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4-[5-Amino-4-(4-fluorophenyl)-3-(pyridin-4-yl)-1H-pyrazol-1-yl]benzotrile

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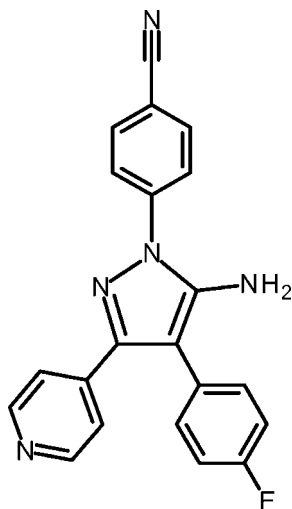
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 Key indicators: single-crystal X-ray study; $T = 193$ K; mean $\sigma(\text{C}-\text{C}) = 0.003$ Å; R factor = 0.038; wR factor = 0.103; data-to-parameter ratio = 12.5.

In the crystal structure of the title compound, $\text{C}_{21}\text{H}_{14}\text{FN}_5$, the pyrazole ring forms dihedral angles of 38.0 (1), 40.0 (1) and 28.5 (1)° with the directly attached 4-fluorophenyl, pyridine and benzonitrile rings, respectively. The crystal packing is characterized by $\text{N}-\text{H}\cdots\text{N}$ hydrogen bonds, which result in a two-dimensional network parallel to the ac -plane.

Related literature

For p38 α MAP kinase inhibitors having a vicinal 4-fluorophenyl/pyridin-4-yl system connected to a five-membered heterocyclic core, see: Abu Thaher *et al.* (2009); Peifer *et al.* (2006). For the inhibitory activity and preparation of the title compound, see: Abu Thaher *et al.* (2012a). For related structures, see: Abu Thaher *et al.* (2012b,c).



Experimental

Crystal data

$\text{C}_{21}\text{H}_{14}\text{FN}_5$
 $M_r = 355.37$
 Orthorhombic, $Pca2_1$
 $a = 10.5189$ (5) Å
 $b = 8.1339$ (3) Å
 $c = 20.0009$ (13) Å
 $V = 1711.27$ (15) Å³
 $Z = 4$
 Cu $K\alpha$ radiation
 $\mu = 0.76$ mm⁻¹
 $T = 193$ K
 $0.50 \times 0.30 \times 0.30$ mm

Data collection

Enraf–Nonius CAD-4 diffractometer
 3163 measured reflections
 3059 independent reflections
 3005 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.026$
 3 standard reflections every 60 min
 intensity decay: 3%

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.038$
 $wR(F^2) = 0.103$
 $S = 1.04$
 3059 reflections
 244 parameters
 1 restraint
 H-atom parameters constrained
 $\Delta\rho_{\text{max}} = 0.17$ e Å⁻³
 $\Delta\rho_{\text{min}} = -0.23$ e Å⁻³
 Absolute structure: Flack (1983),
 1381 Friedel pairs
 Flack parameter: -0.17 (18)

Table 1

Hydrogen-bond geometry (Å, °).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$\text{N6}-\text{H6A}\cdots\text{N26}^i$	0.88	2.14	2.938 (2)	150
$\text{N6}-\text{H6B}\cdots\text{N14}^{ii}$	0.86	2.58	3.292 (3)	141

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

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *CORINC* (Dräger & Gattow, 1971); program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *PLATON*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: IM2359).

References

- Abu Thaher, B., Arnsmann, M., Totzke, F., Ehlert, J. E., Kubbutat, M. H. G., Schächtele, C., Zimmermann, M. O., Koch, P., Boeckler, F. M. & Laufer, S. A. (2012a). *J. Med. Chem.* **55**, 961–965.
 Abu Thaher, B., Koch, P., Schattel, V. & Laufer, S. (2009). *J. Med. Chem.* **52**, 2613–2617.
 Abu Thaher, B., Koch, P., Schollmeyer, D. & Laufer, S. (2012b). *Acta Cryst.* **E68**, o632.
 Abu Thaher, B., Koch, P., Schollmeyer, D. & Laufer, S. (2012c). *Acta Cryst.* **E68**, o633.
 Altomare, A., Burla, M. C., Camalli, M., Cascarano, G. L., Giacovazzo, C., Guagliardi, A., Moliterni, A. G. G., Polidori, G. & Spagna, R. (1999). *J. Appl. Cryst.* **32**, 115–119.
 Dräger, M. & Gattow, G. (1971). *Acta Chem. Scand.* **25**, 761–762.
 Enraf–Nonius (1989). *CAD-4 Software*. Enraf–Nonius, Delft, The Netherlands.
 Flack, H. D. (1983). *Acta Cryst.* **A39**, 876–881.
 Peifer, C., Wagner, G. & Laufer, S. (2006). *Curr. Top. Med. Chem.* **6**, 113–149.
 Sheldrick, G. M. (2008). *Acta Cryst.* **A64**, 112–122.
 Spek, A. L. (2009). *Acta Cryst.* **D65**, 148–155.

