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Ethyl 2-(6-bromo-2-phenyl-1*H*-imidazo[4,5-*b*]-pyridin-1-yl)acetate

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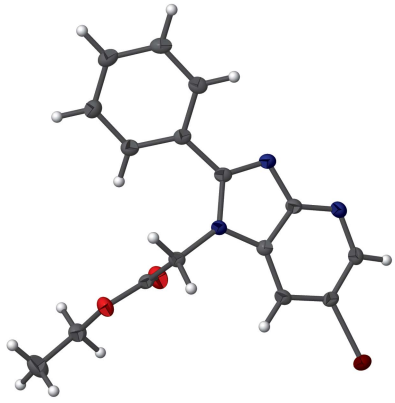
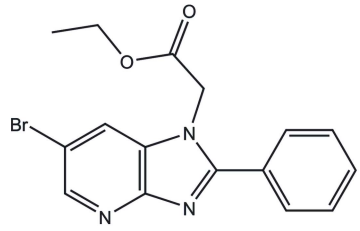
Structural data: full structural data are available from iucrdata.iucr.org

In the title compound, $C_{16}H_{14}BrN_3O_2$, the fused-ring system is essentially planar, with the largest deviation from the mean plane being 0.0216 (15) Å for the substituted N atom of the five-membered ring, the plane of which makes dihedral angles of 28.50 (7) and 77.48 (7)° with the terminal phenyl ring and the ethoxycarbonylmethyl group mean planes, respectively. In the crystal, C—H···N hydrogen bonds link the molecules into inversion dimers. These combine with weak C—H···N contacts to stack the molecules into columns along the *b*-axis direction.

3D view



Chemical scheme



Structure description

Imidazo[4,5-*b*]pyridine derivatives are often defined as precursors in the synthesis of a variety of therapeutic agents. Indeed, heterocyclic compounds containing this motif are endowed with anticancer activity (Guo *et al.*, 2005), antibacterial (Aridoss *et al.*, 2006), tuberculostatic (Bukowski & Janowiec, 1989) and antimitotic activity (Temple, 1990).

In the previous study, we have alkylated 6-bromo-2-phenyl-3*H*-imidazo[4,5-*b*]pyridine at positions N4 and N3 (Ouzidan *et al.*, 2010, 2011). In this work, we report the synthesis of ethyl 2-(6-bromo-2-phenyl-3*H*-imidazo[4,5-*b*]pyridin-3-yl) acetate, by the reaction of ethyl 2-bromoacetate on 6-bromo-2-phenyl-3*H*-imidazo[4,5-*b*]pyridine in phase-transfer catalysis conditions.

In the title compound (Fig. 1), the fused ring system is essentially planar, with the largest deviation from the mean plane being 0.0216 (15) Å for the substituted N atom of

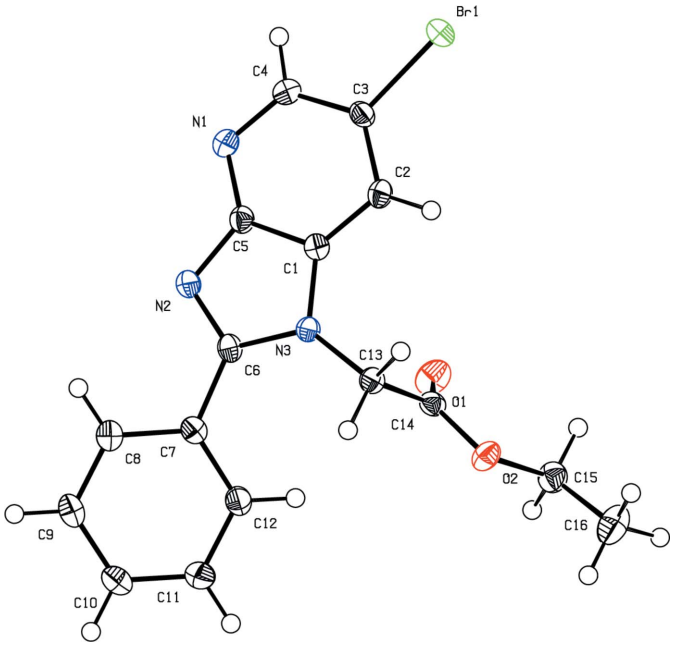


Figure 1
The molecular structure of the title compound, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.

the five-membered ring. It makes dihedral angles of 28.50 (7) and 77.48 (7)°, respectively, with the terminal phenyl ring (C7–C12) and the mean plane of the ethoxycarbonylmethyl group (C13, C14, O1, O2, C15 and C16).

