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# Crystal structure and Hirshfeld surface analysis of 1-[6-bromo-2-(4-fluorophenyl)-1,2,3,4-tetrahydroquinolin-4-yl]pyrrolidin-2-one

**Anastasia A. Pronina,[a] Alexandra G. Podrezova,[a] Mikhail S. Grigoriev,[b] Khudayar I. Hasanov,[c,d] Nurlana D. Sadikhova,[e] Mehmet Akkurt[f]* and Ajaya Bhattarai[g]***

[a]RUDN University, 6 Miklukho-Maklaya St., Moscow, 117198, Russian Federation, [b]Frumkin Institute of Physical Chemistry and Electrochemistry, Russian Academy of Sciences, Leninskiy prospect 31-4, Moscow 119071, Russian Federation, [c]Western Caspian University, Istiqlaliyyat Street 31, AZ1001, Baku, Azerbaijan, [d]Azerbaijan Medical University, Scientific Research Centre (SRC), A. Kasumzade St. 14. AZ 1022, Baku, Azerbaijan, [e]Department of Chemistry, Baku State University, Z. Xalilov Str, Az 1148 Baku, Azerbaijan, [f]Department of Physics, Faculty of Sciences, Erciyes University, 38039 Kayseri, Türkiye, and [g]Department of Chemistry, M.M.A.M.C (Tribhuvan University) Biratnagar, Nepal. *Correspondence e-mail: akkurt@erciyes.edu.tr, ajaya.bhattarai@mmamc.tu.edu.np

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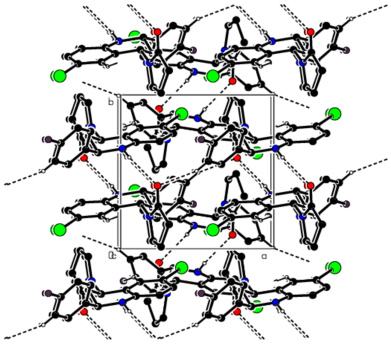
In the title compound, $C_{19}H_{18}BrFN_2O$, the pyrrolidine ring adopts an envelope conformation. In the crystal, molecules are linked by intermolecular N—H···O, C—H···O, C—H···F and C—H···Br hydrogen bonds, forming a three-dimensional network. In addition, C—H···$\pi$ interactions connect molecules into ribbons along the *b*-axis direction, consolidating the molecular packing. The intermolecular interactions in the crystal structure were quantified and analysed using Hirshfeld surface analysis.

## 1. Chemical context

As a result of their presence in many plants, tetrahydroquinoline derivatives have long been of great interest to organic chemists and biochemists. The tetrahydroquinoline moiety can be found in many alkaloids that possess antimalarial and antimicrobial properties (Ghashghaei *et al.*, 2018; Khalilov *et al.*, 2021; Safavora *et al.*, 2019). Various studies show that tetrahydroquinolines have a wide spectrum of biological activity, and some are already being used as pharmaceutical agents (Sridharan *et al.*, 2011; Akbari Afkhami *et al.*, 2017; Abdelhamid *et al.*, 2011). Modification of tetrahydroquinoline derivatives is effective in the search, design, and development of new drugs. However, thousands of compounds are required to find a structure that exhibits biological activity, which is why an efficient synthetic methodology for obtaining tetrahydroquinoline derivatives is necessary (Astudillo *et al.*, 2009; Kouznetsov *et al.*, 2004, 2007). One of the most widely used approaches for the synthesis of tetrahydroquinolines is the Povarov reaction, known as the aza-Diels–Alder reaction (Palacios *et al.*, 2010; Zubkov *et al.*, 2010; Zaitsev *et al.*, 2009). Herein, we have synthesized 1-[6-bromo-2-(4-fluorophenyl)-1,2,3,4-tetrahydroquinolin-4-yl]-pyrrolidin-2-one (I) by the reaction of (*E*)-*N*-(4-bromophenyl)-1-(4-fluorophenyl)methanimine with 1-vinylpyrrolidin-2-one in the presence of the most commonly used Lewis acid, diethyl ether of boron trifluoride (Fig. 1). The mild conditions and efficiency of the cycloaddition of aromatic imines with electronically enriched alkenes make the Povarov reaction a useful tool in the synthesis of tetrahydroquinolines, optimization of the search for potential drugs, and obtaining hits. It should be mentioned that the conformation of the obtained



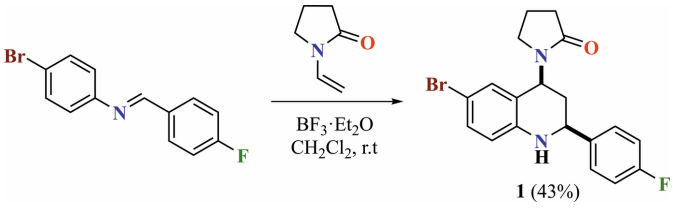
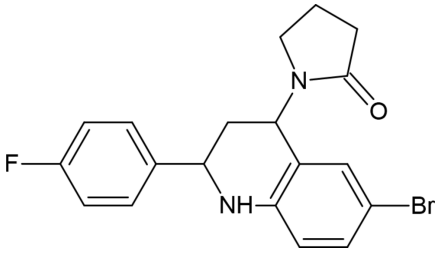



**Figure 1**
Synthesis of 1-[6-bromo-2-(4-fluorophenyl)-1,2,3,4-tetrahydroquinolin-4-yl]pyrrolidin-2-one (I).

1,2,3,4-tetrahydroquinoline cycle plays a key role in the biological activity of a potential drug. The attached halogens (–F and –Br) as well as NH or C═O groups can participate in various sorts of intermolecular interactions (Gurbanov *et al.*, 2020, 2022*a*,*b*; Kopylovich *et al.*, 2011*a*,*b*; Mahmoudi *et al.*, 2017*a*,*b*), which can improve the solubility of this compound. Thus, this communication is devoted to the elucidation of the spatial peculiarities of the partly hydrogenated quinoline fragment in the products of the Povarov reaction.




