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tert-Butyl 3-amino-5-bromo-1*H*-indazole-1-carboxylate

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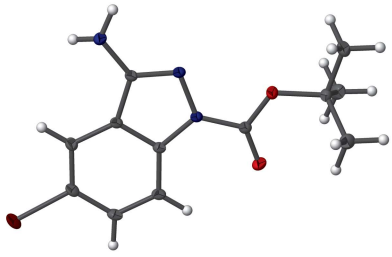
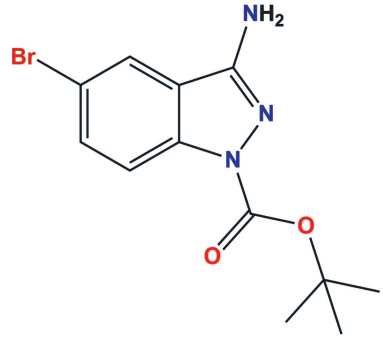
Structural data: full structural data are available from iucrdata.iucr.org

In the title compound, $C_{12}H_{14}BrN_3O_2$, the pyrazole and benzene rings are nearly co-planar with a dihedral angle between the rings of 2.36 (5)°. In the crystal, inversion dimers linked by pairwise N—H···N hydrogen bonds generate $R_2^2(8)$ loops. The dimers are linked into a three-dimensional network by weak aromatic π–π stacking interactions [centroid–centroid separation = 3.7394 (6) Å] and C—H···O and C—H···Br hydrogen bonds.

3D view



Chemical scheme



Structure description

Indazole derivatives possess pharmacological properties against infectious, neurodegenerative and inflammatory disorders and are also good anti-microbial agents (*e.g.*, Kusanur & Mahesh, 2013). To generate a library of compounds using 3-amino-6-bromo indazole, the boc protection of the ring NH group was carried out to form the title compound. From the crystal data, it is confirmed that, as expected, the boc protection happened only at the ring NH grouping.

In this structure (Fig. 1), the fused pyrazole (N1/N2/C7/C6/C1) and benzene (C1–C6) rings are nearly co-planar, subtending a dihedral angle of 2.36 (5)°. The dihedral angle between the C8/O1/O2 ester group and the fused-ring system is 10.01 (4)°. One of the methyl groups (C10) of the *tert*-butyl substituent lies close to the ester-group plane [displacement = −0.068 (1) Å], whereas C11 and C12 are displaced above and below it. Very weak C2—H2···O2, C11—H11*C*···O2 and C12—H12*B*···O2 intramolecular interactions are present (Table 1).

In the extended structure, pairwise N3—H3*B*···N2 links form centrosymmetric dimers with an $R_2^2(8)$ ring motif (Fig. 2). The dimers are linked into a three-dimensional network by C2—H2···O2, C5—H5···Br1 and C12—H12*A*···O2 hydrogen bonds and a π–π

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

D—H···A	D—H	H···A	D···A	D—H···A
C2—H2···O2	0.95	2.46	2.9609 (13)	113
C11—H11C···O2	0.98	2.38	2.9559 (15)	117
C12—H12B···O2	0.98	2.46	3.0475 (15)	118
N3—H3B···N2^{i}	0.865 (18)	2.165 (19)	3.0249 (12)	172.8 (16)
C2—H2···O2^{ii}	0.95	2.62	3.4133 (12)	141
C5—H5···Br1^{iii}	0.95	3.11	3.8871 (10)	140
C12—H12A···O2^{iv}	0.98	2.62	3.5582 (14)	161

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

stacking interaction (Fig. 3) also occurs with $Cg1\cdots Cg1(2-x, 1-y, -z)$ = 3.7394 (6) Å, where $Cg1$ is the centroid of the pyrazole ring.

Synthesis and crystallization

5-Bromo-1*H*-indazol-3-amine (1): To a solution of 5-bromo-2-fluoro benzonitrile (1.0 mmol) in ethanol (20 ml) was added hydrazine hydrate (99%) (10.0 mmol). The reaction mixture was heated in sealed tube at 343 K for 4 h and progress of the reaction was monitored by TLC. The reaction mixture was concentrated to dryness. The brown-coloured solid was purified by recrystallization from ethanol solution to afford pale-yellow needles (90%), m.p. 407 K (Fig. 4).

