research communications

Isoquinolinium 5-(2,4-dinitrophenyl)-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate: crystal structure, Hirshfeld surface analysis and pharmacological evaluation

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The asymmetric unit of the title salt $C_9H_8N^+ \cdot C_{12}H_9N_4O_7^-$, which exhibits anticonvulsant and hypnotic activities, comprises one anion and one cation interacting *via* an N—H···O hydrogen bond. In the anion, the six-membered rings are inclined each to other at 42.78 (9)°. The nitro groups in the 2,4-dinitrophenyl fragment attached to the aromatic ring in the *para* and *ortho* positions are twisted from its plane by 3.1 (2) and 45.5 (2)°, respectively. In the crystal, weak C—H···O hydrogen bonds consolidate the crystal packing. The Hirshfeld surface analysis revealed that O···H/H···O intermolecular contacts predominate in the crystal packing.

1. Chemical context

Barbiturates play a significant role in biological systems (Hueso-Ureña *et al.*, 2003). Epilepsy (convulsion) is a life-threatening neurological disorder which requires immediate treatment with suitable drugs (Shorvon, 2004). Barbiturates have been proved to be potent drugs for this dreadful disorder (Nadkarni *et al.*, 2005). The isoquinoline unit also displays a wide spectrum of activity and it is an important component of many biologically active alkaloids (Montalban, 2011). Since 2008, we have been periodically synthesizing new barbiturate derivatives and exploring their anticonvulsant activity (Kalaivani *et al.*, 2008; Kalaivani & Malarvizhi, 2009; Kalaivani & Buvaneswari, 2010; Manickkam & Kalaivani, 2011; Baby-kala & Kalaivani, 2012; Buvaneswari & Kalaivani, 2013; Vaduganathan & Doraisamyraja, 2014; Gomathi & Kalaivani, 2015). The title molecular salt, which is a new derivative of 1,3-dimethylbarbituric acid (barbiturate), was recently obtained by our group. Herewith we report its crystal structure.
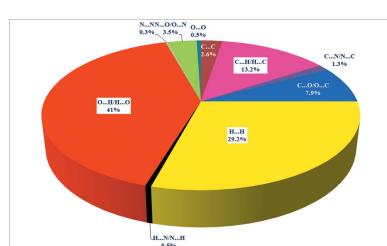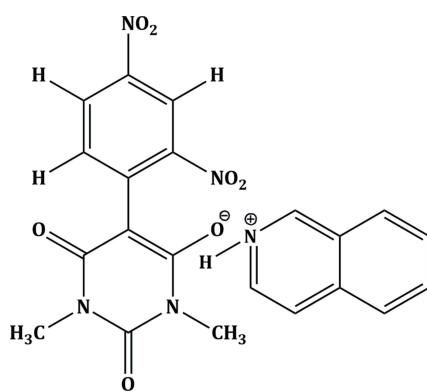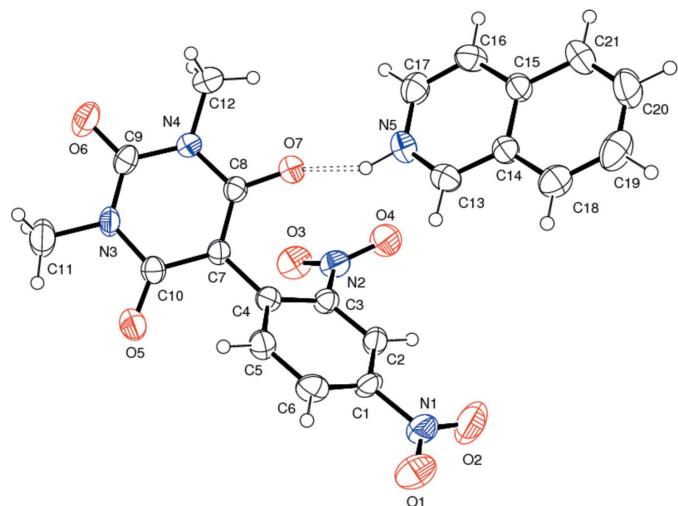
Figure 1
The asymmetric unit of (I) showing the atom numbering and 40% probability displacement ellipsoids. The doubled-dashed line denotes the N—H···O hydrogen bond between the cation and anion.

