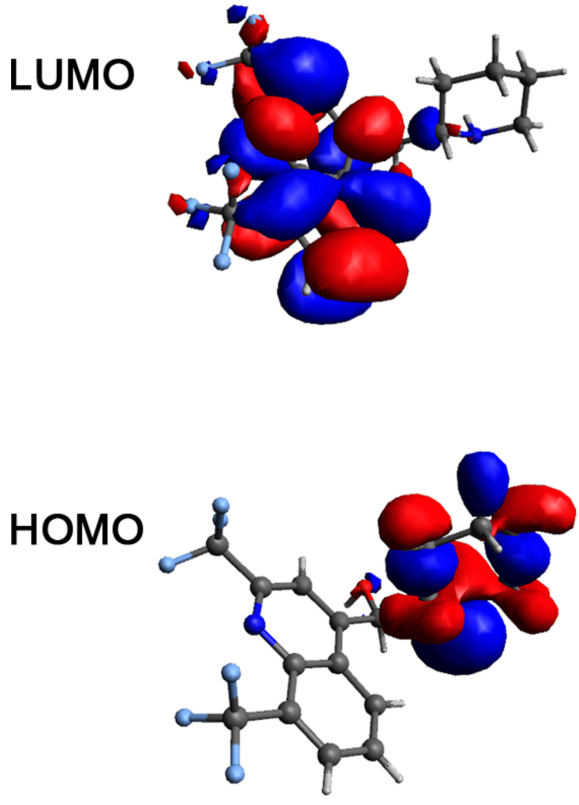


Figure 2
The computed frontier molecular orbitals of the title compound.

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

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1···O2^{i}	0.89 (2)	1.72 (2)	2.6057 (16)	179 (2)
N2—H2N···O1^{ii}	0.85 (2)	2.33 (2)	3.1077 (15)	154.0 (19)
C18—H18C···F3A	0.92 (3)	2.53 (3)	3.193 (2)	129 (2)
O2—H2O···N2^{iii}	0.81 (3)	1.87 (3)	2.6711 (18)	174 (3)

Symmetry codes: (i) $-x+1, -y+1, -z+1$; (ii) $-y+\frac{5}{4}, -x+\frac{5}{4}, -z+\frac{5}{4}$; (iii) $x, y-\frac{1}{2}, -z+1$.

3. Supramolecular features

Apart from crystallizing in a space group of particularly high symmetry in contrast to previously reported structures, further notable differences can be observed in the intermolecular hydrogen-bonding interactions (Table 1). The present structure exhibits hydrogen-bonding interactions between the hydroxymethine O1/H atoms and atom O2 of the methanol solvate molecule, which then acts as hydrogen-bonding donor to the piperidinyl N2 atom, resulting in a hydrogen-bonding ring structure involving two mefloquine and two methanol molecules (Fig. 3). In contrast, the structure for *rac*-mefloquine contains arrangements of four mefloquine molecules held directly together by hydrogen bonds involving the hydroxymethine O atom and the piperidinyl N atom. The C—O, O—H and N—H bond lengths of the current structure are 1.4144 (15) and 0.898 (2) and 0.85 (2) Å, respectively (Table 1). In the crystal, the molecules associate *via* O—H···O, N—H···O, O—H···N and C—H···F interactions.

Crystal packing diagrams are presented in Fig. 4. The structures of the chiral mefloquine molecules appear to associate exclusively through intermolecular hydrogen bonds. The packing pattern consists of stacked ribbons, which alternately protrude through the crystal along the crystallographic