In the crystal, C9—H9···N1 ($-x+1, -y, -z+1$) hydrogen bonds (Table 1) link the molecules into inversion dimers. These combine with weak C13—H13*A*···N2(x, $y+1$, z) contacts to stack the molecules into columns along the *b*-axis direction (Fig. 2).

Synthesis and crystallization

To a solution 6-bromo-2-phenyl-1*H*-imidazo[4,5-*b*]pyridine (0.30 g, 1.1 mmol), potassium carbonate (0.20 g, 1.42 mmol) and tetra-*n*-butylammonium bromide 0.035 g (0,11 mmol) in DMF (15 ml) was added ethyl 2-bromoacetate (0.14 ml, 1.30 mmol). Stirring was continued at room temperature for 12 h. The salt was removed by filtration and the filtrate concentrated under reduced pressure. The residue was separated by chromatography on a column of silica gel with ethyl acetate/hexane (1/2) as eluent. Reddish crystals were isolated when the solvent was allowed to evaporate (yield = 28%)

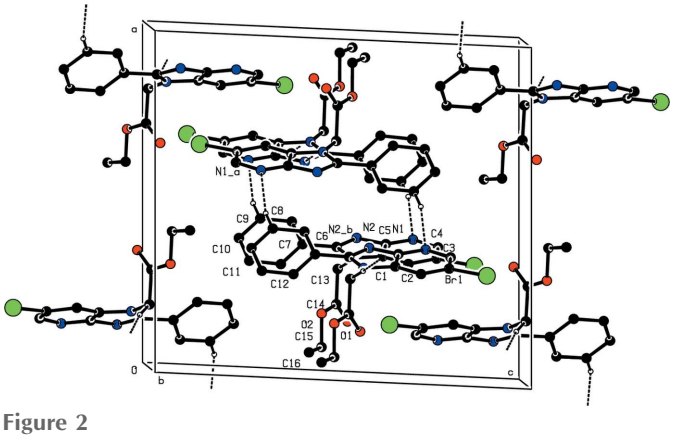


Figure 2
A view along the *b* axis of the crystal packing of the title compound. The hydrogen bonds are shown as dashed lines and H atoms not involved in these interactions have been omitted for clarity.

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

D—H···A	D—H	H···A	D···A	D—H···A
C9—H9···N1^{i}	0.95	2.60	3.529 (2)	166
C13—H13*A*···N2^{ii}	0.99	2.31	3.2755 (19)	165

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

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{16}H_{14}BrN_3O_2$
M_r	360.21
Crystal system, space group	Monoclinic, $P2_1/n$
Temperature (K)	150
a, b, c (Å)	14.6923 (8), 6.1988 (3), 16.2254 (8)
β (°)	92.911 (1)
V (Å^3)	1475.82 (13)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	2.80
Crystal size (mm)	0.21 × 0.15 × 0.06
Data collection	
Diffractometer	Bruker SMART APEX CCD
Absorption correction	Multi-scan (*SADABS*; Bruker, 2015)
T_{min}, T_{max}	0.70, 0.85
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	27419, 3981, 3236
R_{int}	0.044
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.686
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.031, 0.081, 1.06
No. of reflections	3981
No. of parameters	200
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.76, −0.35

Computer programs: *APEX2* and *SAINT* (Bruker, 2015), *SHELXT* (Sheldrick, 2015*a*), *SHELXL2014* (Sheldrick, 2015*b*), *PLATON* (Spek, 2009) and *publCIF* (Westrip, 2010).

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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Ethyl 2-(6-bromo-2-phenyl-1*H*-imidazo[4,5-*b*]pyridin-1-yl)acetate

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Ethyl 2-(6-bromo-2-phenyl-1*H*-imidazo[4,5-*b*]pyridin-1-yl)acetate

Crystal data

$C_{16}H_{14}BrN_3O_2$
M_r = 360.21
Monoclinic, $P2_1/n$
a = 14.6923 (8) Å
b = 6.1988 (3) Å
c = 16.2254 (8) Å
β = 92.911 (1)°
V = 1475.82 (13) Å^3
Z = 4
$F(000)$ = 728
D_x = 1.621 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 9736 reflections
θ = 2.5–29.1°
μ = 2.80 mm^{-1}
T = 150 K
Plate, colourless
0.21 × 0.15 × 0.06 mm

