Bis(mefloquinium) butanedioate ethanol monosolvate: crystal structure and Hirshfeld surface analysis

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Bis(mefloquinium) butanedioate ethanol monosolvate: crystal structure and Hirshfeld surface analysis

James L. Wardell,a‡ Mukesh M. Jotani b and Edward R. T. Tiekink c*

The asymmetric unit of the centrosymmetric title salt solvate, $2\text{C}_17\text{H}_17\text{F}_6\text{N}_2\text{O}^+\cdot\text{C}_4\text{H}_4\text{O}_4^{2-}\cdot\text{C}_0\cdot\text{CH}_3\text{CH}_2\text{OH}$, (systematic name: 2-[[2,8-bis(trifluoromethyl)quinolin-4-yl](hydroxy)methyl]piperidin-1-ium butanedioate ethanol monosolvate) comprises two independent cations, with almost superimposable conformations and each approximating the shape of the letter L, a butanedioate dianion with an all-trans conformation and an ethanol solvent molecule. In the crystal, supramolecular chains along the $a$-axis direction are sustained by charge-assisted hydroxy-O—H/C1/C1/O(carboxylate) and ammonium-N—H/C1/C1/O(carboxylate) hydrogen bonds. These are connected into a layer via C—F/C1/C1/C1/C25(pyridyl) contacts and C25—C25 stacking interactions between quinolinyl-C6 and –NC5 rings of the independent cations of the asymmetric unit [inter-centroid separations = 3.6784 (17) and 3.6866 (17) Å]. Layers stack along the $c$-axis direction with no directional interactions between them. The analysis of the calculated Hirshfeld surface reveals the significance of the fluorine atoms in surface contacts. Thus, by far the greatest contribution to the surface contacts, i.e. 41.2%, are of the type F/C1/C1/H/H/C1/C1/F and many of these occur in the inter-layer region. However, these contacts occur at separations beyond the sum of the van der Waals radii for these atoms. It is noted that H/C1/C1/C1/H contacts contribute 29.8% to the overall surface, with smaller contributions from O/C1/C1/H/H (14.0%) and F/C1/C1/F (5.7%) contacts.

1. Chemical context

Malaria continues to be a major worldwide health issue and vast populations in tropical countries, including visitors to those regions, are susceptible to the disease, which is spread by parasites such as Plasmodium falciparum (Maguire et al., 2006). The problem is compounded by the parasites’ abilities to develop resistance to drugs, such as to the once popular chloroquine (Grabias & Kumar, 2016). Mefloquine, [2,8-bis(trifluoromethyl)quinolin-4-yl]-piperidin-2-ylmethanol, is a drug used against malaria (Tickell-Painter et al., 2017). The molecule contains two adjacent chiral centres, i.e. one at the carbon atom carrying the hydroxy group and one at the link connecting the piperidinyl ring to the rest of the molecule. The drug is commonly marketed as Lariam, which is the hydrochloride salt, comprising ($R^*,S^*$)-(2-[[2,8-bis(trifluoromethyl)quinolin-4-yl](hydroxy)methyl]piperidin-1-ium chloride and its ($S^*,R^*$) enantiomer. While the former is effective against malaria, the latter has an affinity for the adenosine acceptors in the brain, inducing serious psychiatric and neurologic side-effects (Nevin, 2017). Hence, experiments at resolving the
enantiomers are of practical importance (Engwerda et al., 2019). Herein, as continuation of our anion-exchange experiments of the racemic salt and attendant structural studies (Wardell et al., 2016; Wardell, Wardell et al., 2018; Wardell, Jotani et al., 2018; Wardell & Tiekink, 2019), the crystal and molecular structures of the butanedioate salt, isolated as an ethanol monosolvate, are described along with an analysis of the calculated Hirshfeld surfaces.

2. Structural commentary

The asymmetric unit of the salt solvate, (I), comprises two mefloquinium cations, a butanedioate dianion and a solvent ethanol molecule; the molecular structures of the ions are shown in Fig. 1. Evidence of proton transfer during crystallization is seen in the relatively small difference in the C⋯O bond lengths of the dianion, i.e. C35—O3, O4 = 1.236 (4) and 1.285 (3) Å, and C38—O5, O6 = 1.255 (4) and 1.271 (4) Å. While normally these bond lengths might be expected to be closer to equivalent, as noted below, each of the O4 and O6 atoms participate in two strong charge-assisted hydrogen bonds, see Supramolecular features, which explains the slightly longer C⋯O bond lengths formed by these atoms. Further support for proton transfer leading to the formation of piperidin-1-ium cations is supported by the pattern of hydrogen bonding involving the ammonium-N—H hydrogen atoms, as discussed below in Supramolecular features.

The cations exhibit very similar molecular geometries, as highlighted in the overlay diagram of Fig. 2. There are two chiral centres in each cation and the illustrated cations are R at C12 and S at C13 for the N1-cation, and R at C29 and S at C30 for the N3-cation, i.e. each conforms to the [(+)–erythro–mefloquinium] isomer; space-group symmetry indicates that the unit cell contains equal numbers of both enantiomers. The r.m.s. deviation for the ten atoms comprising the N1-quinolinyl residue is 0.0254 Å [0.0256 Å for the N3-quinolinyl residue], with the hydroxy-O1 and ammonium-N2 atoms lying to either side of the plane, i.e. /C0.323 (4) and 1.302 (6) Å, respectively [0.255 (4) Å for O2 and /C0.1348 (6) Å for N4]. The dihedral angle of 72.55 (9) /C14 [71.48 (9) /C14] formed between the fused ring system and the least-squares plane through the piperinium ring indicates that, to a first approximation, the molecule has the shape of the letter L. Referring to Table 1, an intramolecular charge-assisted ammonium-N +—H hydrogen-bond is formed as the hydroxyl-O1 and ammonium-N2 atoms lie to the same side of the cation with

| D—H⋯A | D—H | H⋯A | D⋯A | D—H⋯A |
|-------|-----|-----|-----|-------|
| N2—H1N⋯O1 | 0.88 (3) | 2.49 (3) | 2.806 (4) | 102 (2) |
| N4—H3N⋯O2 | 0.88 (2) | 2.54 (3) | 2.863 (4) | 103 (2) |
| O1—H1O⋯O6 | 0.84 (3) | 1.81 (3) | 2.653 (3) | 175 (2) |
| O2—H2O⋯O4 | 0.84 (2) | 1.82 (2) | 2.656 (3) | 170 (3) |
| N2—H1N⋯O5 | 0.88 (3) | 1.97 (3) | 2.830 (4) | 163 (3) |
| N2—H2N⋯O4 | 0.88 (3) | 1.82 (3) | 2.694 (4) | 173 (3) |
| N4—H3N⋯O3 | 0.88 (2) | 1.99 (3) | 2.832 (4) | 161 (3) |
| N4—H4N⋯O6 | 0.89 (3) | 1.92 (3) | 2.789 (4) | 168 (3) |
| O7—H7O⋯O5 | 0.85 (3) | 1.88 (3) | 2.729 (4) | 176 (7) |
| C30—H30⋯O7 | 1.00 | 2.40 | 3.296 (4) | 149 |
| C10—F3⋯Cg1 | 1.32 (1) | 3.28 (1) | 4.101 (3) | 120 (1) |

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

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

Cg1 is the centroid of the (N1,C1–C4,C9) ring.

Figure 1
The molecular structures of the ionic components of the asymmetric unit of (I) showing the atom-labelling scheme and displacement ellipsoids at the 50% probability level: (a) the N1-containing cation, (b) the N3-cation and (c) the butanedioate dianion.