supporting information

Acta Cryst. (2012). E68, o935 [https://doi.org/10.1107/S160053681200877X]

4-[5-Amino-4-(4-fluorophenyl)-3-(pyridin-4-yl)-1H-pyrazol-1-yl]benzotrile**Bassam Abu Thaher, Pierre Koch, Dieter Schollmeyer and Stefan Laufer****S1. Comment**

Compounds having a vicinal 4-fluorophenyl/pyridin-4-yl system connected to a five-membered heterocyclic core have been considered to be potential p38 α MAP kinase inhibitors (Abu Thaher *et al.* 2009, Peifer *et al.* 2006). We showed that the regioisomeric switch from 3-(4-fluorophenyl)-4-(pyridin-4-yl)-1-(aryl)-1H-pyrazol-5-amine to 4-(4-fluorophenyl)-3-(pyridin-4-yl)-1-(aryl)-1H-pyrazol-5-amine completely changed the inhibitory profile from p38 α MAP kinase to kinases relevant in cancer (Abu Thaher *et al.* 2012a). Recently, we reported similar crystal structures (Abu Thaher *et al.* 2012b,c).

In the crystal structure of the title compound (Fig. 1) the pyrazole ring forms dihedral angles of 38.0 (1)°, 40.0 (1)°, 28.5 (1)° with the directly attached 4-fluorophenyl, pyridine and benzonitrile rings, respectively. The 4-fluorophenyl ring encloses dihedral angles of 57.7 (1)° and 22.1 (9)° toward the pyridine and benzonitrile rings, respectively. The pyridine ring is oriented at a dihedral angle of 35.6 (1)° toward the benzonitrile ring.

The crystal packing (Fig. 2) shows that the amino function acts as a hydrogen bond donor of two intermolecular hydrogen bonds formed to two different molecules - one to the nitrogen atom (N26) of the pyridine ring and one to the nitrogen atom (N14) of the nitrile group. The length of the hydrogen bonds is 2.14 Å and 2.58 Å, respectively (Table 1). The two hydrogen bonds result in a two dimensional network parallel to the *ac*-plane.

S2. Experimental

20 mmol of LDA were added to 30 ml of dry THF in a three neck flask and cooled to 194 K. 14 mmol of 4-fluorophenyl-acetonitril in 10 ml THF were added dropwise and the reaction mixture was stirred for 45 min. 5 mmol of *N*-(4-cyanophenyl)-4-pyridinecarbohydrazonoyl chloride were added slowly and stirring of the reaction mixture was continued for 1 h. After warming to 293 K, 50 ml of water were added to the reaction mixture which then was extracted with ethyl acetate (2x 50 mL). The combined organic layers were dried over Na₂SO₄. The organic solution was concentrated to about 5 ml and the product precipitated as pure pale brown crystals which were washed with diethyl ether. Yield 62%.

S3. Refinement

Hydrogen atoms attached to carbons were placed at calculated positions with C—H = 0.95 Å (aromatic) or 0.98–0.99 Å (*sp*³ C-atom). All H atoms were refined in the riding-model approximation with isotropic displacement parameters (set at 1.2–1.5 times of the *U*_{eq} of the parent atom).

