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Synthesis, characterization, crystal structure and Hirshfeld surface analysis of isobutyl 4-[4-(difluoromethoxy)phenyl]-2,6,6-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate

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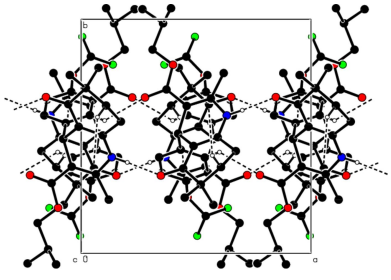
In the title compound, $C_{24}H_{29}F_2NO_4$, which crystallizes in the orthorhombic $Pca2_1$ space group with $Z = 4$, the 1,4-dihydropyridine ring adopts a distorted boat conformation, while the cyclohexene ring is in a distorted half-chair conformation. In the crystal, the molecules are linked by N—H···O and C—H···O interactions, forming supramolecular chains parallel to the *a* axis. These chains pack with C—H···π interactions between them, forming layers parallel to the (010) plane. The cohesion of the crystal structure is ensured by van der Waals interactions between these layers. Hirshfeld surface analysis shows the major contributions to the crystal packing are from H···H (56.9%), F···H/H···F (15.7%), O···H/H···O (13.7%) and C···H/H···C (9.5%) contacts.

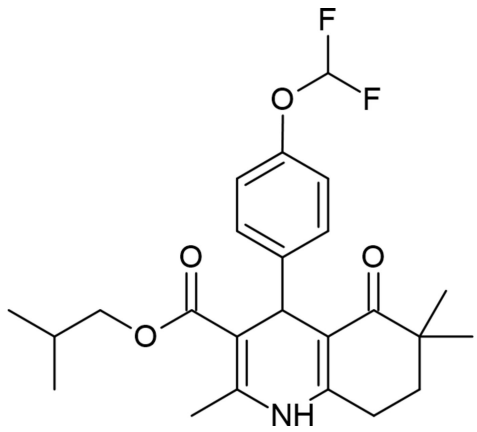
1. Chemical context

Hexahydroquinoline (HHQ) ring systems occupy a prominent place in medicinal chemistry, attracting the attention of researchers for their versatile structural attributes and pharmacological potential. These ring systems, characterized by a unique combination of pyridine and cyclohexane rings, have shown remarkable bioactivity across a spectrum of therapeutic areas. Their capacity to interact with specific biological targets has led to the development of HHQ-based compounds with diverse medicinal properties, including antimicrobial, anti-inflammatory, and anticancer activities (Ranjbar *et al.*, 2019). Recent studies have shown that these compounds are effective in cancer-related inflammatory pathways such as TGF-β (Längle *et al.*, 2019). Additionally, they have been demonstrated to have inhibitory effects on receptors involved in cancer development, such as EGFR, or to reverse multi-drug resistance (Abo Al-Hamd *et al.*, 2023; Shahraki *et al.*, 2020).

The choice to synthesize HHQs is also fueled by the accessibility of various synthetic routes and the opportunity to fine-tune their chemical structure to optimize drug-like properties. Multi-component reactions and cyclization strategies provide versatile platforms for their synthesis, allowing for systematic modifications to explore structure–activity relationships (SAR; Batista *et al.*, 2016). As a result, the strategic pursuit of hexahydroquinoline synthesis continues to be a compelling avenue in medicinal chemistry, promising



innovative solutions to pressing medical challenges and drug discovery endeavors.



In this study, isobutyl 4-(4-difluoromethoxyphenyl)-2,6,6-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate was synthesized and its molecular structure was confirmed by IR, ^{1}H NMR, ^{13}C NMR, HRMS and X-ray crystallography. The intermolecular interactions observed in the crystal packing were investigated by Hirshfeld surface analysis.

2. Structural commentary

The 1,4-dihydropyridine ring (N1/C1/C6–C9) of the title compound (Fig. 1), which crystallizes in the orthorhombic $Pca2_1$ space group with Z = 4, adopts a distorted boat conformation [puckering parameters (Cremer & Pople, 1975) are Q_T = 0.2779 (16) Å, θ = 73.7 (3)° and φ = 179.1 (3)°], while the cyclohexene ring (C1–C6) has a distorted half-chair conformation [puckering parameters are Q_T = 0.4464 (18) Å, θ = 48.9 (2)° and φ = 126.3 (3)°]. The 4-(4-difluoromethoxyphenyl) ring (C18–C23) makes a dihedral angle of 88.73 (6)° with the mean plane of the quinoline ring system [N1/C1–C9; maximum deviation = 0.415 (2) Å for C3]. The geometrical parameters of the title compound are in agreement with those reported for similar compounds in the *Database survey* section.

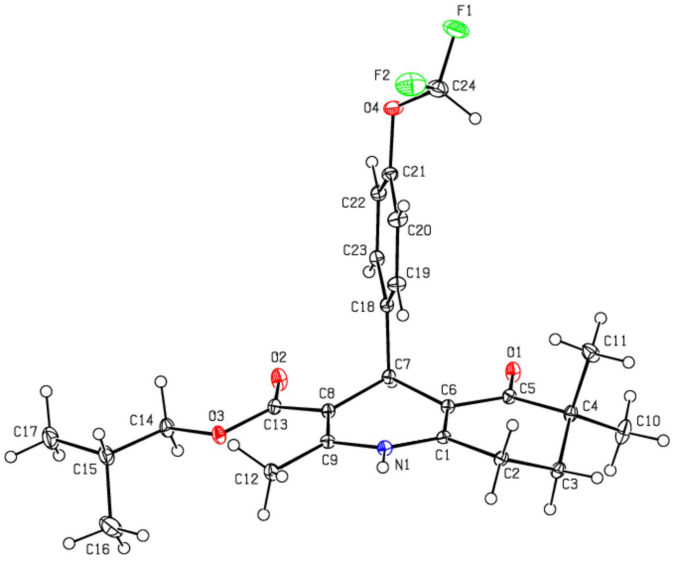


Figure 1
View of the title molecule. Displacement ellipsoids are drawn at the 30% probability level.

