1-(2,4-Dichlorophenyl)-5-(2-nitroanilino)-1H-pyrazole-4-carbonitrile

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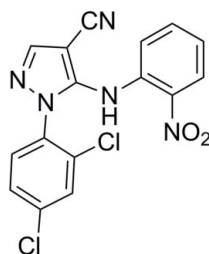
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In the title compound, $C_{16}H_9Cl_2N_5O_2$, the folded molecular conformation is characterized by a dihedral angle between the two benzene rings of 74.03 (5)°. An intramolecular N—H⋯O hydrogen bond is observed between the H atom of the amide group and a nitro-group O atom. Intermolecular C—H⋯O and N—H⋯N hydrogen bonds feature in the crystal packing.

Related literature

For general background to N-1-diaryl-1H-pyrazol-5-amine derivatives as synthetic intermediates in the preparation of medicinal compounds and the synthesis of the title compound, see: Markwalder et al. (2004); Mehdi et al. (2010). For the pharmacological activity of the 5-aminopyrazole nucleus, see: Nils et al. (2010); Aymn et al. (2005).

Experimental

Crystal data

$C_{16}H_9Cl_2N_5O_2$	Orthorhombic, $Pbcn$
$M_r = 374.18$	$a = 13.878$ (3) Å
$b = 13.475$ (3) Å	Mo $K\alpha$ radiation
$c = 17.421$ (4) Å	$\mu = 0.42$ mm^{-1}
$V = 3257.7$ (11) Å^3	$T = 293$ K
$Z = 8$	$0.20 \times 0.18 \times 0.12$ mm

Data collection

Rigaku Saturn724 CCD diffractometer	31011 measured reflections
Absorption correction: multi-scan (*CrystalClear*; Rigaku/MSC, 2005)	3888 independent reflections
	2738 reflections with $I > 2\sigma(I)$
$T_{min} = 0.921$, $T_{max} = 0.951$	$R_{int} = 0.050$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.052$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.142$	
$S = 1.04$	
3888 reflections	$\Delta\rho_{max} = 0.24$ e Å^{-3}
231 parameters	$\Delta\rho_{min} = -0.24$ e Å^{-3}

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

D—H⋯A	D—H	H⋯A	D⋯A	D—H⋯A
C9—H9⋯O2^i	0.93	2.51	3.050 (3)	117
C5—H5⋯O1^{ii}	0.93	2.58	3.374 (3)	143
N4—H4⋯N3^{iii}	0.82 (3)	2.62 (3)	3.201 (3)	129 (2)
N4—H4⋯O1	0.82 (3)	2.02 (3)	2.608 (2)	128 (2)

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

Data collection: *RAPID-AUTO* (Rigaku, 1998); cell refinement: *RAPID-AUTO*; data reduction: *CrystalClear* (Rigaku/MSC, 2005); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXTL*.

References

Aymn, E. R., Ahmed, H. S., Mohamed, I. H. & Hassan, M. A. (2005). *Acta Chim. Slov.* **52**, 429–434.

Markwalder, J. A., Arnone, M. R., Benfield, P. A., Boisclair, M., Burton, C. R., Chang, C. H., Cox, S. S., Czerniak, P. M., Dean, C. L., Doleniak, D., Grafstrom, R., Harrison, B. A., Kaltenbach, R. F., Nugiel, D. A., Rossi, K. A., Sherk, S. R., Sisk, L. M., Stouten, P., Trainor, G. L., Worland, P. & Seitz, S. P. (2004). *J. Med. Chem.* **47**, 5894–5911.

Mehdi, B., Ghodsieh, B., Maryam, V., Ali, S., Mehdi, P., Mansour, M., Parvaneh, P. & Maryam, A. (2010). *Tetrahedron*, **60**, 2897–2902.

Nils, G., Lars, B., Heinrich, M., Dirk, S., Nicole, T., Klemens, L., Raimund, K. & Peter, K. (2010). *Bioorg. Med. Chem. Lett.* **20**, 5891–5894.

Rigaku (1998). *RAPID-AUTO*. Rigaku Corporation, Tokyo, Japan.