***tert*-Butyl 3-amino-5-bromo-1*H*-indazole-1-carboxylate (2):** To a solution of compound (**1**) (5.0 mmol) in dichloromethane (40 ml) was added DMAP (5.0 mmol). The reaction mixture cooled to 273 K and boc anhydride (5.0 mmol) was added. The reaction mixture was slowly warmed to room temperature and stirred for 15 h. Progress of the reaction was monitored by TLC. The reaction mixture was diluted with dichloromethane (50 ml) and washed with water and brine (25 ml), dried over

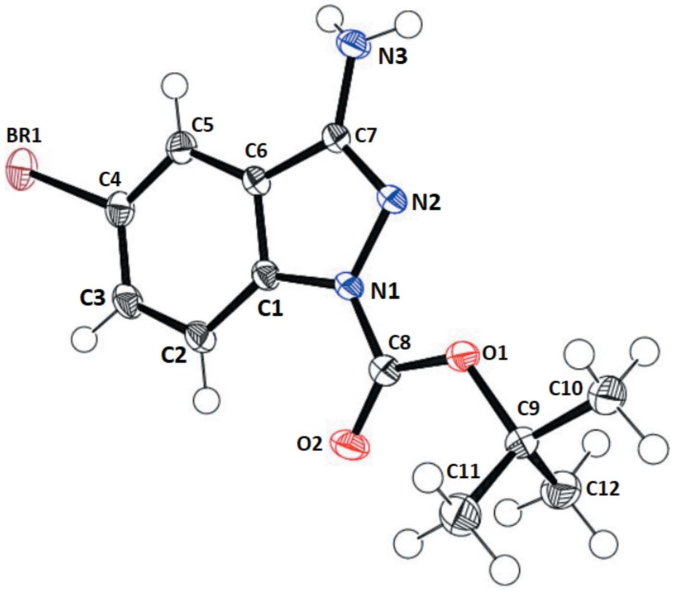


Figure 1
A view of the structure of the title compound with displacement ellipsoids drawn at the 70% probability level.

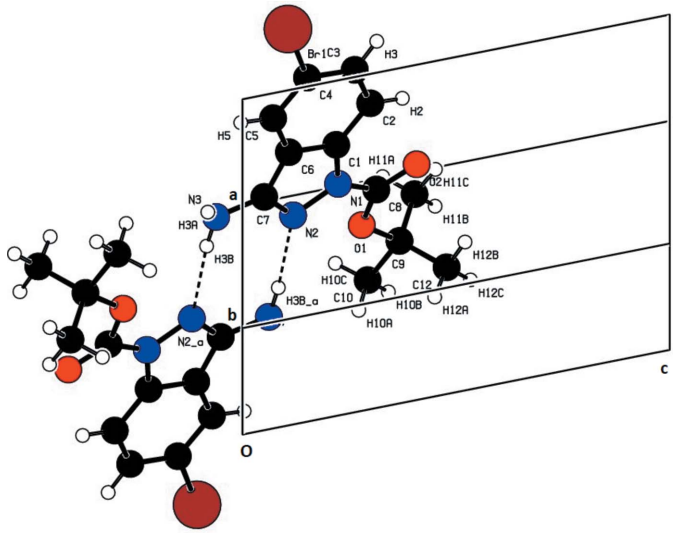


Figure 2
Partial packing viewed along b-axis direction showing the $R_2^2(8)$ ring motif.

