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Crystal structure of (3*E*)-5-nitro-3-(2-phenylhydrazinylidene)-1*H*-indol-2(3*H*)-one

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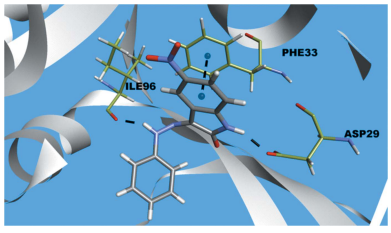
The reaction between 5-nitroisatin and phenylhydrazine in acidic ethanol yields the title compound, $C_{14}H_{10}N_4O_3$, whose molecular structure deviates slightly from a planar geometry (r.m.s. deviation = 0.065 Å for the mean plane through all non-H atoms). An intramolecular N—H···O hydrogen bond is present, forming a ring of graph-set motif *S*(6). In the crystal, molecules are linked by N—H···O and C—H···O hydrogen-bonding interactions into a two-dimensional network along (120), and rings of graph-set motif $R_2^2(8)$, $R_2^2(26)$ and $R_4^4(32)$ are observed. Additionally, a Hirshfeld surface analysis suggests that the molecules are stacked along [100] through C═O···*Cg* interactions and indicates that the most important contributions for the crystal structure are O···H (28.5%) and H···H (26.7%) interactions. An *in silico* evaluation of the title compound with the DHFR enzyme (dihydrofolate reductase) was performed. The isatin–hydrazone derivative and the active site of the selected enzyme show N—H···O(*ASP29*), N—H···O(*ILE96*) and *Cg*···*Cg*(*PHE33*) interactions.

1. Chemical context

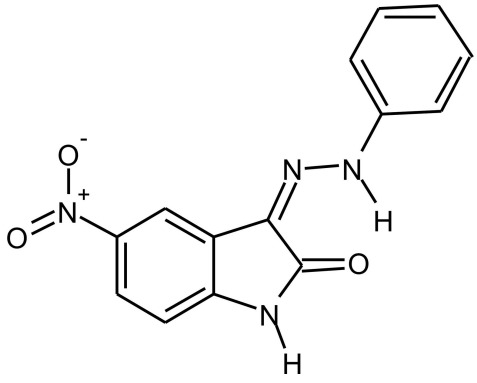
The first reports on isatin and the synthesis of isatin derivatives were published independently in Germany and France over 170 years ago (Erdmann, 1841*a*,*b*; Laurent, 1841). After the 19th Century, isatin chemistry changed rapidly into a major group of compounds with a wide range of applications in different scientific disciplines, with special attention to medicinal chemistry. For example, the synthesis, *in silico* evaluation and *in vitro* inhibition of Chikungunya virus replication by an isatin–thiosemicarbazone derivative was performed recently (Mishra *et al.*, 2016). Other isatin derivatives synthesized in the 1950s (Campaigne & Archer, 1952) had their pharmacological properties *in vitro* successfully tested against Cruzain, Falcipain-2 and Rhodesian in the 2000s (Chiyanzu *et al.*, 2003), and the crystal structure of one of the derivatives was determined by X-ray diffraction in the 2010s (Pederzolli *et al.*, 2011). The crystal structure determination of isatin-based molecules is an intensive research field, especially in medicinal chemistry. As part of our studies in this area, we now describe the synthesis and structure of the title compound, (I).



2. Structural commentary

For the title compound, the molecular structure matches the asymmetric unit and one intramolecular N4—H5···O1 inter-

action of graph-set $S(6)$ is observed (Fig. 1). The molecule is nearly planar with an r.m.s. deviation from the mean plane of the non–H atoms of 0.065 Å and a maximum deviation of 0.1907 (9) Å for atom O2 of the nitro group. The dihedral angle between the indole unit and the phenyl ring is 0.9 (4)°. The plane through the nitro group is rotated by 6.21 (6)° with respect to the indole ring.



3. Supramolecular features

In the crystal, the molecules are connected by centrosymmetric pairs of N1—H1···O1^{i} interactions (Table 1) into dimers with graph-set motif $R_2^2(8)$. In addition, C10—H6···O3^{ii} and C12—H8···O2^{iii} interactions complete a two-dimensional hydrogen-bonded network with rings of graph-set motif $R_2^2(26)$ and $R_4^4(32)$ (Fig. 2, Table 1). As suggested by Hirshfeld surface analysis, the dimensionality of the structure increases to three-dimensional through the C=O···*Cg* interactions [C1···*Cg* = 3.5427 (7) Å, O1···*Cg* = 3.2004 (7) Å; *Cg* is the centroid of the C9–C14 ring], building a chain along [100] (Fig. 3). The separation between the C1 and C14 atoms of adjacent molecules in the chain is 3.1744 (11) Å, which is shorter than the sum of the van der Waals radii for carbon atoms (Bondi, 1964; Rowland & Taylor, 1996).

