IUCrData

ISSN 2414-3146

A polymorph of *N*′-[(4-hydroxyphenyl)methylidene]pyridine-4-carbohydrazide

Lincy Tom,[a]* Jerry P. Jasinski,[b]‡ Victoria A. Smolenski[b] and M. R. Prathapachandra Kurup[c]

[a]Department of Chemistry, Nirmala College Muvattupuzha, Ernakulam, 686661, Kerala, India, [b]Department of Chemistry, Keene, State College, 229 Main Street, Keene, NH03435-2001, USA, and [c]Department of Chemistry, Central University of Kerala, Tejaswini Hills, Periye, Kasaragod 671 320, Kerala, India. *Correspondence e-mail: lincytom@nirmalacollege.ac.in

Received 11 March 2026
Accepted 24 March 2026

Edited by M. Weil, Vienna University of Technology, Austria

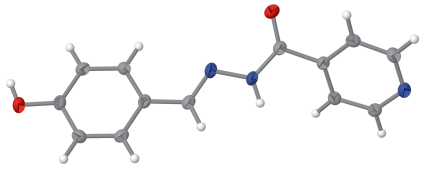
‡ Deceased.

Keywords: isoniazid; crystal structure; hydrogen bonding; packing polymorphism; Hirshfeld.

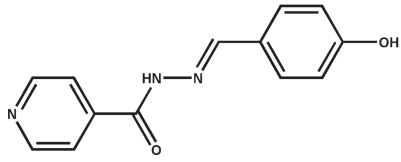
Structural data: full structural data are available from iucrdata.iucr.org

The synthesis and single-crystal X-ray diffraction analysis of a polymorphic form of the isoniazid derivative *N*′-[(4-hydroxyphenyl)methylidene]pyridine-4-carbohydrazide, $C_{13}H_{11}N_3O_2$, are reported, revealing that both the molecular conformation and the hydrogen-bonding scheme differ in the two polymorphs. The crystal packing of the title polymorph is primarily consolidated by N—H···O and O—H···N hydrogen-bonding interactions, leading to the formation of a supramolecular layer parallel to (001). The intermolecular contacts were further quantified and analysed using Hirshfeld surface analysis.

3D view



Chemical scheme



Structure description

N-containing heterocycles constitute a major class of natural products and possess a wide range of applications (Goetz *et al.*, 2015). They are widely used as starting materials for the synthesis of biologically important compounds. Among them, isoniazid-based scaffolds, which contain nitrogen heterocycles, have attracted considerable attention in medicinal chemistry due to their diverse biological activities, including anti-carcinogenic, anti-fungal, anti-mycobacterial, analgesic, antibacterial, and antiviral properties (Tom *et al.*, 2020; Rodrigues *et al.*, 2014; Mohanram & Meshram, 2014; Judge *et al.*, 2013; Hu *et al.*, 2017; Costa *et al.*, 2024). Among these, their anti-tubercular activity is particularly significant. As part of our ongoing research in this field, we report here on the synthesis and crystal structure of a polymorph of *N*′-[(4-hydroxyphenyl)methylidene]pyridine-4-carbohydrazide, an isoniazid-derived molecule with potential antitubercular activity.

Single-crystal X-ray diffraction analysis of the title compound, $C_{13}H_{11}N_3O_2$, revealed that it is dimorphic. The title P_A polymorph (Fig. 1) crystallizes in the monoclinic space group $P2_1/c$. The previously reported polymorph P_B (Deng *et al.*, 2005) crystallizes in the

OPEN ACCESS
Published under a CC BY 4.0 licence

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O1^{i}	0.86	2.34	3.1452 (15)	156
O2—H2···N3^{ii}	0.82	1.96	2.7356 (16)	159

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

same space group type but with different unit-cell parameters. The differences between the P_A and P_B forms can mainly be attributed to crystal-packing effects. An additional monohydrated orthorhombic form has also been reported (Tai *et al.*, 2007). The overlay of the two molecules of the polymorphs (Fig. 2) indicates that they possess distinct molecular conformations. P_A adopts a slightly twisted conformation compared to the more planar P_B form. The dihedral angles between the pyridine ring (C2, C3, C4, N3, C5, C6) and hydrazide moiety (N1, N2, C1, O1, C7) are 36.14 (8)° in P_A and 9.59 (8)° in P_B. Similarly, the dihedral angles between the hydrazide moiety and phenol ring are 23.97 (8)° in P_A and 3.96 (7)° in P_B.