Rigaku/MSC (2005). *Crystal Structure*. Rigaku/MSC, The Woodlands, Texas, USA.

Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.

supporting information

1-(2,4-Dichlorophenyl)-5-(2-nitroanilino)-1*H*-pyrazole-4-carbonitrile

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S1. Comment

N-1-Diaryl-1*H*-pyrazol-5-amine derivatives possess therapeutic value. They are synthetic intermediates in the preparation of medicinal compounds (Markwalder *et al.*, 2004; Mehdi *et al.*, 2010). 5-Aminopyrazole nucleus is associated with several pharmacological activities such as selective adenosine A1 receptor antagonists (Nils *et al.*, 2010) and antimicrobial activity (Aymn *et al.*, 2005). In view of this biological importance a part of our ongoing studies of pyrazole derivatives includes the crystal structure determination of the title compound. The folded molecular conformation is characterised by the dihedral angle between the two benzene rings of 74.03 (5) ° (Fig. 1). Intramolecular N—H⋯O hydrogen bond between the hydrogen of the amide group and the nitro group O atom is observed. The crystal packing is stabilised by intermolecular C—H⋯O and N—H⋯N hydrogen bonds (Table 1).

S2. Experimental

To a mixture of 5-amino-1-(2,4-dichlorophenyl)-1*H*-pyrazole-4-carbonitrile (3.0 g, 11.85 mmol) and *o*-nitrochloro-benzene (3.74 g, 23.74 mmol) in dimethyl sulfoxide (10 mL) lithium hydroxide monohydrate (0.74 g, 17.87 mmol) was added. The solution was heated at 343 K for 4.5 h. After cooling to 293 K, 50 mL of water was added to the reaction mixture. The resulting precipitate was collected by filtration, washed with ethanol to yield the title compound as a brown yellow solid (3.28 g, 73.95%). Crystals suitable for X-ray analysis were obtained from ethanol:acetone (1:1) solution by slow evaporation.

S3. Refinement

All H atoms were geometrically positioned (C—H 0.93–0.98 Å) and treated as riding, with U_{iso}(H) = 1.2Ueq(C).
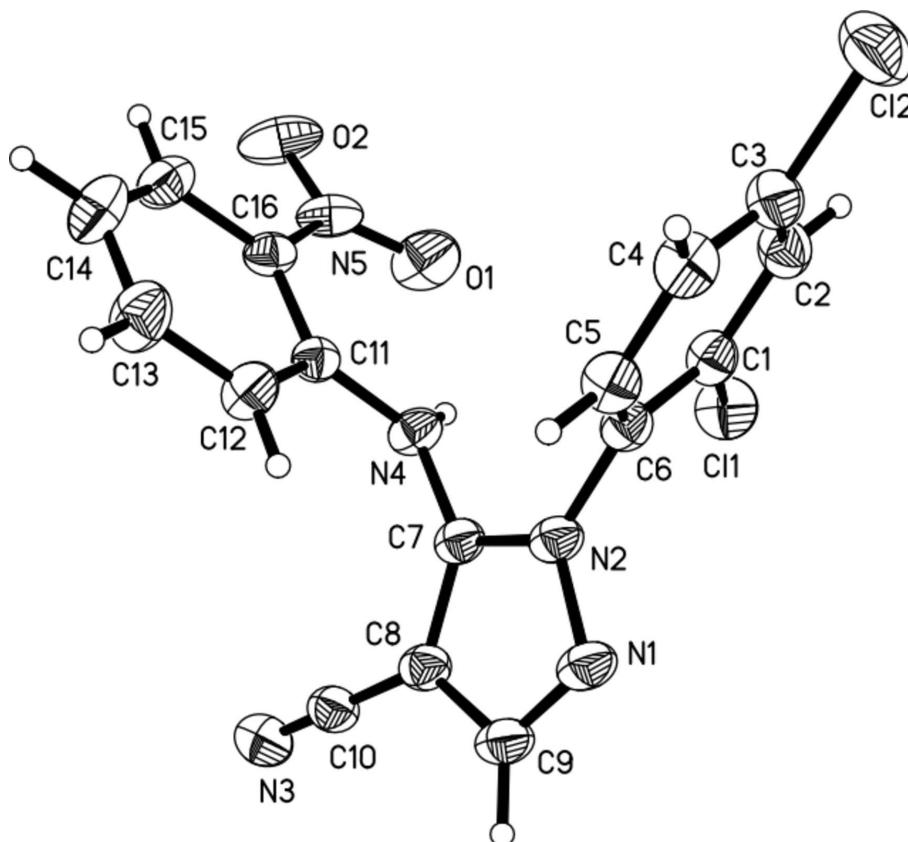
Figure 1
The structure of $C_{16}H_9Cl_2N_5O_2$ with all non-H atom-labelling scheme and ellipsoids drawn at the 50% probability level.