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

*Cg*3 is the centroid the benzene ring of the 4-(4-difluoromethoxyphenyl group of the title compound.

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1*N*···O1^{i}	0.87 (2)	1.98 (2)	2.8426 (17)	173 (2)
C19—H19*A*···O2^{i}	0.95	2.43	3.100 (2)	127
C3—H3*A*···*Cg*3^{ii}	0.99	2.84	3.7345 (18)	151

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

3. Supramolecular features and Hirshfeld surface analysis

In the crystal, the molecules are linked by N—H···O and C—H···O interactions, forming supramolecular chains parallel to the *a*-axis direction (see Table 1; Figs. 2 and 3). These chains pack with C—H···π interactions between them,

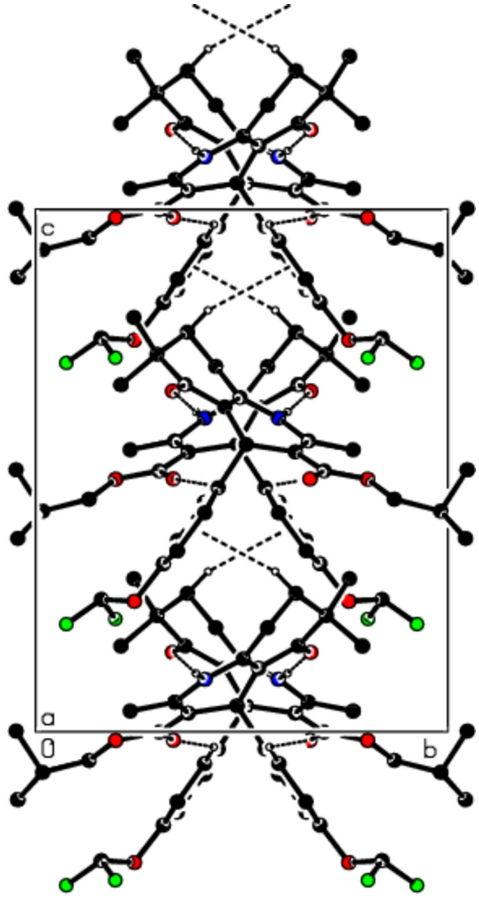


Figure 2
A view of the molecular packing of the title compound along the *a*-axis with the N—H···O, C—H···O hydrogen bonds and C—H···π interactions shown as dashed lines.

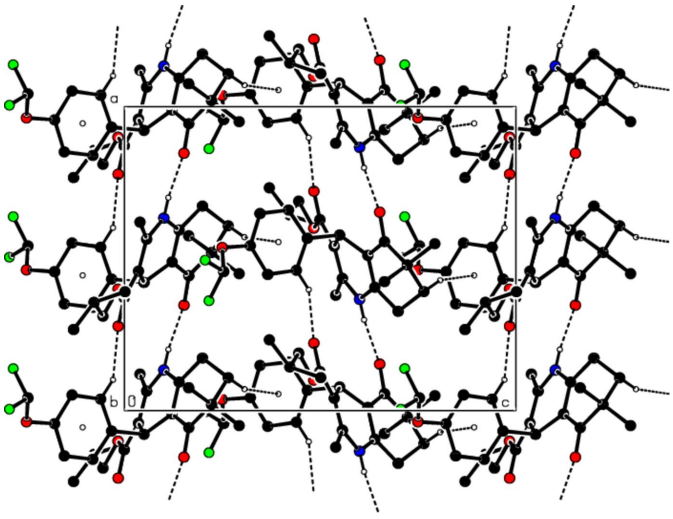


Figure 3
View of the molecular packing along the *b*-axis. Hydrogen bonds are shown as dashed lines.

forming layers parallel to the (010) plane (Fig. 4). The cohesion of the crystal structure is ensured by van der Waals interactions between these layers.

The Hirshfeld surfaces and their corresponding two-dimensional fingerprint plots were calculated using the software package *Crystal Explorer 17.5* (Spackman *et al.*, 2021). The $d_{\rm norm}$ surfaces are mapped over a fixed color scale from −0.5961 (red) to 1.9017 (blue) a.u. Red spots on the surface correspond to O···H/H···O interactions (Tables 1 and 2; Fig. 5*a*,*b*).

