Acta Cryst E CRYSTALLOGRAPHIC COMMUNICATIONS

ISSN 2056-9890

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

Ezgi Pehlivanlar,[a,b] Sema Öztürk Yıldırım,[c,d] Rahime Şimşek,[a] Mehmet Akkurt,[d] Ray J. Butcher[e] and Ajaya Bhattarai[f]*

[a]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hacettepe University, 06100 Ankara, Türkiye, [b]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Karadeniz Technical University, 61000 Trabzon, Türkiye, [c]Department of Physics, Faculty of Science, Eskisehir Technical University, Yunus Emre Campus 26470 Eskisehir, Türkiye, [d]Department of Physics, Faculty of Science, Erciyes University, 38039 Kayseri, Türkiye, [e]Department of Chemistry, Howard University, Washington DC 20059, USA, and [f]Department of Chemistry, M.M.A.M.C (Tribhuvan University), Biratnagar, Nepal. *Correspondence e-mail: ajaya.bhattarai@mmamc.tu.edu.np

Received 22 May 2023
Accepted 21 June 2023

Edited by A. Briceno, Venezuelan Institute of Scientific Research, Venezuela

Keywords: crystal structure; hydrogen bonds; van der Waals forces; C—H···F interactions; Hirshfeld surface analysis.

CCDC reference: 2271384

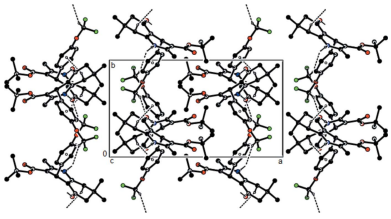
Supporting information: this article has supporting information at journals.iucr.org/e

The 1,4-dihydropyridine ring of the title compound, $C_{24}H_{29}F_2NO_4$, adopts a distorted boat conformation, while the cyclohexene ring is in an almost twist-boat conformation. In the crystal, N—H···O and C—H···O hydrogen bonds as well as C—H···π interactions connect molecules, forming layers parallel to the (100) plane. These layers are linked by van der Waals forces and C—H···F interactions, which consolidate the crystal structure. Hirshfeld surface analysis shows the major contributions to the crystal packing are from H···H (54.1%), F···H/H···F (16.9%), O···H/H···O (15.4%) and C···H/H···C (12.6%) contacts.

1. Chemical context

Inflammation is the natural and basic response of an organism to signals from tissue damage or pathogenic infections. In this way, the integrity of the organism is preserved. Chronic diseases that cause death and economic losses in the world are constantly increasing. It has been found that chronic diseases occur through inflammation-mediated mechanisms. In recent years, it has been proven that cardiovascular diseases, cancer, diabetes mellitus, chronic kidney disease, non-alcoholic fatty liver disease, autoimmune and neurodegenerative diseases are caused by inflammation. In this context, managing inflammatory mediators and inflammatory processes can be a treatment method for many chronic diseases (Furman *et al.*, 2019; Tu *et al.*, 2022).

Chronic or local inflammation first occurs with the activation of immune system cells such as cytokines, proteases, chemokines, oxygen-independent radicals, which generate signals from damaged cells or pathogens that are dangerous to the tissue. The immune system cells released in the circulatory system increase the pro-inflammatory response and reach the infected tissue area, but if this response is insufficient or excessive, the balance of the immune system is disturbed. This imbalance causes an excessive amount of distress signals and local or systemic tissue damage. This defect in the immune response causes the inflammation to change from acute to chronic, and the disease progresses and results in death. A better understanding of inflammation and its processes enables the discovery of new and effective therapeutic ways to



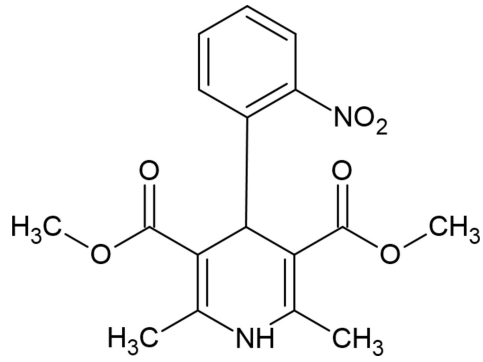
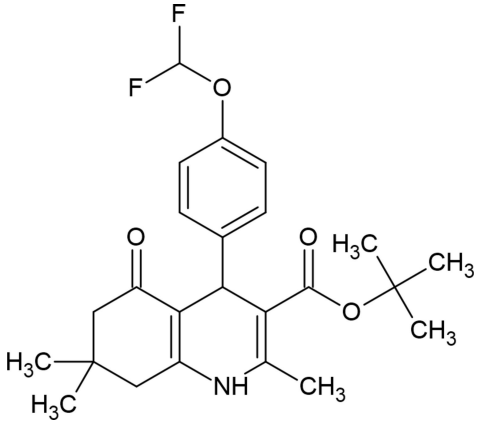


Figure 1
Structure of nifedipine.

target and regulate inflammation. Drug therapy is widely used for the treatment of inflammation. Therefore, there is a need for new molecules that are more active and have minimal side effects (Tu *et al.*, 2022). The 1,4-DHP ring, which is a partially saturated derivative of the pyridine ring, is involved in the structure of many bioactive compounds. Nifedipine, which has a 1,4-DHP structure, was introduced as an antihypertensive treatment about 50 years ago (Fig. 1). The therapeutic success of nifedipine has led to the preparation of analogue derivatives. In this ongoing process, various compounds such as amlodipine and benidipine, which have a 1,4-DHP structure, are used as antihypertensives. Studies have shown that the 1,4-DHP ring has various activities such as neuroprotective, antiplatelet, anti-ischemic, anti-Alzheimer's, antituberculer, antiulcer and anticancer (Khot *et al.*, 2021; Abdelwahab *et al.*, 2022).

The hexahydroquinoline ring system is obtained by condensing 1,4-DHP with cyclohexane. This ring system also has a variety of pharmacological activities such as calcium channel antagonist, anticancer, antimicrobial, anti-Alzheimer's. In current studies, 1,4-DHP derivatives and condensed analogues were found to be effective inflammation mediators of chronic inflammation in addition to their various biological activities.