Data collection

Bruker SMART APEX CCD diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
Detector resolution: 8.3333 pixels mm^{-1}
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2015)
T_{min} = 0.70, T_{max} = 0.85
27419 measured reflections
3981 independent reflections
3236 reflections with $I > 2\sigma(I)$
R_{int} = 0.044
θ_{max} = 29.2°, θ_{min} = 1.8°
h = −20→20
k = −8→8
l = −22→21

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.031
$wR(F^2)$ = 0.081
S = 1.06
3981 reflections
200 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0468P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.76 e Å^{-3}
$\Delta\rho_{min}$ = −0.35 e Å^{-3}

Special details

Experimental. The diffraction data were obtained from 3 sets of 400 frames, each of width 0.5° in ω, collected at φ = 0.00, 90.00 and 180.00° and 2 sets of 800 frames, each of width 0.45° in φ, collected at ω = –30.00 and 210.00°. The scan time was 25 sec/frame.

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. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger. H-atoms attached to carbon were placed in calculated positions (C—H = 0.95 - 0.99 Å). All were included as riding contributions with isotropic displacement parameters 1.2 - 1.5 times those of the attached atoms.

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

	x	*y*	*z*	U_{iso}*/U_{eq}
Br1	0.34865 (2)	0.81843 (3)	0.85417 (2)	0.02759 (8)
O1	0.16616 (9)	0.7148 (2)	0.52092 (9)	0.0307 (3)
O2	0.19431 (8)	1.0034 (2)	0.44255 (7)	0.0233 (3)
N1	0.40277 (11)	0.2935 (2)	0.70896 (9)	0.0248 (3)
N2	0.39950 (10)	0.2709 (2)	0.56003 (9)	0.0209 (3)
N3	0.34936 (10)	0.6079 (2)	0.53338 (8)	0.0180 (3)
C1	0.35738 (11)	0.5886 (3)	0.61830 (10)	0.0178 (3)
C2	0.34280 (12)	0.7307 (3)	0.68207 (11)	0.0201 (3)
H2	0.3232	0.8754	0.6734	0.024*
C3	0.35958 (12)	0.6417 (3)	0.75984 (10)	0.0200 (3)
C4	0.38704 (12)	0.4271 (3)	0.77089 (10)	0.0240 (4)
H4	0.3949	0.3738	0.8257	0.029*
C5	0.38838 (12)	0.3781 (3)	0.63395 (10)	0.0197 (3)
C6	0.37482 (12)	0.4107 (3)	0.50189 (10)	0.0188 (3)
C7	0.37627 (12)	0.3570 (3)	0.41311 (10)	0.0187 (3)
C8	0.43728 (12)	0.1963 (3)	0.39011 (11)	0.0208 (4)
H8	0.4771	0.1310	0.4308	0.025*
C9	0.43990 (13)	0.1322 (3)	0.30827 (11)	0.0237 (4)
H9	0.4808	0.0220	0.2932	0.028*
C10	0.38293 (13)	0.2289 (3)	0.24859 (11)	0.0257 (4)
H10	0.3858	0.1876	0.1924	0.031*
C11	0.32184 (14)	0.3858 (3)	0.27083 (11)	0.0268 (4)
H11	0.2823	0.4507	0.2298	0.032*
C12	0.31791 (13)	0.4489 (3)	0.35259 (10)	0.0232 (4)
H12	0.2752	0.5554	0.3674	0.028*
C13	0.32126 (12)	0.8060 (2)	0.49161 (10)	0.0185 (3)
H13B	0.3434	0.8054	0.4350	0.022*
H13A	0.3493	0.9307	0.5214	0.022*
C14	0.21847 (13)	0.8314 (3)	0.48722 (10)	0.0190 (3)
C15	0.09723 (12)	1.0579 (3)	0.44032 (11)	0.0254 (4)
H15A	0.0754	1.0633	0.4970	0.031*
H15B	0.0614	0.9477	0.4086	0.031*
C16	0.08622 (15)	1.2742 (3)	0.39969 (15)	0.0369 (5)
H16A	0.1244	1.3802	0.4299	0.055*
H16B	0.0223	1.3189	0.4000	0.055*