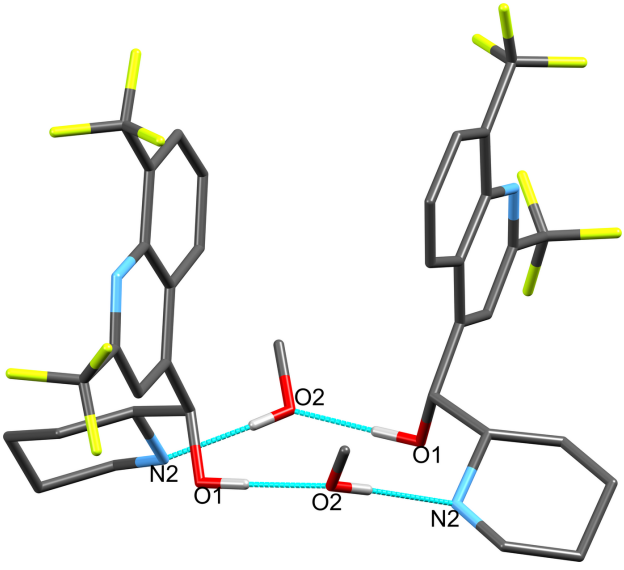


Figure 3
Hydrogen-bonding interactions between the hydroxy atoms of the hydroxymethine moiety and the methanol solvate and the piperidinyl nitrogen atom. H atoms not involved in the hydrogen bonds are omitted for clarity. Symmetry codes: $-x+1, -y+1, -z+1$ (methanol at the front); $x, y-\frac{1}{2}, -z+1$ (mefloquine to the right).

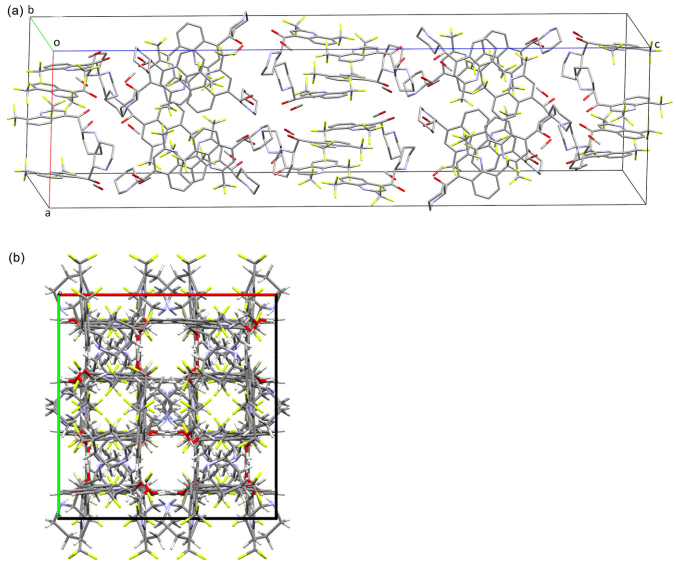


Figure 4
Packing diagram in the crystals of the title compound viewed along the *b* axis (top). The atoms are unlabeled, and all H atoms are omitted for clarity. Below the packing in the crystal shown along the crystallographic *c* axis exhibiting a grid motif (bottom).

a- and *b*-axis directions, resulting in grid or chessboard-like structures when viewed along the crystallographic *c* axis. Where the resulting rows at the 0, 1/2, and 1 *x* regions and those at the 1/4 and 3/4 *y* regions cross each other, the structure bears small nearly spherical voids of 114.36 Å^3 size comprising merely 0.7% of the unit-cell volume.

In order to gain more insight into the intermolecular interactions among neighboring molecules in the crystal packing of the title compound, a Hirshfeld surface analysis was performed using *CrystalExplorer 21* (Spackman, *et al.*, 2021). The 3D surface map of the title compound is shown in Fig. 5. The d_{norm} Hirshfeld surface map reveals strong inter-

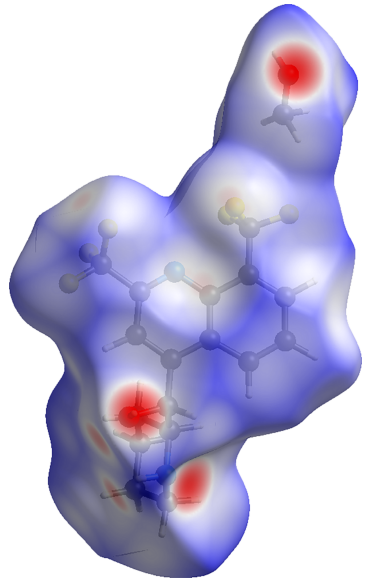


Figure 5
The d_{norm} Hirshfeld surface map for the title compound.