In this study, the title compound, *tert*-butyl 4-[4-(difluoromethoxy)phenyl]-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate was obtained by using modified Hantzsch one-pot synthesis (Ghosh *et al.*, 2013). The reaction of 4-difluoromethoxybenzaldehyde with 5,5-dimethylcyclohexane-1,3-dione and *tert*-butyl acetoacetate gives the target compound in methanol in the presence of ammonium acetate as nitrogen source (Çetin *et al.*, 2022). The structure of the compound was elucidated by IR, ^{1}H-NMR, ^{13}C-NMR and HRMS analysis. X-ray analysis was undertaken to determine the crystal structure. Biological activity tests will be conducted in independent studies to determine the inhibition potential of inflammation mediators.

2. Structural commentary

As seen in Fig. 2, the 1,4-dihydropyridine ring (N1/C1/C6–C9) of the title compound adopts a distorted boat conformation [puckering parameters (Cremer & Pople, 1975) are Q_T = 0.2940 (18) Å, θ = 72.1 (4)° and φ = 182.9 (4)°], while the cyclohexene ring (C1–C6) has an almost twist-boat conformation [puckering parameters are Q_T = 0.4617 (19) Å, θ = 124.5 (2)° and φ = 313.8 (3)°]. The 4-[4-(difluoromethoxy]phenyl ring (C18–C23) makes a dihedral angle of 89.88 (7)° with the mean plane of the quinoline ring system [N1/C1–C9; maximum deviation = 0.358 (2) Å for C4]. The geometrical parameters of the title compound are in agreement with those reported for similar compounds in the *Database survey* section.

3. Supramolecular features and Hirshfeld surface analysis

The molecules in the crystal are connected by N—H···O and C—H···O hydrogen bonds, as well as C—H···π interactions, resulting in the formation of layers parallel to the (100) plane (see Table 1; Figs. 3 and 4). These layers are linked by van der

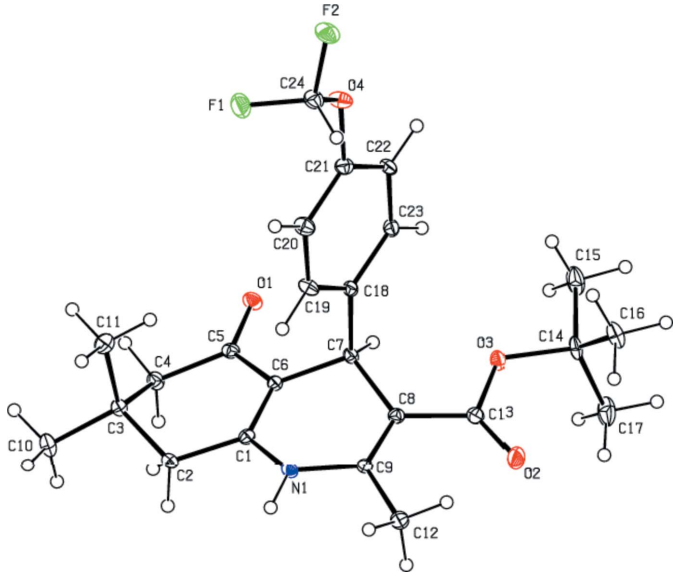


Figure 2
View of the title molecule. Displacement ellipsoids are drawn at the 30% probability level.

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

*Cg*3 is the centroid of the C18–C23 ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1*N*···O1^{i}	0.91 (2)	1.96 (2)	2.866 (2)	176.6 (18)
C12—H12*A*···O2	0.98	2.25	2.800 (2)	114
C16—H16*A*···O2	0.98	2.36	2.938 (2)	117
C17—H17*C*···O2	0.98	2.37	2.958 (3)	118
C20—H20*A*···F1	0.95	2.46	2.989 (2)	115
C24—H24*A*···O1^{ii}	1.00	2.35	3.230 (2)	147
C2—H2*A*···*Cg*3^{iii}	0.99	2.74	3.6959 (19)	162

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

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

H11*C*···H10*A*	2.49	$2-x, -\frac{1}{2}+y, \frac{1}{2}-z$
F2···H19*A*	2.51	$x, \frac{1}{2}-y, \frac{1}{2}+z$
O1···H24*A*	2.35	$x, 1+y, z$
O1···H1*N*	1.96	$x, \frac{1}{2}-y, -\frac{1}{2}+z$
H12*A*···O2	2.61	$1-x, 1-y, -z$
H15*A*···H12*A*	2.40	$1-x, \frac{1}{2}+y, \frac{1}{2}-z$
H22*A*···H16*B*	2.38	$1-x, 1-y, 1-z$

Waals forces and C—H···F interactions, which consolidate the crystal structure (Fig. 5).

The Hirshfeld surfaces and their corresponding two-dimensional fingerprint plots were calculated using the *Crystal Explorer 17.5* (Spackman *et al.*, 2021) software package. The d_{norm} surfaces are mapped over a fixed colour scale from −0.5814 (red) to +1.6362 (blue) a.u. Red spots on the surface correspond to N···H/H···N and O···H/H···O interactions (Tables 1 and 2; Fig. 6*a*,*b*).

Fingerprint plots of the most important non-covalent interactions for the title compound are shown in Fig. 7. The major contributions to the crystal packing are from H···H (54.1%), F···H/H···F (16.9%), O···H/H···O (15.4%) and

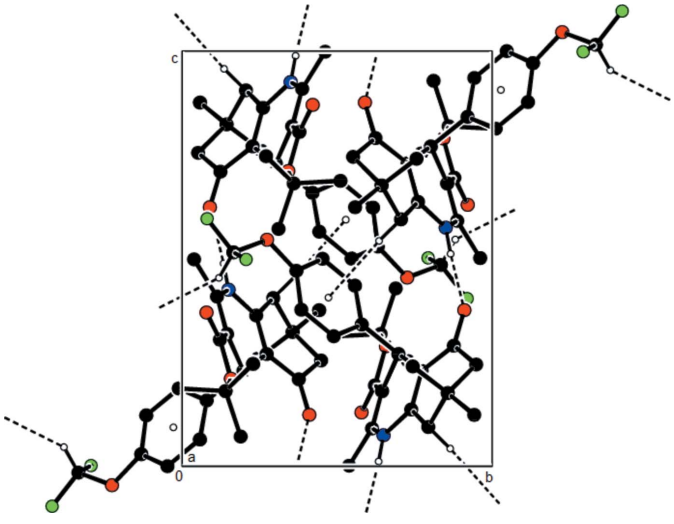


Figure 3
A view of the molecular packing of the title compound along the *a* axis by the N—H···O, C—H···O hydrogen bonds and C—H···π interactions (dashed lines).