## 2. Structural commentary

In the title compound (Fig. 2), the 1,2,3,4-tetrahydropyridine ring (N1/C2–C4/C4*A*/C8*A*) of the 1,2,3,4-tetrahydroquinoline ring system (N1/C2–C4/C4*A*/C5–C8/C8*A*) adopts an envelope conformation [the puckering parameters (Cremer & Pople, 1975) are $Q_T$ = 0.509 (2) Å, $\theta$ = 46.3 (2)°, $\varphi$ = 121.4 (3)°], while the benzene ring (C4*A*/C5–C8/C8*A*) is essentially planar (r.m.s. deviation = 0.002 Å). The plane (r.m.s deviation = 0.002 Å) of the 1,2,3,4-tetrahydroquinoline ring system forms angles of 65.91 (8) and 81.17 (9)°, respectively, with the fluorobenzene ring (C21–C26) and the pyrrolidine ring (N11/C12–C15) (r.m.s deviation = 0.002 Å), which has an envelope conformation [the puckering parameters are $Q(2)$ = 0.195 (2) Å, $\varphi(2)$ = 107.4 (6)°]. The angle between the pyrrolidine and fluorobenzene rings is 71.16 (11)°. The geometric parameters in the molecule are normal and in good agreement with those in the compounds discussed in the *Database survey* section.

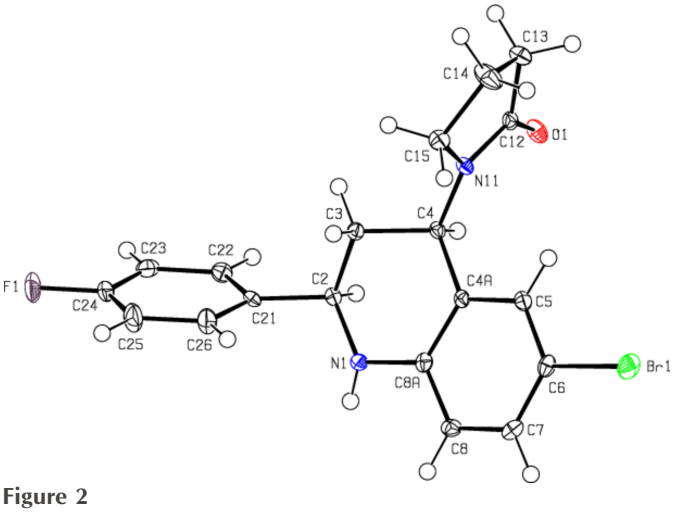



**Figure 2**
View of the title molecule. Displacement ellipsoids are drawn at the 50% probability level.

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

*Cg*3 is the centroid of the C4*A*/C5–C8/C8*A* ring.

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| N1—H1···O1$^{i}$ | 0.85 (2) | 2.43 (2) | 3.217 (2) | 154 (2) |
| C5—H5*A*···F1$^{ii}$ | 0.95 | 2.50 | 3.393 (2) | 157 |
| C23—H23*A*···O1$^{iii}$ | 0.95 | 2.46 | 3.365 (2) | 159 |
| C15—H15*B*···Br1$^{iv}$ | 0.99 | 2.98 | 3.703 (2) | 131 |
| C2—H2*A*···*Cg*3$^{i}$ | 1.00 | 2.68 | 3.676 (2) | 172 |
| C15—H15*A*···*Cg*3$^{v}$ | 0.99 | 2.94 | 3.386 (2) | 109 |
| C15—H15*B*···*Cg*3$^{v}$ | 0.99 | 2.97 | 3.386 (2) | 106 |

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

## 3. Supramolecular features and Hirshfeld surface analysis

In the crystal, molecules are linlked by intermolecular N—H···O, C—H···O, C—H···F and C—H···Br hydrogen bonds, forming a three-dimensional network (Table 1; Figs. 3,

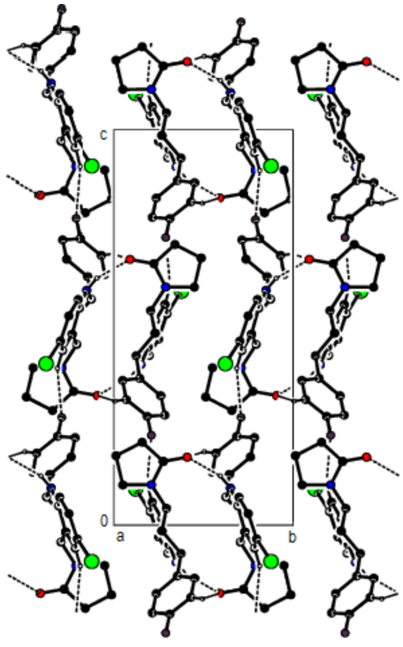



**Figure 3**
A view of the molecular packing along the *a* axis of the title compound, showing the N—H···O, C—H···O, C—H···F and C—H···Br hydrogen bonds.