The molecular packing and hydrogen-bonding patterns differ significantly in the two extended structures of P_A and P_B. The polymorphs exhibit different combinations of hydrogen-bonding donor and acceptor sites, leading to distinct supramolecular networks. The P_A polymorph reported here exhibits two types of classical hydrogen-bonding interactions (Table 1). The NH group of the N═NH—C═O moiety is hydrogen-bonded to the O atom of the same moiety of a neighbouring molecule into chains extending parallel to [100]. These chains are connected through O—H···N hydrogen-bonding interactions involving the phenol OH group and the pyridine N atom, leading to the formation of a supramolecular layer extending parallel to (001) (Fig. 3). In polymorph P_B, the NH group of the N═NH—C═O moiety bonds to the pyridine N atom, and the phenol OH group forms bifurcated

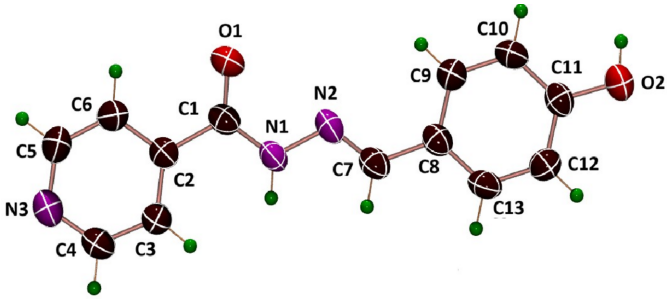


Figure 1
Molecular structure of polymorph P_A with displacement ellipsoids drawn at the 30% probability level.

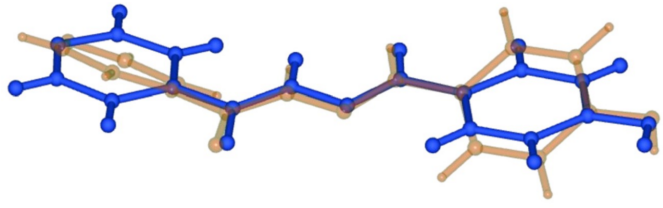


Figure 2
Superimposition of the molecular structures of P_A (gold) and P_B (blue).

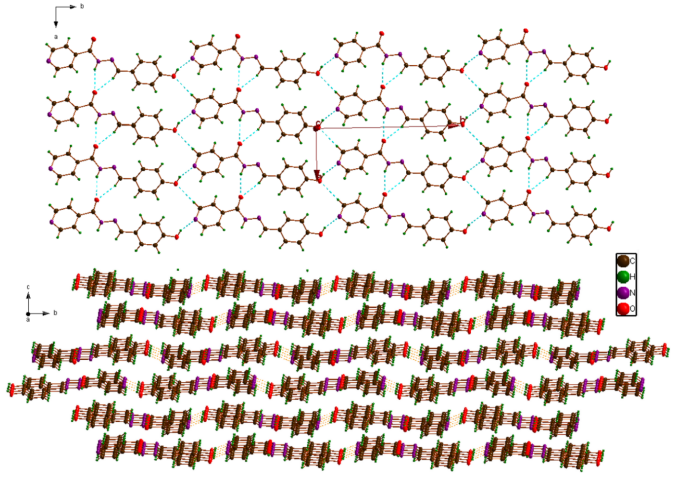


Figure 3
Formation of supramolecular (001) layers in the crystal structure of P_A. Hydrogen bonds are shown as dotted lines.

hydrogen bonds to the N═NH—C═O moiety and the carbonyl O atom of neighbouring molecules, thus leading to a different supramolecular arrangement.

To visualize and quantify the contributions of intermolecular interactions in the supramolecular assembly of the title compound, a Hirshfeld surface (HS) analysis (Spackman & Jayatilaka, 2009) was performed using *CrystalExplorer* (Spackman *et al.*, 2021). The Hirshfeld surface mapped over d_{norm} is shown in Fig. 4, where prominent deep-red spots correspond to significant intermolecular contacts. These spots

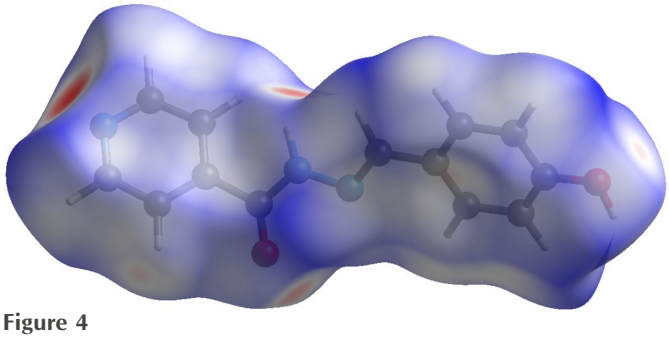


Figure 4
The Hirshfeld surface of P_A mapped over d_{norm}.