1-(2,4-Dichlorophenyl)-5-(2-nitroanilino)-1*H*-pyrazole-4-carbonitrile

Crystal data

$C_{16}H_9Cl_2N_5O_2$	$F(000) = 1520$
$M_r = 374.18$	$D_x = 1.526$ Mg m^{-3}
Orthorhombic, *Pbcn*	Mo *Kα* radiation, $\lambda = 0.71073$ Å
Hall symbol: -P2n2ab	Cell parameters from 7017 reflections
$a = 13.878$ (3) Å	$\theta = 2.4–28.0°$
$b = 13.475$ (3) Å	$\mu = 0.42$ mm^{-1}
$c = 17.421$ (4) Å	$T = 293$ K
$V = 3257.7$ (11) Å^3	Prism, yellow
$Z = 8$	$0.20 \times 0.18 \times 0.12$ mm

Data collection

Rigaku Saturn724 CCD diffractometer	31011 measured reflections
Radiation source: rotating anode	3888 independent reflections
Multilayer monochromator	2738 reflections with $I > 2\sigma(I)$
Detector resolution: 7.31 pixels mm^{-1}	$R_{int} = 0.050$
ω scans	$\theta_{max} = 27.9°$, $\theta_{min} = 2.3°$
Absorption correction: multi-scan (*CrystalClear*; Rigaku/MSC, 2005)	$h = -17 \rightarrow 17$
	$k = -17 \rightarrow 16$
$T_{min} = 0.921$, $T_{max} = 0.951$	$l = -22 \rightarrow 22$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.052$

$wR(F^2) = 0.142$

$S = 1.04$

3888 reflections

231 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 atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0759P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} = 0.001$

$\Delta\rho_{max} = 0.24$ e Å^{-3}

$\Delta\rho_{min} = -0.24$ e Å^{-3}

Extinction correction: *SHELXL97* (Sheldrick, 2008), Fc*=kFc[1+0.001xFc$^2\lambda^3$/sin(2θ)]$^{-1/4}$

Extinction coefficient: 0.0166 (13)

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 (Å^2)

	x	y	z	U_{iso}*/U_{eq}
Cl1	0.15552 (5)	0.60779 (4)	0.46994 (4)	0.0673 (2)
Cl2	−0.14562 (5)	0.48959 (6)	0.30041 (5)	0.0881 (3)
O1	0.35014 (15)	0.63038 (12)	0.30863 (12)	0.0858 (6)
O2	0.41521 (15)	0.62525 (14)	0.19700 (10)	0.0914 (6)
N1	0.20172 (14)	0.33598 (13)	0.53423 (10)	0.0540 (5)
N2	0.20985 (13)	0.39203 (11)	0.46920 (9)	0.0467 (4)
N3	0.54146 (17)	0.37889 (14)	0.51865 (12)	0.0667 (5)
N4	0.32727 (13)	0.46781 (13)	0.38776 (9)	0.0477 (4)
N5	0.37959 (14)	0.58365 (14)	0.25298 (11)	0.0609 (5)
C1	0.09266 (15)	0.51444 (13)	0.42412 (12)	0.0481 (5)
C2	0.00946 (15)	0.53705 (15)	0.38503 (13)	0.0558 (6)
H2A	−0.0128	0.6021	0.3830	0.067*
C3	−0.04013 (16)	0.46247 (16)	0.34907 (13)	0.0556 (6)
C4	−0.00852 (16)	0.36558 (16)	0.35107 (13)	0.0575 (6)
H4A	−0.0428	0.3158	0.3261	0.069*
C5	0.07443 (15)	0.34366 (14)	0.39045 (12)	0.0521 (5)
H5	0.0962	0.2785	0.3925	0.063*
C6	0.12581 (15)	0.41746 (14)	0.42708 (11)	0.0446 (5)
C7	0.30239 (15)	0.41365 (13)	0.45245 (11)	0.0438 (5)
C8	0.35782 (15)	0.37153 (15)	0.50928 (12)	0.0476 (5)
C9	0.29092 (16)	0.32434 (15)	0.55794 (11)	0.0536 (5)
H9	0.3079	0.2890	0.6018	0.064*
C10	0.45966 (19)	0.37500 (15)	0.51458 (12)	0.0516 (5)