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N4—H5···O1	0.88	2.03	2.7479 (10)	137
N1—H1···O1^{i}	0.88	1.96	2.8310 (10)	171
C10—H6···O3^{ii}	0.95	2.63	3.5542 (13)	166
C12—H8···O2^{iii}	0.95	2.47	3.3943 (13)	163

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

4. Hirshfeld surface analysis

The Hirshfeld surface analysis of the crystal structure indicates that the contribution of O···H intermolecular interactions to the crystal packing amounts to 28.5% and the H···H interactions amount to 26.7%. Other important intermolecular contacts for the cohesion of the structure are (in %): H···C = 17.7, H···N = 8.9, C···O = 8.2, C···C = 5.5 and C···N = 3.3. The Hirshfeld surface graphical representation with transparency and labelled atoms (Figs. 4 and 5) indicates, in magenta, the locations of the strongest intermolecular contacts. The H1, H8, O1 and O2 atoms are the most important for the intermolecular hydrogen bonding, while the C1 and C14 atoms are the most important for C···C interactions. The O···H contribution to the crystal packing is shown as a Hirshfeld surface fingerprint two-dimensional plot with cyan dots (Wolff *et al.*, 2012). The d_e (*y* axis) and d_i (*x* axis) values are the closest external and internal distances (in Å) from given points on the Hirshfeld surface (Fig. 6). The magenta colour on graphical representations of the Hirshfeld surface

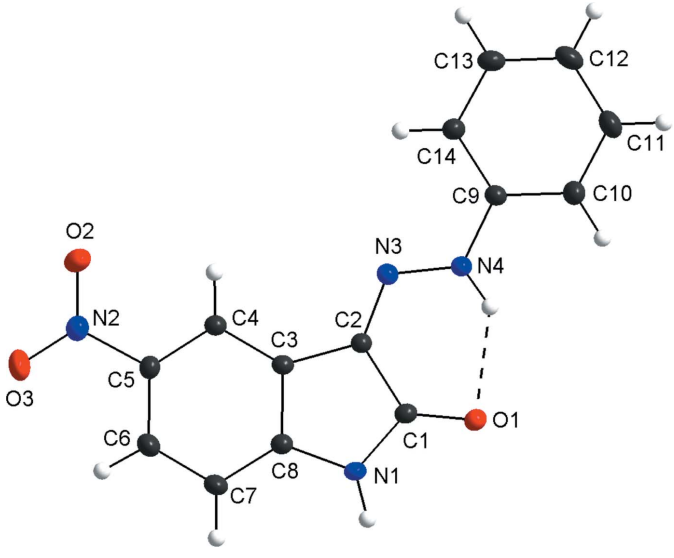


Figure 1
The molecular structure of the title compound, showing displacement ellipsoids drawn at the 50% probability level. The intramolecular hydrogen bond is shown as a dashed line.

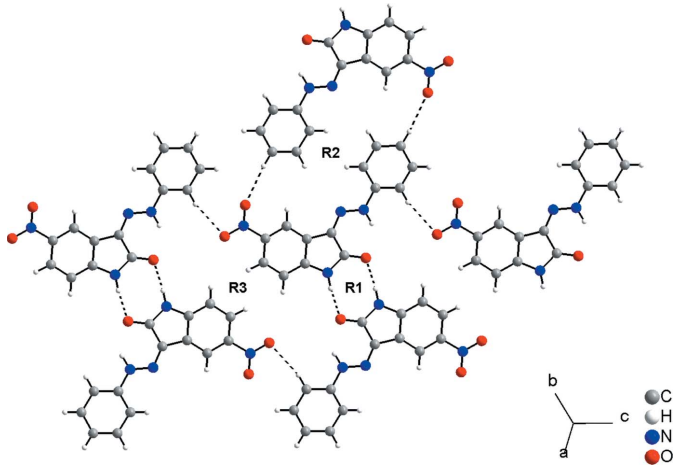


Figure 2
A packing diagram of the title compound, showing the N—H···O and C—H···O interactions (dashed lines) connecting the molecules into a two-dimensional network in the (120) plane. The graph-set motifs for the crystal packing are: R1 = $R_2^2(8)$, R2 = $R_2^2(26)$ and R3 = $R_4^4(32)$.