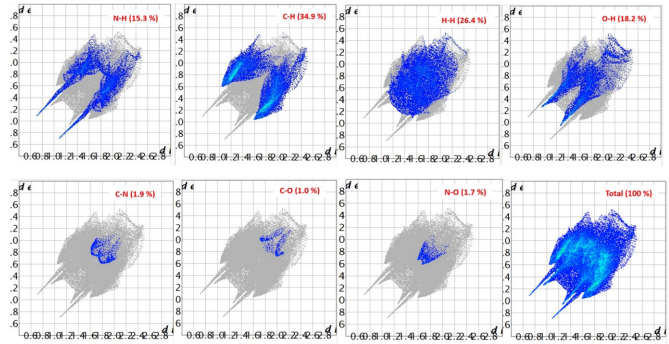


Figure 5
The two-dimensional fingerprint plots for P_A for different contact types.

appear around atoms N3, N1, O1 and O2, indicating that these atoms participate in the intermolecular hydrogen bonds, as discussed above. The associated two-dimensional fingerprint plots provide quantitative insight into the various non-covalent interactions contributing to the crystal packing. The H···H, C···H, N···H and O···H, interactions dominate the packing, collectively accounting for approximately 95% of the total Hirshfeld surface area (Fig. 5).

Synthesis and crystallization

A mixture of *p*-hydroxybenzaldehyde (1 mmol) and isonicotinic hydrazide (1 mmol) was refluxed in methanol (20 ml) at 343 K for 30 min. After completion of the reaction, the mixture was allowed to cool to room temperature. Colourless crystals suitable for X-ray diffraction were obtained by slow evaporation of the solution at room temperature.

Refinement

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

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{13}H_{11}N_3O_2$
M_r	241.25
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	293
a, b, c (Å)	5.36340 (13), 14.4462 (4), 14.6619 (4)
β (°)	91.229 (3)
V (Å^3)	1135.75 (5)
Z	4
Radiation type	Cu $K\alpha$
μ (mm^{-1})	0.81
Crystal size (mm)	0.42 × 0.33 × 0.29
Data collection	
Diffractometer	Rigaku Oxford Diffraction Gemini Eos
Absorption correction	Multi-scan (*CrysAlis PRO*; Rigaku OD, 2015)
T_{min}, T_{max}	0.858, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	7898, 2185, 1901
R_{int}	0.027
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.624
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.039, 0.112, 1.05
No. of reflections	2185
No. of parameters	164
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.22, −0.25

Computer programs: *CrysAlis PRO* (Rigaku OD, 2015), *SHELXT* (Sheldrick, 2015*a*), *SHELXL* (Sheldrick, 2015*b*), *ORTEP-3 for Windows* (Farrugia, 2012), *Mercury* (Macrae *et al.*, 2020) and *publCIF* (Westrip, 2010).

Acknowledgements

The NSF–MRI program (grant No. CHE-1039027) is acknowledged for funds to purchase the Rigaku X-ray diffractometer.