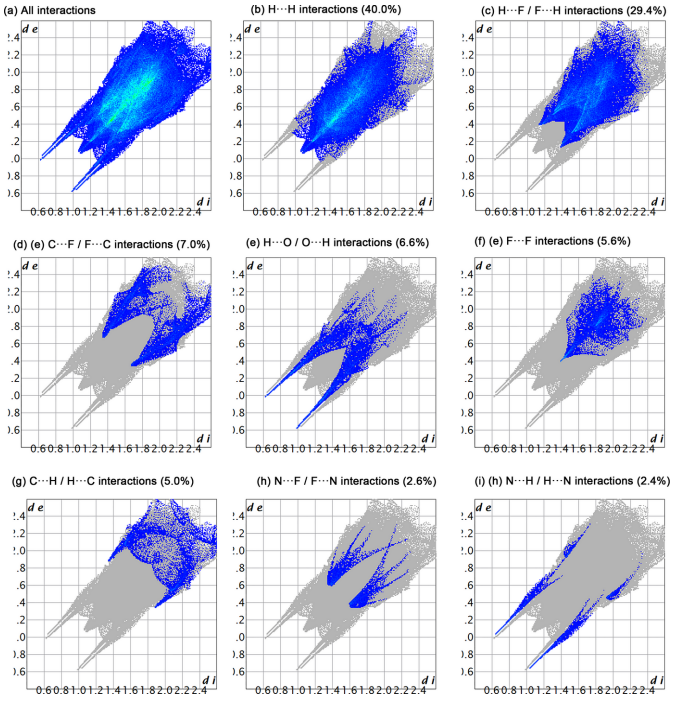


Figure 6
Two dimensional fingerprint plots for the title compound, showing (*a*) all interactions, and delineated into (*b*) H···H, (*c*) H···F/ F···H, (*d*) C···F/ F···C (*e*) H···O/ O···H, (*g*) C···H/ H···C, (*h*) N···F/ F···N, and (*i*) N···H/ H···N interactions with their relative contributions.

molecular forces (dark-red-colored regions), which are attributed to N···H and H···O interactions involving the piperidinyl N—H, the methanol O—H, as well as the solvated methanol O—H. The d_{norm} Hirshfeld surface map also reveals C—H···F interactions (light red) in the vicinity of the CF_3 group. The 2D fingerprint plots were assessed to provide quantitative information about the non-covalent interactions in the crystal packing. As revealed by the 2D fingerprint plots (Fig. 6), the H···H and H···F/ F···H interactions are the most prominent, accounting for 40.0% and 29.4%, respectively, of the overall intermolecular interactions. Other notable contributions include, C···F/ F···C (7.0%), H···O/ O···H (6.6%), F···F (5.6%) and C···H/ H···C (5.0%). The weakest interactions are N···F/ F···N (2.6%) and N···H/ H···N (2.4%).

4. Database survey

A survey of the Cambridge Structural Database version 2025.1.0 (Groom *et al.*, 2016; accessed March 2025) using CONQUEST (Bruno *et al.*, 2002) for the unmodified mefloquine structural motif in cationic or neutral form was carried out. The search returned 16 hit structures of which a large proportion were refined with multiple molecules in their asymmetric units or contain co-crystallized molecules other than solvent and/or counter-ions. Four or even more molecules in the asymmetric unit are found for neutral (*e.g.* QIYREX; Dassonville-Klimpt *et al.*, 2013) as well as for cationic (*e.g.* BIGTIV; Karle & Karle, 2002) mefloquine species. A better-defined single-crystal structure of the neutral form with only two molecules in the asymmetric unit is available from the database with refcode LEBYAT (Skórska *et al.*, 2006). A well representative hydrochloride form with only a single molecule in the a.u. was reported by Mendes do Prado *et al.* (2014) (refcode HAJSAO01). All metrical parameters of the title compound and its closely related structures are well comparable and there are not even notable differences between protonated and neutral forms discernible.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{17}H_{16}F_6N_2O{\cdot}CH_4O$
M_r	410.36
Crystal system, space group	Tetragonal, $I4_1/acd$
Temperature (K)	100
a, c (Å)	15.9788 (6), 59.997 (3)
V (Å^3)	15318.6 (14)
Z	32
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.13
Crystal size (mm)	0.44 × 0.40 × 0.36
Data collection	
Diffractometer	Bruker D8 Venture Duo
Absorption correction	Multi-scan (Blessing, 1995)
T_{min}, T_{max}	0.85, 0.95
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	158826, 5423, 4871
R_{int}	0.052
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.696
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.053, 0.146, 1.06
No. of reflections	5423
No. of parameters	333
H-atom treatment	All H-atom parameters refined
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.65, −0.55

Computer programs: *SAINT* (Bruker, 2019), *SHELXT2018/2* (Sheldrick, 2015*a*), *SHELXL2019/1* (Sheldrick, 2015*b*), *ShelXle* (Hübschle *et al.*, 2011) and *publCIF* (Westrip, 2010).