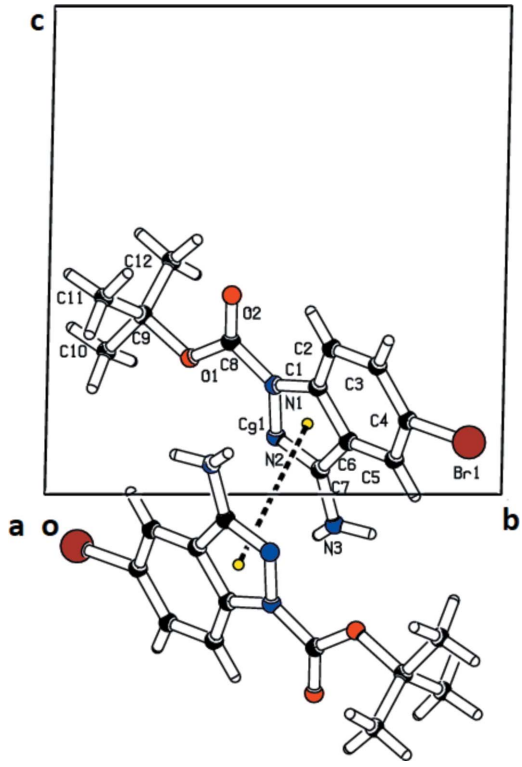


Figure 3
A view of the π–π interaction along the a-axis direction.

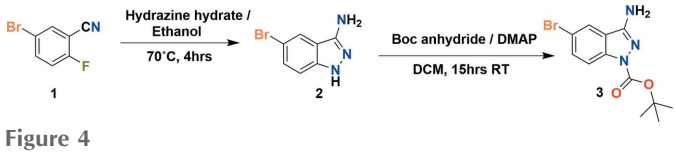


Figure 4
Synthesis scheme for the title compound.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{12}H_{14}BrN_3O_2$
M_r	312.17
Crystal system, space group	Triclinic, $P\overline{1}$
Temperature (K)	100
a, b, c (Å)	5.8281 (2), 10.5313 (3), 11.0917 (3)
α, β, γ (°)	85.954 (1), 78.801 (2), 75.105 (1)
V (Å^3)	645.23 (3)
Z	2
Radiation type	Mo $K\alpha$
μ (mm^{-1})	3.18
Crystal size (mm)	0.45 × 0.32 × 0.30
Data collection	
Diffractometer	Bruker SMART APEXII CCD
Absorption correction	Multi-scan (*SADABS*; Bruker, 2012)
T_{min}, T_{max}	0.502, 0.748
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	19603, 7076, 5872
R_{int}	0.018
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.895
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.027, 0.070, 1.08
No. of reflections	7076
No. of parameters	174
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.59, −0.53

Computer programs: *APEX2* and *SAINT* (Bruker, 2012), *SHELXS97* (Sheldrick, 2008), *SHELXL2018/3* (Sheldrick, 2015), *ORTEP-3 for Windows* (Farrugia, 2012), *PLATON* (Spek, 2020) and *publCIF* (Westrip, 2010).

anhydrous sodium sulfate and concentrated. The crude compound was purified by column chromatography (silica gel, 20–30% ethyl acetate in hexane) to afford a gummy solid, which solidifies as transparent crystals after 2 d (62%), m.p. 389 K.

Refinement

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

Acknowledgements

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full crystallographic data

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tert-Butyl 3-amino-5-bromo-1*H*-indazole-1-carboxylate

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tert-Butyl 3-amino-5-bromo-1*H*-indazole-1-carboxylate

Crystal data

$C_{12}H_{14}BrN_3O_2$
$M_r = 312.17$
Triclinic, $P\overline{1}$
$a = 5.8281$ (2) Å
$b = 10.5313$ (3) Å
$c = 11.0917$ (3) Å
$\alpha = 85.954$ (1)°
$\beta = 78.801$ (2)°
$\gamma = 75.105$ (1)°
$V = 645.23$ (3) Å^3
$Z = 2$
$F(000) = 316$
$D_x = 1.607$ Mg m^{-3}
Melting point: 389 K
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 2120 reflections
$\theta = 2.7$–$25.5°$
$\mu = 3.18$ mm^{-1}
$T = 100$ K
Fragment, colourless
0.45 × 0.32 × 0.30 mm