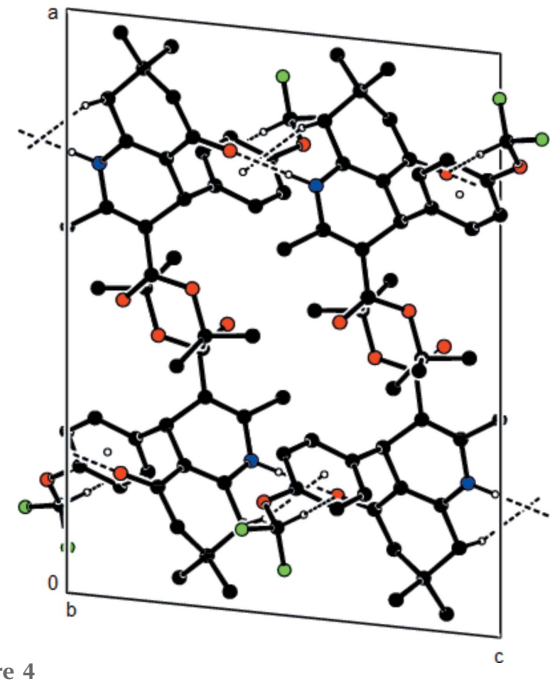


Figure 4
View of the molecular packing along [010]. Hydrogen bonds are shown as dashed lines.

C···H/H···C (12.6) contacts. N···H/H···N (0.5%), F···N/N···F (0.3%) and F···F (0.2%) contacts, which contribute less than 1%, are not shown in Fig. 7.

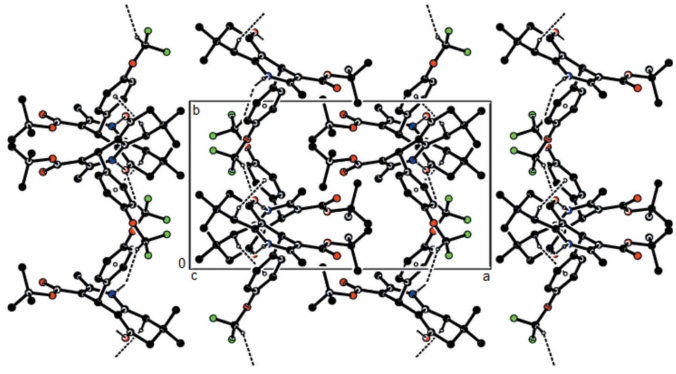


Figure 5
View of the molecular packing along [001]. Hydrogen bonds are shown as dashed lines.

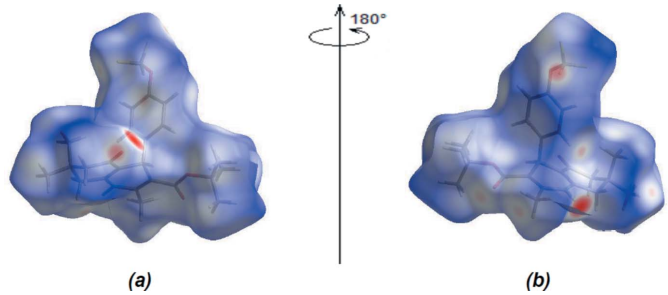


Figure 6
(*a*) Front and (*b*) back views of the three-dimensional Hirshfeld surface for the title compound.

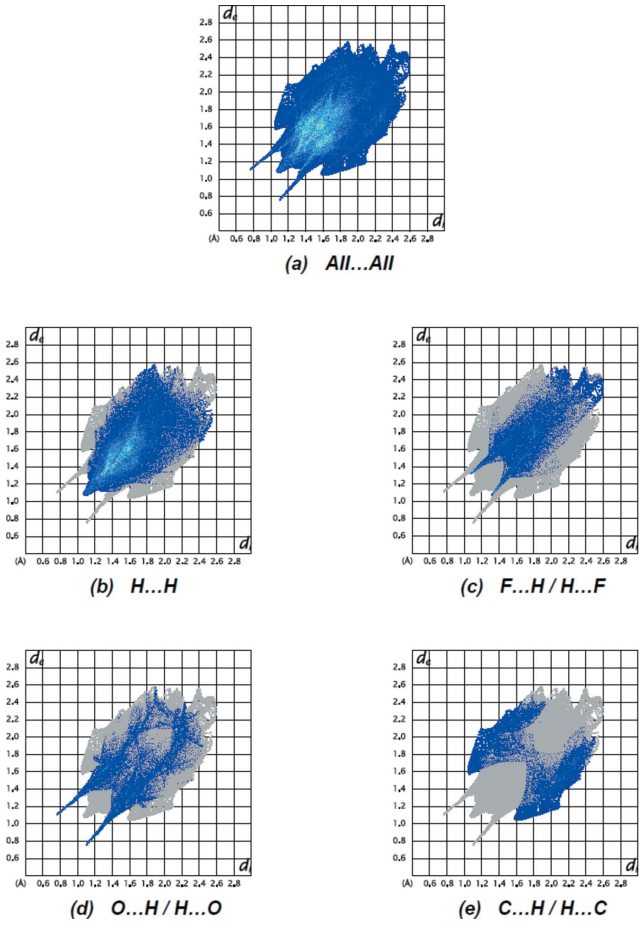


Figure 7
The two-dimensional fingerprint plots for the title compound showing (*a*) all interactions, and delineated into (*b*) H···H, (*c*) F···H/H···F, (*d*) O···H/H···O and (*e*) C···H/H···C interactions. The d_i and d_e values are the closest internal and external distances (in Å) from given points on the Hirshfeld surface.