5. Synthesis and crystallization

Sodium methoxide (137 mg, 2.54 mmol) was placed in a 25 mL Schlenk tube followed by 3 mL MeOH. In a separate vial, mefloquine hydrochloride (502.0 mg, 1.21 mmol) was dissolved in MeOH (5 mL) then added dropwise to the sodium methoxide solution. The solution was stirred for 3 h during which time it became slightly turbid. The solvent was reduced to *ca.* 5 mL *in vacuo*. The resulting precipitate was filtered under vacuum, and washed with small amounts of cold MeOH. The filtrate was collected and placed in a 10 mL Erlenmeyer flask. A slow evaporation of the filtrate resulted in colorless prism-like crystals suitable for X-ray crystallography. IR (ATR, cm^{-1} intensity): 3411 *br* (*m*), 2949 (*w*), 2920 (*w*), 2856 (*w*), 1641 (*m*), 1602 (*m*), 1431 (*m*), 1381 (*w*) 1367 (*w*) 1305 (*s*), 1265 (*w*), 1210 (*w*), 1185 (*w*), 1104 (*vs*), 1128 (*vs*), 1039 (*m*), 1006 (*w*), 939 (*w*), 890 (*w*), 865 (*w*), 835 (*m*), 768 (*s*), 736 (*w*), 715 (*w*), 686 (*w*), 669 (*m*), 648 (*m*), 616 (*w*). ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) δ 8.69 (*d*, *J* = 8.8 Hz, 1H, qnl-*H*), 8.32 (*d*, *J* = 7.2 Hz, 1H, qnl-*H*), 8.06 (*s*, 1H, qnl-*H*), 7.89 (*dd*, *J* = 8.7, 7.2 Hz, 1H, qnl-*H*), 5.93 (*br s*, 1H, O-*H*), 5.29 (*d*, *J* = 5.4 Hz, 1H, C(OH)*H*), 2.67–2.92 (*m*, 2H, pip-*H*), 2.34 (*t*, *J* =

11.1 Hz, 1H, pip-*H*), 1.82 (*br s*, 1H, N—*H*), 1.02–1.32 (*m*, 6H, pip-*H*). ^{19}F NMR (DMSO-d_6, 376 MHz,) δ −58.88, −66.64.

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2.

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Crystal structure and Hirshfeld surface analysis of [(*R*,*S*)-2,8-bis(trifluoromethyl)quinolin-4-yl](piperidin-2-yl)methanol methanol monosolvate

Dennis Awasabisah, Navamoney Arulsamy, Mason Primrose and Guoxing Lin

Computing details

[(*R*,*S*)-2,8-Bis(trifluoromethyl)quinolin-4-yl](piperidin-2-yl)methanol methanol monosolvate

Crystal data

$C_{17}H_{16}F_6N_2O\cdot CH_4O$
$M_r = 410.36$
Tetragonal, $I4_1/acd$
$a = 15.9788$ (6) Å
$c = 59.997$ (3) Å
$V = 15318.6$ (14) Å^3
$Z = 32$
$F(000) = 6784$
$D_x = 1.423$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 9494 reflections
$\theta = 2.6$–29.4°
$\mu = 0.13$ mm^{-1}
$T = 100$ K
Prism, colourless
0.44 × 0.40 × 0.36 mm

Data collection

Bruker D8 Venture Duo diffractometer
Detector resolution: 7.3910 pixels mm^{-1}
ω and φ scans
Absorption correction: multi-scan (Blessing, 1995)
$T_{min} = 0.85$, $T_{max} = 0.95$
158826 measured reflections
5423 independent reflections
4871 reflections with $I > 2\sigma(I)$
$R_{int} = 0.052$
$\theta_{max} = 29.7°$, $\theta_{min} = 1.9°$
$h = -22\rightarrow22$
$k = -21\rightarrow22$
$l = -83\rightarrow83$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.053$
$wR(F^2) = 0.146$
$S = 1.06$
5423 reflections
333 parameters
0 restraints
Primary atom site location: dual
Hydrogen site location: difference Fourier map
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0776P)^2 + 19.8214P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.65$ e Å^{-3}
$\Delta\rho_{min} = -0.55$ e Å^{-3}