Figure 2
An overlay diagram of the N1- (red image) and N3-containing cations. The cations have been superimposed so that the CgN rings of the quinolinyl residues are coincident.
the O1—C12—C13—N2 torsion angle of $-63.4$ ($3^\circ$) indicating a + syn-clinal relationship [O2—C29—C30—N4 = $-68.4$ ($3^\circ$)].

In the butanedioate dianion, the C35—C36—C38—C39 torsion angle of $175.4$ ($3^\circ$) indicates an all-trans conformation (+ anti-periplanar). The dihedral angle formed between the terminal carboxylate residues is $51.0$ ($2^\circ$), indicating that the dianion is considerably twisted.

3. Supramolecular features

The most prominent feature of the molecular packing is the formation of twisted supramolecular chains propagating parallel to the $a$-axis direction, Table 1 and Fig. 3a. Each of the cation-bound hydroxy groups forms a charge-assisted hydroxy-O—H···O(carboxylate) hydrogen bond to a carboxylate-O atom, at opposite ends of the butanedioate dianion. In addition, each of the four ammonium-N—H hydrogen atoms connects to a carboxylate-O atom, each derived from a different carboxylate residue, via a charge-assisted ammonium-N—H···O(carboxylate) hydrogen bond. Thus, each of the O4 and O6 atoms accept two charge-assisted hydrogen bonds. The carboxylate-O5 atom accepts a hydrogen bond from the solvent ethanol molecule, while ethanol-O7 participates in a methine-C—H···O interaction, Table 1. The carboxylate-O3 atom forms only one hydrogen bond. The number and strength of hydrogen bonds formed by the carboxylate-O atoms correlates with the magnitude of the C—O bond lengths, e.g. the C35—O3 < C38—O5 < C38—O6 C35—O4 (see comment in Structural Commentary).

The connections between the chains leading to supramolecular layers that stack along the $c$-axis direction are of the type C—F···(pyridyl), Table 1, occurring between N1-containing cations, and $\pi$—$\pi$ stacking interactions between the independent molecules comprising the asymmetric unit. The latter occur between the $C_6$ ring of the N1-quinolinyl residue (C4–C9) and each of the N3-quinolinyl-bound pyridyl (N3,C18–C21,C26) [inter-centroid separation = 3.6784 ($17^\circ$), angle of inclination = 4.27 ($14^\circ$)] and $C_6$ (C21–C26) [3.6866 ($17^\circ$), angle of inclination = 3.67 ($14^\circ$)] rings. A view of the unit-cell contents is shown in Fig. 3b.

4. Hirshfeld surface analysis

The analysis of Hirshfeld surface calculations for (I) was performed in order to learn more about the supramolecular association, in particular, about the inter-layer connections, following established procedures (Tan et al., 2019) and employing Crystal Explorer 17 (Turner et al., 2017). Such analyses have proven useful for salts with multiple components comprising the asymmetric unit (Jotani et al., 2019).

It is clearly evident from the numerous characteristic red spots on the Hirshfeld surfaces mapped over $d_{norm}$ for the constituents of (I), shown in Fig. 4, that the butanedioate dianion plays a crucial role in forming significant interactions with each of the two independent mefloquinium cations as well as with the ethanol solvent molecule. The O—H···O and N—H···O hydrogen bonds summarized in Table 1 are characterized as bright-red spots on the Hirshfeld surface mapped over $d_{norm}$ for the dianion, Fig. 4a and b, and near the
The effects of the short inter-atomic contacts on the packing of (I), summarized in Table 2, are also evident as the faint-red spots near the respective atoms, Fig. 4. The blue and red regions corresponding to positive and negative potentials, respectively, around the atoms of the dianion and solvent ethanol molecule, Fig. 5, and cations, Fig. 6, on the Hirshfeld surfaces mapped over electrostatic potential also represent donors and acceptors of the respective hydrogen bonds. }

The additional influence of the C—F⋯C1/C1/C1/C1/C1/C25 contacts involving the F2 and F3 atoms interacting with the (C4–C9) and N1-pyridyl rings of the N1-quinolinyl residue are viewed as blue bumps and bright-orange concave regions, respectively, on the Hirshfeld surfaces of the ethanol molecule, Fig. 4c, and mefloquinium cations in Fig. 4d and e.

**Table 2**

| Contact | Distance (Å) | Symmetry operation |
|---------|--------------|-------------------|
| F1⋯H6  | 2.50         | 1 + x, y, z       |
| F6⋯C32 | 3.096 (4)    | x, −1 + y, z      |
| O1⋯H37B| 2.45         | x, y, z           |
| O1⋯C38 | 3.038 (4)    | −x, −y, −1 − z    |
| O2⋯H36B| 2.50         | −1 + x, y, z      |
| O2⋯C36 | 3.090 (4)    | −1 + x, y, z      |
| O4⋯H12 | 2.53         | 1 + x, y, z       |
| O6⋯H22 | 2.50         | x, y, z           |
| O7⋯H31B| 2.55         | x, y, z           |
| H1O⋯H37B| 2.14       | x, y, z           |
| H12⋯H29| 2.06         | x, y, z           |
| H34A⋯H39A| 2.22     | −x, 2 − y, −z     |

Notes: (a) The interatomic distances are calculated in Crystal Explorer (Turner et al., 2017) whereby the X—H bond lengths are adjusted to their neutron values.
The relatively small percentage contribution from H contacts to the Hirshfeld surface are summarized in Table 3. Percentage contributions from the different inter-atomic F, major contributor of contacts to the surface is of the type Hirshfeld surface of (I), as highlighted in Table 3. Indeed, the trifluoromethyl groups in each of the independent cations in the long list of contacts in Table 3. The presence of two dianions and solvent ethanol molecule. This is well-evidenced molecular interactions between the constituent cations, due to the formation of a wide range of different inter-contacts to the Hirshfeld surface in the overall packing of (I) is.

The overall two-dimensional fingerprint plot for (I), Fig. 9a, and those delineated into specific H· · ·H, O· · ·H/H· · ·O, F· · ·H/H· · ·F, C· · ·F/· · ·C and C· · ·O/O· · ·C contacts (McKinnon et al., 2007) are illustrated in Fig. 9b–e; the percentage contributions from the different inter-atomic contacts to the Hirshfeld surface are summarized in Table 3. The relatively small percentage contribution from H· · ·H contacts to the Hirshfeld surface in the overall packing of (I) is due to the formation of a wide range of different inter-molecular interactions between the constituent cations, dianions and solvent ethanol molecule. This is well-evidenced in the long list of contacts in Table 3. The presence of two trifluoromethyl groups in each of the independent cations results in a major contribution from fluorine atoms to the Hirshfeld surface of (I), as highlighted in Table 3. Indeed, the major contributor of contacts to the surface is of the type F· · ·H/H· · ·F, at 41.2%. Many of these occur in the inter-layer Hirshfeld surface mapped with the shape-index property in Fig. 7. The π–π contacts formed between the (C4–C9) ring of the O1-cation and each of the (C21–C26) and N3-pyridyl rings of the O2-cation are illustrated in Fig. 8.