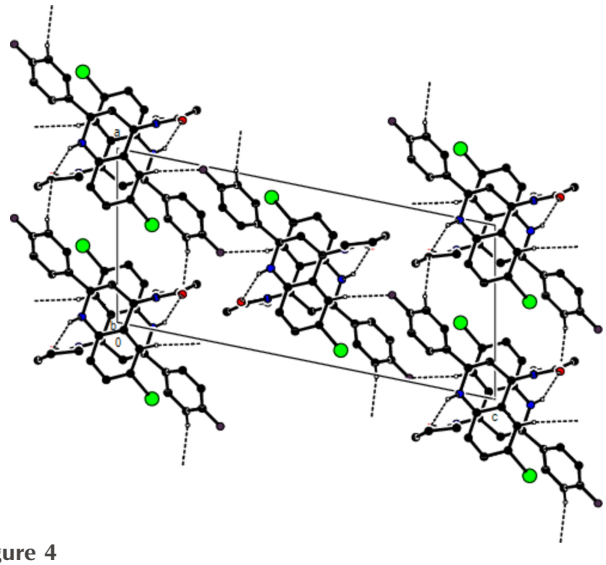


**Figure 4**
A view of the molecular packing along the *b* axis of the title compound.

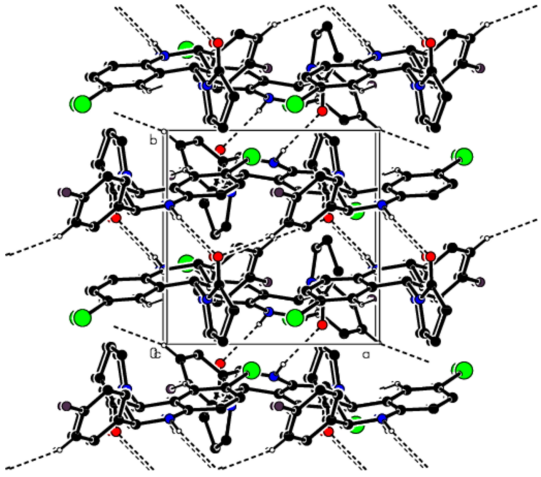


**Figure 5**
A view of the molecular packing along the *c* axis of the title compound.

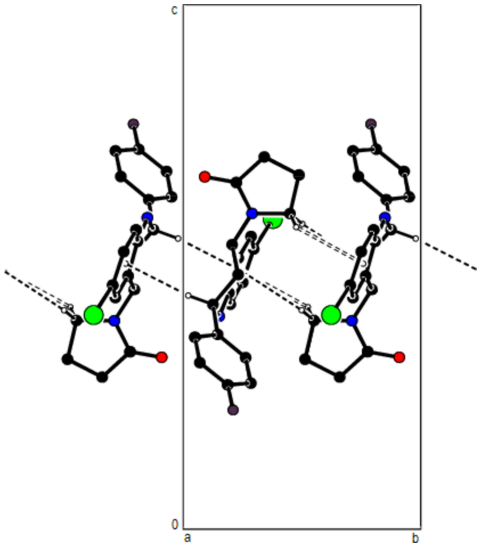


**Figure 6**
A view of the molecular packing along the *a* axis of the title compound, showing the C—H···$\pi$ interactions.

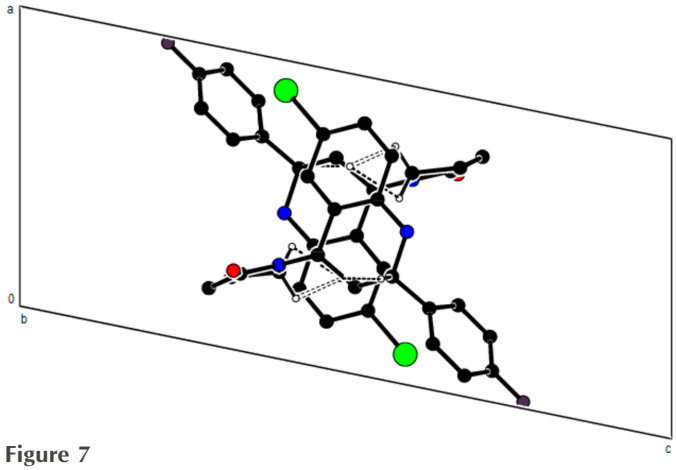


**Figure 7**
A view of the molecular packing along the *b* axis.

4 and 5). In addition, C—H···$\pi$ interactions connect molecules, forming ribbons along the *b*-axis direction and consolidating molecular packing (Table 1; Figs. 6, 7 and 8).

To quantify the intermolecular interactions in the crystal, the Hirshfeld surfaces of the title molecule and the two-dimensional fingerprints were generated with *CrystalExplorer17.5* (Spackman *et al.*, 2021). The $d_{norm}$ mappings for the title compound were performed in the range −0.2398 (red) to +1.3617 (blue) a.u. On the $d_{norm}$ surfaces, bright-red spots show the locations of the N—H···O, C—H···O and C—H···F interactions (Table 1; Fig. 9*a*,*b*).

The overall two-dimensional fingerprint plot for the title compound and those delineated into H···H (Fig. 10*b*; 38.7%),

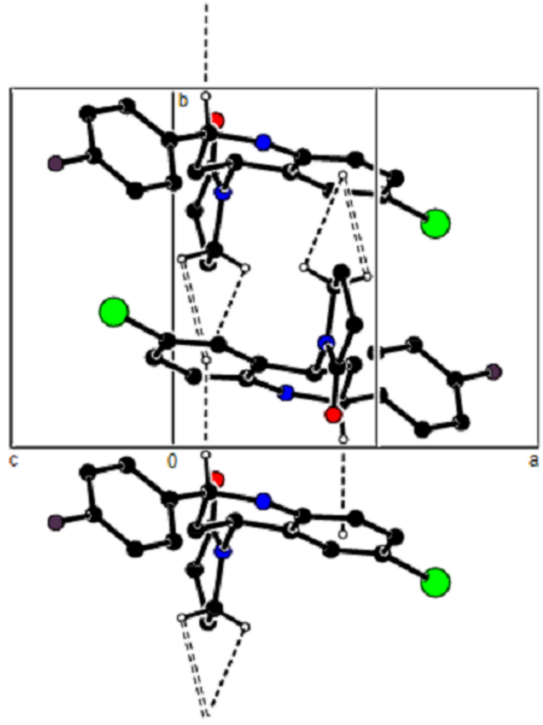


**Figure 8**
A view of the molecular packing of the title compound showing supramolecular ribbons running along the *c*-axis direction.

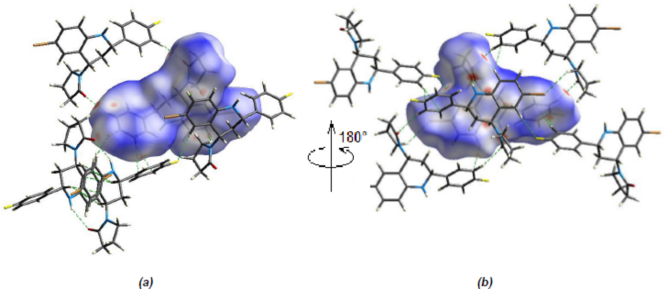



**Figure 9**
(*a*) Front and (*b*) back views of the three-dimensional Hirshfeld surface for the title compound. Some N—H···O, C—H···O and C—H···F interactions are shown as dashed lines.

C···H/H···C (Fig. 10*c*; 24.3%), Br···H/H···Br (Fig. 10*d*; 14.9%) and F···H/H···F (Fig. 10*e*; 9.6%) contacts are shown in Fig. 10. O···H/H···O (8.8%), Br···C/C···Br (1.8%), F···O/O···F (0.6%), F···C/C···F (0.6%), N···H/H···N (0.5%), Br···N/N···Br (0.1%) and Br···Br (0.1%) contacts have little directional influence on the molecular packing.