Special details

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

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

	x	*y*	*z*	U_{iso}*/U_{eq}
N1	0.61574 (7)	0.47489 (7)	0.52401 (2)	0.0173 (2)
C1	0.62308 (7)	0.55818 (8)	0.52001 (2)	0.0161 (2)
C2	0.63270 (8)	0.58539 (9)	0.49753 (2)	0.0218 (3)
C3	0.63376 (9)	0.52166 (10)	0.47904 (2)	0.0270 (3)
F3A	0.64063 (10)	0.55938 (8)	0.45905 (2)	0.0548 (4)
F3B	0.69710 (6)	0.46825 (7)	0.48036 (2)	0.0380 (3)
F3C	0.56412 (6)	0.47602 (6)	0.47807 (2)	0.0308 (2)
C4	0.63991 (11)	0.66807 (10)	0.49261 (2)	0.0297 (3)
H4	0.6452 (14)	0.6859 (14)	0.4777 (4)	0.035 (5)*
C5	0.63740 (11)	0.72894 (10)	0.50962 (2)	0.0304 (3)
H5	0.6424 (13)	0.7854 (14)	0.5055 (4)	0.035 (5)*
C6	0.62771 (9)	0.70536 (8)	0.53134 (2)	0.0230 (3)
H6	0.6259 (13)	0.7465 (13)	0.5425 (3)	0.029 (5)*
C7	0.62047 (8)	0.61947 (8)	0.53718 (2)	0.0161 (2)
C8	0.60924 (7)	0.59137 (8)	0.55946 (2)	0.0155 (2)
C9	0.60064 (8)	0.50698 (8)	0.56305 (2)	0.0184 (2)
H9	0.5933 (13)	0.4863 (13)	0.5777 (3)	0.030 (5)*
C10	0.60476 (8)	0.45281 (8)	0.54478 (2)	0.0180 (2)
C11	0.59709 (11)	0.35957 (9)	0.54840 (3)	0.0277 (3)
F11A	0.67126 (8)	0.32145 (6)	0.54678 (2)	0.0484 (3)
F11B	0.54795 (7)	0.32345 (6)	0.53352 (2)	0.0407 (3)
F11C	0.56779 (11)	0.34104 (7)	0.56857 (2)	0.0599 (4)
C12	0.60708 (8)	0.65098 (8)	0.57910 (2)	0.0164 (2)
H122	0.5744 (11)	0.6990 (12)	0.5748 (3)	0.020 (4)*
O1	0.57190 (6)	0.61217 (7)	0.59810 (2)	0.0214 (2)
H1	0.5169 (14)	0.6183 (13)	0.5967 (3)	0.030 (5)*
C13	0.69512 (8)	0.68156 (8)	0.58533 (2)	0.0167 (2)
H13	0.7168 (10)	0.7145 (11)	0.5729 (3)	0.015 (4)*
C14	0.75681 (9)	0.61117 (9)	0.59016 (2)	0.0215 (3)
H14A	0.7634 (12)	0.5749 (12)	0.5774 (3)	0.027 (5)*
H14B	0.7337 (13)	0.5741 (13)	0.6018 (3)	0.030 (5)*
C15	0.84104 (9)	0.64723 (10)	0.59736 (3)	0.0269 (3)
H15A	0.8781 (14)	0.6024 (14)	0.6002 (4)	0.037 (5)*
H15B	0.8649 (13)	0.6771 (13)	0.5852 (3)	0.030 (5)*
C16	0.82988 (10)	0.70462 (11)	0.61745 (3)	0.0325 (3)
H16A	0.8095 (15)	0.6707 (14)	0.6309 (4)	0.039 (6)*
H16B	0.8838 (16)	0.7324 (17)	0.6214 (4)	0.053 (7)*
C17	0.76620 (9)	0.77248 (10)	0.61218 (3)	0.0288 (3)
H17A	0.7554 (14)	0.8067 (13)	0.6255 (4)	0.038 (5)*
H17B	0.7877 (13)	0.8080 (13)	0.6003 (4)	0.032 (5)*
N2	0.68546 (7)	0.73889 (7)	0.60436 (2)	0.0197 (2)
H2N	0.6627 (13)	0.7113 (13)	0.6147 (3)	0.030 (5)*
C18	0.62912 (17)	0.41400 (13)	0.42266 (5)	0.0577 (7)
H18A	0.673 (2)	0.396 (2)	0.4292 (7)	0.090 (11)*
H18B	0.671 (3)	0.436 (3)	0.4125 (9)	0.140 (19)*