In Fig. 6, fingerprint plots of the most important non-covalent interactions for the title compound are shown. The major contributions to the crystal packing are from H···H (56.9%), F···H/H···F (15.7%), O···H/H···O (13.7%) and C···H/H···C (9.5%) contacts. O···C/C···O (1.1%), F···C/C···F (1.0%), C···C (0.7%), F···O/O···F (0.6%), O···N/

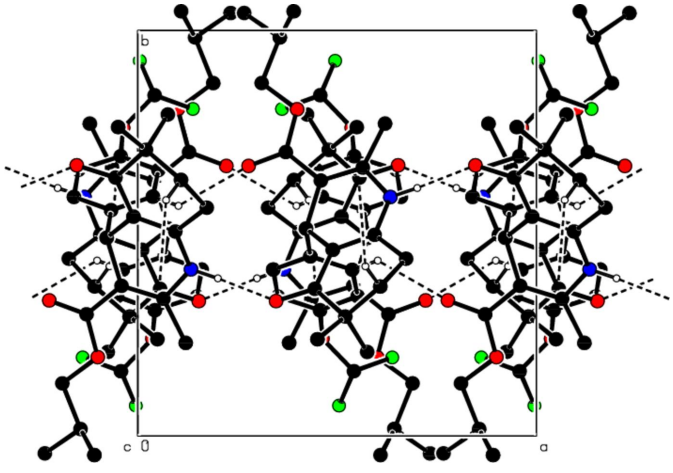


Figure 4
View of the molecular packing along the *c*-axis. Hydrogen bonds are shown as dashed lines.

Table 2
Summary of short interatomic contacts (Å) in the title compound.

H15*A*···H10*B*	2.37	$1-x, 1-y, -\frac{1}{2}+z$
F2···H11*B*	2.83	$\frac{1}{2}-x, y, -\frac{1}{2}+z$
O1···H1*N*	1.98	$\frac{1}{2}+x, 1-y, z$
H10*A*···H22*A*	2.47	$\frac{3}{2}-x, y, \frac{1}{2}+z$
H17*B*···H22*A*	2.58	$x, -1+y, z$
H12*A*···H17*C*	2.54	$-\frac{1}{2}+x, -y, z$

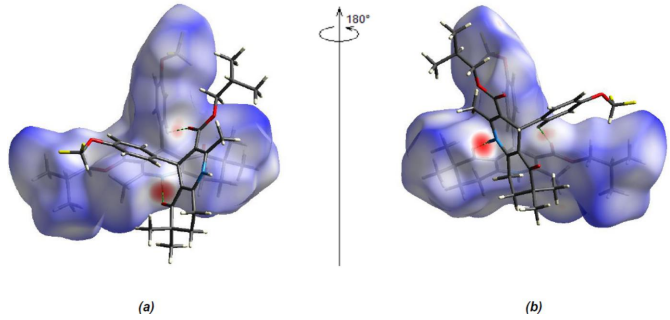


Figure 5
(*a*) Front and (*b*) back views of the three-dimensional Hirshfeld surface for the title compound.

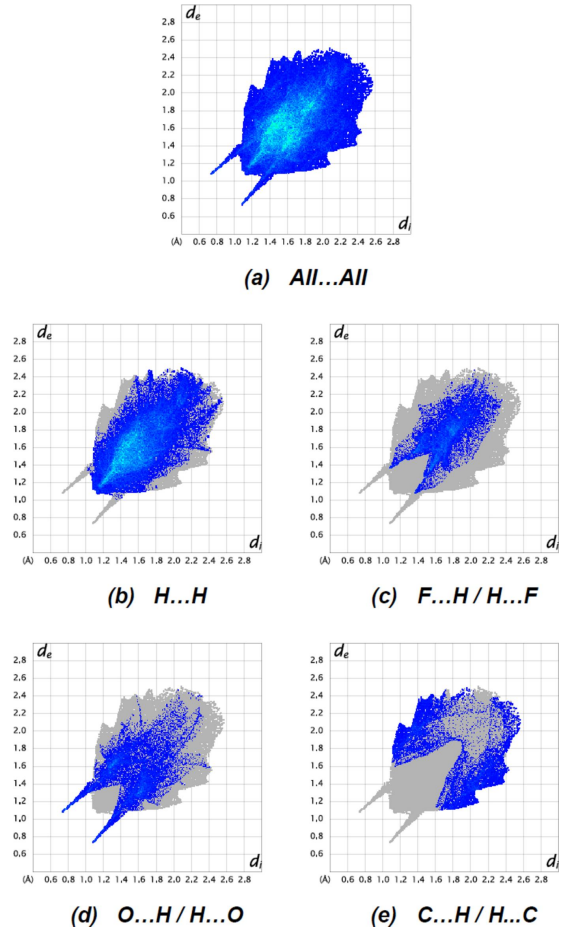


Figure 6
The two-dimensional fingerprint plots for the title compound showing (*a*) all interactions, and delineated into (*b*) H···H, (*c*) F···H/H···F, (*d*) O···H/H···O and (*e*) C···H/H···C interactions. The d_i and d_e values are the closest internal and external distances (in Å) from given points on the Hirshfeld surface.

N···O (0.5%) and N···H/H···N (0.2%) contacts, which contribute less than 1.1%, are not shown in Fig.7.

4. Database survey

A search of the Cambridge Structural Database (CSD, Version 5.42, update of September 2021; Groom *et al.*, 2016) for similar structures with the 1,4,5,6,7,8-hexahydroquinoline group showed that the nine most closely related to the title compound are LIMYUF (Pehlivanlar *et al.*, 2023), WEZJUK (Yıldırım *et al.*, 2023), ECUCUE (Yıldırım *et al.*, 2022), LOQCAX (Steiger *et al.*, 2014), NEQMON (Öztürk Yildirim, *et al.*, 2013), PECPUK (Gündüz *et al.*, 2012), IMEJOA (Linden *et al.*, 2011), PUGCIE (Mookiah *et al.*, 2009), UCOLOO (Linden *et al.*, 2006) and DAYJET (Linden *et al.*, 2005). In all of these compounds, molecules are linked by N—H···O hydrogen bonds. Furthermore, C—H···F hydrogen bonds in LIMYUF, C—H···O hydrogen bonds in WEZJUK, ECUCUE, NEQMON, IMEJOA and PUGCIE and C—H···π interactions in LIMYUF, WEZJUK and ECUCUE were also observed.