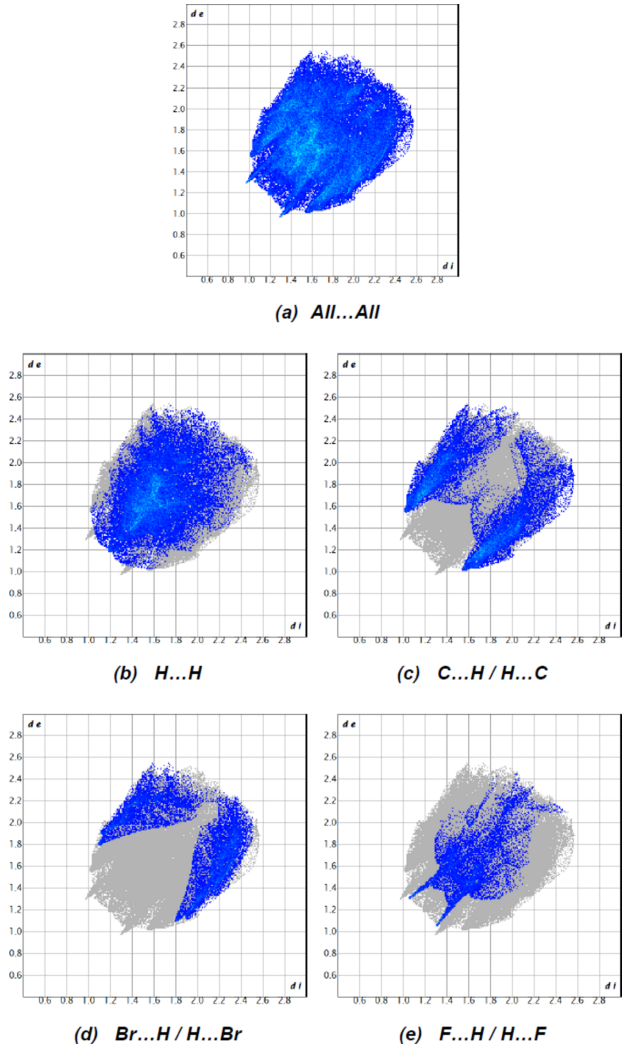



**Figure 10**
The two-dimensional fingerprint plots for the title compound showing (*a*) all interactions, and delineated into (*b*) H···H, (*c*) C···H/H···C, (*d*) Br···H/H···Br and (*e*) F···H/H···F interactions. The $d_i$ and $d_e$ values are the closest internal and external distances (in Å) from 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 1,2,3,4-tetrahydroquinoline unit showed that the six most closely related species to the title compound are those with refcodes WACWOO (Çelik *et al.*, 2010*a*), CEDNUW (Çelik *et al.*, 2010*b*), SUFDEE (Jeyaseelan, *et al.*, 2015*c*), NOVGAI (Jeyaseelan *et al.*, 2015*a*), WUFBEG (Jeyaseelan *et al.*, 2015*b*) and EZOMIR (Çelik *et al.*, 2016).

The crystal structure of WACWOO is consolidated by weak aromatic $\pi$–$\pi$ interactions [centroid–centroid distance = 3.802 (4) Å] between the pyridine and benzene rings of the quinoline ring systems of adjacent molecules. In the crystal of CEDNUW, $\pi$–$\pi$ stacking interactions are present between the pyridine and benzene rings of adjacent molecules [centroid–centroid distances = 3.634 (4) Å], and short Br···Br contacts [3.4443 (13) Å] occur. In the crystal of SUFDEE, molecules are linked by weak C—H···O hydrogen bonds, generating *C*(8) and *C*(4) chains propagating along [100] and [010], respectively, which together generate (001) sheets. In the crystal of NOVGAI, inversion dimers linked by pairs of C—H···O hydrogen bonds generate $R_2^2(8)$ loops. In the crystal of WUFBEG, inversion dimers linked by pairs of C—H···O hydrogen bonds generate $R_2^2(10)$ loops. Additional intermolecular C—H···O hydrogen bonds generate *C*(7) chains along [100]. In the crystal of EZOMIR, inversion dimers linked by pairs of N—H···N hydrogen bonds generate $R_2^2(12)$ loops.

## 5. Synthesis and crystallization

***N*-[(*E*)-(4-Fluorophenyl)methylidene]-4-bromaniline:** Anhydrous $MgSO_4$ (3.61 g, 0.030 mol) and 4-fluorobenzaldehyde (1.86 g, 0.015 mol) were successively added to a solution of 4-bromaniline (2.60 g, 0.015 mol) in $CH_2Cl_2$ (35 mL). After 24 h at room temperature, the reaction mixture was filtered through a silica gel layer (2 × 3 cm), eluent – $CH_2Cl_2$ (2 × 25 mL). The solvent was evaporated under reduced pressure and the residue was recrystallized from hexane/EtOAc. Azomethine was obtained as a light-yellow powder in a yield of 92% (3.88 g).

**1-[6-Bromo-2-(4-fluorophenyl)-1,2,3,4-tetrahydroquinolin-4-yl]pyrrolidin-2-one (1):** Boron trifluoride ether (0.33 mL, 0.0026 mol) and *N*-vinylpyrrolidone (1.50 mL, 0.014 mol) were added to a cooled solution (275–277 K) of the previously obtained azomethine (3.50 g, 0.013 mol) in freshly distilled $CH_2Cl_2$ (30 mL). After that, the suspension was mixed at room temperature for 24 h and treated with a small amount of water (0.2–0.3 mL) to decompose the catalyst. The reaction mixture was filtered through a layer of silica gel (2 × 3 cm), washed with $CH_2Cl_2$ (2 × 6 mL) and the solvent was