H16C	0.1048	1.2648	0.3426	0.055*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Br1	0.03435 (13)	0.02850 (12)	0.01993 (10)	0.00701 (8)	0.00138 (7)	−0.00537 (7)
O1	0.0275 (8)	0.0289 (7)	0.0360 (8)	−0.0040 (6)	0.0036 (6)	0.0112 (6)
O2	0.0215 (7)	0.0225 (6)	0.0261 (6)	0.0019 (5)	0.0015 (5)	0.0076 (5)
N1	0.0308 (9)	0.0205 (8)	0.0228 (7)	0.0063 (6)	−0.0008 (6)	0.0014 (6)
N2	0.0247 (8)	0.0169 (7)	0.0210 (7)	0.0018 (6)	0.0008 (6)	−0.0021 (6)
N3	0.0232 (8)	0.0130 (6)	0.0176 (6)	0.0007 (6)	0.0005 (5)	0.0004 (5)
C1	0.0169 (8)	0.0172 (8)	0.0195 (7)	−0.0014 (6)	0.0025 (6)	0.0000 (6)
C2	0.0210 (9)	0.0154 (8)	0.0239 (8)	0.0010 (7)	0.0008 (7)	0.0005 (7)
C3	0.0192 (9)	0.0231 (9)	0.0178 (8)	0.0020 (7)	0.0023 (6)	−0.0034 (6)
C4	0.0274 (10)	0.0248 (9)	0.0195 (8)	0.0042 (8)	−0.0006 (7)	0.0024 (7)
C5	0.0209 (9)	0.0166 (8)	0.0216 (8)	0.0011 (7)	0.0010 (7)	−0.0011 (6)
C6	0.0195 (9)	0.0146 (8)	0.0224 (8)	−0.0017 (7)	0.0021 (6)	−0.0020 (6)
C7	0.0207 (9)	0.0158 (8)	0.0199 (8)	−0.0034 (6)	0.0038 (7)	−0.0005 (6)
C8	0.0186 (9)	0.0178 (8)	0.0262 (8)	−0.0025 (7)	0.0032 (7)	0.0000 (7)
C9	0.0233 (10)	0.0201 (8)	0.0284 (9)	−0.0012 (7)	0.0081 (7)	−0.0042 (7)
C10	0.0302 (11)	0.0259 (9)	0.0213 (8)	−0.0026 (8)	0.0041 (7)	−0.0046 (7)
C11	0.0321 (11)	0.0267 (9)	0.0212 (8)	0.0019 (8)	−0.0014 (7)	−0.0023 (7)
C12	0.0231 (9)	0.0229 (9)	0.0237 (8)	0.0027 (7)	0.0016 (7)	−0.0029 (7)
C13	0.0236 (9)	0.0124 (7)	0.0195 (7)	−0.0017 (6)	0.0020 (6)	0.0012 (6)
C14	0.0250 (9)	0.0155 (8)	0.0164 (7)	−0.0017 (7)	0.0006 (6)	−0.0015 (6)
C15	0.0207 (9)	0.0274 (10)	0.0282 (9)	0.0007 (7)	−0.0001 (7)	−0.0013 (8)
C16	0.0300 (12)	0.0300 (11)	0.0500 (13)	0.0049 (9)	−0.0060 (10)	0.0038 (10)

Geometric parameters (Å, º)

Br1—C3	1.8955 (17)	C7—C8	1.403 (3)
O1—C14	1.206 (2)	C8—C9	1.388 (2)
O2—C14	1.328 (2)	C8—H8	0.9500
O2—C15	1.464 (2)	C9—C10	1.384 (3)
N1—C4	1.332 (2)	C9—H9	0.9500
N1—C5	1.332 (2)	C10—C11	1.384 (3)
N2—C6	1.318 (2)	C10—H10	0.9500
N2—C5	1.388 (2)	C11—C12	1.387 (2)
N3—C1	1.382 (2)	C11—H11	0.9500
N3—C6	1.384 (2)	C12—H12	0.9500
N3—C13	1.453 (2)	C13—C14	1.517 (2)
C1—C2	1.384 (2)	C13—H13B	0.9900
C1—C5	1.401 (2)	C13—H13A	0.9900
C2—C3	1.388 (2)	C15—C16	1.499 (3)
C2—H2	0.9500	C15—H15A	0.9900
C3—C4	1.399 (2)	C15—H15B	0.9900
C4—H4	0.9500	C16—H16A	0.9800
C6—C7	1.480 (2)	C16—H16B	0.9800