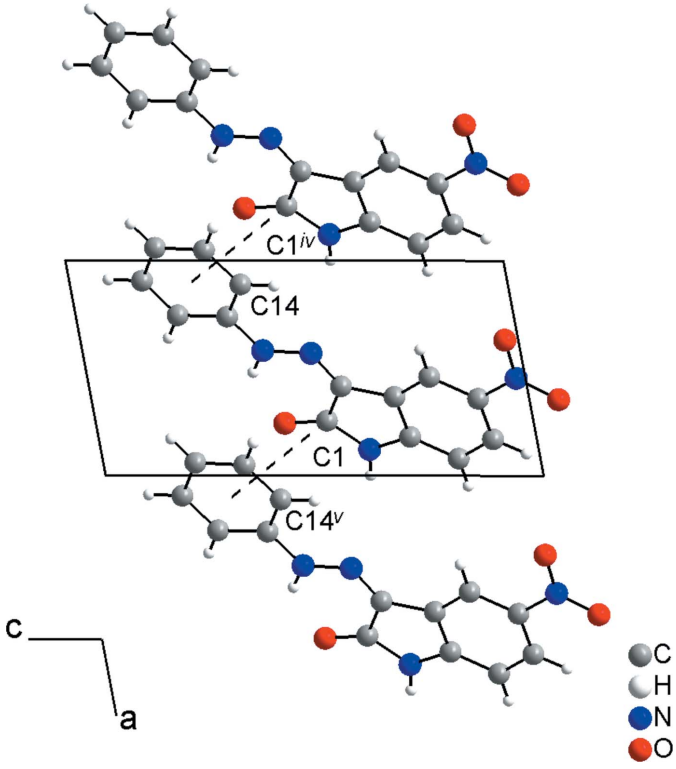


Figure 3
A packing diagram of the title compound showning the C···*Cg* interactions (as dashed lines) building a chain along [100]. [Symmetry codes: (iv) $x-1, y, z$; (v) $x+1, y, z$.]

matches the N1—H1···O1^{i}, C10—H6···O3^{ii} and C12—H8···O2^{iii} interactions described above. In the same way, the C···*Cg* interactions can be seen more clearly on the C1═O1 and C14 atoms.

5. Molecular docking evaluation

Finally, for a lock-and-key supramolecular analysis, a molecular docking evaluation between the title compound and the

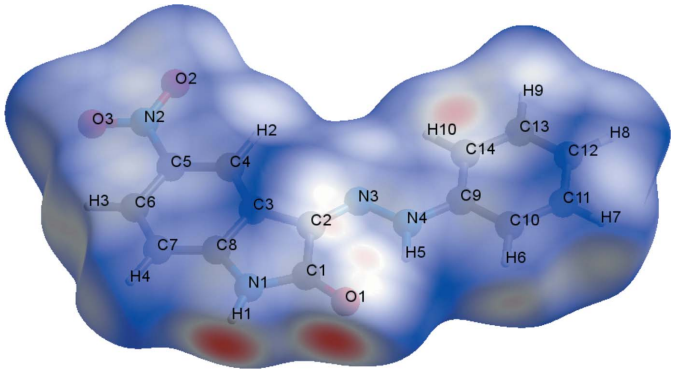


Figure 4
A Hirshfeld surface graphical representation (d_{norm}) for the title compound. The surface is drawn with transparency and all atoms are labelled. The surface regions with strongest intermolecular interactions for atoms H1, O1 and C14 are shown in magenta.

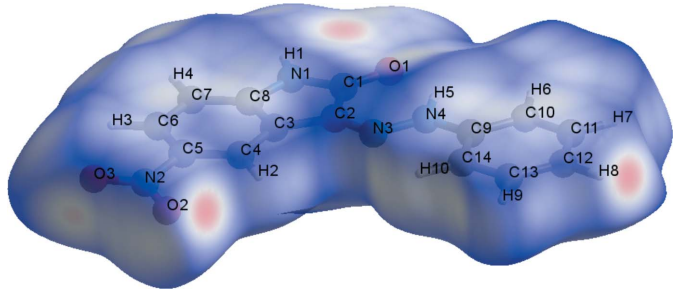


Figure 5
A Hirshfeld surface graphical representation (d_{norm}) for the title compound. The surface is drawn with transparency and all atoms are labelled. The surface regions with strongest intermolecular interactions for atoms H8, O2 and C1 are shown in magenta.