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 WEZJUK (Yıldırım *et al.*, 2023), ECUCUE (Yıldırım *et al.*, 2022), LOQCAX (Steiger *et al.*, 2014), NEQMON (Öztürk Yıldırım *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 these compounds, molecules are linked by N—H···O hydrogen bonds. Furthermore, C—H···O hydrogen bonds in WEZJUK, ECUCUE, NEQMON, IMEJOA and PUGCIE and C—H···π interactions in WEZJUK and ECUCUE were also observed.

5. Synthesis and crystallization

The target compound was synthesized by refluxing 5,5-dimethylcyclohexane-1,3-dione (1 mmol), 4-difluoromethoxybenzaldehyde (1 mmol), *tert*-butylacetoacetate (1 mmol) and ammonium acetate (5 mmol) for 8 h in absolute methanol (10 ml). The reaction mixture was monitored by TLC, and after completion of the reaction was cooled to room temperature. The obtained precipitate was filtered and recrystallized from methanol for further purification. The synthetic route is shown in Fig. 8.

Yellow solid, m.p. 487–488 K; yield: 65.32%. IR (ν, cm^{-1}) 3211 (N—H, stretching), 3080 (C—H stretching, aromatic), 2968 (C—H stretching, aliphatic) 1697 (C═O stretching, ester), 1641 (C═O stretching, ketone). ^{1}H NMR (DMSO-d_6) δ: 0.84 (3H; *s*; 7-CH_3), 1.00 (3H; *s*; 7-CH_3), 1.31 [9H, *s*, $C(CH_3)_3$], 1.95–1.99 (2H; *d*; J = 16 Hz; quinoline H8), 2.13–2.16 (H; *d*; J = 16.1; quinoline H8), 2.25 (3H; *s*; 2-CH_3), 2.26–2.30 (H; *d*; J = 16.95 quinoline H6), 2.37–2.41 (H; *d*; J =1 6.95 quinoline H6), 4.78 (1H; *s*; quinoline H4), 6.99–7.01 (2*H*, *d*, J = 8.5 Hz Ar—H3), 7.14 (1H; *t*; J = 74.4 Hz; $OCHF_2$), 7.17–7.18 (2*H*, *d*, J = 10 Ar—H2), 8.99 (1*H*,*s*; NH). ^{13}C NMR (DMSO-

Table 3
Experimental details.

Crystal data	
Chemical formula	$C_{24}H_{29}F_2NO_4$
M_r	433.48
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	100
a, b, c (Å)	17.6062 (11), 9.7588 (7), 13.1509 (9)
β (°)	95.905 (2)
V (Å^3)	2247.5 (3)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.10
Crystal size (mm)	0.26 × 0.20 × 0.14
Data collection	
Diffractometer	Bruker D8 Quest with Photon 2 detector
Absorption correction	Multi-scan (*SADABS*; Bruker, 2018)
T_{min}, T_{max}	0.657, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	31708, 4599, 3208
R_{int}	0.111
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.625
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.046, 0.110, 1.02
No. of reflections	4599
No. of parameters	290
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.21, −0.26

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).

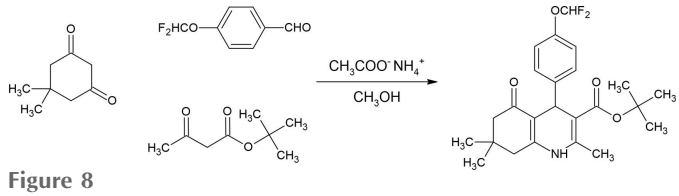


Figure 8
Synthetic scheme.

d_6) δ: 18.7 (2-CH_3), 27.0 (7-CH_3), 28.3 [$COOC(CH_3)_3$], 29.4 (C-7), 32.0 (C-8), 36.2 (C-4), 50.6 (C-6), 79.2 [$COOC(CH_3)_3$], 105.4 (C-3), 110.0 (C-4a), 114.8 (C_3'), 116.9, 118.4, 118.9 ($OCHF_2$), 129.4 (C_2'), 144.5 (C_1'), 145.3 (C-2), 149.3 (C-8a), 150.0 (C_4'), 166.7 [$COOC(CH_3)_3$], 194.6 (C-5). HRMS (ESI/Q-TOF) *m*/*z*: $[M + H]^+$ Calculated for $C_{24}H_{29}F_2NO_4$ 433.2065; found 434.2328 (M + H).

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* = 0.91 (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 1.5 U_{eq}(C).

Acknowledgements

Authors' contributions are as follows. Conceptualization, *RS* and SÖY; methodology, *RS* and EP; investigation, *RS* and SÖY; writing (original draft), EP 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*.

References

Bruker (2018). *APEX2*, *SAINT* and *SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA.

Çetin, G., Çetin, B., Çolak, B., Aşan, M., Birlik Demirel, G., Cansaran-Duman, D., Akçelik, N. & Şimşek, R. (2022). *J. Res. Pharm.* **26**, 219–230.

Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.

Elwahy, A. H. M., Eid, E. M., Abdel-Latif, S. A., Hassaneen, H. M. E. & Abdelhamid, I. A. (2022). *Polycyclic Aromat. Compd.* pp. 1–30.

Farrugia, L. J. (2012). *J. Appl. Cryst.* **45**, 849–854.

Furman, D., Campisi, J., Verdin, E., Carrera-Bastos, P., Targ, S., Franceschi, C., Ferrucci, L., Gilroy, D. W., Fasano, A., Miller, G. W., Miller, A. H., Mantovani, A., Weyand, C. M., Barzilai, N., Goronzy, J. J., Rando, T. A., Effros, R. B., Lucia, A., Kleinstreuer, N. & Slavich, G. M. (2019). *Nat. Med.* **25**, 1822–1832.

Ghosh, S., Saikh, F., Das, J. & Pramanik, A. K. (2013). *Tetrahedron Lett.* **54**, 58–62.