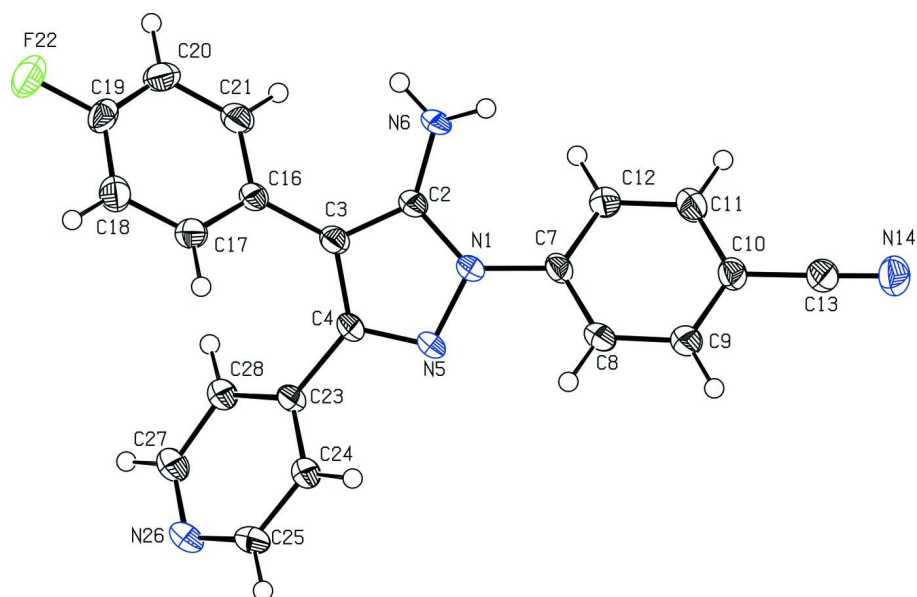


Figure 1

View of the title compound. Displacement ellipsoids are drawn at the 50% probability level. H atoms are depicted as circles of arbitrary size.

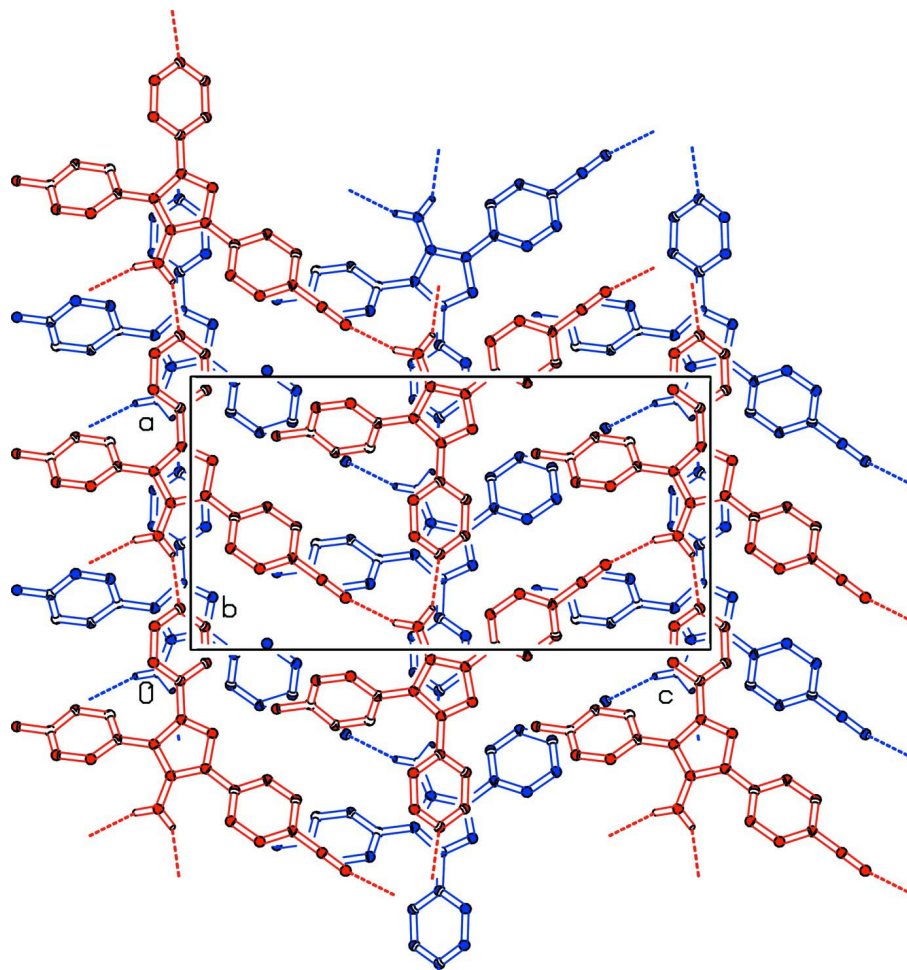


Figure 2

A packing section of the crystal viewed down the *b* axis. Hydrogen bonds are shown as dashed lines. Separated layers are indicated by different colours.