DHFR enzyme (dihydrofolate reductase) was carried out. Initially, the semi-empirical equilibrium energy of the small molecule was obtained using the PM6 Hamiltonian, but the experimental bond lengths were conserved. The calculated parameters were: heat of formation = 149.41 kJ mol^{-1}, gradient normal = 0.763, HOMO = −8.96 eV, LUMO =-1.66 eV and energy gap = 7.30 eV. The target prediction for 5-nitroisatin-3-phenylhydrazone was calculated with the *SwissTargetPrediction* webserver based on the bioisosteric similarity to the isatin entity (Gfeller *et al.*, 2013). As result of this screening, the title compound showed a promising theo-

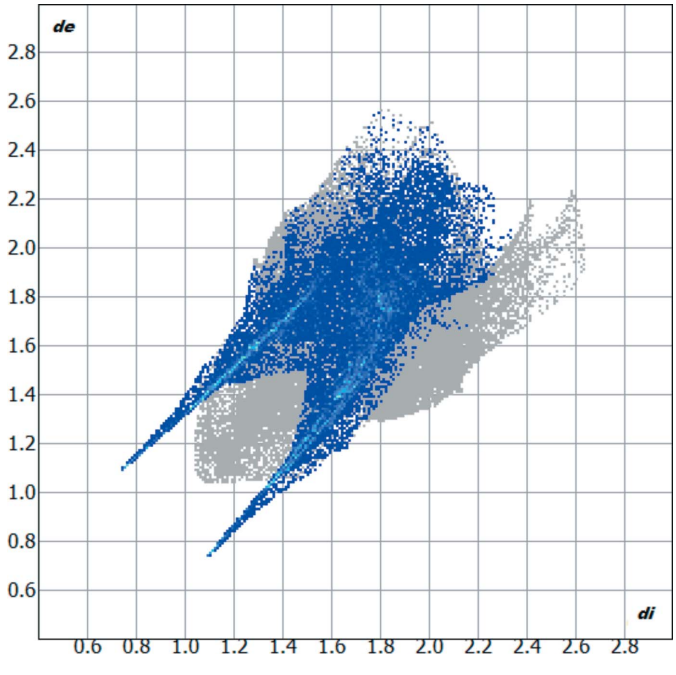


Figure 6
Hirshfeld surface fingerprint two-dimensional plot for the 5-nitroisatin-3-phenylhydrazone crystal structure showing the O···H contacts in detail (cyan dots). The O···H contribution for the crystal packing amounts to 28.5%, being the most important intermolecular connection. The d_e (y axis) and d_i (x axis) values are the closest external and internal distances [in Å] from given points on the Hirshfeld surface.

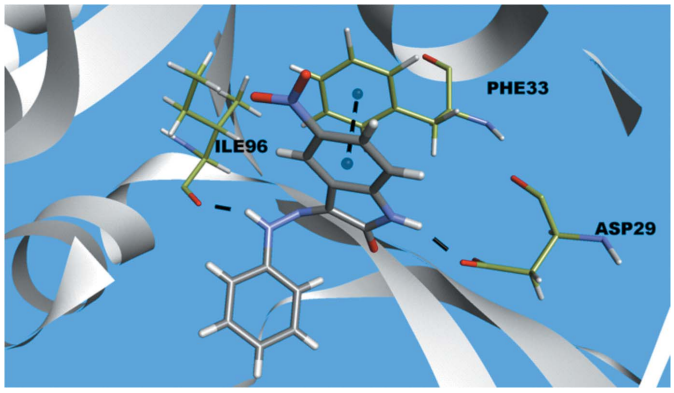


Figure 7
Intermolecular interactions between the title compound and the dihydrofolate reductase enzyme. The interactions are shown as dashed lines and the figure is simplified for clarity.