evaporated under reduced pressure. The obtained product was recrystallized from a mixture of hexane/EtOAc. A white microcrystalline precipitate of the title compound was isolated in a yield of 43% (2.17 g), m.p. 460.3–462.3 K. IR (KBr), $\nu$ ($cm^{-1}$): 3344 (NH), 2956 (Ph), 2897 (Ph), 1666 (N—C═O). $^1$H NMR (700 MHz, $CDCl_3$, 298 K) ($J$, Hz): $\delta$ 2.00–2.10 ($m$, 4H, H-3 + H-4-pyrrole), 2.43–2.47 ($m$, 1H, H-3-pyrrole-A), 2.52–2.57 ($m$, 1H, H-3-pyrrole-B), 3.19–3.26 ($m$, 2H, H-5-pyrrole), 4.56 ($dd$, $J$ = 9.5, $J$ = 5.0, 1H, H-2), 5.65–5.68 ($m$, 1H, H-4), 6.48 ($d$, $J$ = 8.3, 1H, H-8), 6.95 ($br.s$, 1H, H-5), 7.05–7.08 ($m$, 2H, H-2,6–$C_6H_4$–F), 7.14 ($dd$, $J$ = 8.6, $J$ = 2.4, 1H, H-7), 7.38–7.40 ($m$, 2H, H-3,5–$C_6H_4$–F) ppm. $^{13}$C NMR{$^1$H} (176 MHz, $CDCl_3$, 298 K) ($J$, Hz): $\delta$ 18.18, 31.19, 34.82, 42.21, 48.07, 55.68, 110.10, 115.65 ($d$, 2C, $^2J_{C,F}$ = 21.6), 116.67, 121.05, 128.06 ($d$, 2C, $^3J_{C,F}$ = 8.1), 129.14, 131.10, 138.15 ($br.s$, 1C), 144.59, 162.38 ($d$, $^1J_{C,F}$ = 245.8), 175.84 ppm. $^{19}$F NMR{$^1$H} (659 MHz, $CDCl_3$, 298 K): $\delta$ −113.93 ($s$, 1F) ppm. Elemental analysis calculated (%) for $C_{19}H_{18}BrFN_2O$: C, 58.62; H, 4.66; N, 7.20; found: C, 58.73; H, 4.53; N, 7.15. Single crystals (colourless prisms) of the title compound were grown from a mixture of hexane and ethyl acetate (∼3:1).

## 6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. The C-bound H atoms were placed in calculated positions (0.95–1.00 Å) and refined as riding with $U_{iso}$(H) = 1.2$U_{eq}$(C). The N-bound H atom was located in a difference map and freely refined.

**Table 2**
Experimental details.

| | |
|---|---|
| Crystal data | |
| Chemical formula | $C_{19}H_{18}BrFN_2O$ |
| $M_r$ | 389.26 |
| Crystal system, space group | Monoclinic, $P2_1/n$ |
| Temperature (K) | 100 |
| $a$, $b$, $c$ (Å) | 9.2092 (6), 9.0576 (6), 20.4085 (13) |
| $\beta$ (°) | 101.518 (2) |
| $V$ (Å$^3$) | 1668.06 (19) |
| $Z$ | 4 |
| Radiation type | Mo $K\alpha$ |
| $\mu$ ($mm^{-1}$) | 2.48 |
| Crystal size (mm) | 0.40 × 0.36 × 0.34 |
| | |
| Data collection | |
| Diffractometer | Bruker Kappa APEXII area-detector diffractometer |
| Absorption correction | Multi-scan (*SADABS*; Krause *et al.*, 2015) |
| $T_{min}$, $T_{max}$ | 0.752, 1.000 |
| No. of measured, independent and observed [$I > 2\sigma(I)$] reflections | 28015, 4882, 3713 |
| $R_{int}$ | 0.057 |
| $(\sin \theta/\lambda)_{max}$ (Å$^{-1}$) | 0.706 |
| | |
| Refinement | |
| $R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, $S$ | 0.035, 0.072, 1.02 |
| No. of reflections | 4882 |
| No. of parameters | 221 |
| H-atom treatment | H atoms treated by a mixture of independent and constrained refinement |
| $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å$^{-3}$) | 0.45, −0.41 |

Computer programs: *APEX3* and *SAINT* (Bruker, 2018), *SHELXT2014/5* (Sheldrick, 2015*a*), *SHELXL2018/3* (Sheldrick, 2015*b*), *ORTEP-3 for Windows* (Farrugia, 2012) and *PLATON* (Spek, 2020).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# supporting information

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## Crystal structure and Hirshfeld surface analysis of 1-[6-bromo-2-(4-fluorophenyl)-1,2,3,4-tetrahydroquinolin-4-yl]pyrrolidin-2-one

**Anastasia A. Pronina, Alexandra G. Podrezova, Mikhail S. Grigoriev, Khudayar I. Hasanov, Nurlana D. Sadikhova, Mehmet Akkurt and Ajaya Bhattarai**

### Computing details

#### 1-[6-Bromo-2-(4-fluorophenyl)-1,2,3,4-tetrahydroquinolin-4-yl]pyrrolidin-2-one

*Crystal data*

$C_{19}H_{18}BrFN_2O$
$M_r$ = 389.26
Monoclinic, $P2_1/n$
$a$ = 9.2092 (6) Å
$b$ = 9.0576 (6) Å
$c$ = 20.4085 (13) Å
$\beta$ = 101.518 (2)°
$V$ = 1668.06 (19) Å$^3$
$Z$ = 4
$F(000)$ = 792
$D_x$ = 1.550 Mg m$^{-3}$
Mo $K\alpha$ radiation, $\lambda$ = 0.71073 Å
Cell parameters from 5298 reflections
$\theta$ = 3.0–27.1°
$\mu$ = 2.48 mm$^{-1}$
$T$ = 100 K
Bulk, colourless
0.40 × 0.36 × 0.34 mm

*Data collection*

Bruker Kappa APEXII area-detector diffractometer
$\varphi$ and $\omega$ scans
Absorption correction: multi-scan (SADABS; Krause *et al.*, 2015)
$T_{min}$ = 0.752, $T_{max}$ = 1.000
28015 measured reflections
4882 independent reflections
3713 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.057
$\theta_{max}$ = 30.1°, $\theta_{min}$ = 3.8°
$h$ = −12→12
$k$ = −12→12
$l$ = −28→28

*Refinement*

Refinement on $F^2$
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.072
$S$ = 1.02
4882 reflections
221 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Hydrogen site location: mixed
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0267P)^2 + 0.8068P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.45 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.40 e Å$^{-3}$