C7—C12	1.392 (2)	C16—H16C	0.9800
C14—O2—C15	115.57 (14)	C8—C9—H9	120.0
C4—N1—C5	114.75 (15)	C11—C10—C9	119.96 (17)
C6—N2—C5	105.27 (14)	C11—C10—H10	120.0
C1—N3—C6	106.32 (13)	C9—C10—H10	120.0
C1—N3—C13	123.09 (14)	C10—C11—C12	120.44 (17)
C6—N3—C13	130.58 (13)	C10—C11—H11	119.8
N3—C1—C2	133.00 (16)	C12—C11—H11	119.8
N3—C1—C5	105.75 (14)	C11—C12—C7	120.33 (17)
C2—C1—C5	121.24 (16)	C11—C12—H12	119.8
C1—C2—C3	113.57 (16)	C7—C12—H12	119.8
C1—C2—H2	123.2	N3—C13—C14	111.61 (13)
C3—C2—H2	123.2	N3—C13—H13B	109.3
C2—C3—C4	122.09 (16)	C14—C13—H13B	109.3
C2—C3—Br1	119.09 (13)	N3—C13—H13A	109.3
C4—C3—Br1	118.79 (13)	C14—C13—H13A	109.3
N1—C4—C3	123.70 (16)	H13B—C13—H13A	108.0
N1—C4—H4	118.1	O1—C14—O2	124.75 (17)
C3—C4—H4	118.1	O1—C14—C13	124.94 (15)
N1—C5—N2	125.49 (16)	O2—C14—C13	110.29 (14)
N1—C5—C1	124.57 (16)	O2—C15—C16	107.47 (15)
N2—C5—C1	109.92 (15)	O2—C15—H15A	110.2
N2—C6—N3	112.71 (14)	C16—C15—H15A	110.2
N2—C6—C7	122.13 (15)	O2—C15—H15B	110.2
N3—C6—C7	125.15 (15)	C16—C15—H15B	110.2
C12—C7—C8	118.81 (16)	H15A—C15—H15B	108.5
C12—C7—C6	123.76 (16)	C15—C16—H16A	109.5
C8—C7—C6	117.35 (16)	C15—C16—H16B	109.5
C9—C8—C7	120.44 (17)	H16A—C16—H16B	109.5
C9—C8—H8	119.8	C15—C16—H16C	109.5
C7—C8—H8	119.8	H16A—C16—H16C	109.5
C10—C9—C8	120.00 (17)	H16B—C16—H16C	109.5
C10—C9—H9	120.0		
C6—N3—C1—C2	179.06 (19)	C13—N3—C6—N2	177.45 (16)
C13—N3—C1—C2	0.4 (3)	C1—N3—C6—C7	179.71 (16)
C6—N3—C1—C5	0.42 (18)	C13—N3—C6—C7	−1.8 (3)
C13—N3—C1—C5	−178.19 (15)	N2—C6—C7—C12	150.93 (18)
N3—C1—C2—C3	−179.97 (18)	N3—C6—C7—C12	−29.9 (3)
C5—C1—C2—C3	−1.5 (2)	N2—C6—C7—C8	−25.8 (3)
C1—C2—C3—C4	−1.0 (3)	N3—C6—C7—C8	153.35 (17)
C1—C2—C3—Br1	176.98 (12)	C12—C7—C8—C9	0.7 (3)
C5—N1—C4—C3	−1.4 (3)	C6—C7—C8—C9	177.63 (15)
C2—C3—C4—N1	2.7 (3)	C7—C8—C9—C10	0.8 (3)
Br1—C3—C4—N1	−175.34 (14)	C8—C9—C10—C11	−1.6 (3)
C4—N1—C5—N2	−179.61 (17)	C9—C10—C11—C12	0.7 (3)
C4—N1—C5—C1	−1.3 (3)	C10—C11—C12—C7	0.8 (3)

C6—N2—C5—N1	177.68 (18)	C8—C7—C12—C11	−1.5 (3)
C6—N2—C5—C1	−0.9 (2)	C6—C7—C12—C11	−178.25 (17)
N3—C1—C5—N1	−178.30 (17)	C1—N3—C13—C14	−81.81 (19)
C2—C1—C5—N1	2.9 (3)	C6—N3—C13—C14	99.9 (2)
N3—C1—C5—N2	0.3 (2)	C15—O2—C14—O1	4.3 (2)
C2—C1—C5—N2	−178.58 (16)	C15—O2—C14—C13	−174.24 (13)
C5—N2—C6—N3	1.2 (2)	N3—C13—C14—O1	7.0 (2)
C5—N2—C6—C7	−179.55 (16)	N3—C13—C14—O2	−174.51 (13)
C1—N3—C6—N2	−1.0 (2)	C14—O2—C15—C16	170.56 (15)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C9—H9···N1^{i}	0.95	2.60	3.529 (2)	166
C13—H13*A*···N2^{ii}	0.99	2.31	3.2755 (19)	165

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