retical structure–activity relationship to kinase proteins sites. The Frequency Target Class for kinases amounts to 44%, while the second best result for phosphatases amounts to 13%. The interactions with enzymes are important features for biologically active molecules, *e.g.* inhibition of tumor cell proliferation, activation of cell apoptosis mechanisms and blocking of bacterial membrane synthesis. Based on a search for a biological target with pharmacological background, the dihydrofolate reductase was selected for the *in silico* evaluation (Chen, 2015; Dias *et al.*, 2014; Verdonk *et al.*, 2003), biological target code: DHFR (Protein Data Bank ID: 4KM0; Wei *et al.*, 2005). The isatin–hydrazone derivative and the active site of the selected enzyme matches and the structure–activity relationship can be assumed by the following observed intermolecular interactions: N1—H1···O(*ASP29*) (1.928 Å), N4—H5···O(*ILE96*) (1.925 Å) and *Cg*···*Cg*(*PHE33*) (3.567 Å) (Fig. 7).

6. Comparison with a related structure

A recently published article (Bittencourt *et al.*, 2016) reports the structure of (3*E*)-5-nitro-3-(2-phenylhydrazinylidene)-1*H*-indol-2(3*H*)-one, which may be compared with that of the title compound. The molecular structure deviates slightly from the ideal planar geometry and the C···C contacts between the planes are observed. The molecules are linked by N—H···O and C—H···Cl interactions into a two-dimensional hydrogen-bonded polymer, a quite similar structure to the title compound. The *in silico* evaluation of 5-chloroisatin-phenylhydrazone, a molecule with similar crystal packing to the title compound, with and the DNA topoisomerase IIα enzyme was performed and the global free energy of −26.59 kJ mol^{-1} was found. The evaluation agrees with the literature data for molecular docking and cytotoxic activity of hydrazone derivatives against breast cancer cells (Dandawate *et al.*, 2012) and supports research on the structural determination of other isatin-based molecules. The title compound is commercially available, but its structural analysis by X–ray single crystal diffraction, Hirshfeld surface calculation and molecular docking evaluation are presented in this work for the first time.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{14}H_{10}N_4O_3$
M_r	282.26
Crystal system, space group	Triclinic, $P\overline{1}$
Temperature (K)	200
a, b, c (Å)	5.7504 (4), 9.7190 (6), 12.1976 (7)
α, β, γ (°)	111.196 (2), 96.759 (2), 98.497 (2)
V (Å^3)	617.69 (7)
Z	2
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.11
Crystal size (mm)	0.48 × 0.16 × 0.10
Data collection	
Diffractometer	Bruker APEXII CCD area detector
Absorption correction	Multi-scan (*SADABS*; Bruker, 2013)
T_{min}, T_{max}	0.949, 0.989
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	11325, 3971, 3281
R_{int}	0.017
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.726
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.039, 0.117, 1.03
No. of reflections	3971
No. of parameters	190
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.37, −0.26

Computer programs: *APEX2* and *SAINT* (Bruker, 2013), *SHELXS97* and *SHELXL97* (Sheldrick, 2008), *DIAMOND* (Brandenburg, 2006), *GOLD* (Verdonk *et al.*, 2003), *Crystal Explorer* (Wolff, *et al.*, 2012), *publCIF* (Westrip, 2010) and *enCIFer* (Allen *et al.*, 2004).

7. Synthesis and crystallization

All starting materials are commercially available and were used without further purification. The synthesis of the title compound was adapted from a procedure reported previously (Fonseca *et al.*, 2011). The glacial acetic acid-catalysed reaction of 5-nitroisatin (2.6 mmol) and phenylhydrazine (2.6 mmol) in ethanol (40 mL) was refluxed for 4 h. After cooling and filtering, an irregular solid was isolated. Single crystals suitable for X-ray diffraction were obtained from a DMF/methanol solution (1:1 *v*/*v*) on slow evaporation of the solvent.

8. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. Hydrogen atoms were located in a difference Fourier map, but were positioned with idealized geometry and refined isotropically using a riding model, with U_{iso}(H) = 1.2U_{eq}(C, N), and with C—H = 0.95 Å and N—H = 0.88 Å.

Acknowledgements

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supporting information

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Crystal structure of (3*E*)-5-nitro-3-(2-phenylhydrazinylidene)-1*H*-indol-2(3*H*)-one

Jecika Maciel Velasques, Vanessa Carratu Gervini, Adaílton João Bortoluzzi, Renan Lira de Farias and Adriano Bof de Oliveira

Computing details

Data collection: *APEX2* (Bruker, 2013); cell refinement: *SAINT* (Bruker, 2013); data reduction: *SAINT* (Bruker, 2013); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *DIAMOND* (Brandenburg, 2006), *GOLD* (Verdonk *et al.*, 2003) and *Crystal Explorer* (Wolff, *et al.*, 2012); software used to prepare material for publication: *publCIF* (Westrip, 2010) and *enCIFer* (Allen *et al.*, 2004).