The presence of a cone-shaped tip at \( d_e + d_i = 2.2 \text{ Å} \) in the fingerprint plot delineated into H· · ·H contacts in Fig. 9b, is an indication of the short interatomic H· · ·H contact between symmetry-related piperidinium-H34A and ethanol-H39A atoms, Table 2. The other short H· · ·H contacts summarized in Table 2 occur between the hydrogen atoms of the cations and dianion within the asymmetric unit. In the fingerprint plot delineated into O· · ·H/H· · ·O contacts, Fig. 9c, the pair of long spikes with their tips at \( d_e + d_i = 1.8 \text{ Å} \) are due to the O–H· · ·O and N–H· · ·O hydrogen bonds involving the carboxylate-O4 atom of the dianion whereas the points corresponding to N–H· · ·O hydrogen bonds involving the O3 and O5 atoms of the dianion and those involved in short interatomic O· · ·H contacts, Table 2, are merged within the plot. The pair of conical tips at \( d_e + d_i = 2.5 \text{ Å} \) in the fingerprint plot delineated into F· · ·H/H· · ·F contacts, Fig. 9d, represent the presence of these short contacts. The effect of inter-molecular C· · ·F/π/· · ·F—C and short interatomic C· · ·F/ F· · ·C contacts on the molecular packing, Table 3, results in a small but measurable contribution of 2.8% to the Hirshfeld surface of (I) and are viewed as the pair of forceps-like tips at \( d_e + d_i = 3.1 \text{ Å} \) in Fig. 9e. The presence of short interatomic C· · ·O/O· · ·C contacts involving the hydroxyl-O1 and -O2 atoms are characterized as a pair of leaf-like tips at \( d_e + d_i \).
inversion axis, a glide plane or a mirror plane. In these circumstances, the enantiomeric molecules are related by non-crystallographic symmetry, e.g. a non-crystallographic centre of inversion. A review of this phenomenon has appeared for organic compounds (Fábián & Brock, 2010) where such behaviour is found in only 0.1% of structures. There are about 30 mefloquine/derivatives in the Cambridge Structural Database (Groom et al., 2016) and of these, there are two examples of kryptoracemates (Jotani et al., 2016; Wardell, Wardell et al., 2016). Further, in a very recent study, 34 new mefloquine salts were reported of which two were kryptoracemates (Engwerda et al., 2019). Such a high adoption of kryptoracemic behaviour by these species suggest that further, systematic structural studies are warranted.

6. Synthesis and crystallization
A solution of mefloquinium chloride (1 mmol) and sodium succinate (2 mmol) in ethanol (15 ml) was refluxed for 30 min. The reaction mixture was left at room temperature and after three days, colourless platy crystals of (I) were collected; m.p. 505–505 K. Yield of recrystallized product 65%.

1H NMR (DMSO-d6): δ: 1.15–1.27 (2H, m), 1.32–1.47 (6H, m), 1.48–1.57 (2H, br. d), 1.65–1.74 (2H, br. d), 2.33 (4H, s; succinate), 2.58–2.67 (2H, br. t), 3.00–3.11 (4H, m), 5.58 (2H, d, J = 8 Hz), 7.95 (2H, t, J = 8 Hz), 8.10 (2H, s), 8.37 (2H, t, J = 7.2 Hz), 8.75 (2H, d, J = 8 Hz), resonances due to OH and NH were not observed. Resonances due to ethanol solvate were also present: 3.45 (q, J = 70 Hz) and 1.07 (t, J = 7.0 Hz). 13C NMR (DMSO-d6): δ: 22.92, 24.28, 24.71, 31.76, 45.55, 60.57, 70.33, 115.58, 119.89 (JC,F = 273.8 Hz), 122.34, 122.64 (JC,F = 271.7 Hz), 127.77 (JC,F = 29.0 Hz), 127.76, 129.40, 129.9 (JC,F = 29.0 Hz), 127.78, 129.40, 129.9 (JC,F = 5.2 Hz), 142.74, 146.56 (JC,F = 34.5 Hz), 153.13, 175.32). 19F NMR (DMSO-d6): δ: −58.83, −66.63. IR (cm⁻¹) 3500–2100 (br), 1589 (br), 1514, 1454, 1430, 1371, 1312, 1267, 1217, 1182, 1111, 1053, 1018, 986, 941, 910, 837, 777, 546, 445.

7. Refinement
Crystal data, data collection and structure refinement details are summarized in Table 4. The carbon-bound H atoms were placed in calculated positions (C—H = 0.95–1.00 Å) and were included in the refinement in the riding-model approximation, with Uiso(H) set to 1.2–1.5 Ueq(C). The O- and N-bound H atoms were refined with distance restraints 0.84±0.01 and 0.88±0.01 Å, respectively, and refined with Uiso(H) = 1.5Ueq(O) and 1.2Ueq(N), respectively. Owing to poor agreement, the (01Ì2) reflection was omitted from the final cycles of refinement.

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Table 4
Experimental details.

| Crystal data | Chemical formula |
|--------------|-----------------|
| M₁          | 2C₁₂H₁₅F₅N₉O⁻·C₄H₆O₄²⁻·C₂H₄O⁺ |
| Crystal system, space group | Triclinic, PT |
| Temperature (K) | 120 |
| a, b, c (Å) | 10.0405 (2), 14.6482 (4), 9.6547 (4) |
| α, β, γ (°) | 100.745 (1), 93.830 (2), 98.497 (2) |
| V (Å³) | 2084.41 (9) |
| Z | 2 |
| Radiation type | Mo Ka |
| μ (mm⁻¹) | 0.14 |
| Crystal size (mm) | 0.42 × 0.05 × 0.03 |

Data collection
Diffractometer
Bruker–Nonius Roper CCD camera on κ-goniostat

Absorption correction
Multi-scan (SADABS; Sheldrick, 2007)

Tmax, Tmin
Max. 0.849, 1.000
Min. 42885, 9545, 6505

No. of measured, independent and observed [I > 2σ(I)] reflections
Rint (sinθ/λ)max (Å⁻¹)
0.085
0.651

Refinement
R[F² > 2σ(F²)], wR(F²), S
0.074, 0.180, 1.04
9543

No. of parameters
590

No. of restraints
7

H-atom treatment
H atoms treated by a mixture of independent and constrained refinement

Δρmax, Δρmin (e Å⁻³)
0.60, −0.58

Computer programs: DENZO (Otwinowski & Minor, 1997) and COLLECT (Hooft, 1998), SHELX97 (Sheldrick, 2008), SHELXL2014 (Sheldrick, 2015), ORTEP-3 for Windows (Farrugia, 2012), DIAMOND (Brandenburg, 2006) and pubICIF (Westrip, 2010).

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sup-1

Supporting information

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Bis(mefloquininium) butanedioate ethanol monosolvate: crystal structure and Hirshfeld surface analysis

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Computing details

Data collection: COLLECT (Hooft, 1998); cell refinement: DENZO (Otwinowski & Minor, 1997) and COLLECT (Hooft, 1998); data reduction: DENZO (Otwinowski & Minor, 1997) and COLLECT (Hooft, 1998); program(s) used to solve structure: SHELXS97 (Sheldrick, 2008); program(s) used to refine structure: SHELXL2014 (Sheldrick, 2015); molecular graphics: ORTEP-3 for Windows (Farrugia, 2012) and DIAMOND (Brandenburg, 2006); software used to prepare material for publication: publCIF (Westrip, 2010).