5. Synthesis and crystallization

The synthesis of the compound was carried out by refluxing 1 mmol of 4-(4-difluoromethoxy)benzaldehyde, isobutyl acetoacetate, 4,4-methyl-1,3-cyclohexandione and 5 mmol of ammonium acetate in methanol. The reaction process was monitored by thin-layer chromatography [ethyl acetate-*n*-hexane (1:1)], and after the reaction was complete, the mixture was allowed to stand at room temperature for a while and then poured into an ice–water mixture (Fig. 7). The resulting precipitates were purified again by crystallization with methanol (Yıldırım *et al.*, 2023).

Isobutyl 4-(4-difluoromethoxyphenyl)-2,6,6-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate

Light-yellow solid, m.p: 489–491 K, yield: 85%. IR (cm^{-1}) 3291 (N—H), 1674 (C═O, ester), 1597 (C═O, ketone). ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.69 [3H, *d*, *J* = 9 Hz, –CH(**CH$_3$**)$_a$], 0.77 [3H, *d*, *J* = 9 Hz, –CH(**CH$_3$**)$_b$], 0.81 (3H, *s*, 6-CH$_3$), 0.97 (3H, *s*, 6-CH$_3$), 1.52–1.65 (2H, *m*, quinoline H$_7$), 1.72–1.81 (H, *m*, –CH–), 2.26 (3H, *s*, 2-CH$_3$), 2.46–2.50 (2H, *m*, quinoline H$_8$), 3.63–3.72 (2H, *m*, –**CH$_2$**)–, 4.94 (H, *s*, quinoline H$_4$), 6.96 (2H, *dd*, *J* = 9.2, 6.8 Hz, Ar-H$_{3,5}$), 7.16 (2H, *dd*, *J* = 9.2, 6.8 Hz, Ar-H$_{4,6}$), 7.26 (H, *s*, O**CH**F$_2$), 9.02 (H, *s*, NH). ^{13}C NMR (100 MHz, DMSO-d_6): 18.6 (2-CH$_3$), 22.3 [–CH(**CH$_3$**)$_a$], 22.9 [–CH(**CH$_3$**)$_b$], 23.4 (C-8), 24.2 (6-CH$_3$), 24.8 (6-CH$_3$), 33.5 (C-7), 34.1 (C-4), 35 (–CH–), 39.5 (C-6), 68.2 (–CH$_2$–), 103.8 (C-3), 108.4 (C-4a), 114.2, 116.7, 125.4, 128.2, 135.5, 157.4 (phenyl carbons), 147.1(C-2), 150.6 (C-8a), 166.9 (–COO–), 168.3 (OCHF$_2$) 199.6 (C-5). HRMS (ESI/Q-TOF) *m*/*z*: [*M* + H]$^+$ calculated for $C_{23}H_{25}F_4NO_3$: 420.1942; found: 420.2150.

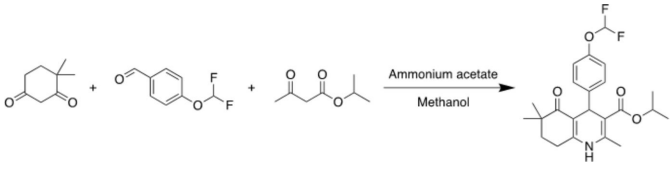


Figure 7
Synthetic scheme.

Table 3
Experimental details.

Crystal data	
Chemical formula	$C_{24}H_{29}F_2NO_4$
M_r	433.48
Crystal system, space group	Orthorhombic, $Pca2_1$
Temperature (K)	100
a, *b*, *c* (Å)	11.9879 (7), 12.1807 (7), 15.4518 (9)
V (Å^3)	2256.3 (2)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.10
Crystal size (mm)	0.27 × 0.24 × 0.16
Data collection	
Diffractometer	Bruker Quest D8 with Photon 2 detector
Absorption correction	Multi-scan (*SADABS*; Krause *et al.*, 2015)
T_{min}, T_{max}	0.718, 0.744
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	103269, 9491, 7264
R_{int}	0.080
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.826
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.045, 0.107, 1.03
No. of reflections	9491
No. of parameters	289
No. of restraints	1
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.32, −0.29
Absolute structure	Flack *x* determined using 2721 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter	0.0 (2)

Computer programs: *APEX2* and *SAINT* (Bruker, 2018), *SHELXT* (Sheldrick, 2015*a*), *SHELXL* (Sheldrick, 2015*b*), *ORTEP-3 for Windows* (Farrugia, 2012) and *PLATON* (Spek, 2020).

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 3. The N-bound H atom was located in a difference-Fourier map and refined freely [N1—H1*N* = 0.87 (2) Å]. All C-bound H atoms were positioned geometrically [C—H = 0.95–1.00 Å] and refined using a riding model with U_{iso}(H) = 1.2 or 1.5U_{eq}(C).