H18C	0.6047 (18)	0.4639 (18)	0.4268 (5)	0.056 (7)*
O2	0.58920 (8)	0.36933 (10)	0.40650 (3)	0.0453 (4)
H2O	0.6152 (18)	0.3277 (19)	0.4034 (5)	0.056 (8)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0157 (5)	0.0189 (5)	0.0173 (5)	−0.0007 (4)	−0.0011 (4)	−0.0035 (4)
C1	0.0150 (5)	0.0203 (5)	0.0130 (5)	−0.0013 (4)	−0.0009 (4)	−0.0012 (4)
C2	0.0235 (6)	0.0293 (7)	0.0125 (5)	−0.0036 (5)	−0.0008 (4)	−0.0017 (5)
C3	0.0266 (7)	0.0402 (8)	0.0142 (6)	−0.0061 (6)	0.0008 (5)	−0.0055 (5)
F3A	0.0955 (10)	0.0575 (7)	0.0115 (4)	−0.0188 (7)	0.0057 (5)	−0.0032 (4)
F3B	0.0197 (4)	0.0582 (7)	0.0362 (5)	0.0018 (4)	0.0018 (4)	−0.0251 (5)
F3C	0.0207 (4)	0.0454 (5)	0.0263 (4)	−0.0039 (4)	−0.0051 (3)	−0.0139 (4)
C4	0.0410 (8)	0.0329 (8)	0.0153 (6)	−0.0069 (6)	−0.0030 (5)	0.0064 (5)
C5	0.0469 (9)	0.0230 (7)	0.0214 (6)	−0.0048 (6)	−0.0062 (6)	0.0065 (5)
C6	0.0320 (7)	0.0181 (6)	0.0191 (6)	−0.0008 (5)	−0.0053 (5)	0.0005 (5)
C7	0.0168 (5)	0.0172 (5)	0.0142 (5)	−0.0002 (4)	−0.0026 (4)	−0.0002 (4)
C8	0.0153 (5)	0.0180 (5)	0.0132 (5)	0.0010 (4)	−0.0016 (4)	−0.0023 (4)
C9	0.0219 (6)	0.0194 (6)	0.0140 (5)	−0.0007 (4)	−0.0003 (4)	0.0005 (4)
C10	0.0198 (5)	0.0144 (5)	0.0197 (6)	0.0001 (4)	−0.0013 (4)	−0.0017 (4)
C11	0.0387 (8)	0.0167 (6)	0.0278 (7)	−0.0016 (5)	−0.0017 (6)	−0.0014 (5)
F11A	0.0455 (6)	0.0213 (5)	0.0784 (9)	0.0100 (4)	−0.0158 (6)	−0.0025 (5)
F11B	0.0463 (6)	0.0221 (4)	0.0536 (6)	−0.0117 (4)	−0.0141 (5)	−0.0033 (4)
F11C	0.1174 (12)	0.0235 (5)	0.0388 (6)	−0.0110 (6)	0.0224 (7)	0.0056 (4)
C12	0.0170 (5)	0.0191 (5)	0.0131 (5)	0.0010 (4)	−0.0010 (4)	−0.0035 (4)
O1	0.0201 (5)	0.0303 (5)	0.0138 (4)	−0.0031 (4)	0.0017 (3)	−0.0024 (3)
C13	0.0156 (5)	0.0207 (5)	0.0137 (5)	0.0008 (4)	−0.0011 (4)	−0.0026 (4)
C14	0.0200 (6)	0.0239 (6)	0.0207 (6)	0.0039 (5)	−0.0029 (5)	−0.0017 (5)
C15	0.0188 (6)	0.0332 (7)	0.0289 (7)	0.0044 (5)	−0.0061 (5)	−0.0005 (6)
C16	0.0237 (7)	0.0428 (9)	0.0310 (7)	0.0007 (6)	−0.0115 (6)	−0.0073 (7)
C17	0.0216 (6)	0.0337 (8)	0.0310 (7)	−0.0034 (5)	−0.0066 (5)	−0.0121 (6)
N2	0.0186 (5)	0.0245 (5)	0.0161 (5)	−0.0021 (4)	−0.0012 (4)	−0.0060 (4)
C18	0.0601 (14)	0.0308 (9)	0.0823 (17)	0.0101 (9)	−0.0426 (14)	−0.0214 (10)
O2	0.0212 (5)	0.0529 (8)	0.0619 (9)	0.0046 (5)	−0.0038 (5)	−0.0334 (7)