2-[(2,8-Bis(trifluoromethyl)quinolin-4-yl)(hydroxy)methyl]piperidin-1-ium butanedioate ethanol monosolvate

Crystal data

2C17H17F6N2O+·C4H4O42−·C2H6O

M_r = 920.79

Triclinic, P

a = 10.0405 (2) Å

b = 14.6482 (4) Å

c = 14.6547 (4) Å

α = 100.745 (1)°

β = 93.830 (2)°

γ = 98.497 (2)°

V = 2084.41 (9) Å

Z = 2

F(000) = 952

D_x = 1.467 Mg m

Mo Kα radiation, λ = 0.71073 Å

Cell parameters from 32862 reflections

θ = 2.9–27.5°

µ = 0.14 mm

T = 120 K

Plate, colourless

0.42 × 0.05 × 0.03 mm

Data collection

Bruker–Nonius Roper CCD camera on κ-goniostat
diffractometer

Radiation source: Bruker–Nonius FR591 rotating anode

Graphite monochromator

Detector resolution: 9.091 pixels mm

φ & ω scans

Absorption correction: multi-scan
(SADABS;Sheldrick, 2007)

Refinement

Refinement on F^2

Least-squares matrix: full

R(F^2 > 2σ(F^2)) = 0.074

wR(F^2) = 0.180

S = 1.04

9543 reflections

590 parameters

7 restraints

Primary atom site location: structure-invariant direct methods

Secondary atom site location: difference Fourier map

Acta Cryst. (2019). E75, 1162-1168  sup-1

electronic reprint
Hydrogen site location: mixed
H atoms treated by a mixture of independent
and constrained refinement

$w = 1/(\sigma^2(F_o^2) + (0.0525P)^2 + 4.9226P)$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\text{max}} < 0.001$
$\Delta \rho_{\text{max}} = 0.60 \text{ e Å}^{-3}$
$\Delta \rho_{\text{min}} = -0.58 \text{ e Å}^{-3}$

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.

Refinement. Owing to poor agreement, possibly to interference from the beam-stop, one reflection, i.e. (0 -1 2), was omitted from the final cycles of refinement.

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

|     | x    | y     | z     | $U_{\text{iso}}$/*$U_{\text{eq}}$ |
|-----|------|-------|-------|-------------------------------|
| F1  | 0.2808 (2) | 0.67260 (18) | 0.16134 (18) | 0.0504 (7) |
| F2  | 0.2712 (2) | 0.65790 (19) | 0.01402 (19) | 0.0506 (7) |
| F3  | 0.2412 (2) | 0.53596 (15) | 0.07419 (19) | 0.0430 (6) |
| F4  | -0.1087 (2) | 0.38548 (14) | 0.16771 (16) | 0.0344 (5) |
| F5  | -0.03229 (19) | 0.48942 (14) | 0.29119 (15) | 0.0319 (5) |
| F6  | -0.2296 (2) | 0.40671 (14) | 0.28320 (16) | 0.0364 (5) |
| O1  | -0.0896 (2) | 0.82971 (15) | -0.04003 (16) | 0.0212 (5) |
| H1O | -0.061 (4) | 0.869 (2) | 0.0096 (16) | 0.032* |
| N1  | -0.0028 (2) | 0.57189 (18) | 0.12924 (19) | 0.0207 (6) |
| N2  | -0.3489 (3) | 0.78367 (18) | -0.13680 (19) | 0.0190 (5) |
| H1N | -0.289 (3) | 0.8273 (18) | -0.152 (2) | 0.023* |
| H2N | -0.390 (3) | 0.811 (2) | -0.0906 (17) | 0.023* |
| C1  | 0.0642 (3) | 0.6271 (2) | 0.0803 (2) | 0.0198 (6) |
| C2  | 0.0089 (3) | 0.6897 (2) | 0.0331 (2) | 0.0190 (6) |
| H2  | 0.0631 | 0.7264 | -0.0019 | 0.023* |
| C3  | -0.1251 (3) | 0.6968 (2) | 0.0384 (2) | 0.0188 (6) |
| C4  | -0.2021 (3) | 0.6417 (2) | 0.0930 (2) | 0.0181 (6) |
| C5  | -0.3393 (3) | 0.6472 (2) | 0.1083 (2) | 0.0223 (7) |
| H5  | -0.3852 | 0.6885 | 0.0799 | 0.027* |
| C6  | -0.4056 (3) | 0.5940 (2) | 0.1630 (2) | 0.0237 (7) |
| H6  | -0.4971 | 0.5989 | 0.1728 | 0.028* |
| C7  | -0.3403 (3) | 0.5318 (2) | 0.2053 (3) | 0.0260 (7) |
| H7  | -0.3881 | 0.4952 | 0.2435 | 0.031* |
| C8  | -0.2090 (3) | 0.5233 (2) | 0.1922 (2) | 0.0217 (7) |
| C9  | -0.1351 (3) | 0.5793 (2) | 0.1366 (2) | 0.0195 (6) |
| C10 | 0.2142 (3) | 0.6225 (2) | 0.0822 (2) | 0.0244 (7) |
| C11 | -0.1435 (3) | 0.4521 (2) | 0.2331 (3) | 0.0259 (7) |
| C12 | -0.1883 (3) | 0.7644 (2) | -0.0125 (2) | 0.0184 (6) |
| H12 | -0.2441 | 0.8000 | 0.0309 | 0.022* |
| C13 | -0.2802 (3) | 0.7122 (2) | -0.1001 (2) | 0.0176 (6) |
| H13 | -0.3506 | 0.6652 | -0.0815 | 0.021* |
| C14 | -0.4440 (3) | 0.7429 (2) | -0.2226 (2) | 0.0263 (7) |
|     | x     | y     | z     | Ueq   |
|-----|-------|-------|-------|-------|
| H14A| -0.4816 | 0.7940 | -0.2457 | 0.032* |
| H14B| -0.5202 | 0.6991 | -0.2071 | 0.032* |
| C15 | -0.3715 (4) | 0.6904 (3) | -0.2983 (2) | 0.0295 (8) |
| H15A| -0.3033 | 0.7359 | -0.3196 | 0.035* |
| H15B| -0.4376 | 0.6596 | -0.3524 | 0.035* |
| C16 | -0.3015 (3) | 0.6160 (2) | -0.2630 (2) | 0.0262 (7) |
| H16A| -0.3704 | 0.5665 | -0.2484 | 0.031* |
| H16B| -0.2501 | 0.5861 | -0.3123 | 0.031* |
| C17 | -0.2054 (3) | 0.6606 (2) | -0.1756 (2) | 0.0201 (6) |
| H17A| -0.1649 | 0.6110 | -0.1517 | 0.024* |
| H17B| -0.1312 | 0.7056 | -0.1918 | 0.024* |
| F7  | -0.6032 (3) | 0.6297 (2) | 0.3672 (3) | 0.0874 (12) |
| F8  | -0.6420 (2) | 0.7695 (2) | 0.3979 (2) | 0.0572 (8) |
| F9  | -0.5432 (2) | 0.7145 (2) | 0.50201 (19) | 0.0670 (9) |
| F10 | -0.1334 (2) | 0.67918 (15) | 0.55849 (15) | 0.0343 (5) |
| F11 | -0.1959 (2) | 0.55632 (14) | 0.44945 (16) | 0.0371 (5) |
| F12 | 0.0147 (2) | 0.60063 (14) | 0.49868 (15) | 0.0332 (5) |
| O2  | -0.4008 (2) | 0.92583 (16) | 0.18909 (16) | 0.0236 (5) |
| H2O | -0.4244 (4) | 0.897 (2) | 0.1338 (12) | 0.035* |
| N3  | -0.3160 (3) | 0.71100 (19) | 0.4089 (2) | 0.0229 (6) |
| N4  | -0.1656 (3) | 1.06682 (18) | 0.20532 (19) | 0.0186 (5) |
| H3N | -0.240 (2) | 1.071 (2) | 0.172 (2) | 0.022* |
| H4N | -0.114 (3) | 1.036 (2) | 0.168 (2) | 0.022* |
| C18 | -0.4157 (3) | 0.7498 (2) | 0.3795 (2) | 0.0239 (7) |
| C19 | -0.4077 (3) | 0.8153 (2) | 0.3206 (2) | 0.0221 (7) |
| H19 | -0.4848 | 0.8413 | 0.3036 | 0.027* |
| C20 | -0.2853 (3) | 0.8408 (2) | 0.2883 (2) | 0.0188 (6) |
| C21 | -0.1731 (3) | 0.7995 (2) | 0.3149 (2) | 0.0188 (6) |
| C22 | -0.0438 (3) | 0.8172 (2) | 0.2819 (2) | 0.0191 (6) |
| H22 | -0.0287 | 0.8594 | 0.2402 | 0.023* |
| C23 | 0.0591 (3) | 0.7740 (2) | 0.3097 (2) | 0.0229 (7) |
| H23 | 0.1448 | 0.7858 | 0.2864 | 0.027* |
| C24 | 0.0399 (3) | 0.7124 (2) | 0.3722 (2) | 0.0224 (7) |
| H24 | 0.1126 | 0.6831 | 0.3907 | 0.027* |
| C25 | -0.0821 (3) | 0.6942 (2) | 0.4067 (2) | 0.0223 (7) |
| C26 | -0.1939 (3) | 0.7360 (2) | 0.3771 (2) | 0.0191 (6) |
| C27 | -0.5505 (3) | 0.7155 (3) | 0.4130 (3) | 0.0339 (8) |
| C28 | -0.1002 (3) | 0.6326 (2) | 0.4778 (2) | 0.0259 (7) |
| C29 | -0.2730 (3) | 0.9119 (2) | 0.2244 (2) | 0.0182 (6) |
| H29 | -0.2221 | 0.8882 | 0.1710 | 0.022* |
| C30 | -0.1964 (3) | 1.0076 (2) | 0.2770 (2) | 0.0187 (6) |
| H30 | -0.1091 | 0.9978 | 0.3076 | 0.022* |
| C31 | -0.0944 (3) | 1.1651 (2) | 0.2457 (2) | 0.0243 (7) |
| H31A| -0.0841 | 1.2015 | 0.1953 | 0.029* |
| H31B| -0.0029 | 1.1628 | 0.2739 | 0.029* |
| C32 | -0.1729 (3) | 1.2135 (2) | 0.3186 (3) | 0.0291 (8) |
| H32A| -0.2611 | 1.2213 | 0.2891 | 0.035* |
| H32B| -0.1223 | 1.2768 | 0.3467 | 0.035* |
C33  -0.1966 (4)  1.1559 (2)  0.3949 (3)  0.0309 (8)
H33A  -0.1087  1.1505  0.4265  0.037*
H33B  -0.2494  1.1880  0.4420  0.037*
C34  -0.2739 (3)  1.0578 (2)  0.3511 (2)  0.0253 (7)
H34A  -0.2880  1.0202  0.4002  0.030*
H34B  -0.3638  1.0634  0.3226  0.030*
C35  -0.2739 (3)  1.0578 (2)  0.3511 (2)  0.0253 (7)
H35A  -0.2880  1.0202  0.4002  0.030*
H35B  -0.3638  1.0634  0.3226  0.030*
C36  -0.3743 (3)  0.9243 (2)  0.0649 (2)  0.0212 (6)
H36A  -0.3096  0.8752  0.1011  0.025*
H36B  -0.3993  0.9762  0.1072  0.025*
C37  -0.2127 (3)  0.6260 (2)  0.0338 (2)  0.0188 (6)
H37A  -0.2407  0.7015  0.0004  0.023*
H37B  -0.1535  0.5118  0.0172  0.023*
C38  -0.1328 (3)  0.9955 (2)  0.1142 (2)  0.0176 (6)
H38A  -0.1253 (3)  1.0539 (3)  0.3588 (2)  0.0587 (9)
H38B  -0.147 (6)  1.052 (4)  0.3036 (17)  0.088*
C39  -0.2349 (6)  1.0663 (5)  0.4209 (4)  0.083 (2)
H39A  -0.2025  1.0473  0.4780  0.100*
H39B  -0.2682  1.1349  0.4375  0.100*
C40  -0.3465 (6)  1.0231 (7)  0.4013 (4)  0.105 (3)
H40A  -0.3264  0.9569  0.4070  0.158*
H40B  -0.4242  1.0552  0.4456  0.158*
H40C  -0.3679  1.0265  0.3377  0.158*