2. Structural commentary

In the title compound, (I) (Fig. 1), all the bond lengths and bond angles are normal and comparable with those observed in the related barbiturates (Sridevi & Kalaivani, 2012; Gunaseelan & Doraisamyraja, 2014). The plane of the dinitroaromatic ring C1–C6 and that of the barbiturate ring C7/C8/N4/C9/N3/C10 form a dihedral angle of 42.78 (9)°. The nitro groups in the 2,4-dinitrophenyl fragment attached to the aromatic ring in the *para* and *ortho* positions are twisted from its plane by 3.1 (2) and 45.5 (2)°, respectively. Thus the *para* nitro group is more involved in delocalizing the negative charge than the *ortho* nitro group in the anionic part. This sort of delocalization of the charge over a large area imparts a maroon red colour to the title compound.

3. Supramolecular features

The aminium group is involved in formation of an N—H···O hydrogen bond (Table 1) between the isoquinolinium cation (N5—H5A) and the deprotonated enol oxygen atom O7. In the crystal, weak C—H···O hydrogen bonds (Table 1) consolidate the crystal packing (Fig. 2). An $R_2^1(6)$ motif is generated by the C—H groups [C13—H13 and C20—H20] of the isoquinolinium cation and oxygen atom O5 of the carbonyl group of the barbiturate ring of the anion. Although there are three rings with cyclically delocalized π electron clouds, no π–π stacking interactions are observed between them.

4. 3D Hirshfeld Surface Analysis and 2D Fingerprint Analysis

Hirshfeld surfaces (Spackman & Jayatilaka, 2009) and the associated 2D-fingerprint plots (McKinnon *et al.*, 2007) of the title molecular salt have been generated using *Crystal Explorer 3.1* (Wolff *et al.*, 2013). Hirshfeld surfaces mapped

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

D—H···A	D—H	H···A	D···A	D—H···A
N5—H5A···O7	0.93 (6)	1.74 (6)	2.592 (6)	150 (5)
C13—H13···O5^i	0.93	2.40	3.260 (7)	153
C16—H16···O6^{ii}	0.93	2.33	3.187 (7)	154
C17—H17···O2^{iii}	0.93	2.61	3.424 (8)	146

Symmetry codes: (i) $x + \frac{1}{2}, -y + \frac{1}{2}, -z + 1$; (ii) $-x + 3, y - \frac{1}{2}, -z + \frac{1}{2}$; (iii) $-x + \frac{5}{2}, -y, z - \frac{1}{2}$.