4-[5-Amino-4-(4-fluorophenyl)-3-(pyridin-4-yl)-1*H*-pyrazol-1-yl]benzonitrile

Crystal data

$C_{21}H_{14}FN_5$

$M_r = 355.37$

Orthorhombic, *Pca*2₁

Hall symbol: P 2c -2ac

$a = 10.5189$ (5) Å

$b = 8.1339$ (3) Å

$c = 20.0009$ (13) Å

$V = 1711.27$ (15) Å³

$Z = 4$

$F(000) = 736$

$D_x = 1.379$ Mg m⁻³

Cu *K*α radiation, $\lambda = 1.54178$ Å

Cell parameters from 25 reflections

$\theta = 65\text{--}70^\circ$

$\mu = 0.76$ mm⁻¹

$T = 193$ K

Block, brown

0.50 × 0.30 × 0.30 mm

Data collection

Enraf–Nonius CAD-4
diffractometer

Radiation source: rotating anode

Graphite monochromator

$\omega/2\theta$ scans

3163 measured reflections

3059 independent reflections

3005 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.026$
 $\theta_{\text{max}} = 69.9^\circ$, $\theta_{\text{min}} = 4.4^\circ$
 $h = -12 \rightarrow 12$
 $k = -9 \rightarrow 9$

$l = -24 \rightarrow 24$
 3 standard reflections every 60 min
 intensity decay: 3%

Refinement

Refinement on F^2
 Least-squares matrix: full
 $R[F^2 > 2\sigma(F^2)] = 0.038$
 $wR(F^2) = 0.103$
 $S = 1.04$
 3059 reflections
 244 parameters
 1 restraint
 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
 $w = 1/[\sigma^2(F_o^2) + (0.0752P)^2 + 0.2913P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\text{max}} < 0.001$
 $\Delta\rho_{\text{max}} = 0.17 \text{ e } \text{\AA}^{-3}$
 $\Delta\rho_{\text{min}} = -0.23 \text{ e } \text{\AA}^{-3}$
 Absolute structure: Flack (1983), 1381 Friedel
 pairs
 Absolute structure parameter: $-0.17 (18)$

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s 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 $F^2 > \sigma(F^2)$ 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.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
N1	0.43666 (14)	0.21998 (19)	0.52903 (8)	0.0245 (3)
C2	0.46323 (15)	0.2397 (2)	0.46188 (10)	0.0233 (4)
C3	0.34814 (17)	0.2656 (2)	0.43004 (10)	0.0234 (4)
C4	0.25715 (16)	0.2607 (2)	0.48226 (9)	0.0236 (4)
N5	0.30861 (14)	0.23527 (19)	0.54156 (8)	0.0253 (3)
N6	0.58360 (15)	0.2377 (2)	0.43736 (9)	0.0322 (4)
H6A	0.6492	0.2547	0.4639	0.048*
H6B	0.5975	0.2425	0.3949	0.048*
C7	0.51679 (16)	0.1880 (2)	0.58436 (10)	0.0240 (4)
C8	0.47853 (17)	0.2416 (3)	0.64701 (11)	0.0307 (4)
H8	0.4014	0.3013	0.6516	0.037*
C9	0.55154 (18)	0.2090 (3)	0.70281 (10)	0.0319 (4)
H9	0.5245	0.2446	0.7457	0.038*
C10	0.66595 (17)	0.1229 (2)	0.69545 (9)	0.0269 (4)
C11	0.70398 (19)	0.0686 (2)	0.63280 (10)	0.0309 (4)
H11	0.7816	0.0102	0.6281	0.037*
C12	0.62949 (18)	0.0992 (2)	0.57720 (10)	0.0287 (4)
H12	0.6548	0.0600	0.5345	0.034*
C13	0.74546 (19)	0.0933 (2)	0.75280 (11)	0.0306 (4)