| Atomic displacement parameters (Å²) |
|-------------------------------------|
|  | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{12}$ | $U^{13}$ | $U^{23}$ |
| F1 | 0.0210 (11) | 0.0686 (16) | 0.0492 (15) | 0.0145 (10) | −0.0092 (10) | −0.0207 (13) |
| F2 | 0.0212 (11) | 0.0813 (18) | 0.0645 (17) | 0.0170 (11) | 0.0168 (10) | 0.0419 (15) |
| F3 | 0.0250 (11) | 0.0294 (11) | 0.0778 (18) | 0.0147 (9) | 0.0100 (11) | 0.0087 (11) |
| F4 | 0.0393 (12) | 0.0239 (10) | 0.0413 (13) | 0.0132 (8) | 0.0039 (9) | 0.0037 (9) |
| F5 | 0.0298 (11) | 0.0327 (11) | 0.0343 (12) | 0.0066 (8) | −0.0040 (9) | 0.0112 (9) |
| F6 | 0.0360 (11) | 0.0318 (11) | 0.0482 (14) | 0.0061 (9) | 0.0097 (10) | 0.0225 (10) |
| O1 | 0.0189 (11) | 0.0214 (11) | 0.0216 (13) | 0.0002 (8) | −0.0014 (9) | 0.0033 (9) |
| N1 | 0.0161 (12) | 0.0221 (13) | 0.0230 (15) | 0.0049 (10) | −0.0009 (10) | 0.0016 (11) |
| N2 | 0.0162 (13) | 0.0197 (13) | 0.0201 (15) | 0.0033 (10) | −0.0002 (10) | 0.0017 (11) |
| C1 | 0.0158 (14) | 0.0208 (15) | 0.0208 (17) | 0.0049 (11) | −0.0011 (12) | −0.0011 (13) |
| C2 | 0.0147 (14) | 0.0213 (15) | 0.0200 (17) | 0.0024 (11) | 0.0014 (11) | 0.0027 (13) |
| C3 | 0.0202 (15) | 0.0163 (14) | 0.0193 (17) | 0.0047 (11) | −0.0001 (12) | 0.0017 (12) |
| C4 | 0.0139 (14) | 0.0192 (15) | 0.0195 (17) | 0.0027 (11) | −0.0001 (11) | 0.0002 (12) |
| C5 | 0.0183 (15) | 0.0226 (16) | 0.0259 (18) | 0.0063 (12) | 0.0009 (12) | 0.0025 (14) |
| C6 | 0.0125 (14) | 0.0267 (16) | 0.0312 (19) | 0.0030 (12) | 0.0026 (12) | 0.0043 (14) |
| C7 | 0.0192 (16) | 0.0276 (17) | 0.032 (2) | 0.0017 (13) | 0.0030 (13) | 0.0078 (15) |
| C8 | 0.0211 (15) | 0.0187 (15) | 0.0241 (18) | 0.0036 (12) | −0.0007 (12) | 0.0021 (13) |
C9 0.0189 (15) 0.0173 (14) 0.0216 (17) 0.0049 (11) 0.0002 (12) 0.0010 (12)
C10 0.0178 (15) 0.0251 (16) 0.0297 (19) 0.0058 (12) −0.0008 (13) 0.0036 (14)
C11 0.0230 (16) 0.0239 (16) 0.031 (2) 0.0034 (13) 0.0022 (14) 0.0075 (15)
C12 0.0127 (14) 0.0198 (15) 0.0229 (17) 0.0040 (11) 0.0000 (11) 0.0047 (13)
C13 0.0156 (14) 0.0219 (15) 0.0165 (16) 0.0045 (11) 0.0022 (11) 0.0052 (12)
C14 0.0243 (16) 0.0326 (18) 0.0203 (18) 0.0088 (13) −0.0045 (13) 0.0002 (14)
C15 0.0336 (19) 0.0365 (19) 0.0172 (18) 0.0116 (15) −0.0039 (14) 0.0003 (15)
C16 0.0264 (17) 0.0268 (17) 0.0230 (19) 0.0041 (13) 0.0033 (13) −0.0013 (14)
C17 0.0205 (15) 0.0176 (15) 0.0228 (18) 0.0039 (11) 0.0038 (12) 0.0045 (13)
F7 0.0547 (18) 0.0618 (19) 0.127 (3) −0.0282 (14) 0.0462 (19) −0.0129 (19)
F8 0.0204 (11) 0.098 (2) 0.0746 (19) 0.0233 (12) 0.0199 (11) 0.0562 (17)
F9 0.0271 (12) 0.144 (3) 0.0493 (17) 0.0202 (14) 0.0152 (11) 0.0595 (19)
F10 0.0382 (12) 0.0429 (12) 0.0272 (12) 0.0135 (9) 0.0061 (9) 0.0139 (10)
C18 0.0174 (15) 0.0301 (17) 0.0241 (18) 0.0027 (12) 0.0015 (12) 0.0058 (14)
C19 0.0144 (14) 0.0258 (16) 0.0272 (19) 0.0059 (12) 0.0034 (12) 0.0053 (14)
C20 0.0171 (14) 0.0190 (15) 0.0186 (17) 0.0019 (11) −0.0005 (11) 0.0006 (12)
C21 0.0143 (14) 0.0207 (15) 0.0198 (17) 0.0015 (11) −0.0004 (11) 0.0021 (13)
C22 0.0184 (13) 0.0215 (15) 0.0172 (16) 0.0033 (11) 0.0008 (11) 0.0034 (12)
C23 0.0138 (14) 0.0256 (16) 0.0281 (19) 0.0037 (12) 0.0014 (12) 0.0024 (14)
C24 0.0211 (15) 0.0201 (15) 0.0252 (18) 0.0057 (12) −0.0020 (12) 0.0023 (13)
C25 0.0219 (15) 0.0207 (15) 0.0232 (18) 0.0026 (12) −0.0024 (12) 0.0041 (13)
C26 0.0187 (15) 0.0184 (14) 0.0185 (17) 0.0024 (11) −0.0009 (12) 0.0007 (12)
C27 0.0206 (17) 0.044 (2) 0.039 (2) 0.0029 (15) 0.0051 (15) 0.0150 (18)
C28 0.0248 (17) 0.0272 (17) 0.0271 (19) 0.0069 (13) 0.0003 (13) 0.0079 (15)
C29 0.0141 (14) 0.0211 (15) 0.0196 (17) 0.0051 (11) 0.0009 (11) 0.0030 (13)
C30 0.0179 (14) 0.0226 (15) 0.0160 (16) 0.0057 (11) 0.0026 (11) 0.0026 (12)
C31 0.0212 (16) 0.0232 (16) 0.0284 (19) 0.0010 (12) −0.0007 (13) 0.0080 (14)
C32 0.0265 (17) 0.0225 (16) 0.036 (2) 0.0081 (13) −0.0040 (14) −0.0009 (15)
C33 0.040 (2) 0.0285 (18) 0.0228 (19) 0.0104 (15) 0.0041 (15) −0.0023 (15)
C34 0.0284 (17) 0.0270 (17) 0.0219 (18) 0.0071 (13) 0.0099 (13) 0.0041 (14)
O3 0.0218 (11) 0.0347 (13) 0.0185 (13) 0.0113 (9) 0.0004 (9) 0.0046 (10)
O4 0.0181 (11) 0.0343 (13) 0.0224 (13) 0.0115 (9) −0.0002 (9) 0.0033 (10)
O5 0.0206 (11) 0.0249 (11) 0.0186 (12) 0.0031 (9) 0.0006 (9) 0.0023 (9)
O6 0.0150 (10) 0.0225 (11) 0.0261 (13) 0.0024 (8) 0.0035 (9) 0.0027 (9)