(3*E*)-5-nitro-3-(2-phenylhydrazinylidene)-1*H*-indol-2(3*H*)-one

Crystal data

$C_{14}H_{10}N_4O_3$
M_r = 282.26
Triclinic, $P\overline{1}$
a = 5.7504 (4) Å
b = 9.7190 (6) Å
c = 12.1976 (7) Å
α = 111.196 (2)°
β = 96.759 (2)°
γ = 98.497 (2)°
V = 617.69 (7) Å^3
Z = 2
$F(000)$ = 292
D_x = 1.518 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 2154 reflections
θ = 2.3–31.0°
μ = 0.11 mm^{-1}
T = 200 K
Prism, yellow
0.48 × 0.16 × 0.10 mm

Data collection

Bruker APEXII CCD area detector diffractometer
Radiation source: fine-focus sealed tube, Bruker APEX2 CCD
Graphite monochromator
φ and ω scans
Absorption correction: multi-scan (SADABS; Bruker, 2013)
T_{min} = 0.949, T_{max} = 0.989
11325 measured reflections
3971 independent reflections
3281 reflections with $I > 2\sigma(I)$
R_{int} = 0.017
θ_{max} = 31.1°, θ_{min} = 1.8°
h = −8→8
k = −14→14
l = −17→17

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.039
$wR(F^2)$ = 0.117
S = 1.03
3971 reflections
190 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
$w = 1/[\sigma^2(F_o^2) + (0.0693P)^2 + 0.1171P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.37$ e Å^{-3}
$\Delta\rho_{min} = -0.26$ 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. 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.

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

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.74444 (16)	0.10997 (10)	0.47144 (8)	0.01734 (17)
C2	0.58388 (16)	0.19030 (10)	0.42434 (8)	0.01692 (17)
C3	0.63293 (16)	0.17378 (10)	0.30690 (8)	0.01701 (17)
C4	0.53990 (17)	0.22036 (10)	0.21904 (8)	0.01863 (18)
H2	0.4130	0.2737	0.2283	0.022*
C5	0.64117 (17)	0.18525 (11)	0.11683 (8)	0.02053 (19)
C6	0.8299 (2)	0.10968 (12)	0.10014 (9)	0.0255 (2)
H3	0.8968	0.0921	0.0299	0.031*
C7	0.92000 (19)	0.06009 (12)	0.18685 (9)	0.0240 (2)
H4	1.0462	0.0062	0.1767	0.029*
C8	0.81885 (16)	0.09218 (10)	0.28844 (8)	0.01844 (17)
C9	0.26077 (16)	0.34671 (10)	0.65458 (8)	0.01776 (17)
C10	0.25473 (19)	0.34151 (12)	0.76695 (9)	0.0244 (2)
H6	0.3603	0.2920	0.7976	0.029*
C11	0.0939 (2)	0.40895 (13)	0.83359 (9)	0.0296 (2)
H7	0.0883	0.4047	0.9099	0.036*
C12	−0.0597 (2)	0.48282 (13)	0.78973 (10)	0.0284 (2)
H8	−0.1711	0.5280	0.8354	0.034*
C13	−0.04899 (19)	0.49000 (11)	0.67893 (9)	0.0248 (2)
H9	−0.1521	0.5418	0.6494	0.030*
C14	0.11070 (18)	0.42243 (11)	0.61027 (9)	0.02091 (19)
H10	0.1173	0.4278	0.5344	0.025*
N1	0.87794 (14)	0.05403 (9)	0.38620 (7)	0.01994 (17)
H1	0.9867	0.0010	0.3923	0.024*
N2	0.54638 (17)	0.23011 (10)	0.02105 (8)	0.02622 (19)
N3	0.43091 (14)	0.26487 (9)	0.47905 (7)	0.01813 (16)
N4	0.41836 (15)	0.27045 (9)	0.58791 (7)	0.01990 (17)
H5	0.5115	0.2250	0.6195	0.024*
O1	0.75650 (12)	0.09474 (8)	0.56864 (6)	0.02078 (15)