C11	0.34423 (13)	0.42402 (14)	0.31790 (11)	0.0407 (4)
C12	0.33508 (16)	0.32211 (15)	0.30894 (12)	0.0559 (6)
H12	0.3164	0.2838	0.3508	0.067*
C13	0.35285 (19)	0.27656 (18)	0.24013 (15)	0.0735 (7)
H13	0.3455	0.2082	0.2360	0.088*
C14	0.3815 (2)	0.3305 (2)	0.17670 (14)	0.0750 (7)
H14	0.3942	0.2988	0.1304	0.090*
C15	0.39084 (16)	0.4299 (2)	0.18286 (12)	0.0608 (6)
H15	0.4098	0.4670	0.1404	0.073*
C16	0.37242 (14)	0.47708 (15)	0.25204 (11)	0.0453 (5)
H4	0.3360 (18)	0.528 (2)	0.3926 (15)	0.077 (8)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0852 (5)	0.0448 (3)	0.0719 (4)	−0.0062 (3)	−0.0050 (3)	−0.0152 (3)
Cl2	0.0593 (4)	0.1038 (6)	0.1013 (6)	0.0108 (3)	−0.0192 (4)	−0.0065 (4)
O1	0.1372 (18)	0.0455 (10)	0.0746 (13)	−0.0036 (9)	0.0066 (11)	0.0082 (9)
O2	0.1296 (16)	0.0868 (13)	0.0577 (11)	−0.0414 (11)	−0.0163 (11)	0.0338 (9)
N1	0.0691 (13)	0.0515 (10)	0.0413 (9)	−0.0029 (8)	0.0045 (8)	0.0103 (7)
N2	0.0577 (11)	0.0429 (9)	0.0394 (9)	−0.0014 (7)	0.0013 (7)	0.0059 (6)
N3	0.0697 (15)	0.0613 (12)	0.0691 (14)	0.0055 (10)	−0.0084 (10)	0.0057 (9)
N4	0.0668 (11)	0.0363 (9)	0.0401 (9)	−0.0063 (8)	0.0028 (8)	0.0020 (7)
N5	0.0745 (13)	0.0594 (12)	0.0488 (12)	−0.0166 (10)	−0.0150 (10)	0.0172 (9)
C1	0.0547 (13)	0.0399 (10)	0.0499 (12)	−0.0017 (9)	0.0047 (10)	−0.0043 (8)
C2	0.0593 (14)	0.0464 (12)	0.0617 (14)	0.0075 (10)	0.0046 (11)	−0.0014 (10)
C3	0.0485 (13)	0.0607 (14)	0.0576 (14)	0.0001 (10)	0.0000 (10)	0.0011 (10)
C4	0.0570 (14)	0.0552 (13)	0.0603 (14)	−0.0137 (11)	0.0003 (11)	−0.0063 (10)
C5	0.0603 (13)	0.0374 (10)	0.0586 (13)	−0.0049 (9)	0.0041 (11)	−0.0001 (9)
C6	0.0504 (12)	0.0412 (10)	0.0421 (11)	−0.0031 (8)	0.0036 (9)	0.0022 (8)
C7	0.0556 (13)	0.0383 (10)	0.0375 (10)	0.0000 (8)	0.0012 (9)	0.0007 (7)
C8	0.0616 (14)	0.0411 (10)	0.0400 (11)	0.0023 (9)	−0.0034 (9)	−0.0011 (8)
C9	0.0733 (16)	0.0472 (12)	0.0401 (11)	0.0021 (10)	−0.0014 (10)	0.0068 (8)
C10	0.0625 (16)	0.0450 (11)	0.0472 (12)	0.0066 (10)	−0.0054 (10)	0.0006 (8)
C11	0.0394 (10)	0.0420 (10)	0.0406 (10)	−0.0025 (8)	−0.0020 (8)	0.0023 (8)
C12	0.0729 (14)	0.0439 (11)	0.0511 (13)	−0.0054 (10)	0.0077 (11)	−0.0017 (9)
C13	0.097 (2)	0.0552 (15)	0.0684 (17)	−0.0038 (12)	0.0093 (14)	−0.0156 (12)
C14	0.0862 (18)	0.0849 (19)	0.0540 (15)	−0.0084 (15)	0.0118 (13)	−0.0203 (13)
C15	0.0567 (14)	0.0836 (17)	0.0422 (12)	−0.0094 (12)	0.0042 (10)	0.0003 (11)
C16	0.0428 (11)	0.0514 (11)	0.0419 (11)	−0.0071 (9)	−0.0053 (8)	0.0061 (8)