C35 0.0149 (14) 0.0185 (15) 0.0261 (18) 0.0035 (11) 0.0024 (12) 0.0071 (13)
C36 0.0194 (15) 0.0266 (16) 0.0194 (17) 0.0082 (12) 0.0030 (12) 0.0056 (13)
C37 0.0146 (14) 0.0222 (15) 0.0193 (17) 0.0042 (11) 0.0012 (11) 0.0028 (13)
C38 0.0170 (14) 0.0190 (15) 0.0189 (17) 0.0068 (11) 0.0015 (11) 0.0061 (12)
O7 0.0374 (16) 0.111 (3) 0.0352 (18) 0.0244 (17) 0.0060 (13) 0.0237 (19)
C39 0.074 (4) 0.136 (6) 0.040 (3) 0.053 (4) −0.015 (3) −0.004 (3)
C40 0.052 (3) 0.220 (9) 0.058 (4) 0.060 (4) 0.004 (3) 0.036 (5)
| Bond                  | Length (Å) | Bond                  | Length (Å) |
|----------------------|------------|----------------------|------------|
| F1—C10               | 1.328 (4)  | N4—C31               | 1.502 (4)  |
| F2—C10               | 1.333 (4)  | N4—C30               | 1.502 (4)  |
| F3—C10               | 1.321 (4)  | N4—H3N               | 0.882 (10) |
| F4—C11               | 1.338 (4)  | N4—H4N               | 0.882 (10) |
| F5—C11               | 1.338 (4)  | C18—C19              | 1.403 (5)  |
| F6—C11               | 1.352 (4)  | C18—C27              | 1.518 (5)  |
| O1—C12               | 1.406 (4)  | C19—C20              | 1.373 (4)  |
| O1—H1O              | 0.840 (10) | C19—H19              | 0.950      |
| N1—C1                | 1.319 (4)  | C20—C21              | 1.419 (4)  |
| N1—C9                | 1.358 (4)  | C20—C29              | 1.522 (4)  |
| N2—C13               | 1.495 (4)  | C21—C22              | 1.421 (4)  |
| N2—C14               | 1.497 (4)  | C21—C26              | 1.423 (4)  |
| N2—H1N              | 0.880 (10) | C22—C23              | 1.366 (4)  |
| N2—H2N              | 0.883 (10) | C22—H22              | 0.950      |
| C1—C2                | 1.401 (4)  | C23—C24              | 1.404 (5)  |
| C1—C10              | 1.517 (4)  | C23—H23              | 0.950      |
| C2—C3                | 1.370 (4)  | C24—C25              | 1.365 (5)  |
| C2—H2                | 0.950     | C24—H24              | 0.950      |
| C3—C4                | 1.425 (4)  | C25—C26              | 1.435 (4)  |
| C3—C12              | 1.530 (4)  | C25—C28              | 1.504 (5)  |
| C4—C5                | 1.422 (4)  | C29—C30              | 1.533 (4)  |
| C4—C9                | 1.428 (4)  | C29—H29              | 1.0000     |
| C5—C6                | 1.357 (5)  | C30—C34              | 1.519 (4)  |
| C5—H5                | 0.950     | C30—H30              | 1.0000     |
| C6—C7                | 1.406 (5)  | C31—C32              | 1.504 (5)  |
| C6—H6                | 0.950     | C31—H31A             | 0.9900     |
| C7—C8                | 1.365 (4)  | C31—H31B             | 0.9900     |
| C7—H7                | 0.950     | C32—C33              | 1.532 (5)  |
| C8—C9                | 1.427 (4)  | C32—H32A             | 0.9900     |
| C8—C11               | 1.503 (4)  | C32—H32B             | 0.9900     |
| C12—C13              | 1.533 (4)  | C33—C34              | 1.529 (5)  |
| C12—H12              | 1.0000    | C33—H33A             | 0.9900     |
| C13—C17              | 1.525 (4)  | C34—C34B             | 0.9900     |
| C13—H13              | 1.0000    | C34—H34A             | 0.9900     |
| C14—C15              | 1.519 (5)  | C34—H34B             | 0.9900     |
| C14—H14A             | 0.9900    | O3—C35               | 1.236 (4)  |
| C14—H14B             | 0.9900    | O4—C35               | 1.285 (4)  |
| C15—C16              | 1.529 (5)  | O5—C38               | 1.255 (4)  |
| C15—H15A             | 0.9900    | O6—C38               | 1.271 (4)  |
| C15—H15B             | 0.9900    | C35—C36              | 1.522 (4)  |
| C16—C17              | 1.527 (5)  | C36—C37              | 1.517 (4)  |
| C16—H16A             | 0.9900    | C36—H36A             | 0.9900     |
| C16—H16B             | 0.9900    | C36—H36B             | 0.9900     |
| C17—H17A             | 0.9900    | C37—C38              | 1.517 (4)  |
| C17—H17B             | 0.9900    | C37—H37A             | 0.9900     |
| F7—C27               | 1.323 (5)  | C37—H37B             | 0.9900     |
F8—C27 1.331 (4) O7—C39 1.347 (6)
F9—C27 1.304 (5) O7—H7O 0.847 (10)
F10—C28 1.340 (4) C39—C40 1.388 (8)
F11—C28 1.341 (4) C39—H39A 0.9900
F12—C28 1.346 (4) C39—H39B 0.9900
O2—C29 1.409 (3) C40—H40A 0.9800
O2—H2O 0.841 (10) C40—H40B 0.9800
N3—C18 1.309 (4) C40—H40C 0.9800
N3—C26 1.363 (4)