Groom, C. R., Bruno, I. J., Lightfoot, M. P. & Ward, S. C. (2016). *Acta Cryst.* B**72**, 171–179.

Gündüz, M. G., Butcher, R. J., Öztürk Yildirim, S., El-Khouly, A., Şafak, C. & Şimşek, R. (2012). *Acta Cryst.* E**68**, o3404–o3405.

Khot, S., Auti, P. B. & Khedkar, S. A. (2021). *Mini Rev. Med. Chem.* **21**, 135–149.

Linden, A., Gündüz, M. G., Şimşek, R. & Şafak, C. (2006). *Acta Cryst.* C**62**, o227–o230.

Linden, A., Şafak, C., Şimşek, R. & Gündüz, M. G. (2011). *Acta Cryst.* C**67**, o80–o84.

Linden, A., Şimşek, R., Gündüz, M. & Şafak, C. (2005). *Acta Cryst.* C**61**, o731–o734.

Mookiah, P., Rajesh, K., Narasimhamurthy, T., Vijayakumar, V. & Srinivasan, N. (2009). *Acta Cryst.* E**65**, o2664.

Öztürk Yildirim, S., Butcher, R. J., Gündüz, M. G., El-Khouly, A., Şimşek, R. & Şafak, C. (2013). *Acta Cryst.* E**69**, o40–o41.

Sheldrick, G. M. (2015*a*). *Acta Cryst.* A**71**, 3–8.

Sheldrick, G. M. (2015*b*). *Acta Cryst.* C**71**, 3–8.

Spackman, P. R., Turner, M. J., McKinnon, J. J., Wolff, S. K., Grimwood, D. J., Jayatilaka, D. & Spackman, M. A. (2021). *J. Appl. Cryst.* **54**, 1006–1011.

Spek, A. L. (2020). *Acta Cryst.* E**76**, 1–11.

Steiger, S. A., Monacelli, A. J., Li, C., Hunting, J. L. & Natale, N. R. (2014). *Acta Cryst.* C**70**, 790–795.

Tu, Z., Zhong, Y., Hu, H., Shao, D., Haag, R., Schirner, M., Lee, J., Sullenger, B. & Leong, K. W. (2022). *Nat. Rev. Mater.* 557–574.

Yıldırım, S. Ö., Akkurt, M., Çetin, G., Şimşek, R., Butcher, R. J. & Bhattarai, A. (2022). *Acta Cryst.* E**78**, 798–803.

Yıldırım, S. Ö., Akkurt, M., Çetin, G., Şimşek, R., Butcher, R. J. & Bhattarai, A. (2023). *Acta Cryst.* E**79**, 187–191.

supporting information

Acta Cryst. (2023). E**79**, 664-668 [https://doi.org/10.1107/S2056989023005455]

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

Ezgi Pehlivanlar, Sema Öztürk Yıldırım, Rahime Şimşek, Mehmet Akkurt, Ray J. Butcher and Ajaya Bhattarai

Computing details

Data collection: *APEX2* (Bruker, 2018); cell refinement: *SAINT* (Bruker, 2018); data reduction: *SAINT* (Bruker, 2018); program(s) used to solve structure: *SHELXT* (Sheldrick, 2015a); program(s) used to refine structure: *SHELXL* (Sheldrick, 2015b); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 2012); software used to prepare material for publication: *PLATON* (Spek, 2020).

tert-Butyl 4-[4-(difluoromethoxy)phenyl]-2,7,7-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
Monoclinic, $P2_1/c$
a = 17.6062 (11) Å
b = 9.7588 (7) Å
c = 13.1509 (9) Å
β = 95.905 (2)°
V = 2247.5 (3) Å^3
Z = 4
$F(000)$ = 920
D_x = 1.281 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 4059 reflections
θ = 2.3–30.3°
μ = 0.10 mm^{-1}
T = 100 K
Prism, colorless
0.26 × 0.20 × 0.14 mm

Data collection

Bruker D8 Quest with Photon 2 detector diffractometer
φ and ω scans
Absorption correction: multi-scan (SADABS; Bruker, 2018)
T_{min} = 0.657, T_{max} = 0.746
31708 measured reflections
4599 independent reflections
3208 reflections with $I > 2\sigma(I)$
R_{int} = 0.111
θ_{max} = 26.4°, θ_{min} = 2.4°
h = −22→22
k = −12→12
l = −16→16

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.046
$wR(F^2)$ = 0.110
S = 1.02
4599 reflections
290 parameters
0 restraints
Primary atom site location: dual
Secondary atom site location: difference Fourier map
Hydrogen site location: mixed
H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0445P)^2 + 0.5785P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$