N14	0.81025 (18)	0.0714 (3)	0.79805 (10)	0.0402 (4)
C16	0.33007 (16)	0.3156 (2)	0.35985 (9)	0.0235 (4)
C17	0.24094 (18)	0.4368 (2)	0.34404 (10)	0.0279 (4)
H17	0.1915	0.4843	0.3788	0.033*
C18	0.22306 (19)	0.4892 (2)	0.27863 (11)	0.0315 (4)
H18	0.1605	0.5693	0.2681	0.038*
C19	0.29837 (19)	0.4220 (3)	0.22958 (9)	0.0303 (4)
C20	0.38681 (19)	0.3029 (3)	0.24196 (10)	0.0329 (4)
H20	0.4369	0.2585	0.2068	0.039*
C21	0.40156 (19)	0.2480 (3)	0.30763 (10)	0.0294 (4)
H21	0.4611	0.1634	0.3170	0.035*
F22	0.28240 (13)	0.47710 (18)	0.16555 (6)	0.0439 (3)
C23	0.11619 (16)	0.2723 (2)	0.47901 (10)	0.0247 (4)
C24	0.04902 (17)	0.3515 (3)	0.52898 (10)	0.0301 (4)
H24	0.0927	0.4043	0.5646	0.036*
C25	-0.08274 (18)	0.3532 (3)	0.52667 (11)	0.0357 (5)
H25	-0.1273	0.4093	0.5611	0.043*
N26	-0.15029 (15)	0.2799 (2)	0.47859 (10)	0.0370 (4)
C27	-0.08439 (19)	0.2038 (3)	0.43060 (12)	0.0362 (5)
H27	-0.1306	0.1511	0.3959	0.043*
C28	0.04695 (18)	0.1972 (3)	0.42836 (11)	0.0301 (4)
H28	0.0891	0.1422	0.3928	0.036*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0145 (6)	0.0350 (8)	0.0241 (8)	-0.0011 (6)	0.0004 (6)	0.0023 (7)
C2	0.0160 (8)	0.0292 (9)	0.0246 (10)	-0.0018 (6)	0.0001 (7)	-0.0011 (7)
C3	0.0177 (8)	0.0267 (8)	0.0259 (9)	-0.0007 (6)	0.0000 (7)	-0.0014 (8)
C4	0.0149 (8)	0.0299 (8)	0.0259 (9)	-0.0019 (6)	-0.0023 (7)	0.0007 (7)
N5	0.0128 (7)	0.0366 (8)	0.0265 (9)	0.0008 (5)	-0.0004 (6)	0.0013 (7)
N6	0.0119 (7)	0.0586 (11)	0.0260 (8)	-0.0022 (7)	0.0012 (6)	-0.0019 (8)
C7	0.0164 (8)	0.0288 (9)	0.0268 (9)	-0.0026 (7)	-0.0035 (7)	0.0019 (8)
C8	0.0175 (8)	0.0447 (11)	0.0298 (10)	0.0032 (7)	0.0008 (8)	-0.0026 (9)
C9	0.0228 (9)	0.0469 (11)	0.0261 (10)	-0.0006 (8)	-0.0003 (7)	-0.0042 (9)
C10	0.0224 (8)	0.0318 (9)	0.0265 (10)	-0.0038 (7)	-0.0041 (7)	0.0022 (8)
C11	0.0252 (9)	0.0357 (10)	0.0320 (10)	0.0068 (8)	-0.0031 (8)	-0.0003 (9)
C12	0.0254 (9)	0.0363 (9)	0.0244 (9)	0.0042 (8)	0.0003 (7)	-0.0028 (8)
C13	0.0260 (8)	0.0365 (10)	0.0291 (9)	-0.0040 (8)	-0.0014 (8)	0.0014 (8)
N14	0.0332 (9)	0.0541 (11)	0.0333 (9)	-0.0074 (8)	-0.0090 (8)	0.0054 (9)
C16	0.0172 (7)	0.0292 (9)	0.0241 (9)	-0.0039 (7)	-0.0008 (6)	-0.0019 (7)
C17	0.0248 (9)	0.0328 (9)	0.0261 (10)	-0.0002 (7)	0.0017 (7)	-0.0024 (8)
C18	0.0297 (10)	0.0336 (10)	0.0314 (10)	-0.0008 (8)	-0.0043 (8)	0.0041 (8)
C19	0.0300 (9)	0.0406 (10)	0.0202 (9)	-0.0136 (8)	-0.0034 (7)	0.0013 (8)
C20	0.0277 (9)	0.0456 (11)	0.0254 (10)	-0.0079 (8)	0.0058 (8)	-0.0078 (9)
C21	0.0202 (9)	0.0367 (10)	0.0313 (10)	-0.0014 (7)	0.0004 (8)	-0.0033 (8)
F22	0.0503 (8)	0.0578 (8)	0.0236 (6)	-0.0142 (6)	-0.0051 (5)	0.0065 (6)
C23	0.0156 (8)	0.0316 (9)	0.0268 (9)	0.0008 (6)	0.0006 (7)	0.0040 (7)