C12—O1—H1O 104 (3) C21—C20—C29 121.6 (3)
C1—N1—C9 116.7 (3) C22—C21—C20 123.7 (3)
C13—N2—C14 113.4 (2) C22—C21—C26 119.0 (3)
C13—N2—H1N 111 (2) C20—C21—C26 120.4 (3)
C14—N2—H1N 106 (2) C23—C22—C21 117.3 (3)
C13—N2—H2N 106 (2) C23—C22—H22 119.8
C14—N2—H2N 112 (2) C21—C22—H22 119.8
H1N—N2—H2N 108 (3) C22—C23—C24 120.8 (3)
N1—C1—C2 125.4 (3) C22—C23—H23 119.6
N1—C1—C10 114.3 (3) C24—C23—H23 119.6
C2—C1—C10 120.2 (3) C25—C24—C23 120.8 (3)
C3—C2—C1 118.6 (3) C25—C24—H24 119.6
C3—C2—H2 120.7 C23—C24—H24 119.6
C1—C2—H2 120.7 C24—C25—C26 120.1 (3)
C2—C3—C4 118.9 (3) C24—C25—C28 120.7 (3)
C2—C3—C12 119.8 (3) C26—C25—C28 119.2 (3)
C4—C3—C12 121.3 (3) N3—C26—C21 123.3 (3)
C5—C4—C3 124.0 (3) N3—C26—C25 117.9 (3)
C5—C4—C9 118.7 (3) C21—C26—C25 118.8 (3)
C3—C4—C9 117.3 (3) F9—C27—F7 107.9 (3)
C6—C5—C4 120.8 (3) F9—C27—F8 106.4 (3)
C6—C5—H5 119.6 F7—C27—F8 105.4 (3)
C4—C5—H5 119.6 F9—C27—C18 113.5 (3)
C5—C6—C7 120.7 (3) F7—C27—C18 111.5 (3)
C5—C6—H6 119.7 F8—C27—C18 111.6 (3)
C7—C6—H6 119.7 F10—C28—F11 107.0 (3)
C8—C7—C6 120.8 (3) F10—C28—F12 106.1 (3)
C8—C7—H7 119.6 F11—C28—F12 106.4 (3)
C6—C7—H7 119.6 F10—C28—C25 112.0 (3)
C7—C8—C9 120.1 (3) F11—C28—C25 113.4 (3)
C7—C8—C11 120.1 (3) F12—C28—C25 111.4 (3)
C9—C8—C11 119.7 (3) O2—C29—C30 111.7 (2)
N1—C9—C8 118.1 (3) O2—C29—C30 107.7 (2)
N1—C9—C4 123.0 (3) C20—C29—C30 110.8 (3)
C8—C9—C4 118.8 (3) O2—C29—H29 108.9
F3—C10—F1 107.1 (3) C20—C29—H29 108.9
F3—C10—F2 106.5 (3) C30—C29—H29 108.9
F1—C10—F2 105.9 (3) N4—C30—C34 110.2 (2)
F3—C10—C1 113.2 (3) N4—C30—C29 106.9 (2)
F1—C10—C1 111.1 (3) C34—C30—C29 113.9 (3)
F2—C10—C1 112.5 (3) N4—C30—H30 108.6
F5—C11—F4 107.0 (3) C34—C30—H30 108.6
F5—C11—F6 106.0 (3) C29—C30—H30 108.6
F4—C11—F6 106.2 (3) N4—C31—C32 110.6 (3)
F5—C11—C8 114.0 (3) N4—C31—H31A 109.5
F4—C11—C8 112.6 (3) C32—C31—H31A 109.5
F6—C11—C8 110.6 (3) C32—C31—H31B 109.5
O1—C12—C3 112.0 (2) C33—C32—C34 109.8
O1—C12—C13 107.7 (2) C33—C32—H32A 109.8
C3—C12—C13 112.0 (2) C33—C32—H32B 109.8
O1—C12—H12 108.4 C34—C33—C32 109.8
C3—C12—H12 108.4 C34—C33—H33A 109.8
C13—C12—H12 108.4 C34—C33—H33B 109.8
N2—C13—C17 110.2 (2) C34—C33—H33B 109.8
N2—C13—C12 107.1 (2) C31—C32—C33 109.4 (3)
N2—C13—C17 107.3 (2) C31—C32—H32A 109.4
C17—C13—C12 113.9 (2) C31—C32—H32B 109.4
C17—C13—C17 108.5 C30—C34—C33 109.4
C12—C13—C17 108.5 C30—C34—H34A 109.4
N2—C14—C15 110.6 (3) C30—C34—H34B 109.4
N2—C14—H14A 109.5 C37—C36—C35 115.7 (3)
C15—C14—H14A 109.5 C37—C36—H36A 114.3 (3)
N2—C14—H14B 109.5 C37—C36—H36B 112.7 (3)
C15—C14—H14B 109.5 C37—C36—H36C 112.7 (3)
H14A—C14—H14B 108.1 C37—C36—H36D 112.7 (3)
C14—C15—C16 111.4 (3) C37—C36—H36E 108.1
C14—C15—H15A 109.4 C37—C36—C37 108.7
C16—C15—H15A 109.4 C37—C36—C37 108.7
C14—C15—H15B 109.4 C38—C37—C36 108.7
C16—C15—H15B 109.4 C38—C37—C37 108.7
H15A—C15—H15B 108.0 C38—C37—C37 108.7
C17—C16—C15 110.5 (3) C38—C37—C37 108.7
C17—C16—H16A 109.5 C38—C37—C37 108.7
C15—C16—H16A 109.5 C38—C37—C37 108.7
C17—C16—H16B 109.5 C38—C37—C37 108.7
C15—C16—H16B 109.5 C38—C37—C37 108.7
H16A—C16—H16B 108.1 C38—C37—C37 108.7
C13—C17—C16 110.9 (2) C38—C37—C37 108.7
C13—C17—H17A 109.5 C38—C37—C37 108.7
C16—C17—H17A 109.5 C38—C37—C37 108.7
C13—C17—H17B 109.5 C38—C37—C37 108.7
C16—C17—H17B 109.5 C38—C37—C37 108.7
H17A—C17—H17B 108.1 C38—C37—C37 108.7
C29—O2—H2O 113 (3) O5—C38—C37 118.3 (3)
C29—O2—H2O 113 (3) O5—C38—C37 118.3 (3)
C29—O2—H2O 113 (3) O5—C38—C37 118.3 (3)
C18—N3—C26 116.1 (3) C39—O7—H7O 112 (4)
C31—N4—C30 114.0 (2)
| Bond                  | Distance (Å) | Angle (°) |
|-----------------------|--------------|-----------|
| C31—N4—H3N           | 108 (2)      |           |
| C30—N4—H3N           | 111 (2)      |           |
| C31—N4—H4N           | 111 (2)      |           |
| C30—N4—H4N           | 105 (2)      |           |
| H3N—N4—H4N           | 108 (3)      |           |
| N3—C18—C19           | 126.2 (3)    |           |
| N3—C18—C27           | 113.7 (3)    |           |
| C19—C18—C27          | 120.0 (3)    |           |
| C20—C19—C18          | 118.0 (3)    |           |
| C20—C19—H19          | 121.0        |           |
| C18—C19—H19          | 121.0        |           |
| C19—C20—C21          | 119.0 (3)    |           |
| C19—C20—C29          | 119.4 (3)    |           |
| C9—N1—C1—C2          | −2.4 (5)     |           |
| C9—N1—C1—C10         | 174.4 (3)    |           |
| N1—C1—C2—C3          | 1.3 (5)      |           |
| C10—C1—C2—C3         | −175.4 (3)   |           |
| C1—C2—C3—C4          | 1.1 (4)      |           |
| C1—C2—C3—C12         | −179.9 (3)   |           |
| C2—C3—C4—C5          | 176.1 (3)    |           |
| C12—C3—C4—C5         | −2.8 (5)     |           |
| C2—C3—C4—C9          | −2.1 (4)     |           |
| C12—C3—C4—C9         | 178.9 (3)    |           |
| C3—C4—C5—C6          | −178.4 (3)   |           |
| C9—C4—C5—C6          | −0.2 (5)     |           |
| C4—C5—C6—C7          | −0.4 (5)     |           |
| C5—C6—C7—C8          | −0.1 (5)     |           |
| C6—C7—C8—C9          | 1.3 (5)      |           |
| C6—C7—C8—C11         | −176.2 (3)   |           |
| C11—N1—C9—C8         | −177.5 (3)   |           |
| C11—N1—C9—C4         | 1.2 (5)      |           |
| C7—C8—C9—N1          | 176.8 (3)    |           |
| C11—C8—C9—N1         | −5.6 (5)     |           |
| C7—C8—C9—C4          | −2.0 (5)     |           |
| C11—C8—C9—C4         | 175.6 (3)    |           |
| C5—C4—C9—N1          | −177.3 (3)   |           |
| C3—C4—C9—N1          | 1.0 (5)      |           |
| C5—C4—C9—C8          | 1.4 (4)      |           |
| C3—C4—C9—C8          | 179.7 (3)    |           |
| N1—C1—C10—F3         | 42.1 (4)     |           |
| N1—C1—C10—F1         | −78.4 (4)    |           |
| C2—C1—C10—F3         | −140.9 (3)   |           |
| C2—C1—C10—F1         | 98.6 (4)     |           |
| N1—C1—C10—F2         | 163.0 (3)    |           |
| C2—C1—C10—F2         | −20.0 (4)    |           |
| C7—C8—C11—F5         | −121.8 (3)   |           |
| C9—C8—C11—F5         | 60.6 (4)     |           |
C7—C8—C11—F4  116.1 (3)  C26—C25—C28—F12  −178.9 (3)
C9—C8—C11—F4  −61.5 (4)  C19—C20—C29—O2  −14.1 (4)
C7—C8—C11—F6  −2.5 (5)   C21—C20—C29—O2  165.5 (3)
C9—C8—C11—F6  179.9 (3)  C19—C20—C29—C30  105.9 (3)
C2—C3—C12—O1  −15.4 (4)  C21—C20—C29—C30  −74.4 (4)
C4—C3—C12—O1  163.5 (3)  C31—N4—C30—C34  53.7 (3)
C2—C3—C12—C13  105.7 (3)  C31—N4—C30—C29  177.9 (2)
C4—C3—C12—C13  −75.4 (4)  O2—C29—C30—N4  −68.4 (3)
C14—N2—C13—C17  56.2 (3)  C20—C29—C30—N4  169.2 (2)
C14—N2—C13—C12  −179.4 (2)  O2—C29—C30—C34  53.6 (3)
O1—C12—C13—N2  −63.4 (3)  C20—C29—C30—C34  −68.9 (3)
C3—C12—C13—N2  173.1 (2)  C30—N4—C31—C32  −54.6 (3)
O1—C12—C13—C17  58.7 (3)   N4—C31—C32—C33  56.3 (4)
C3—C12—C13—C17  −64.8 (3)  N4—C31—C32—C33  −58.7 (4)
C13—N2—C14—C15  −55.5 (4)  N4—C30—C34—C33  −55.2 (4)
N2—C14—C15—C16  54.4 (4)   C29—C30—C34—C33  −175.3 (3)
C14—C15—C16—C17  −55.4 (4)  C32—C33—C34—C30  58.3 (4)
N2—C13—C17—C16  −55.8 (3)  O3—C35—C36—C37  −3.0 (4)
C12—C13—C17—C16  −176.1 (3)  O4—C35—C36—C37  177.4 (3)
C15—C16—C17—C13  56.0 (3)   C35—C36—C37—C38  175.4 (3)
C26—N3—C18—C19  −1.4 (5)   C36—C37—C38—O5  55.5 (4)
C26—N3—C18—C27  177.0 (3)  C36—C37—C38—O6  −124.1 (3)
N3—C18—C19—C20  1.5 (5)