O2	0.36881 (18)	0.28657 (11)	0.03076 (8)	0.0393 (2)
O3	0.64526 (18)	0.20633 (12)	−0.06636 (8)	0.0416 (2)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0163 (4)	0.0189 (4)	0.0187 (4)	0.0066 (3)	0.0039 (3)	0.0081 (3)
C2	0.0171 (4)	0.0202 (4)	0.0165 (4)	0.0077 (3)	0.0050 (3)	0.0084 (3)
C3	0.0160 (4)	0.0198 (4)	0.0176 (4)	0.0072 (3)	0.0050 (3)	0.0081 (3)
C4	0.0187 (4)	0.0222 (4)	0.0182 (4)	0.0089 (3)	0.0055 (3)	0.0091 (3)
C5	0.0229 (5)	0.0257 (4)	0.0165 (4)	0.0093 (4)	0.0049 (3)	0.0103 (3)
C6	0.0278 (5)	0.0344 (5)	0.0206 (4)	0.0158 (4)	0.0107 (4)	0.0125 (4)
C7	0.0242 (5)	0.0326 (5)	0.0217 (4)	0.0162 (4)	0.0100 (4)	0.0121 (4)
C8	0.0183 (4)	0.0217 (4)	0.0179 (4)	0.0084 (3)	0.0047 (3)	0.0085 (3)
C9	0.0181 (4)	0.0201 (4)	0.0169 (4)	0.0075 (3)	0.0053 (3)	0.0071 (3)
C10	0.0269 (5)	0.0326 (5)	0.0187 (4)	0.0138 (4)	0.0066 (4)	0.0120 (4)
C11	0.0357 (6)	0.0389 (6)	0.0195 (4)	0.0163 (5)	0.0127 (4)	0.0117 (4)
C12	0.0293 (5)	0.0329 (5)	0.0256 (5)	0.0152 (4)	0.0133 (4)	0.0085 (4)
C13	0.0250 (5)	0.0260 (4)	0.0274 (5)	0.0138 (4)	0.0085 (4)	0.0107 (4)
C14	0.0235 (5)	0.0236 (4)	0.0208 (4)	0.0112 (3)	0.0076 (3)	0.0111 (3)
N1	0.0203 (4)	0.0257 (4)	0.0196 (4)	0.0133 (3)	0.0068 (3)	0.0111 (3)
N2	0.0310 (5)	0.0332 (4)	0.0206 (4)	0.0144 (4)	0.0074 (3)	0.0136 (3)
N3	0.0184 (4)	0.0215 (3)	0.0171 (3)	0.0076 (3)	0.0056 (3)	0.0085 (3)
N4	0.0216 (4)	0.0265 (4)	0.0172 (3)	0.0130 (3)	0.0069 (3)	0.0108 (3)
O1	0.0218 (3)	0.0259 (3)	0.0201 (3)	0.0108 (3)	0.0059 (3)	0.0122 (3)
O2	0.0468 (5)	0.0577 (6)	0.0299 (4)	0.0370 (5)	0.0134 (4)	0.0241 (4)
O3	0.0475 (5)	0.0687 (6)	0.0280 (4)	0.0299 (5)	0.0198 (4)	0.0305 (4)

Geometric parameters (Å, º)

C1—O1	1.2421 (11)	C9—C14	1.3942 (12)
C1—N1	1.3669 (11)	C9—N4	1.4029 (11)
C1—C2	1.4848 (12)	C10—C11	1.3845 (14)
C2—N3	1.3119 (11)	C10—H6	0.9500
C2—C3	1.4490 (12)	C11—C12	1.3913 (16)
C3—C4	1.3882 (12)	C11—H7	0.9500
C3—C8	1.4144 (12)	C12—C13	1.3863 (15)
C4—C5	1.3900 (13)	C12—H8	0.9500
C4—H2	0.9500	C13—C14	1.3919 (13)
C5—C6	1.3923 (13)	C13—H9	0.9500
C5—N2	1.4631 (12)	C14—H10	0.9500
C6—C7	1.3902 (13)	N1—H1	0.8800
C6—H3	0.9500	N2—O2	1.2267 (12)
C7—C8	1.3838 (13)	N2—O3	1.2316 (12)
C7—H4	0.9500	N3—N4	1.3202 (11)
C8—N1	1.3915 (11)	N4—H5	0.8800
C9—C10	1.3939 (13)		