Acknowledgements

Authors' contributions are as follows. Conceptualization, RS and SÖY; methodology, RS and GÇ; investigation, RS and SÖY; writing (original draft), GÇ and MA; writing (review and editing of the manuscript), RS and SÖY; crystal data production and validation, RJB and SÖY; visualization, MA; funding acquisition, RJB; resources, AB, RJB and RS.

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supporting information

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Synthesis, characterization, crystal structure and Hirshfeld surface analysis of isobutyl 4-[4-(difluoromethoxy)phenyl]-2,6,6-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate

Sema Öztürk Yıldırım, Mehmet Akkurt, Gökalp Çetin, Rahime Şimşek, Ray J. Butcher and Ajaya Bhattarai

Computing details

Isobutyl 4-[4-(difluoromethoxy)phenyl]-2,6,6-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate

Crystal data

$C_{24}H_{29}F_2NO_4$
M_r = 433.48
Orthorhombic, $Pca2_1$
a = 11.9879 (7) Å
b = 12.1807 (7) Å
c = 15.4518 (9) Å
V = 2256.3 (2) Å^3
Z = 4
$F(000)$ = 920
D_x = 1.276 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 9859 reflections
θ = 2.4–32.7°
μ = 0.10 mm^{-1}
T = 100 K
Chunk, light yellow
0.27 × 0.24 × 0.16 mm

Data collection

Bruker Quest D8 with Photon 2 detector diffractometer
φ and ω scans
Absorption correction: multi-scan (SADABS; Krause *et al.*, 2015)
T_{min} = 0.718, T_{max} = 0.744
103269 measured reflections
9491 independent reflections
7264 reflections with $I > 2\sigma(I)$
R_{int} = 0.080
θ_{max} = 36.0°, θ_{min} = 2.4°
h = −18→19
k = −20→19
l = −25→21

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.045
$wR(F^2)$ = 0.107
S = 1.03
9491 reflections
289 parameters
1 restraint
Hydrogen site location: mixed
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0508P)^2 + 0.3823P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.32 e Å^{-3}
$\Delta\rho_{min}$ = −0.29 e Å^{-3}
Absolute structure: Flack x determined using 2721 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter: 0.0 (2)

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	0.49509 (14)	0.92511 (11)	0.20621 (10)	0.0455 (4)
F2	0.36176 (12)	0.80630 (13)	0.21602 (10)	0.0467 (4)
O1	0.65307 (10)	0.66738 (10)	0.65205 (8)	0.0198 (2)
O2	0.72200 (10)	0.33422 (10)	0.48402 (9)	0.0239 (3)
O3	0.60039 (10)	0.19451 (9)	0.48360 (8)	0.0184 (2)
O4	0.53670 (11)	0.76006 (11)	0.24983 (8)	0.0236 (3)
N1	0.36644 (10)	0.41080 (11)	0.60065 (9)	0.0143 (2)
H1N	0.299 (2)	0.3886 (19)	0.6122 (14)	0.019 (5)*
C1	0.40589 (12)	0.50413 (12)	0.63969 (10)	0.0128 (3)
C2	0.32686 (12)	0.56285 (13)	0.69932 (10)	0.0149 (3)
H2A	0.279873	0.508580	0.730076	0.018*
H2B	0.277189	0.611193	0.665143	0.018*
C3	0.39163 (14)	0.63141 (13)	0.76504 (11)	0.0171 (3)
H3A	0.429018	0.581636	0.806558	0.021*
H3B	0.338594	0.677625	0.797973	0.021*
C4	0.47947 (13)	0.70546 (13)	0.72264 (11)	0.0165 (3)
C5	0.55598 (12)	0.63711 (12)	0.66451 (10)	0.0142 (3)
C6	0.51077 (12)	0.54097 (12)	0.62178 (10)	0.0134 (3)
C7	0.57801 (12)	0.48870 (12)	0.54998 (10)	0.0129 (2)
H7A	0.658250	0.488219	0.567679	0.015*
C8	0.54078 (12)	0.37018 (12)	0.53589 (10)	0.0135 (3)
C9	0.43551 (13)	0.33826 (12)	0.55678 (10)	0.0142 (3)
C10	0.54927 (15)	0.76147 (18)	0.79303 (13)	0.0285 (4)
H10A	0.584192	0.705497	0.829657	0.043*
H10B	0.500970	0.808215	0.828535	0.043*
H10C	0.607286	0.806523	0.765913	0.043*
C11	0.42455 (16)	0.79274 (14)	0.66419 (14)	0.0246 (4)
H11A	0.482159	0.841376	0.640633	0.037*
H11B	0.371361	0.835939	0.698245	0.037*
H11C	0.385240	0.756348	0.616550	0.037*
C12	0.37972 (13)	0.22972 (13)	0.53973 (11)	0.0186 (3)
H12A	0.400712	0.203315	0.482072	0.028*
H12B	0.298580	0.238862	0.542595	0.028*
H12C	0.403522	0.176294	0.583404	0.028*
C13	0.62870 (13)	0.30006 (12)	0.49936 (10)	0.0150 (3)
C14	0.68925 (15)	0.12977 (14)	0.44523 (12)	0.0208 (3)
H14A	0.751816	0.122384	0.486642	0.025*
H14B	0.717478	0.166562	0.392459	0.025*
C15	0.64362 (16)	0.01733 (14)	0.42246 (14)	0.0260 (4)