*Special details*

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

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

| | *x* | *y* | *z* | $U_{iso}$*/$U_{eq}$ |
|---|---|---|---|---|
| C2 | 0.64897 (19) | 0.1250 (2) | 0.42863 (9) | 0.0113 (3) |
| H2A | 0.664204 | 0.021487 | 0.445624 | 0.014* |
| C3 | 0.7094 (2) | 0.2311 (2) | 0.48563 (9) | 0.0114 (4) |
| H3A | 0.695266 | 0.334338 | 0.469667 | 0.014* |
| H3B | 0.816813 | 0.213924 | 0.501577 | 0.014* |
| C4 | 0.62722 (19) | 0.2058 (2) | 0.54273 (9) | 0.0098 (3) |
| H4A | 0.639259 | 0.099050 | 0.555148 | 0.012* |
| C4A | 0.46344 (19) | 0.23196 (19) | 0.51703 (9) | 0.0097 (3) |
| C5 | 0.3722 (2) | 0.2855 (2) | 0.55836 (9) | 0.0125 (4) |
| H5A | 0.413562 | 0.314242 | 0.602937 | 0.015* |
| C6 | 0.2210 (2) | 0.2968 (2) | 0.53445 (10) | 0.0132 (4) |
| C7 | 0.1569 (2) | 0.2503 (2) | 0.47072 (10) | 0.0144 (4) |
| H7A | 0.052477 | 0.253929 | 0.455694 | 0.017* |
| C8 | 0.2472 (2) | 0.1984 (2) | 0.42916 (10) | 0.0127 (4) |
| H8A | 0.204136 | 0.166365 | 0.385250 | 0.015* |
| C8A | 0.4015 (2) | 0.19234 (19) | 0.45099 (9) | 0.0110 (4) |
| C12 | 0.74202 (19) | 0.2236 (2) | 0.66142 (9) | 0.0117 (4) |
| C13 | 0.8116 (2) | 0.3412 (2) | 0.70995 (10) | 0.0170 (4) |
| H13A | 0.921011 | 0.333787 | 0.718707 | 0.020* |
| H13B | 0.777820 | 0.331985 | 0.752877 | 0.020* |
| C14 | 0.7601 (3) | 0.4872 (2) | 0.67578 (10) | 0.0247 (5) |
| H14A | 0.677041 | 0.529078 | 0.693974 | 0.030* |
| H14B | 0.842211 | 0.559631 | 0.682281 | 0.030* |
| C15 | 0.7101 (2) | 0.4493 (2) | 0.60191 (10) | 0.0146 (4) |
| H15A | 0.617049 | 0.501351 | 0.582257 | 0.018* |
| H15B | 0.787199 | 0.475484 | 0.576387 | 0.018* |
| C21 | 0.7300 (2) | 0.1449 (2) | 0.37154 (9) | 0.0113 (4) |
| C22 | 0.8453 (2) | 0.0493 (2) | 0.36616 (10) | 0.0144 (4) |
| H22A | 0.866503 | −0.031520 | 0.396188 | 0.017* |
| C23 | 0.9300 (2) | 0.0700 (2) | 0.31764 (10) | 0.0169 (4) |
| H23A | 1.008962 | 0.004965 | 0.314036 | 0.020* |
| C24 | 0.8955 (2) | 0.1873 (3) | 0.27535 (10) | 0.0195 (4) |
| C25 | 0.7829 (2) | 0.2849 (3) | 0.27849 (11) | 0.0251 (5) |
| H25A | 0.762472 | 0.365242 | 0.248101 | 0.030* |
| C26 | 0.6999 (2) | 0.2627 (2) | 0.32732 (10) | 0.0184 (4) |
| H26A | 0.621590 | 0.328838 | 0.330588 | 0.022* |
| Br1 | 0.10063 (2) | 0.37706 (2) | 0.59152 (2) | 0.02069 (7) |
| F1 | 0.97779 (13) | 0.20988 (16) | 0.22741 (6) | 0.0311 (3) |
| N1 | 0.48956 (17) | 0.15098 (18) | 0.40598 (8) | 0.0127 (3) |

| | | | | |
|---|---|---|---|---|
| N11 | 0.68720 (16) | 0.28987 (17) | 0.60227 (7) | 0.0101 (3) |
| O1 | 0.73676 (15) | 0.09059 (14) | 0.67215 (7) | 0.0159 (3) |
| H1 | 0.446 (3) | 0.094 (3) | 0.3753 (12) | 0.022 (6)* |