C24	0.0205 (8)	0.0449 (11)	0.0250 (9)	0.0002 (7)	-0.0024 (7)	-0.0022 (9)
C25	0.0213 (9)	0.0538 (12)	0.0318 (10)	0.0055 (8)	0.0055 (8)	-0.0036 (9)
N26	0.0160 (7)	0.0569 (11)	0.0382 (10)	-0.0002 (7)	0.0001 (7)	0.0016 (9)
C27	0.0206 (9)	0.0542 (12)	0.0337 (11)	-0.0049 (8)	-0.0040 (8)	-0.0026 (10)
C28	0.0210 (8)	0.0428 (11)	0.0265 (9)	-0.0017 (7)	-0.0020 (8)	-0.0022 (9)

Geometric parameters (Å, °)

N1—N5	1.376 (2)	C13—N14	1.147 (3)
N1—C2	1.381 (3)	C16—C17	1.397 (3)
N1—C7	1.415 (2)	C16—C21	1.399 (3)
C2—N6	1.358 (2)	C17—C18	1.389 (3)
C2—C3	1.384 (2)	C17—H17	0.9500
C3—C4	1.417 (3)	C18—C19	1.374 (3)
C3—C16	1.474 (3)	C18—H18	0.9500
C4—N5	1.320 (2)	C19—C20	1.366 (3)
C4—C23	1.487 (2)	C19—F22	1.367 (2)
N6—H6A	0.8816	C20—C21	1.396 (3)
N6—H6B	0.8621	C20—H20	0.9500
C7—C8	1.386 (3)	C21—H21	0.9500
C7—C12	1.395 (3)	C23—C24	1.383 (3)
C8—C9	1.380 (3)	C23—C28	1.389 (3)
C8—H8	0.9500	C24—C25	1.387 (3)
C9—C10	1.400 (3)	C24—H24	0.9500
C9—H9	0.9500	C25—N26	1.336 (3)
C10—C11	1.388 (3)	C25—H25	0.9500
C10—C13	1.440 (3)	N26—C27	1.336 (3)
C11—C12	1.383 (3)	C27—C28	1.383 (3)
C11—H11	0.9500	C27—H27	0.9500
C12—H12	0.9500	C28—H28	0.9500
N5—N1—C2	111.40 (14)	C17—C16—C21	117.97 (18)
N5—N1—C7	117.21 (15)	C17—C16—C3	119.80 (17)
C2—N1—C7	131.39 (15)	C21—C16—C3	122.22 (17)
N6—C2—N1	122.58 (16)	C18—C17—C16	121.39 (18)
N6—C2—C3	130.64 (18)	C18—C17—H17	119.3
N1—C2—C3	106.74 (15)	C16—C17—H17	119.3
C2—C3—C4	104.33 (17)	C19—C18—C17	118.20 (18)
C2—C3—C16	126.37 (16)	C19—C18—H18	120.9
C4—C3—C16	128.50 (17)	C17—C18—H18	120.9
N5—C4—C3	112.93 (16)	C20—C19—F22	119.08 (19)
N5—C4—C23	117.26 (16)	C20—C19—C18	123.03 (18)
C3—C4—C23	129.75 (18)	F22—C19—C18	117.90 (18)
C4—N5—N1	104.59 (15)	C19—C20—C21	118.24 (19)
C2—N6—H6A	120.7	C19—C20—H20	120.9
C2—N6—H6B	120.9	C21—C20—H20	120.9
H6A—N6—H6B	117.0	C20—C21—C16	121.13 (19)
C8—C7—C12	120.14 (18)	C20—C21—H21	119.4