Geometric parameters (Å, º)

Cl1—C1	1.726 (2)	C4—C5	1.372 (3)
Cl2—C3	1.731 (2)	C4—H4A	0.9300
O1—N5	1.226 (3)	C5—C6	1.380 (3)
O2—N5	1.229 (2)	C5—H5	0.9300
N1—C9	1.314 (3)	C7—C8	1.376 (3)

N1—N2	1.366 (2)	C8—C9	1.409 (3)
N2—C7	1.349 (3)	C8—C10	1.417 (3)
N2—C6	1.420 (3)	C9—H9	0.9300
N3—C10	1.139 (3)	C11—C12	1.388 (3)
N4—C11	1.373 (2)	C11—C16	1.407 (3)
N4—C7	1.386 (2)	C12—C13	1.369 (3)
N4—H4	0.82 (3)	C12—H12	0.9300
N5—C16	1.440 (3)	C13—C14	1.381 (3)
C1—C2	1.375 (3)	C13—H13	0.9300
C1—C6	1.386 (3)	C14—C15	1.350 (3)
C2—C3	1.370 (3)	C14—H14	0.9300
C2—H2A	0.9300	C15—C16	1.386 (3)
C3—C4	1.378 (3)	C15—H15	0.9300
C9—N1—N2	104.40 (16)	N2—C7—C8	106.71 (18)
C7—N2—N1	112.17 (16)	N2—C7—N4	121.77 (18)
C7—N2—C6	128.19 (16)	C8—C7—N4	131.51 (19)
N1—N2—C6	119.60 (17)	C7—C8—C9	104.52 (19)
C11—N4—C7	122.49 (17)	C7—C8—C10	126.21 (19)
C11—N4—H4	119.2 (18)	C9—C8—C10	129.26 (19)
C7—N4—H4	118.1 (18)	N1—C9—C8	112.19 (18)
O1—N5—O2	121.8 (2)	N1—C9—H9	123.9
O1—N5—C16	119.88 (18)	C8—C9—H9	123.9
O2—N5—C16	118.3 (2)	N3—C10—C8	179.2 (2)
C2—C1—C6	120.40 (18)	N4—C11—C12	120.61 (17)
C2—C1—Cl1	119.47 (15)	N4—C11—C16	123.50 (17)
C6—C1—Cl1	120.13 (17)	C12—C11—C16	115.88 (18)
C3—C2—C1	119.08 (19)	C13—C12—C11	121.7 (2)
C3—C2—H2A	120.5	C13—C12—H12	119.1
C1—C2—H2A	120.5	C11—C12—H12	119.1
C2—C3—C4	121.6 (2)	C12—C13—C14	121.1 (2)
C2—C3—Cl2	119.61 (17)	C12—C13—H13	119.5
C4—C3—Cl2	118.80 (17)	C14—C13—H13	119.5
C5—C4—C3	118.9 (2)	C15—C14—C13	119.1 (2)
C5—C4—H4A	120.5	C15—C14—H14	120.4
C3—C4—H4A	120.5	C13—C14—H14	120.4
C4—C5—C6	120.63 (19)	C14—C15—C16	120.4 (2)
C4—C5—H5	119.7	C14—C15—H15	119.8
C6—C5—H5	119.7	C16—C15—H15	119.8
C5—C6—C1	119.4 (2)	C15—C16—C11	121.82 (19)
C5—C6—N2	119.31 (17)	C15—C16—N5	117.01 (19)
C1—C6—N2	121.28 (17)	C11—C16—N5	121.12 (18)
C9—N1—N2—C7	0.7 (2)	N4—C7—C8—C9	−178.5 (2)
C9—N1—N2—C6	178.77 (16)	N2—C7—C8—C10	179.56 (19)
C6—C1—C2—C3	0.0 (3)	N4—C7—C8—C10	0.3 (4)
Cl1—C1—C2—C3	−179.77 (17)	N2—N1—C9—C8	−0.3 (2)
C1—C2—C3—C4	−0.1 (3)	C7—C8—C9—N1	−0.3 (2)