*Atomic displacement parameters (Å²)*

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{12}$ | $U^{13}$ | $U^{23}$ |
|---|---|---|---|---|---|---|
| C2 | 0.0122 (8) | 0.0126 (9) | 0.0094 (9) | −0.0001 (7) | 0.0027 (7) | 0.0007 (7) |
| C3 | 0.0121 (8) | 0.0117 (9) | 0.0106 (9) | −0.0017 (7) | 0.0029 (7) | −0.0004 (7) |
| C4 | 0.0124 (8) | 0.0090 (9) | 0.0084 (9) | −0.0013 (7) | 0.0027 (7) | −0.0007 (7) |
| C4A | 0.0128 (8) | 0.0071 (8) | 0.0094 (9) | −0.0022 (7) | 0.0029 (7) | 0.0016 (7) |
| C5 | 0.0159 (9) | 0.0114 (9) | 0.0106 (9) | −0.0022 (7) | 0.0037 (7) | −0.0005 (7) |
| C6 | 0.0132 (9) | 0.0111 (9) | 0.0171 (10) | 0.0006 (7) | 0.0072 (8) | −0.0006 (7) |
| C7 | 0.0104 (8) | 0.0125 (9) | 0.0203 (10) | −0.0008 (7) | 0.0030 (8) | 0.0011 (8) |
| C8 | 0.0137 (9) | 0.0105 (9) | 0.0131 (9) | −0.0029 (7) | 0.0007 (7) | −0.0011 (7) |
| C8A | 0.0136 (9) | 0.0069 (9) | 0.0129 (9) | −0.0016 (7) | 0.0039 (7) | 0.0011 (7) |
| C12 | 0.0094 (8) | 0.0164 (10) | 0.0102 (9) | 0.0024 (7) | 0.0038 (7) | 0.0011 (7) |
| C13 | 0.0177 (10) | 0.0207 (11) | 0.0113 (10) | −0.0011 (8) | −0.0001 (8) | −0.0019 (8) |
| C14 | 0.0411 (13) | 0.0161 (11) | 0.0148 (11) | −0.0047 (9) | 0.0005 (10) | −0.0031 (8) |
| C15 | 0.0183 (9) | 0.0106 (9) | 0.0147 (10) | −0.0024 (7) | 0.0027 (8) | −0.0012 (7) |
| C21 | 0.0126 (8) | 0.0136 (10) | 0.0071 (8) | −0.0010 (7) | 0.0008 (7) | −0.0021 (7) |
| C22 | 0.0153 (9) | 0.0138 (10) | 0.0140 (10) | 0.0004 (7) | 0.0025 (8) | −0.0012 (8) |
| C23 | 0.0116 (9) | 0.0220 (11) | 0.0167 (10) | −0.0004 (8) | 0.0016 (8) | −0.0069 (8) |
| C24 | 0.0140 (9) | 0.0356 (12) | 0.0103 (10) | −0.0018 (9) | 0.0053 (8) | −0.0017 (9) |
| C25 | 0.0218 (11) | 0.0363 (13) | 0.0188 (11) | 0.0066 (9) | 0.0080 (9) | 0.0138 (10) |
| C26 | 0.0162 (9) | 0.0233 (11) | 0.0171 (10) | 0.0070 (8) | 0.0064 (8) | 0.0074 (8) |
| Br1 | 0.01630 (10) | 0.02401 (11) | 0.02408 (12) | 0.00192 (9) | 0.00963 (8) | −0.00610 (10) |
| F1 | 0.0234 (7) | 0.0555 (9) | 0.0186 (7) | 0.0011 (6) | 0.0141 (5) | 0.0060 (6) |
| N1 | 0.0116 (7) | 0.0173 (9) | 0.0096 (8) | −0.0032 (6) | 0.0026 (6) | −0.0037 (6) |
| N11 | 0.0137 (7) | 0.0084 (7) | 0.0079 (7) | −0.0002 (6) | 0.0013 (6) | −0.0002 (6) |
| O1 | 0.0228 (7) | 0.0126 (7) | 0.0118 (7) | 0.0042 (5) | 0.0025 (6) | 0.0031 (5) |

*Geometric parameters (Å, º)*

| | | | |
|---|---|---|---|
| C2—N1 | 1.467 (2) | C12—C13 | 1.508 (3) |
| C2—C21 | 1.514 (2) | C13—C14 | 1.525 (3) |
| C2—C3 | 1.526 (2) | C13—H13A | 0.9900 |
| C2—H2A | 1.0000 | C13—H13B | 0.9900 |
| C3—C4 | 1.528 (2) | C14—C15 | 1.525 (3) |
| C3—H3A | 0.9900 | C14—H14A | 0.9900 |
| C3—H3B | 0.9900 | C14—H14B | 0.9900 |
| C4—N11 | 1.447 (2) | C15—N11 | 1.459 (2) |
| C4—C4A | 1.513 (2) | C15—H15A | 0.9900 |
| C4—H4A | 1.0000 | C15—H15B | 0.9900 |
| C4A—C5 | 1.391 (2) | C21—C26 | 1.389 (3) |
| C4A—C8A | 1.401 (3) | C21—C22 | 1.391 (3) |
| C5—C6 | 1.384 (3) | C22—C23 | 1.390 (3) |
| C5—H5A | 0.9500 | C22—H22A | 0.9500 |

| | | | |
|---|---|---|---|
| C6—C7 | 1.382 (3) | C23—C24 | 1.365 (3) |
| C6—Br1 | 1.9053 (18) | C23—H23A | 0.9500 |
| C7—C8 | 1.383 (3) | C24—F1 | 1.367 (2) |
| C7—H7A | 0.9500 | C24—C25 | 1.374 (3) |
| C8—C8A | 1.403 (3) | C25—C26 | 1.386 (3) |
| C8—H8A | 0.9500 | C25—H25A | 0.9500 |
| C8A—N1 | 1.393 (2) | C26—H26A | 0.9500 |
| C12—O1 | 1.227 (2) | N1—H1 | 0.85 (2) |
| C12—N11 | 1.352 (2) | | |

| | | | |
|---|---|---|---|
| N1—C2—C21 | 110.74 (14) | C14—C13—H13A | 110.7 |
| N1—C2—C3 | 109.20 (15) | C12—C13—H13B | 110.7 |
| C21—C2—C3 | 110.55 (14) | C14—C13—H13B | 110.7 |
| N1—C2—H2A | 108.8 | H13A—C13—H13B | 108.8 |
| C21—C2—H2A | 108.8 | C15—C14—C13 | 105.17 (17) |
| C3—C2—H2A | 108.8 | C15—C14—H14A | 110.7 |
| C2—C3—C4 | 109.03 (14) | C13—C14—H14A | 110.7 |
| C2—C3—H3A | 109.9 | C15—C14—H14B | 110.7 |
| C4—C3—H3A | 109.9 | C13—C14—H14B | 110.7 |
| C2—C3—H3B | 109.9 | H14A—C14—H14B | 108.8 |
| C4—C3—H3B | 109.9 | N11—C15—C14 | 103.49 (16) |
| H3A—C3—H3B | 108.3 | N11—C15—H15A | 111.1 |
| N11—C4—C4A | 113.30 (14) | C14—C15—H15A | 111.1 |
| N11—C4—C3 | 113.41 (14) | N11—C15—H15B | 111.1 |
| C4A—C4—C3 | 108.86 (15) | C14—C15—H15B | 111.1 |
| N11—C4—H4A | 107.0 | H15A—C15—H15B | 109.0 |
| C4A—C4—H4A | 107.0 | C26—C21—C22 | 118.86 (17) |
| C3—C4—H4A | 107.0 | C26—C21—C2 | 121.75 (16) |
| C5—C4A—C8A | 119.53 (17) | C22—C21—C2 | 119.20 (16) |
| C5—C4A—C4 | 121.70 (16) | C23—C22—C21 | 121.23 (18) |
| C8A—C4A—C4 | 118.66 (15) | C23—C22—H22A | 119.4 |
| C6—C5—C4A | 119.94 (18) | C21—C22—H22A | 119.4 |
| C6—C5—H5A | 120.0 | C24—C23—C22 | 117.51 (18) |
| C4A—C5—H5A | 120.0 | C24—C23—H23A | 121.2 |
| C7—C6—C5 | 121.30 (17) | C22—C23—H23A | 121.2 |
| C7—C6—Br1 | 120.02 (14) | C23—C24—F1 | 118.44 (18) |
| C5—C6—Br1 | 118.67 (14) | C23—C24—C25 | 123.63 (18) |
| C6—C7—C8 | 118.99 (17) | F1—C24—C25 | 117.93 (19) |
| C6—C7—H7A | 120.5 | C24—C25—C26 | 118.0 (2) |
| C8—C7—H7A | 120.5 | C24—C25—H25A | 121.0 |
| C7—C8—C8A | 120.88 (18) | C26—C25—H25A | 121.0 |
| C7—C8—H8A | 119.6 | C25—C26—C21 | 120.77 (18) |
| C8A—C8—H8A | 119.6 | C25—C26—H26A | 119.6 |
| N1—C8A—C4A | 121.61 (16) | C21—C26—H26A | 119.6 |
| N1—C8A—C8 | 119.18 (17) | C8A—N1—C2 | 120.88 (16) |
| C4A—C8A—C8 | 119.19 (16) | C8A—N1—H1 | 113.3 (15) |
| O1—C12—N11 | 125.02 (18) | C2—N1—H1 | 115.7 (15) |
| O1—C12—C13 | 127.12 (17) | C12—N11—C4 | 121.86 (16) |