Data collection

Bruker SMART APEXII CCD diffractometer
φ and ω scans
Absorption correction: multi-scan (SADABS; Bruker, 2012)
$T_{min} = 0.502$, $T_{max} = 0.748$
19603 measured reflections
7076 independent reflections
5872 reflections with $I > 2\sigma(I)$
$R_{int} = 0.018$
$\theta_{max} = 39.5°$, $\theta_{min} = 1.9°$
$h = -10\rightarrow10$
$k = -18\rightarrow18$
$l = -19\rightarrow19$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.027$
$wR(F^2) = 0.070$
$S = 1.08$
7076 reflections
174 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: mixed
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0327P)^2 + 0.1773P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.002$
$\Delta\rho_{max} = 0.59$ e Å^{-3}
$\Delta\rho_{min} = -0.53$ 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. The amino –NH_2 H atoms were located in a difference Fourier map and their positions were freely refined. The C-bound H atoms were placed in calculated positions (C—H = 0.95–0.98 Å) and were refined with U_{iso}(H) = 1.2U_{eq}(C) or 1.5U_{eq}(methyl C).

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

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.90907 (17)	0.59306 (9)	0.21941 (9)	0.01265 (14)
C2	1.04771 (18)	0.62182 (10)	0.29904 (9)	0.01532 (16)
H2	1.063744	0.574273	0.374242	0.018*
C3	1.16027 (19)	0.72288 (10)	0.26285 (10)	0.01661 (17)
H3	1.255405	0.745757	0.314333	0.020*
C4	1.13572 (18)	0.79194 (10)	0.15122 (10)	0.01534 (16)
C5	1.00073 (18)	0.76403 (10)	0.07169 (9)	0.01467 (16)
H5	0.987132	0.811006	−0.003982	0.018*
C6	0.88544 (17)	0.66311 (9)	0.10852 (9)	0.01246 (14)
C7	0.73941 (17)	0.60237 (9)	0.05102 (9)	0.01226 (14)
C8	0.76837 (18)	0.40037 (10)	0.31328 (9)	0.01421 (15)
C9	0.61429 (18)	0.20590 (10)	0.36754 (9)	0.01514 (16)
C10	0.5067 (2)	0.12827 (12)	0.29308 (11)	0.0236 (2)
H10A	0.356430	0.184090	0.272305	0.035*
H10B	0.472695	0.051548	0.341495	0.035*
H10C	0.621570	0.099056	0.217351	0.035*
C11	0.8457 (2)	0.11997 (11)	0.40268 (11)	0.02108 (19)
H11A	0.963638	0.090441	0.328004	0.032*
H11B	0.810398	0.043417	0.450934	0.032*
H11C	0.912110	0.170719	0.451721	0.032*
C12	0.4299 (2)	0.26645 (12)	0.47786 (11)	0.0218 (2)
H12A	0.285095	0.320478	0.450072	0.033*
H12B	0.498911	0.321461	0.521026	0.033*
H12C	0.386670	0.196475	0.533695	0.033*
Br1	1.30179 (2)	0.92671 (2)	0.10637 (2)	0.01982 (3)
N1	0.78125 (15)	0.49788 (8)	0.22385 (8)	0.01335 (13)
N2	0.67956 (15)	0.50413 (8)	0.11849 (7)	0.01299 (13)
N3	0.67793 (17)	0.63640 (9)	−0.06185 (8)	0.01576 (15)
O1	0.66674 (15)	0.31183 (8)	0.27930 (7)	0.01632 (13)
O2	0.84393 (16)	0.40048 (8)	0.40767 (7)	0.01973 (15)
H3A	0.669 (3)	0.7159 (19)	−0.0811 (17)	0.029 (5)*
H3B	0.575 (3)	0.6006 (17)	−0.0839 (16)	0.025 (4)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0122 (4)	0.0141 (4)	0.0128 (3)	−0.0042 (3)	−0.0033 (3)	−0.0017 (3)
C2	0.0155 (4)	0.0186 (4)	0.0141 (4)	−0.0059 (3)	−0.0051 (3)	−0.0017 (3)
C3	0.0160 (4)	0.0194 (4)	0.0172 (4)	−0.0068 (3)	−0.0054 (3)	−0.0041 (3)
C4	0.0148 (4)	0.0145 (4)	0.0181 (4)	−0.0059 (3)	−0.0020 (3)	−0.0031 (3)
C5	0.0160 (4)	0.0137 (4)	0.0156 (4)	−0.0059 (3)	−0.0031 (3)	−0.0004 (3)