Hydrogen-bond geometry (Å, °)

Hydrogen-bond geometry (Å, °)

Cg1 is the centroid of the (N1,C1–C4,C9) ring.

| D—H···A  | D—H  | H···A  | D···A  | D—H···A |
|----------|------|-------|-------|---------|
| N2—H1N···O1  | 0.88 (3)  | 2.49 (3)  | 2.806 (4)  | 102 (2) |
| N4—H3N···O2  | 0.88 (2)  | 2.54 (3)  | 2.863 (4)  | 103 (2) |
| O1—H1O···O6  | 0.84 (3)  | 1.81 (3)  | 2.653 (3)  | 175 (2) |
| O2—H2O···O4  | 0.84 (2)  | 1.82 (2)  | 2.656 (3)  | 170 (3) |
| N2—H1N···O5  | 0.88 (3)  | 1.97 (3)  | 2.830 (4)  | 165 (3) |
| N2—H2N···O4  | 0.88 (3)  | 1.82 (3)  | 2.694 (4)  | 173 (3) |
| N4—H3N···O3  | 0.88 (2)  | 1.99 (3)  | 2.832 (4)  | 161 (3) |
| N4—H4N···O6  | 0.89 (3)  | 1.92 (3)  | 2.789 (4)  | 168 (3) |
| O7—H7O···O5  | 0.85 (3)  | 1.88 (3)  | 2.729 (4)  | 176 (7) |
| C30—H30···O7  | 1.00  | 2.40  | 3.296 (4)  | 149 |
| C10—F3···Cg1 | 1.32 (1)  | 3.28 (1)  | 4.101 (3)  | 120 (1) |

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