O1—C1—N1	126.00 (8)	C14—C9—N4	121.93 (8)
O1—C1—C2	127.42 (8)	C11—C10—C9	119.56 (9)
N1—C1—C2	106.58 (7)	C11—C10—H6	120.2
N3—C2—C3	126.40 (8)	C9—C10—H6	120.2
N3—C2—C1	126.92 (8)	C10—C11—C12	120.53 (9)
C3—C2—C1	106.67 (7)	C10—C11—H7	119.7
C4—C3—C8	119.72 (8)	C12—C11—H7	119.7
C4—C3—C2	134.01 (8)	C13—C12—C11	119.47 (9)
C8—C3—C2	106.26 (7)	C13—C12—H8	120.3
C3—C4—C5	116.83 (8)	C11—C12—H8	120.3
C3—C4—H2	121.6	C12—C13—C14	120.93 (9)
C5—C4—H2	121.6	C12—C13—H9	119.5
C4—C5—C6	123.62 (9)	C14—C13—H9	119.5
C4—C5—N2	118.74 (8)	C13—C14—C9	118.93 (9)
C6—C5—N2	117.64 (8)	C13—C14—H10	120.5
C7—C6—C5	119.64 (9)	C9—C14—H10	120.5
C7—C6—H3	120.2	C1—N1—C8	110.92 (7)
C5—C6—H3	120.2	C1—N1—H1	124.5
C8—C7—C6	117.46 (9)	C8—N1—H1	124.5
C8—C7—H4	121.3	O2—N2—O3	123.29 (9)
C6—C7—H4	121.3	O2—N2—C5	118.18 (8)
C7—C8—N1	127.81 (8)	O3—N2—C5	118.50 (9)
C7—C8—C3	122.66 (8)	C2—N3—N4	116.98 (8)
N1—C8—C3	109.53 (8)	N3—N4—C9	121.85 (8)
C10—C9—C14	120.56 (9)	N3—N4—H5	119.1
C10—C9—N4	117.49 (8)	C9—N4—H5	119.1

O1—C1—C2—N3	2.70 (16)	C14—C9—C10—C11	1.64 (16)
N1—C1—C2—N3	−177.67 (9)	N4—C9—C10—C11	−176.92 (9)
O1—C1—C2—C3	−178.71 (9)	C9—C10—C11—C12	−0.59 (17)
N1—C1—C2—C3	0.91 (10)	C10—C11—C12—C13	−0.70 (18)
N3—C2—C3—C4	−2.73 (17)	C11—C12—C13—C14	0.97 (17)
C1—C2—C3—C4	178.67 (10)	C12—C13—C14—C9	0.06 (16)
N3—C2—C3—C8	176.72 (9)	C10—C9—C14—C13	−1.37 (15)
C1—C2—C3—C8	−1.87 (10)	N4—C9—C14—C13	177.12 (9)
C8—C3—C4—C5	−1.17 (14)	O1—C1—N1—C8	−179.93 (9)
C2—C3—C4—C5	178.23 (10)	C2—C1—N1—C8	0.44 (10)
C3—C4—C5—C6	−1.17 (15)	C7—C8—N1—C1	177.81 (10)
C3—C4—C5—N2	179.09 (8)	C3—C8—N1—C1	−1.68 (11)
C4—C5—C6—C7	2.57 (17)	C4—C5—N2—O2	−5.61 (15)
N2—C5—C6—C7	−177.69 (9)	C6—C5—N2—O2	174.63 (10)
C5—C6—C7—C8	−1.48 (16)	C4—C5—N2—O3	175.99 (10)
C6—C7—C8—N1	179.74 (10)	C6—C5—N2—O3	−3.77 (15)
C6—C7—C8—C3	−0.83 (16)	C3—C2—N3—N4	−177.84 (8)
C4—C3—C8—C7	2.21 (15)	C1—C2—N3—N4	0.47 (14)
C2—C3—C8—C7	−177.34 (9)	C2—N3—N4—C9	−179.85 (8)
C4—C3—C8—N1	−178.26 (8)	C10—C9—N4—N3	177.74 (9)
C2—C3—C8—N1	2.18 (10)	C14—C9—N4—N3	−0.80 (15)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N4—H5···O1	0.88	2.03	2.7479 (10)	137
N1—H1···O1^{i}	0.88	1.96	2.8310 (10)	171
C10—H6···O3^{ii}	0.95	2.63	3.5542 (13)	166
C12—H8···O2^{iii}	0.95	2.47	3.3943 (13)	163

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