$\Delta\rho_{max} = 0.21$ e Å^{-3}
$\Delta\rho_{min} = -0.26$ 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 (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
F1	0.92250 (6)	0.20646 (12)	0.49817 (9)	0.0351 (3)
F2	0.86051 (6)	0.08089 (11)	0.59614 (9)	0.0311 (3)
O1	0.78594 (7)	0.91033 (13)	0.37607 (9)	0.0202 (3)
O2	0.51155 (7)	0.57880 (16)	0.12973 (10)	0.0338 (4)
O3	0.54282 (7)	0.65743 (13)	0.28906 (9)	0.0189 (3)
O4	0.80976 (7)	0.27398 (13)	0.54548 (9)	0.0242 (3)
N1	0.74130 (8)	0.64973 (15)	0.07479 (12)	0.0155 (3)
H1N	0.7556 (11)	0.634 (2)	0.0116 (16)	0.027 (6)*
C1	0.78375 (9)	0.73899 (17)	0.13677 (13)	0.0141 (4)
C2	0.85366 (9)	0.79398 (18)	0.09469 (13)	0.0160 (4)
H2A	0.838042	0.864711	0.042740	0.019*
H2B	0.878600	0.718755	0.060078	0.019*
C3	0.91163 (10)	0.85665 (18)	0.17650 (13)	0.0164 (4)
C4	0.86773 (10)	0.94844 (18)	0.24516 (14)	0.0184 (4)
H4A	0.903915	0.984065	0.301593	0.022*
H4B	0.846852	1.027890	0.204631	0.022*
C5	0.80277 (10)	0.87635 (17)	0.29047 (13)	0.0155 (4)
C6	0.76121 (9)	0.77274 (17)	0.22958 (13)	0.0140 (4)
C7	0.69507 (9)	0.69774 (18)	0.27054 (13)	0.0146 (4)
H7A	0.666791	0.764154	0.310637	0.018*
C8	0.64044 (10)	0.64486 (17)	0.18117 (13)	0.0148 (4)
C9	0.66713 (9)	0.61265 (18)	0.09115 (13)	0.0153 (4)
C10	0.96912 (11)	0.9421 (2)	0.12400 (15)	0.0245 (4)
H10A	1.008339	0.977719	0.175509	0.037*
H10B	0.942644	1.018719	0.087535	0.037*
H10C	0.993191	0.884569	0.075323	0.037*
C11	0.95397 (11)	0.7439 (2)	0.24056 (15)	0.0257 (5)
H11A	0.990465	0.785721	0.292795	0.039*
H11B	0.981403	0.685259	0.196126	0.039*
H11C	0.917130	0.688629	0.273739	0.039*
C12	0.62714 (10)	0.5386 (2)	0.00161 (14)	0.0209 (4)
H12A	0.588198	0.477760	0.025035	0.031*
H12B	0.664249	0.484180	−0.031788	0.031*
H12C	0.602762	0.605142	−0.047102	0.031*
C13	0.55921 (10)	0.62201 (18)	0.19487 (14)	0.0174 (4)
C14	0.46412 (10)	0.64012 (19)	0.31875 (15)	0.0212 (4)

C15	0.47276 (12)	0.6890 (2)	0.42836 (16)	0.0338 (5)
H15A	0.487156	0.786090	0.430522	0.051*
H15B	0.512507	0.635304	0.467906	0.051*
H15C	0.424214	0.677487	0.457741	0.051*
C16	0.44228 (11)	0.4893 (2)	0.31253 (16)	0.0272 (5)
H16A	0.438276	0.459295	0.241063	0.041*
H16B	0.393032	0.476330	0.339800	0.041*
H16C	0.481471	0.435070	0.352732	0.041*
C17	0.40767 (11)	0.7291 (2)	0.25328 (19)	0.0358 (6)
H17A	0.424720	0.824723	0.257522	0.054*
H17B	0.357177	0.721817	0.278004	0.054*
H17C	0.404679	0.698213	0.182077	0.054*
C18	0.72353 (10)	0.57950 (18)	0.34146 (13)	0.0151 (4)
C19	0.77883 (10)	0.48904 (19)	0.31318 (14)	0.0207 (4)
H19A	0.796943	0.499218	0.248000	0.025*
C20	0.80838 (11)	0.38451 (19)	0.37706 (14)	0.0218 (4)
H20A	0.846835	0.325229	0.356664	0.026*
C21	0.78073 (10)	0.36846 (18)	0.47084 (14)	0.0185 (4)
C22	0.72373 (10)	0.45291 (19)	0.49978 (14)	0.0192 (4)
H22A	0.703948	0.439405	0.563564	0.023*
C23	0.69559 (10)	0.55749 (19)	0.43512 (13)	0.0179 (4)
H23A	0.656394	0.615290	0.455307	0.021*
C24	0.85104 (11)	0.16566 (19)	0.51508 (15)	0.0223 (4)
H24A	0.824329	0.118997	0.453797	0.027*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
F1	0.0253 (6)	0.0380 (7)	0.0430 (8)	−0.0014 (5)	0.0079 (5)	0.0154 (6)
F2	0.0389 (7)	0.0244 (6)	0.0305 (7)	0.0009 (5)	0.0062 (5)	0.0127 (5)
O1	0.0250 (7)	0.0224 (7)	0.0140 (7)	−0.0035 (6)	0.0055 (5)	−0.0038 (5)
O2	0.0210 (7)	0.0590 (10)	0.0214 (8)	−0.0140 (7)	0.0026 (6)	−0.0078 (7)
O3	0.0145 (6)	0.0228 (7)	0.0204 (7)	−0.0024 (5)	0.0062 (5)	−0.0030 (6)
O4	0.0342 (8)	0.0217 (7)	0.0169 (7)	0.0053 (6)	0.0039 (6)	0.0042 (6)
N1	0.0168 (8)	0.0190 (8)	0.0113 (8)	−0.0013 (6)	0.0045 (6)	−0.0025 (6)
C1	0.0139 (9)	0.0133 (9)	0.0149 (9)	0.0020 (7)	0.0001 (7)	0.0013 (7)
C2	0.0175 (9)	0.0158 (9)	0.0156 (9)	0.0005 (7)	0.0051 (7)	0.0010 (7)
C3	0.0165 (9)	0.0166 (9)	0.0166 (9)	−0.0011 (7)	0.0035 (7)	−0.0002 (8)
C4	0.0200 (10)	0.0175 (9)	0.0179 (10)	−0.0043 (8)	0.0036 (8)	−0.0018 (8)
C5	0.0173 (9)	0.0146 (9)	0.0147 (9)	0.0031 (7)	0.0014 (7)	0.0022 (7)
C6	0.0129 (9)	0.0156 (9)	0.0136 (9)	0.0011 (7)	0.0017 (7)	0.0017 (7)
C7	0.0150 (9)	0.0158 (9)	0.0135 (9)	−0.0009 (7)	0.0040 (7)	−0.0001 (7)
C8	0.0164 (9)	0.0138 (9)	0.0141 (9)	−0.0002 (7)	0.0008 (7)	0.0015 (7)
C9	0.0150 (9)	0.0150 (9)	0.0158 (9)	−0.0006 (7)	0.0010 (7)	0.0025 (7)
C10	0.0211 (10)	0.0255 (11)	0.0287 (11)	−0.0057 (8)	0.0107 (8)	−0.0022 (9)
C11	0.0203 (10)	0.0299 (11)	0.0265 (11)	0.0033 (9)	−0.0001 (8)	0.0027 (9)
C12	0.0220 (10)	0.0240 (10)	0.0167 (10)	−0.0049 (8)	0.0018 (8)	−0.0031 (8)
C13	0.0185 (10)	0.0183 (10)	0.0156 (9)	−0.0012 (7)	0.0024 (8)	0.0009 (8)