C1—C2—C3—Cl2	179.38 (17)	C10—C8—C9—N1	−179.1 (2)
C2—C3—C4—C5	0.3 (3)	C7—C8—C10—N3	45 (19)
Cl2—C3—C4—C5	−179.17 (17)	C9—C8—C10—N3	−136 (19)
C3—C4—C5—C6	−0.4 (3)	C7—N4—C11—C12	1.3 (3)
C4—C5—C6—C1	0.3 (3)	C7—N4—C11—C16	−177.99 (18)
C4—C5—C6—N2	178.21 (19)	N4—C11—C12—C13	−179.1 (2)
C2—C1—C6—C5	−0.1 (3)	C16—C11—C12—C13	0.2 (3)
Cl1—C1—C6—C5	179.68 (16)	C11—C12—C13—C14	0.5 (4)
C2—C1—C6—N2	−177.94 (18)	C12—C13—C14—C15	−0.8 (4)
Cl1—C1—C6—N2	1.8 (3)	C13—C14—C15—C16	0.3 (4)
C7—N2—C6—C5	110.9 (2)	C14—C15—C16—C11	0.4 (3)
N1—N2—C6—C5	−66.7 (2)	C14—C15—C16—N5	−177.1 (2)
C7—N2—C6—C1	−71.2 (3)	N4—C11—C16—C15	178.6 (2)
N1—N2—C6—C1	111.1 (2)	C12—C11—C16—C15	−0.7 (3)
N1—N2—C7—C8	−0.9 (2)	N4—C11—C16—N5	−3.9 (3)
C6—N2—C7—C8	−178.74 (17)	C12—C11—C16—N5	176.78 (18)
N1—N2—C7—N4	178.39 (17)	O1—N5—C16—C15	168.9 (2)
C6—N2—C7—N4	0.6 (3)	O2—N5—C16—C15	−10.8 (3)
C11—N4—C7—N2	−88.3 (2)	O1—N5—C16—C11	−8.7 (3)
C11—N4—C7—C8	90.8 (3)	O2—N5—C16—C11	171.6 (2)
N2—C7—C8—C9	0.7 (2)		

Hydrogen-bond geometry (Å, °)

D—H⋯A	D—H	H⋯A	D⋯A	D—H⋯A
C9—H9⋯O2[i]	0.93	2.51	3.050 (3)	117
C5—H5⋯O1[ii]	0.93	2.58	3.374 (3)	143
N4—H4⋯N3[iii]	0.82 (3)	2.62 (3)	3.201 (3)	129 (2)
N4—H4⋯O1	0.82 (3)	2.02 (3)	2.608 (2)	128 (2)

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