| | | | |
|---|---|---|---|
| N11—C12—C13 | 107.85 (16) | C12—N11—C15 | 114.52 (16) |
| C12—C13—C14 | 105.05 (16) | C4—N11—C15 | 123.22 (15) |
| C12—C13—H13A | 110.7 | | |

| | | | |
|---|---|---|---|
| N1—C2—C3—C4 | 59.01 (19) | N1—C2—C21—C22 | −140.90 (18) |
| C21—C2—C3—C4 | −178.91 (15) | C3—C2—C21—C22 | 97.9 (2) |
| C2—C3—C4—N11 | 173.65 (15) | C26—C21—C22—C23 | 0.0 (3) |
| C2—C3—C4—C4A | −59.24 (19) | C2—C21—C22—C23 | −175.11 (17) |
| N11—C4—C4A—C5 | −22.0 (2) | C21—C22—C23—C24 | −0.2 (3) |
| C3—C4—C4A—C5 | −149.14 (17) | C22—C23—C24—F1 | 179.79 (18) |
| N11—C4—C4A—C8A | 162.03 (16) | C22—C23—C24—C25 | 0.2 (3) |
| C3—C4—C4A—C8A | 34.9 (2) | C23—C24—C25—C26 | 0.0 (3) |
| C8A—C4A—C5—C6 | 1.1 (3) | F1—C24—C25—C26 | −179.62 (19) |
| C4—C4A—C5—C6 | −174.83 (17) | C24—C25—C26—C21 | −0.2 (3) |
| C4A—C5—C6—C7 | 2.6 (3) | C22—C21—C26—C25 | 0.2 (3) |
| C4A—C5—C6—Br1 | −177.82 (14) | C2—C21—C26—C25 | 175.16 (19) |
| C5—C6—C7—C8 | −3.2 (3) | C4A—C8A—N1—C2 | 9.6 (3) |
| Br1—C6—C7—C8 | 177.20 (14) | C8—C8A—N1—C2 | −172.17 (17) |
| C6—C7—C8—C8A | 0.1 (3) | C21—C2—N1—C8A | −156.30 (16) |
| C5—C4A—C8A—N1 | 174.11 (16) | C3—C2—N1—C8A | −34.3 (2) |
| C4—C4A—C8A—N1 | −9.8 (3) | O1—C12—N11—C4 | −5.8 (3) |
| C5—C4A—C8A—C8 | −4.1 (3) | C13—C12—N11—C4 | 173.15 (15) |
| C4—C4A—C8A—C8 | 171.96 (16) | O1—C12—N11—C15 | −178.77 (17) |
| C7—C8—C8A—N1 | −174.75 (17) | C13—C12—N11—C15 | 0.2 (2) |
| C7—C8—C8A—C4A | 3.5 (3) | C4A—C4—N11—C12 | 115.73 (18) |
| O1—C12—C13—C14 | −169.00 (18) | C3—C4—N11—C12 | −119.53 (17) |
| N11—C12—C13—C14 | 12.1 (2) | C4A—C4—N11—C15 | −71.9 (2) |
| C12—C13—C14—C15 | −19.0 (2) | C3—C4—N11—C15 | 52.8 (2) |
| C13—C14—C15—N11 | 18.7 (2) | C14—C15—N11—C12 | −12.3 (2) |
| N1—C2—C21—C26 | 44.1 (2) | C14—C15—N11—C4 | 174.87 (16) |
| C3—C2—C21—C26 | −77.1 (2) | | |

*Hydrogen-bond geometry (Å, º)*

*Cg*3 is the centroid of the C4*A*/C5–C8/C8*A* ring.

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| N1—H1···O1$^{i}$ | 0.85 (2) | 2.43 (2) | 3.217 (2) | 154 (2) |
| C5—H5*A*···F1$^{ii}$ | 0.95 | 2.50 | 3.393 (2) | 157 |
| C23—H23*A*···O1$^{iii}$ | 0.95 | 2.46 | 3.365 (2) | 159 |
| C15—H15*B*···Br1$^{iv}$ | 0.99 | 2.98 | 3.703 (2) | 131 |
| C2—H2*A*···*Cg*3$^{i}$ | 1.00 | 2.68 | 3.676 (2) | 172 |
| C15—H15*A*···*Cg*3$^{v}$ | 0.99 | 2.94 | 3.386 (2) | 109 |
| C15—H15*B*···*Cg*3$^{v}$ | 0.99 | 2.97 | 3.386 (2) | 106 |

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