C8—C7—N1	118.43 (16)	C16—C21—H21	119.4
C12—C7—N1	121.39 (18)	C24—C23—C28	117.64 (16)
C9—C8—C7	120.58 (17)	C24—C23—C4	120.48 (17)
C9—C8—H8	119.7	C28—C23—C4	121.79 (17)
C7—C8—H8	119.7	C23—C24—C25	119.40 (18)
C8—C9—C10	119.30 (19)	C23—C24—H24	120.3
C8—C9—H9	120.4	C25—C24—H24	120.3
C10—C9—H9	120.4	N26—C25—C24	123.45 (19)
C11—C10—C9	120.12 (18)	N26—C25—H25	118.3
C11—C10—C13	119.92 (17)	C24—C25—H25	118.3
C9—C10—C13	119.95 (18)	C27—N26—C25	116.60 (16)
C12—C11—C10	120.38 (18)	N26—C27—C28	124.0 (2)
C12—C11—H11	119.8	N26—C27—H27	118.0
C10—C11—H11	119.8	C28—C27—H27	118.0
C11—C12—C7	119.46 (19)	C27—C28—C23	118.87 (19)
C11—C12—H12	120.3	C27—C28—H28	120.6
C7—C12—H12	120.3	C23—C28—H28	120.6
N14—C13—C10	178.9 (2)		
N5—N1—C2—N6	176.84 (17)	C8—C7—C12—C11	-1.5 (3)
C7—N1—C2—N6	-3.2 (3)	N1—C7—C12—C11	-179.04 (17)
N5—N1—C2—C3	-1.1 (2)	C2—C3—C16—C17	-136.16 (19)
C7—N1—C2—C3	178.89 (17)	C4—C3—C16—C17	32.0 (3)
N6—C2—C3—C4	-177.24 (19)	C2—C3—C16—C21	42.5 (3)
N1—C2—C3—C4	0.45 (19)	C4—C3—C16—C21	-149.42 (18)
N6—C2—C3—C16	-6.8 (3)	C21—C16—C17—C18	0.1 (3)
N1—C2—C3—C16	170.87 (17)	C3—C16—C17—C18	178.76 (17)
C2—C3—C4—N5	0.3 (2)	C16—C17—C18—C19	-1.9 (3)
C16—C3—C4—N5	-169.81 (17)	C17—C18—C19—C20	2.1 (3)
C2—C3—C4—C23	-176.61 (17)	C17—C18—C19—F22	-178.44 (16)
C16—C3—C4—C23	13.2 (3)	F22—C19—C20—C21	-179.87 (17)
C3—C4—N5—N1	-0.97 (19)	C18—C19—C20—C21	-0.4 (3)
C23—C4—N5—N1	176.39 (15)	C19—C20—C21—C16	-1.5 (3)
C2—N1—N5—C4	1.26 (19)	C17—C16—C21—C20	1.7 (3)
C7—N1—N5—C4	-178.71 (15)	C3—C16—C21—C20	-176.99 (18)
N5—N1—C7—C8	-27.3 (2)	N5—C4—C23—C24	38.6 (3)
C2—N1—C7—C8	152.71 (19)	C3—C4—C23—C24	-144.6 (2)
N5—N1—C7—C12	150.24 (17)	N5—C4—C23—C28	-137.84 (19)
C2—N1—C7—C12	-29.7 (3)	C3—C4—C23—C28	39.0 (3)
C12—C7—C8—C9	0.5 (3)	C28—C23—C24—C25	0.0 (3)
N1—C7—C8—C9	178.05 (18)	C4—C23—C24—C25	-176.60 (18)
C7—C8—C9—C10	0.9 (3)	C23—C24—C25—N26	0.8 (3)
C8—C9—C10—C11	-1.1 (3)	C24—C25—N26—C27	-0.8 (3)
C8—C9—C10—C13	177.70 (19)	C25—N26—C27—C28	0.1 (3)
C9—C10—C11—C12	0.1 (3)	N26—C27—C28—C23	0.6 (4)
C13—C10—C11—C12	-178.77 (19)	C24—C23—C28—C27	-0.6 (3)
C10—C11—C12—C7	1.3 (3)	C4—C23—C28—C27	175.92 (19)

Hydrogen-bond geometry (Å, °)

<i>D</i> —H \cdots <i>A</i>	<i>D</i> —H	H \cdots <i>A</i>	<i>D</i> \cdots <i>A</i>	<i>D</i> —H \cdots <i>A</i>
N6—H6A \cdots N26 ⁱ	0.88	2.14	2.938 (2)	150
N6—H6B \cdots N14 ⁱⁱ	0.86	2.58	3.292 (3)	141

Symmetry codes: (i) $x+1, y, z$; (ii) $-x+3/2, y, z-1/2$.