C14	0.0141 (9)	0.0236 (10)	0.0280 (11)	−0.0036 (8)	0.0119 (8)	−0.0044 (8)
C15	0.0263 (11)	0.0417 (13)	0.0362 (13)	−0.0094 (10)	0.0172 (10)	−0.0157 (11)
C16	0.0265 (11)	0.0233 (11)	0.0347 (12)	−0.0060 (9)	0.0169 (9)	−0.0047 (9)
C17	0.0184 (10)	0.0345 (12)	0.0560 (16)	0.0035 (9)	0.0117 (10)	0.0062 (11)
C18	0.0152 (9)	0.0173 (9)	0.0128 (9)	−0.0051 (7)	0.0016 (7)	−0.0010 (7)
C19	0.0262 (10)	0.0224 (10)	0.0146 (10)	0.0007 (8)	0.0072 (8)	0.0007 (8)
C20	0.0259 (10)	0.0212 (10)	0.0191 (10)	0.0033 (8)	0.0062 (8)	−0.0008 (8)
C21	0.0223 (10)	0.0163 (10)	0.0165 (9)	−0.0032 (8)	−0.0003 (8)	0.0010 (8)
C22	0.0204 (10)	0.0252 (10)	0.0126 (9)	−0.0049 (8)	0.0051 (7)	0.0015 (8)
C23	0.0149 (9)	0.0230 (10)	0.0161 (9)	−0.0027 (7)	0.0035 (7)	−0.0019 (8)
C24	0.0257 (11)	0.0186 (10)	0.0228 (10)	−0.0026 (8)	0.0032 (8)	0.0046 (8)

Geometric parameters (Å, º)

F1—C24	1.360 (2)	C10—H10B	0.9800
F2—C24	1.346 (2)	C10—H10C	0.9800
O1—C5	1.238 (2)	C11—H11A	0.9800
O2—C13	1.212 (2)	C11—H11B	0.9800
O3—C13	1.346 (2)	C11—H11C	0.9800
O3—C14	1.487 (2)	C12—H12A	0.9800
O4—C24	1.366 (2)	C12—H12B	0.9800
O4—C21	1.404 (2)	C12—H12C	0.9800
N1—C1	1.363 (2)	C14—C15	1.511 (3)
N1—C9	1.393 (2)	C14—C17	1.519 (3)
N1—H1N	0.91 (2)	C14—C16	1.521 (3)
C1—C6	1.362 (2)	C15—H15A	0.9800
C1—C2	1.500 (2)	C15—H15B	0.9800
C2—C3	1.532 (2)	C15—H15C	0.9800
C2—H2A	0.9900	C16—H16A	0.9800
C2—H2B	0.9900	C16—H16B	0.9800
C3—C10	1.530 (2)	C16—H16C	0.9800
C3—C11	1.532 (2)	C17—H17A	0.9800
C3—C4	1.536 (2)	C17—H17B	0.9800
C4—C5	1.516 (2)	C17—H17C	0.9800
C4—H4A	0.9900	C18—C23	1.389 (2)
C4—H4B	0.9900	C18—C19	1.393 (2)
C5—C6	1.442 (2)	C19—C20	1.388 (3)
C6—C7	1.520 (2)	C19—H19A	0.9500
C7—C8	1.530 (2)	C20—C21	1.381 (3)
C7—C18	1.535 (2)	C20—H20A	0.9500
C7—H7A	1.0000	C21—C22	1.382 (3)
C8—C9	1.355 (2)	C22—C23	1.387 (3)
C8—C13	1.477 (2)	C22—H22A	0.9500
C9—C12	1.495 (2)	C23—H23A	0.9500
C10—H10A	0.9800	C24—H24A	1.0000
C13—O3—C14	120.42 (13)	C9—C12—H12B	109.5
C24—O4—C21	118.04 (14)	H12A—C12—H12B	109.5

C1—N1—C9	122.61 (15)	C9—C12—H12C	109.5
C1—N1—H1N	117.9 (13)	H12A—C12—H12C	109.5
C9—N1—H1N	116.9 (12)	H12B—C12—H12C	109.5
C6—C1—N1	119.88 (16)	O2—C13—O3	122.80 (16)
C6—C1—C2	124.75 (16)	O2—C13—C8	125.12 (17)
N1—C1—C2	115.38 (15)	O3—C13—C8	112.06 (15)
C1—C2—C3	113.36 (14)	O3—C14—C15	102.09 (14)
C1—C2—H2A	108.9	O3—C14—C17	111.05 (15)
C3—C2—H2A	108.9	C15—C14—C17	110.84 (17)
C1—C2—H2B	108.9	O3—C14—C16	109.44 (14)
C3—C2—H2B	108.9	C15—C14—C16	110.92 (17)
H2A—C2—H2B	107.7	C17—C14—C16	112.07 (16)
C10—C3—C11	109.42 (15)	C14—C15—H15A	109.5
C10—C3—C2	108.94 (14)	C14—C15—H15B	109.5
C11—C3—C2	110.54 (15)	H15A—C15—H15B	109.5
C10—C3—C4	110.11 (15)	C14—C15—H15C	109.5
C11—C3—C4	109.96 (15)	H15A—C15—H15C	109.5
C2—C3—C4	107.85 (14)	H15B—C15—H15C	109.5
C5—C4—C3	113.96 (14)	C14—C16—H16A	109.5
C5—C4—H4A	108.8	C14—C16—H16B	109.5
C3—C4—H4A	108.8	H16A—C16—H16B	109.5
C5—C4—H4B	108.8	C14—C16—H16C	109.5
C3—C4—H4B	108.8	H16A—C16—H16C	109.5
H4A—C4—H4B	107.7	H16B—C16—H16C	109.5
O1—C5—C6	122.52 (16)	C14—C17—H17A	109.5
O1—C5—C4	119.59 (15)	C14—C17—H17B	109.5
C6—C5—C4	117.87 (15)	H17A—C17—H17B	109.5
C1—C6—C5	119.29 (15)	C14—C17—H17C	109.5
C1—C6—C7	120.37 (15)	H17A—C17—H17C	109.5
C5—C6—C7	120.29 (15)	H17B—C17—H17C	109.5
C6—C7—C8	109.52 (14)	C23—C18—C19	117.37 (16)
C6—C7—C18	111.30 (13)	C23—C18—C7	122.12 (16)
C8—C7—C18	110.69 (14)	C19—C18—C7	120.51 (16)
C6—C7—H7A	108.4	C20—C19—C18	122.20 (17)
C8—C7—H7A	108.4	C20—C19—H19A	118.9
C18—C7—H7A	108.4	C18—C19—H19A	118.9
C9—C8—C13	119.93 (16)	C21—C20—C19	118.65 (17)
C9—C8—C7	120.16 (15)	C21—C20—H20A	120.7
C13—C8—C7	119.83 (15)	C19—C20—H20A	120.7
C8—C9—N1	119.31 (16)	C20—C21—C22	120.74 (17)
C8—C9—C12	128.53 (16)	C20—C21—O4	124.23 (16)
N1—C9—C12	112.15 (15)	C22—C21—O4	114.93 (16)
C3—C10—H10A	109.5	C21—C22—C23	119.59 (17)
C3—C10—H10B	109.5	C21—C22—H22A	120.2
H10A—C10—H10B	109.5	C23—C22—H22A	120.2
C3—C10—H10C	109.5	C22—C23—C18	121.37 (17)
H10A—C10—H10C	109.5	C22—C23—H23A	119.3
H10B—C10—H10C	109.5	C18—C23—H23A	119.3