References

Costa, W. D., da Silva Mendes, F. R., Almeida-Neto, F. W. Q., Marinho, E. S., Barreto, A. C. H., Braga, M. F. B. M., Guedes, J. M., Marinho, M. M., Julião, M. S. S., Canuto, K. M., Teixeira, A. M. R. & Silva dos Santos, H. (2024). *J. Mol. Struct.* **1309**, 138117–138126.
Deng, Q.-L., Yu, M., Chen, X., Diao, C.-H., Jing, Z.-L. & Fan, Z. (2005). *Acta Cryst.* E**61**, o2545–o2546.
Farrugia, L. J. (2012). *J. Appl. Cryst.* **45**, 849–854.
Goetz, A. E., Shah, T. K. & Garg, N. K. (2015). *Chem. Commun.* **51**, 34–45.
Hu, Y.-Q., Zhang, S., Zhao, F., Gao, C., Feng, L.-S., Lv, Z.-S., Xu, Z. & Wu, X. (2017). *Eur. J. Med. Chem.* **133**, 255–267.
Judge, V., Narasimhan, B., Ahuja, M., Sriram, D., Yogeeswari, P., De Clercq, E., Pannecouque, C. & Balzarini, J. (2013). *Med. Chem.* **9**, 53–76.
Macrae, C. F., Sovago, I., Cottrell, S. J., Galek, P. T. A., McCabe, P., Pidcock, E., Platings, M., Shields, G. P., Stevens, J. S., Towler, M. & Wood, P. A. (2020). *J. Appl. Cryst.* **53**, 226–235.
Mohanram, I. & Meshram, J. (2014). *Med. Chem. Res.* **23**, 939–947.
Rigaku OD (2015). *CrysAlis PRO*. Rigaku Americas, The Woodlands, Texas, USA.
Rodrigues, F. A. R., Oliveira, A. C., Cavalcanti, B. C., Pessoa, C., Pinheiro, A. C. & de Souza, M. V. (2014). *Sci. Pharm.* **82**, 21–28.
Sheldrick, G. M. (2015*a*). *Acta Cryst.* A**71**, 3–8.
Sheldrick, G. M. (2015*b*). *Acta Cryst.* C**71**, 3–8.
Spackman, M. A. & Jayatilaka, D. (2009). *CrystEngComm* **11**, 19–32.
Spackman, P. R., Turner, M. J., McKinnon, J. J., Wolff, S. K., Grimwood, D. J., Jayatilaka, D. & Spackman, M. A. (2021). *J. Appl. Cryst.* **54**, 1006–1011.
Tai, X.-S., Kong, F.-Y. & Yin, J. (2007). *Acta Cryst.* E**63**, o79–o80.
Tom, L., Nirmal, C. R., Dusthackeer, A., Magizhaveni, B. & Kurup, M. R. P. (2020). *New J. Chem.* **44**, 4467–4477.
Westrip, S. P. (2010). *J. Appl. Cryst.* **43**, 920–925.

full crystallographic data

IUCrData (2026). **11**, x260314 [https://doi.org/10.1107/S2414314626003147]

A polymorph of *N*′-[(4-hydroxyphenyl)methylidene]pyridine-4-carbohydrazide

Lincy Tom, Jerry P. Jasinski, Victoria A. Smolenski and M. R. Prathapachandra Kurup

N′-[(4-Hydroxyphenyl)methylidene]pyridine-4-carbohydrazide

Crystal data

$C_{13}H_{11}N_3O_2$
M_r = 241.25
Monoclinic, $P2_1/c$
a = 5.36340 (13) Å
b = 14.4462 (4) Å
c = 14.6619 (4) Å
β = 91.229 (3)°
V = 1135.75 (5) Å^3
Z = 4
$F(000)$ = 504
D_x = 1.411 Mg m^{-3}
Cu $K\alpha$ radiation, λ = 1.54184 Å
Cell parameters from 3210 reflections
θ = 4.3–71.3°
μ = 0.81 mm^{-1}
T = 293 K
Block, pale yellow
0.42 × 0.33 × 0.29 mm

Data collection

Rigaku Oxford Diffraction Gemini Eos diffractometer
Radiation source: Enhance (Cu) X-ray Source
ω scans
Absorption correction: multi-scan (CrysAlisPro; Rigaku OD, 2015)
T_{min} = 0.858, T_{max} = 1.000
7898 measured reflections
2185 independent reflections
1901 reflections with $I > 2\sigma(I)$
R_{int} = 0.027
θ_{max} = 74.3°, θ_{min} = 4.3°
h = −6→5
k = −17→17
l = −17→18