C6	0.0123 (4)	0.0132 (4)	0.0131 (3)	−0.0039 (3)	−0.0038 (3)	−0.0009 (3)
C7	0.0119 (3)	0.0136 (4)	0.0124 (3)	−0.0042 (3)	−0.0032 (3)	−0.0006 (3)
C8	0.0144 (4)	0.0157 (4)	0.0136 (4)	−0.0049 (3)	−0.0041 (3)	0.0008 (3)
C9	0.0158 (4)	0.0163 (4)	0.0147 (4)	−0.0065 (3)	−0.0044 (3)	0.0039 (3)
C10	0.0311 (6)	0.0252 (5)	0.0218 (5)	−0.0178 (4)	−0.0103 (4)	0.0064 (4)
C11	0.0169 (4)	0.0192 (4)	0.0260 (5)	−0.0022 (3)	−0.0055 (4)	0.0031 (4)
C12	0.0161 (4)	0.0275 (5)	0.0193 (4)	−0.0035 (4)	−0.0008 (4)	0.0033 (4)
Br1	0.01951 (5)	0.01624 (5)	0.02640 (6)	−0.00958 (4)	−0.00275 (4)	−0.00328 (4)
N1	0.0151 (3)	0.0157 (3)	0.0120 (3)	−0.0067 (3)	−0.0058 (3)	0.0013 (3)
N2	0.0140 (3)	0.0156 (3)	0.0115 (3)	−0.0055 (3)	−0.0052 (3)	0.0005 (3)
N3	0.0205 (4)	0.0166 (4)	0.0136 (3)	−0.0080 (3)	−0.0077 (3)	0.0022 (3)
O1	0.0216 (3)	0.0177 (3)	0.0137 (3)	−0.0105 (3)	−0.0069 (3)	0.0039 (2)
O2	0.0260 (4)	0.0218 (4)	0.0159 (3)	−0.0096 (3)	−0.0111 (3)	0.0037 (3)

Geometric parameters (Å, º)

C1—N1	1.3874 (12)	C9—O1	1.4835 (12)
C1—C6	1.4006 (13)	C9—C10	1.5177 (15)
C1—C2	1.4019 (13)	C9—C12	1.5185 (16)
C2—C3	1.3859 (15)	C9—C11	1.5222 (15)
C2—H2	0.9500	C10—H10A	0.9800
C3—C4	1.4039 (15)	C10—H10B	0.9800
C3—H3	0.9500	C10—H10C	0.9800
C4—C5	1.3815 (14)	C11—H11A	0.9800
C4—Br1	1.9021 (10)	C11—H11B	0.9800
C5—C6	1.3954 (13)	C11—H11C	0.9800
C5—H5	0.9500	C12—H12A	0.9800
C6—C7	1.4453 (13)	C12—H12B	0.9800
C7—N2	1.3141 (12)	C12—H12C	0.9800
C7—N3	1.3671 (12)	N1—N2	1.3998 (11)
C8—O2	1.2122 (12)	N3—H3A	0.840 (19)
C8—O1	1.3351 (12)	N3—H3B	0.865 (18)
C8—N1	1.3824 (13)		
N1—C1—C6	106.05 (8)	C10—C9—C11	110.23 (10)
N1—C1—C2	132.33 (9)	C12—C9—C11	112.91 (9)
C6—C1—C2	121.59 (9)	C9—C10—H10A	109.5
C3—C2—C1	116.85 (9)	C9—C10—H10B	109.5
C3—C2—H2	121.6	H10A—C10—H10B	109.5
C1—C2—H2	121.6	C9—C10—H10C	109.5
C2—C3—C4	120.95 (9)	H10A—C10—H10C	109.5
C2—C3—H3	119.5	H10B—C10—H10C	109.5
C4—C3—H3	119.5	C9—C11—H11A	109.5
C5—C4—C3	122.74 (9)	C9—C11—H11B	109.5
C5—C4—Br1	118.85 (8)	H11A—C11—H11B	109.5
C3—C4—Br1	118.40 (7)	C9—C11—H11C	109.5
C4—C5—C6	116.38 (9)	H11A—C11—H11C	109.5
C4—C5—H5	121.8	H11B—C11—H11C	109.5