C3—C11—H11A	109.5	F2—C24—F1	105.56 (14)
C3—C11—H11B	109.5	F2—C24—O4	105.67 (15)
H11A—C11—H11B	109.5	F1—C24—O4	110.52 (15)
C3—C11—H11C	109.5	F2—C24—H24A	111.6
H11A—C11—H11C	109.5	F1—C24—H24A	111.6
H11B—C11—H11C	109.5	O4—C24—H24A	111.6
C9—C12—H12A	109.5		

C9—N1—C1—C6	14.1 (2)	C7—C8—C9—C12	168.75 (17)
C9—N1—C1—C2	−165.54 (15)	C1—N1—C9—C8	−12.6 (3)
C6—C1—C2—C3	18.1 (2)	C1—N1—C9—C12	167.69 (16)
N1—C1—C2—C3	−162.30 (14)	C14—O3—C13—O2	2.1 (3)
C1—C2—C3—C10	−165.09 (15)	C14—O3—C13—C8	−179.04 (14)
C1—C2—C3—C11	74.64 (19)	C9—C8—C13—O2	−2.2 (3)
C1—C2—C3—C4	−45.59 (19)	C7—C8—C13—O2	−178.97 (18)
C10—C3—C4—C5	172.96 (15)	C9—C8—C13—O3	179.00 (16)
C11—C3—C4—C5	−66.40 (19)	C7—C8—C13—O3	2.2 (2)
C2—C3—C4—C5	54.20 (19)	C13—O3—C14—C15	178.94 (16)
C3—C4—C5—O1	147.75 (16)	C13—O3—C14—C17	−62.9 (2)
C3—C4—C5—C6	−34.2 (2)	C13—O3—C14—C16	61.4 (2)
N1—C1—C6—C5	−174.53 (15)	C6—C7—C18—C23	134.13 (17)
C2—C1—C6—C5	5.1 (3)	C8—C7—C18—C23	−103.82 (18)
N1—C1—C6—C7	8.1 (2)	C6—C7—C18—C19	−46.2 (2)
C2—C1—C6—C7	−172.29 (15)	C8—C7—C18—C19	75.88 (19)
O1—C5—C6—C1	−178.91 (16)	C23—C18—C19—C20	−3.1 (3)
C4—C5—C6—C1	3.1 (2)	C7—C18—C19—C20	177.17 (16)
O1—C5—C6—C7	−1.5 (3)	C18—C19—C20—C21	1.3 (3)
C4—C5—C6—C7	−179.50 (15)	C19—C20—C21—C22	1.3 (3)
C1—C6—C7—C8	−27.6 (2)	C19—C20—C21—O4	−174.90 (16)
C5—C6—C7—C8	155.05 (15)	C24—O4—C21—C20	−20.1 (3)
C1—C6—C7—C18	95.14 (19)	C24—O4—C21—C22	163.51 (16)
C5—C6—C7—C18	−82.24 (19)	C20—C21—C22—C23	−1.9 (3)
C6—C7—C8—C9	29.0 (2)	O4—C21—C22—C23	174.61 (15)
C18—C7—C8—C9	−94.12 (19)	C21—C22—C23—C18	0.0 (3)
C6—C7—C8—C13	−154.26 (15)	C19—C18—C23—C22	2.5 (3)
C18—C7—C8—C13	82.65 (19)	C7—C18—C23—C22	−177.84 (15)
C13—C8—C9—N1	172.33 (15)	C21—O4—C24—F2	−169.91 (14)
C7—C8—C9—N1	−10.9 (2)	C21—O4—C24—F1	76.36 (19)
C13—C8—C9—C12	−8.0 (3)		

Hydrogen-bond geometry (Å, º)

*Cg*3 is the centroid of the C18–C23 ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1*N*···O1^{i}	0.91 (2)	1.96 (2)	2.866 (2)	176.6 (18)
C12—H12*A*···O2	0.98	2.25	2.800 (2)	114
C16—H16*A*···O2	0.98	2.36	2.938 (2)	117
C17—H17*C*···O2	0.98	2.37	2.958 (3)	118

C20—H20*A*···F1	0.95	2.46	2.989 (2)	115
C24—H24*A*···O1^{ii}	1.00	2.35	3.230 (2)	147
C2—H2*A*···*Cg*3^{iii}	0.99	2.74	3.6959 (19)	162

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