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.039
$wR(F^2)$ = 0.112
S = 1.05
2185 reflections
164 parameters
0 restraints
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0635P)^2 + 0.3435P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.25 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}
C1	0.4746 (3)	0.44240 (9)	0.39335 (9)	0.0229 (3)
C2	0.5399 (2)	0.34115 (9)	0.39757 (9)	0.0211 (3)
C3	0.7526 (2)	0.30837 (9)	0.43964 (9)	0.0235 (3)
H3	0.863180	0.348585	0.469094	0.028*
C4	0.7997 (3)	0.21405 (10)	0.43747 (10)	0.0252 (3)
H4	0.943707	0.192648	0.466990	0.030*
C5	0.4466 (3)	0.18484 (10)	0.35751 (10)	0.0269 (3)
H5	0.337940	0.143061	0.329277	0.032*
C6	0.3834 (2)	0.27780 (10)	0.35686 (9)	0.0246 (3)
H6	0.235113	0.297153	0.328877	0.029*
C7	0.8580 (3)	0.63450 (9)	0.36248 (9)	0.0236 (3)
H7	0.996667	0.598599	0.349456	0.028*
C8	0.8798 (2)	0.73497 (9)	0.35866 (9)	0.0218 (3)
C9	0.6961 (2)	0.79454 (10)	0.39373 (9)	0.0237 (3)
H9	0.554751	0.769727	0.420074	0.028*
C10	0.7254 (3)	0.88975 (10)	0.38910 (10)	0.0262 (3)
H10	0.605271	0.928803	0.412908	0.031*
C11	0.9400 (3)	0.92725 (10)	0.34775 (10)	0.0252 (3)
C12	1.1243 (3)	0.86858 (10)	0.31337 (10)	0.0250 (3)
H12	1.265131	0.893409	0.286667	0.030*
C13	1.0954 (3)	0.77356 (10)	0.31942 (10)	0.0240 (3)
H13	1.218714	0.734688	0.297531	0.029*
N1	0.6758 (2)	0.49791 (8)	0.38618 (8)	0.0244 (3)
H1	0.821556	0.473419	0.383314	0.029*
N2	0.6528 (2)	0.59354 (8)	0.38331 (8)	0.0252 (3)
N3	0.6540 (2)	0.15252 (8)	0.39630 (8)	0.0265 (3)
O1	0.25700 (19)	0.46875 (7)	0.39380 (8)	0.0327 (3)
O2	0.9794 (2)	1.01946 (7)	0.34003 (9)	0.0354 (3)
H2	0.858366	1.047600	0.359096	0.053*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0241 (7)	0.0206 (7)	0.0240 (7)	0.0022 (5)	−0.0011 (5)	−0.0009 (5)
C2	0.0210 (7)	0.0194 (7)	0.0230 (7)	0.0008 (5)	0.0024 (5)	0.0005 (5)
C3	0.0216 (7)	0.0219 (7)	0.0268 (7)	−0.0018 (5)	−0.0013 (5)	0.0003 (5)
C4	0.0217 (7)	0.0237 (7)	0.0301 (7)	0.0009 (5)	−0.0008 (6)	0.0024 (6)
C5	0.0259 (7)	0.0232 (7)	0.0315 (8)	−0.0046 (6)	−0.0012 (6)	−0.0026 (6)
C6	0.0198 (7)	0.0258 (7)	0.0280 (7)	−0.0008 (5)	−0.0018 (5)	0.0008 (5)
C7	0.0246 (7)	0.0200 (7)	0.0259 (7)	0.0038 (5)	−0.0027 (5)	−0.0017 (5)
C8	0.0230 (7)	0.0188 (7)	0.0233 (7)	0.0017 (5)	−0.0049 (5)	−0.0001 (5)
C9	0.0203 (6)	0.0212 (7)	0.0295 (7)	−0.0009 (5)	0.0006 (5)	0.0004 (5)
C10	0.0215 (7)	0.0238 (7)	0.0334 (7)	0.0039 (5)	0.0011 (6)	−0.0028 (6)
C11	0.0261 (7)	0.0186 (7)	0.0308 (7)	0.0002 (5)	−0.0040 (6)	0.0008 (5)
C12	0.0207 (6)	0.0254 (7)	0.0290 (7)	−0.0022 (5)	0.0018 (5)	0.0017 (6)

C13	0.0211 (7)	0.0237 (7)	0.0273 (7)	0.0049 (5)	−0.0008 (5)	−0.0027 (5)
N1	0.0238 (6)	0.0153 (6)	0.0340 (7)	0.0029 (4)	−0.0011 (5)	−0.0004 (5)
N2	0.0285 (6)	0.0166 (6)	0.0306 (6)	0.0017 (5)	−0.0021 (5)	−0.0013 (5)
N3	0.0269 (6)	0.0195 (6)	0.0332 (7)	0.0003 (5)	0.0028 (5)	0.0004 (5)
O1	0.0240 (5)	0.0257 (5)	0.0484 (7)	0.0053 (4)	−0.0031 (4)	0.0013 (5)
O2	0.0307 (6)	0.0174 (5)	0.0583 (8)	−0.0003 (4)	0.0063 (5)	0.0003 (5)