Geometric parameters (Å, º)

N1—C10	1.3070 (17)	C12—C13	1.5356 (17)
N1—C1	1.3575 (17)	C12—H122	0.962 (19)
C1—C7	1.4220 (16)	O1—H1	0.89 (2)
C1—C2	1.4252 (17)	C13—N2	1.4719 (16)
C2—C4	1.359 (2)	C13—C14	1.5233 (18)
C2—C3	1.5058 (19)	C13—H13	0.974 (17)
C3—F3B	1.3263 (19)	C14—C15	1.526 (2)
C3—F3C	1.3318 (17)	C14—H14A	0.97 (2)
C3—F3A	1.3468 (17)	C14—H14B	0.99 (2)
C4—C5	1.410 (2)	C15—C16	1.525 (2)

C4—H4	0.94 (2)	C15—H15A	0.95 (2)
C5—C6	1.3653 (19)	C15—H15B	0.95 (2)
C5—H5	0.94 (2)	C16—C17	1.520 (2)
C6—C7	1.4213 (18)	C16—H16A	1.03 (2)
C6—H6	0.94 (2)	C16—H16B	1.00 (3)
C7—C8	1.4213 (16)	C17—N2	1.4740 (17)
C8—C9	1.3725 (18)	C17—H17A	0.98 (2)
C8—C12	1.5155 (16)	C17—H17B	0.97 (2)
C9—C10	1.3983 (17)	N2—H2N	0.85 (2)
C9—H9	0.95 (2)	C18—O2	1.363 (2)
C10—C11	1.5106 (19)	C18—H18A	0.85 (4)
C11—F11B	1.3216 (18)	C18—H18B	0.97 (5)
C11—F11C	1.3306 (19)	C18—H18C	0.92 (3)
C11—F11A	1.336 (2)	O2—H2O	0.81 (3)
C12—O1	1.4144 (15)		

C10—N1—C1	116.43 (11)	C8—C12—H122	107.8 (11)
N1—C1—C7	122.98 (11)	C13—C12—H122	108.0 (11)
N1—C1—C2	118.41 (11)	C12—O1—H1	105.6 (13)
C7—C1—C2	118.60 (12)	N2—C13—C14	112.33 (10)
C4—C2—C1	120.74 (12)	N2—C13—C12	106.91 (10)
C4—C2—C3	119.78 (12)	C14—C13—C12	113.85 (11)
C1—C2—C3	119.47 (12)	N2—C13—H13	107.0 (10)
F3B—C3—F3C	106.73 (13)	C14—C13—H13	108.3 (10)
F3B—C3—F3A	106.18 (13)	C12—C13—H13	108.1 (10)
F3C—C3—F3A	105.90 (12)	C13—C14—C15	110.22 (12)
F3B—C3—C2	113.58 (12)	C13—C14—H14A	111.3 (12)
F3C—C3—C2	113.16 (12)	C15—C14—H14A	110.8 (12)
F3A—C3—C2	110.75 (13)	C13—C14—H14B	109.6 (12)
C2—C4—C5	120.75 (13)	C15—C14—H14B	110.9 (12)
C2—C4—H4	120.5 (14)	H14A—C14—H14B	103.9 (17)
C5—C4—H4	118.8 (14)	C16—C15—C14	110.34 (12)
C6—C5—C4	120.22 (14)	C16—C15—H15A	112.7 (14)
C6—C5—H5	121.7 (13)	C14—C15—H15A	108.6 (14)
C4—C5—H5	118.0 (13)	C16—C15—H15B	110.6 (13)
C5—C6—C7	120.74 (13)	C14—C15—H15B	108.9 (12)
C5—C6—H6	119.5 (12)	H15A—C15—H15B	105.6 (18)
C7—C6—H6	119.8 (12)	C17—C16—C15	110.04 (12)
C6—C7—C8	123.18 (11)	C17—C16—H16A	109.1 (14)
C6—C7—C1	118.94 (11)	C15—C16—H16A	110.0 (13)
C8—C7—C1	117.87 (11)	C17—C16—H16B	108.1 (16)
C9—C8—C7	118.09 (11)	C15—C16—H16B	110.7 (15)
C9—C8—C12	119.54 (11)	H16A—C16—H16B	109 (2)
C7—C8—C12	122.38 (11)	N2—C17—C16	113.10 (13)
C8—C9—C10	118.70 (11)	N2—C17—H17A	107.9 (14)
C8—C9—H9	120.2 (13)	C16—C17—H17A	110.2 (13)
C10—C9—H9	121.1 (13)	N2—C17—H17B	106.7 (12)
N1—C10—C9	125.92 (12)	C16—C17—H17B	109.4 (13)