C6—C5—H5	121.8	C9—C12—H12A	109.5
C5—C6—C1	121.49 (8)	C9—C12—H12B	109.5
C5—C6—C7	133.15 (9)	H12A—C12—H12B	109.5
C1—C6—C7	105.28 (8)	C9—C12—H12C	109.5
N2—C7—N3	122.92 (9)	H12A—C12—H12C	109.5
N2—C7—C6	111.54 (8)	H12B—C12—H12C	109.5
N3—C7—C6	125.46 (9)	C8—N1—C1	126.18 (8)
O2—C8—O1	127.43 (9)	C8—N1—N2	122.33 (8)
O2—C8—N1	121.75 (9)	C1—N1—N2	111.27 (8)
O1—C8—N1	110.82 (8)	C7—N2—N1	105.85 (8)
O1—C9—C10	102.25 (8)	C7—N3—H3A	113.2 (13)
O1—C9—C12	109.28 (9)	C7—N3—H3B	118.0 (12)
C10—C9—C12	110.83 (9)	H3A—N3—H3B	117.7 (17)
O1—C9—C11	110.84 (8)	C8—O1—C9	119.35 (8)
N1—C1—C2—C3	177.48 (10)	O2—C8—N1—C1	10.52 (16)
C6—C1—C2—C3	0.02 (15)	O1—C8—N1—C1	−169.07 (9)
C1—C2—C3—C4	−0.25 (15)	O2—C8—N1—N2	−175.37 (10)
C2—C3—C4—C5	−0.10 (16)	O1—C8—N1—N2	5.04 (13)
C2—C3—C4—Br1	−178.60 (8)	C6—C1—N1—C8	175.41 (9)
C3—C4—C5—C6	0.68 (15)	C2—C1—N1—C8	−2.34 (17)
Br1—C4—C5—C6	179.17 (7)	C6—C1—N1—N2	0.75 (11)
C4—C5—C6—C1	−0.91 (14)	C2—C1—N1—N2	−177.00 (10)
C4—C5—C6—C7	−177.26 (10)	N3—C7—N2—N1	177.97 (9)
N1—C1—C6—C5	−177.46 (9)	C6—C7—N2—N1	0.84 (11)
C2—C1—C6—C5	0.59 (15)	C8—N1—N2—C7	−175.90 (9)
N1—C1—C6—C7	−0.22 (10)	C1—N1—N2—C7	−1.00 (11)
C2—C1—C6—C7	177.83 (9)	O2—C8—O1—C9	6.31 (16)
C5—C6—C7—N2	176.37 (10)	N1—C8—O1—C9	−174.13 (8)
C1—C6—C7—N2	−0.41 (11)	C10—C9—O1—C8	−179.09 (9)
C5—C6—C7—N3	−0.68 (18)	C12—C9—O1—C8	63.43 (12)
C1—C6—C7—N3	−177.45 (9)	C11—C9—O1—C8	−61.63 (12)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C2—H2···O2	0.95	2.46	2.9609 (13)	113
C11—H11*C*···O2	0.98	2.38	2.9559 (15)	117
C12—H12*B*···O2	0.98	2.46	3.0475 (15)	118
N3—H3*B*···N2^{i}	0.865 (18)	2.165 (19)	3.0249 (12)	172.8 (16)
C2—H2···O2^{ii}	0.95	2.62	3.4133 (12)	141
C5—H5···Br1^{iii}	0.95	3.11	3.8871 (10)	140
C12—H12*A*···O2^{iv}	0.98	2.62	3.5582 (14)	161

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