Geometric parameters (Å, º)

C1—O1	1.2279 (18)	C7—H7	0.9300
C1—N1	1.3501 (18)	C8—C9	1.4132 (19)
C1—C2	1.5049 (18)	C8—C13	1.417 (2)
C2—C3	1.3696 (19)	C9—C10	1.3862 (19)
C2—C6	1.3701 (19)	C9—H9	0.9300
C3—C4	1.3862 (19)	C10—C11	1.420 (2)
C3—H3	0.9300	C10—H10	0.9300
C4—N3	1.3212 (18)	C11—O2	1.3538 (17)
C4—H4	0.9300	C11—C12	1.404 (2)
C5—N3	1.3234 (18)	C12—C13	1.3844 (19)
C5—C6	1.385 (2)	C12—H12	0.9300
C5—H5	0.9300	C13—H13	0.9300
C6—H6	0.9300	N1—N2	1.3875 (16)
C7—N2	1.2916 (19)	N1—H1	0.8600
C7—C8	1.4573 (18)	O2—H2	0.8200
O1—C1—N1	125.28 (12)	C13—C8—C7	118.31 (12)
O1—C1—C2	121.43 (12)	C10—C9—C8	120.38 (13)
N1—C1—C2	113.26 (12)	C10—C9—H9	119.8
C3—C2—C6	117.50 (13)	C8—C9—H9	119.8
C3—C2—C1	123.05 (12)	C9—C10—C11	119.56 (13)
C6—C2—C1	119.44 (12)	C9—C10—H10	120.2
C2—C3—C4	118.69 (13)	C11—C10—H10	120.2
C2—C3—H3	120.7	O2—C11—C12	116.86 (13)
C4—C3—H3	120.7	O2—C11—C10	122.71 (13)
N3—C4—C3	124.43 (13)	C12—C11—C10	120.43 (13)
N3—C4—H4	117.8	C13—C12—C11	119.66 (13)
C3—C4—H4	117.8	C13—C12—H12	120.2
N3—C5—C6	123.26 (13)	C11—C12—H12	120.2
N3—C5—H5	118.4	C12—C13—C8	120.64 (13)
C6—C5—H5	118.4	C12—C13—H13	119.7
C2—C6—C5	119.81 (13)	C8—C13—H13	119.7
C2—C6—H6	120.1	C1—N1—N2	121.55 (11)
C5—C6—H6	120.1	C1—N1—H1	119.2
N2—C7—C8	122.33 (12)	N2—N1—H1	119.2
N2—C7—H7	118.8	C7—N2—N1	112.82 (11)
C8—C7—H7	118.8	C4—N3—C5	116.27 (12)
C9—C8—C13	119.31 (13)	C11—O2—H2	109.5
C9—C8—C7	122.37 (13)		

O1—C1—C2—C3	−147.48 (14)	C8—C9—C10—C11	0.8 (2)
N1—C1—C2—C3	34.59 (18)	C9—C10—C11—O2	179.30 (13)
O1—C1—C2—C6	33.4 (2)	C9—C10—C11—C12	−1.3 (2)
N1—C1—C2—C6	−144.56 (13)	O2—C11—C12—C13	179.82 (13)
C6—C2—C3—C4	1.1 (2)	C10—C11—C12—C13	0.4 (2)
C1—C2—C3—C4	−178.08 (13)	C11—C12—C13—C8	1.0 (2)
C2—C3—C4—N3	0.8 (2)	C9—C8—C13—C12	−1.50 (19)
C3—C2—C6—C5	−1.6 (2)	C7—C8—C13—C12	179.42 (12)
C1—C2—C6—C5	177.62 (13)	O1—C1—N1—N2	3.5 (2)
N3—C5—C6—C2	0.2 (2)	C2—C1—N1—N2	−178.65 (11)
N2—C7—C8—C9	12.3 (2)	C8—C7—N2—N1	−177.78 (11)
N2—C7—C8—C13	−168.67 (13)	C1—N1—N2—C7	−170.07 (12)
C13—C8—C9—C10	0.57 (19)	C3—C4—N3—C5	−2.1 (2)
C7—C8—C9—C10	179.61 (12)	C6—C5—N3—C4	1.6 (2)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···O1^{i}	0.86	2.34	3.1452 (15)	156
O2—H2···N3^{ii}	0.82	1.96	2.7356 (16)	159

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