H15A	0.576642	0.027434	0.384717	0.031*
C16	0.6088 (3)	−0.04712 (19)	0.5015 (2)	0.0529 (8)
H16A	0.544199	−0.011657	0.528503	0.079*
H16B	0.670705	−0.049424	0.542902	0.079*
H16C	0.588934	−0.122088	0.484414	0.079*
C17	0.7331 (2)	−0.04286 (16)	0.37018 (15)	0.0330 (4)
H17A	0.747606	−0.002683	0.316403	0.050*
H17B	0.706990	−0.117084	0.356413	0.050*
H17C	0.801872	−0.047357	0.404232	0.050*
C18	0.56699 (12)	0.55695 (12)	0.46724 (10)	0.0137 (3)
C19	0.46204 (13)	0.59010 (14)	0.43930 (11)	0.0184 (3)
H19A	0.398046	0.567489	0.470878	0.022*
C20	0.44827 (14)	0.65559 (15)	0.36621 (12)	0.0208 (3)
H20A	0.375930	0.676416	0.347231	0.025*
C21	0.54288 (14)	0.68982 (13)	0.32165 (11)	0.0183 (3)
C22	0.64869 (13)	0.65619 (13)	0.34636 (11)	0.0175 (3)
H22A	0.712375	0.678221	0.314155	0.021*
C23	0.66020 (13)	0.58949 (13)	0.41925 (11)	0.0159 (3)
H23A	0.732370	0.565862	0.436503	0.019*
C24	0.45780 (18)	0.84020 (16)	0.25354 (14)	0.0294 (4)
H24A	0.444326	0.863192	0.314777	0.035*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
F1	0.0608 (9)	0.0302 (6)	0.0454 (8)	0.0086 (6)	0.0104 (7)	0.0181 (6)
F2	0.0317 (7)	0.0612 (9)	0.0474 (8)	0.0089 (6)	−0.0074 (6)	0.0154 (7)
O1	0.0120 (5)	0.0199 (5)	0.0276 (6)	−0.0016 (4)	0.0042 (4)	−0.0068 (5)
O2	0.0134 (5)	0.0212 (5)	0.0371 (7)	−0.0005 (4)	0.0070 (5)	−0.0075 (5)
O3	0.0158 (5)	0.0142 (5)	0.0252 (6)	0.0018 (4)	0.0030 (4)	−0.0036 (4)
O4	0.0262 (6)	0.0255 (6)	0.0191 (6)	0.0043 (5)	0.0044 (5)	0.0068 (5)
N1	0.0093 (5)	0.0162 (6)	0.0173 (6)	−0.0009 (4)	0.0014 (5)	−0.0004 (5)
C1	0.0110 (6)	0.0149 (6)	0.0124 (6)	0.0015 (5)	0.0006 (5)	0.0011 (5)
C2	0.0116 (6)	0.0179 (6)	0.0153 (7)	0.0009 (5)	0.0033 (5)	−0.0012 (5)
C3	0.0151 (7)	0.0203 (7)	0.0158 (7)	−0.0002 (6)	0.0034 (5)	−0.0026 (6)
C4	0.0129 (6)	0.0187 (7)	0.0177 (7)	−0.0003 (5)	0.0031 (5)	−0.0051 (5)
C5	0.0122 (7)	0.0156 (6)	0.0148 (6)	0.0015 (5)	0.0004 (5)	−0.0007 (5)
C6	0.0113 (6)	0.0143 (6)	0.0145 (6)	0.0004 (5)	0.0005 (5)	−0.0005 (5)
C7	0.0095 (6)	0.0147 (6)	0.0145 (6)	0.0001 (5)	0.0017 (5)	−0.0013 (5)
C8	0.0110 (6)	0.0141 (6)	0.0154 (6)	0.0006 (5)	0.0009 (5)	−0.0011 (5)
C9	0.0130 (6)	0.0151 (6)	0.0146 (7)	0.0004 (5)	−0.0001 (5)	0.0012 (5)
C10	0.0201 (8)	0.0368 (10)	0.0285 (9)	−0.0063 (7)	0.0049 (7)	−0.0175 (8)
C11	0.0202 (8)	0.0184 (7)	0.0353 (10)	0.0029 (6)	0.0080 (7)	0.0023 (7)
C12	0.0159 (7)	0.0172 (7)	0.0229 (8)	−0.0034 (5)	0.0021 (6)	−0.0016 (6)
C13	0.0141 (6)	0.0153 (6)	0.0156 (7)	0.0010 (5)	−0.0002 (5)	−0.0020 (5)
C14	0.0185 (7)	0.0177 (7)	0.0261 (8)	0.0051 (6)	0.0032 (6)	−0.0039 (6)
C15	0.0286 (9)	0.0163 (7)	0.0331 (10)	0.0030 (6)	0.0065 (7)	−0.0029 (7)
C16	0.0751 (19)	0.0233 (10)	0.0603 (17)	0.0074 (11)	0.0366 (15)	0.0097 (10)