N1—C10—C11	114.47 (11)	H17A—C17—H17B	109.5 (18)
C9—C10—C11	119.61 (12)	C13—N2—C17	112.43 (11)
F11B—C11—F11C	107.94 (14)	C13—N2—H2N	107.0 (14)
F11B—C11—F11A	106.18 (13)	C17—N2—H2N	109.4 (14)
F11C—C11—F11A	106.07 (15)	O2—C18—H18A	122 (2)
F11B—C11—C10	112.45 (13)	O2—C18—H18B	94 (3)
F11C—C11—C10	112.25 (12)	H18A—C18—H18B	81 (4)
F11A—C11—C10	111.54 (13)	O2—C18—H18C	116.6 (17)
O1—C12—C8	111.12 (10)	H18A—C18—H18C	121 (3)
O1—C12—C13	107.89 (10)	H18B—C18—H18C	98 (4)
C8—C12—C13	111.62 (10)	C18—O2—H2O	111 (2)
O1—C12—H122	110.4 (11)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1···O2^{i}	0.89 (2)	1.72 (2)	2.6057 (16)	179 (2)
N2—H2*N*···O1^{ii}	0.85 (2)	2.33 (2)	3.1077 (15)	154.0 (19)
C18—H18*C*···F3*A*	0.92 (3)	2.53 (3)	3.193 (2)	129 (2)
O2—H2*O*···N2^{iii}	0.81 (3)	1.87 (3)	2.6711 (18)	174 (3)

Symmetry codes: (i) −*x*+1, −*y*+1, −*z*+1; (ii) −*y*+5/4, −*x*+5/4, −*z*+5/4; (iii) *x*, *y*−1/2, −*z*+1.

Parameter	DFT
N1-C10	1.306
C1-C7	1.430
C2-C4	1.371
C3-F3B	1.344
C3-F3A	1.354
C4-H4	1.080
C5-H5	1.081
C6-H6	1.080
C8-C9	1.374
C9-C10	1.406
C10-C11	1.523
C11-F11C	1.351
C12-O1	1.428
C12-H122	1.093
C13-N2	1.465
C13-H13	1.096
C14-H14A	1.093
C15-C16	1.531
C15-H15B	1.092
C16-H16A	1.095
C17-N2	1.464
C17-H17B	1.096
N1-C1	1.352
C1-C2	1.427
C2-C3	1.514

C3-F3C	1.344
C4-C5	1.409
C5-C6	1.369
C6-C7	1.418
C7-C8	1.426
C8-C12	1.520
C9-H9	1.078
C11-F11B	1.338
C11-F11A	1.347
C12-C13	1.542
O1-H1	0.961
C13-C14	1.537
C14-C15	1.534
C14-H14B	1.092
C15-H15A	1.096
C16-C17	1.532
C16-H16B	1.093
C17-H17A	1.091
N2-H2N	1.014