C17	0.0388 (11)	0.0202 (8)	0.0401 (11)	0.0047 (7)	0.0097 (9)	−0.0055 (8)
C18	0.0115 (6)	0.0139 (6)	0.0157 (7)	−0.0003 (5)	0.0021 (5)	−0.0013 (5)
C19	0.0124 (6)	0.0234 (7)	0.0195 (7)	0.0007 (6)	0.0024 (5)	0.0035 (6)
C20	0.0144 (7)	0.0279 (8)	0.0201 (8)	0.0024 (6)	0.0000 (6)	0.0044 (7)
C21	0.0202 (7)	0.0183 (7)	0.0164 (7)	0.0010 (6)	0.0036 (6)	0.0019 (6)
C22	0.0160 (7)	0.0176 (7)	0.0190 (7)	−0.0020 (5)	0.0049 (6)	−0.0007 (6)
C23	0.0118 (6)	0.0160 (6)	0.0200 (7)	−0.0013 (5)	0.0023 (5)	−0.0015 (5)
C24	0.0336 (10)	0.0265 (9)	0.0280 (10)	0.0059 (7)	0.0031 (8)	0.0076 (7)

Geometric parameters (Å, º)

F1—C24	1.343 (2)	C10—H10B	0.9800
F2—C24	1.354 (3)	C10—H10C	0.9800
O1—C5	1.2361 (19)	C11—H11A	0.9800
O2—C13	1.2166 (19)	C11—H11B	0.9800
O3—C13	1.3518 (18)	C11—H11C	0.9800
O3—C14	1.4520 (19)	C12—H12A	0.9800
O4—C24	1.360 (2)	C12—H12B	0.9800
O4—C21	1.403 (2)	C12—H12C	0.9800
N1—C1	1.371 (2)	C14—C15	1.516 (2)
N1—C9	1.388 (2)	C14—H14A	0.9900
N1—H1N	0.87 (2)	C14—H14B	0.9900
C1—C6	1.363 (2)	C15—C16	1.511 (3)
C1—C2	1.503 (2)	C15—C17	1.530 (3)
C2—C3	1.527 (2)	C15—H15A	1.0000
C2—H2A	0.9900	C16—H16A	0.9800
C2—H2B	0.9900	C16—H16B	0.9800
C3—C4	1.533 (2)	C16—H16C	0.9800
C3—H3A	0.9900	C17—H17A	0.9800
C3—H3B	0.9900	C17—H17B	0.9800
C4—C5	1.530 (2)	C17—H17C	0.9800
C4—C10	1.532 (2)	C18—C19	1.390 (2)
C4—C11	1.543 (2)	C18—C23	1.398 (2)
C5—C6	1.449 (2)	C19—C20	1.392 (2)
C6—C7	1.512 (2)	C19—H19A	0.9500
C7—C8	1.527 (2)	C20—C21	1.391 (2)
C7—C18	1.531 (2)	C20—H20A	0.9500
C7—H7A	1.0000	C21—C22	1.386 (2)
C8—C9	1.359 (2)	C22—C23	1.396 (2)
C8—C13	1.469 (2)	C22—H22A	0.9500
C9—C12	1.505 (2)	C23—H23A	0.9500
C10—H10A	0.9800	C24—H24A	1.0000
C13—O3—C14	113.95 (12)	C9—C12—H12B	109.5
C24—O4—C21	116.16 (14)	H12A—C12—H12B	109.5
C1—N1—C9	122.48 (13)	C9—C12—H12C	109.5
C1—N1—H1N	119.2 (15)	H12A—C12—H12C	109.5
C9—N1—H1N	117.1 (15)	H12B—C12—H12C	109.5

C6—C1—N1	120.11 (14)	O2—C13—O3	121.40 (14)
C6—C1—C2	123.32 (14)	O2—C13—C8	122.38 (14)
N1—C1—C2	116.55 (13)	O3—C13—C8	116.23 (13)
C1—C2—C3	110.33 (12)	O3—C14—C15	108.70 (14)
C1—C2—H2A	109.6	O3—C14—H14A	109.9
C3—C2—H2A	109.6	C15—C14—H14A	109.9
C1—C2—H2B	109.6	O3—C14—H14B	109.9
C3—C2—H2B	109.6	C15—C14—H14B	109.9
H2A—C2—H2B	108.1	H14A—C14—H14B	108.3
C2—C3—C4	112.76 (13)	C16—C15—C14	112.43 (19)
C2—C3—H3A	109.0	C16—C15—C17	111.82 (17)
C4—C3—H3A	109.0	C14—C15—C17	107.61 (16)
C2—C3—H3B	109.0	C16—C15—H15A	108.3
C4—C3—H3B	109.0	C14—C15—H15A	108.3
H3A—C3—H3B	107.8	C17—C15—H15A	108.3
C5—C4—C10	109.37 (13)	C15—C16—H16A	109.5
C5—C4—C3	110.02 (13)	C15—C16—H16B	109.5
C10—C4—C3	109.49 (14)	H16A—C16—H16B	109.5
C5—C4—C11	106.68 (13)	C15—C16—H16C	109.5
C10—C4—C11	109.99 (15)	H16A—C16—H16C	109.5
C3—C4—C11	111.25 (13)	H16B—C16—H16C	109.5
O1—C5—C6	121.47 (14)	C15—C17—H17A	109.5
O1—C5—C4	119.58 (14)	C15—C17—H17B	109.5
C6—C5—C4	118.88 (13)	H17A—C17—H17B	109.5
C1—C6—C5	121.21 (14)	C15—C17—H17C	109.5
C1—C6—C7	120.13 (14)	H17A—C17—H17C	109.5
C5—C6—C7	118.37 (13)	H17B—C17—H17C	109.5
C6—C7—C8	110.30 (12)	C19—C18—C23	118.43 (15)
C6—C7—C18	109.76 (12)	C19—C18—C7	119.69 (13)
C8—C7—C18	111.67 (12)	C23—C18—C7	121.86 (13)
C6—C7—H7A	108.3	C18—C19—C20	121.71 (15)
C8—C7—H7A	108.3	C18—C19—H19A	119.1
C18—C7—H7A	108.3	C20—C19—H19A	119.1
C9—C8—C13	126.22 (14)	C21—C20—C19	118.47 (15)
C9—C8—C7	120.53 (13)	C21—C20—H20A	120.8
C13—C8—C7	113.25 (12)	C19—C20—H20A	120.8
C8—C9—N1	119.20 (14)	C22—C21—C20	121.41 (15)
C8—C9—C12	128.48 (14)	C22—C21—O4	116.50 (14)
N1—C9—C12	112.32 (13)	C20—C21—O4	122.09 (15)
C4—C10—H10A	109.5	C21—C22—C23	118.99 (15)
C4—C10—H10B	109.5	C21—C22—H22A	120.5
H10A—C10—H10B	109.5	C23—C22—H22A	120.5
C4—C10—H10C	109.5	C22—C23—C18	120.93 (15)
H10A—C10—H10C	109.5	C22—C23—H23A	119.5
H10B—C10—H10C	109.5	C18—C23—H23A	119.5
C4—C11—H11A	109.5	F1—C24—F2	106.55 (17)
C4—C11—H11B	109.5	F1—C24—O4	107.35 (17)
H11A—C11—H11B	109.5	F2—C24—O4	110.76 (17)

C4—C11—H11C	109.5	F1—C24—H24A	110.7
H11A—C11—H11C	109.5	F2—C24—H24A	110.7
H11B—C11—H11C	109.5	O4—C24—H24A	110.7
C9—C12—H12A	109.5		

C9—N1—C1—C6	13.6 (2)	C13—C8—C9—C12	−7.0 (3)
C9—N1—C1—C2	−168.22 (14)	C7—C8—C9—C12	173.21 (15)
C6—C1—C2—C3	−25.9 (2)	C1—N1—C9—C8	−13.9 (2)
N1—C1—C2—C3	155.98 (14)	C1—N1—C9—C12	165.30 (14)
C1—C2—C3—C4	50.56 (18)	C14—O3—C13—O2	−1.8 (2)
C2—C3—C4—C5	−53.48 (18)	C14—O3—C13—C8	178.30 (14)
C2—C3—C4—C10	−173.70 (14)	C9—C8—C13—O2	−178.39 (17)
C2—C3—C4—C11	64.52 (17)	C7—C8—C13—O2	1.4 (2)
C10—C4—C5—O1	−31.4 (2)	C9—C8—C13—O3	1.5 (2)
C3—C4—C5—O1	−151.72 (15)	C7—C8—C13—O3	−178.68 (13)
C11—C4—C5—O1	87.49 (18)	C13—O3—C14—C15	−174.28 (15)
C10—C4—C5—C6	151.64 (15)	O3—C14—C15—C16	−64.8 (2)
C3—C4—C5—C6	31.3 (2)	O3—C14—C15—C17	171.65 (16)
C11—C4—C5—C6	−89.44 (17)	C6—C7—C18—C19	−48.25 (19)
N1—C1—C6—C5	−177.73 (14)	C8—C7—C18—C19	74.40 (18)
C2—C1—C6—C5	4.2 (2)	C6—C7—C18—C23	130.33 (15)
N1—C1—C6—C7	8.5 (2)	C8—C7—C18—C23	−107.02 (16)
C2—C1—C6—C7	−169.55 (14)	C23—C18—C19—C20	−1.0 (2)
O1—C5—C6—C1	176.01 (15)	C7—C18—C19—C20	177.62 (15)
C4—C5—C6—C1	−7.1 (2)	C18—C19—C20—C21	−1.3 (3)
O1—C5—C6—C7	−10.1 (2)	C19—C20—C21—C22	2.8 (3)
C4—C5—C6—C7	166.76 (14)	C19—C20—C21—O4	−176.98 (16)
C1—C6—C7—C8	−26.47 (19)	C24—O4—C21—C22	−142.79 (17)
C5—C6—C7—C8	159.58 (13)	C24—O4—C21—C20	37.0 (2)
C1—C6—C7—C18	96.98 (16)	C20—C21—C22—C23	−2.1 (3)
C5—C6—C7—C18	−76.97 (17)	O4—C21—C22—C23	177.71 (14)
C6—C7—C8—C9	26.2 (2)	C21—C22—C23—C18	−0.2 (2)
C18—C7—C8—C9	−96.17 (17)	C19—C18—C23—C22	1.8 (2)
C6—C7—C8—C13	−153.64 (13)	C7—C18—C23—C22	−176.84 (14)
C18—C7—C8—C13	84.02 (15)	C21—O4—C24—F1	151.23 (16)
C13—C8—C9—N1	172.06 (15)	C21—O4—C24—F2	−92.82 (19)
C7—C8—C9—N1	−7.7 (2)		

Hydrogen-bond geometry (Å, º)

*Cg*3 is the centroid the benzene ring of the 4-(4-difluoromethoxyphenyl group of the title compound.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1*N*···O1^{i}	0.87 (2)	1.98 (2)	2.8426 (17)	173 (2)
C12—H12*A*···O3	0.98	2.40	2.817 (2)	105
C19—H19*A*···O2^{i}	0.95	2.43	3.100 (2)	127
C3—H3*A*···*Cg*3^{ii}	0.99	2.84	3.7345 (18)	151

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