with different properties, *e.g.* d_e, d_{norm}, d_i, shapeindex, curvedness, have proven to be a useful visualization tool for the analysis of intermolecular interactions. The 2D-fingerprint plots of Hirshfeld surfaces have been used to pinpoint and scrutinize the percentage of hydrogen-bonding interactions present in the crystal structure. The presented graphical plots use the same red-white-blue color scheme, wherein red highlights the shortest intermolecular atomic contacts (negative d_{norm} values), white is used for contacts around the van der Waals separation, and blue corresponds to longer ones (positive d_{norm} values). Hirshfeld surface analysis of the new barbiturate of present interest has d_{norm} values ranging from −0.723 (red) to 1.464 (blue), as specified in Fig. 3. The globularity value (a measure of the degree to which the surface area differs from that of the shape) is less than 1
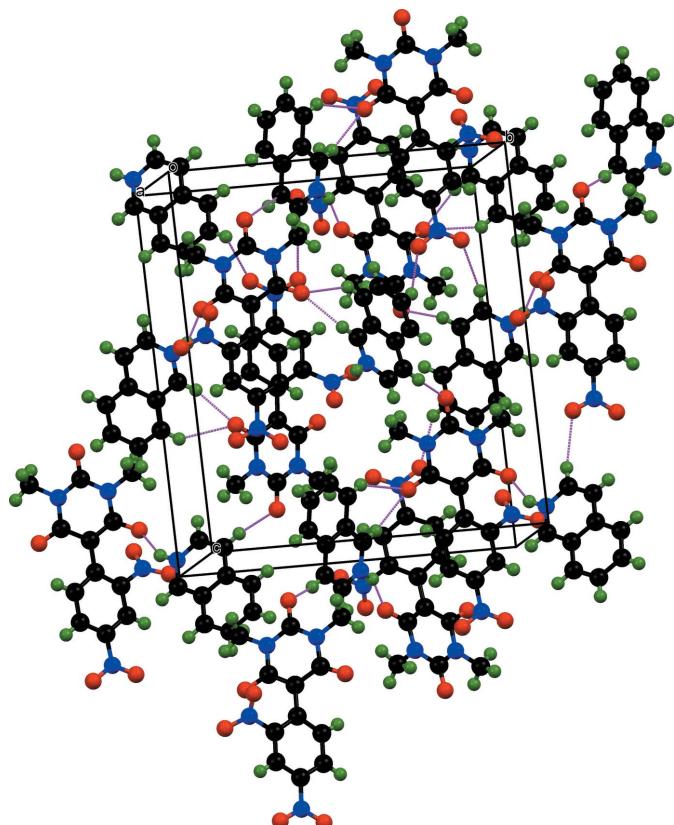

Figure 2
Crystal packing of (I) viewed approximately down the *a* axis. Hydrogen bonds are shown as purple dotted lines.
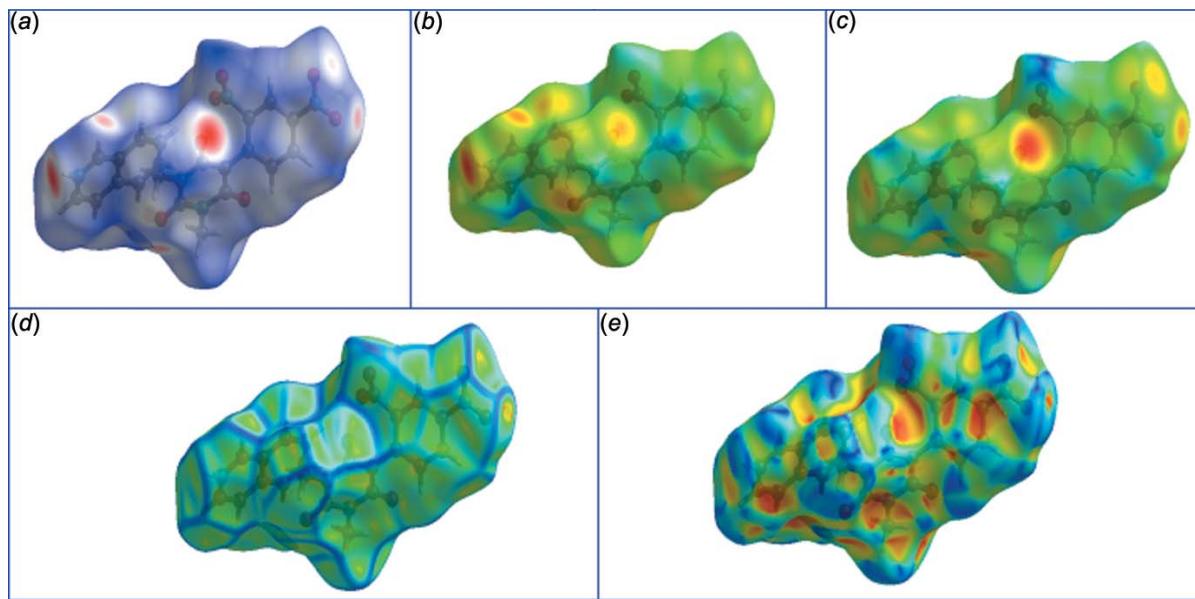
Figure 3
3D Hirshfeld surface analysis of (I) mapped over (a) d_{norm} ranging from −0.723 (red) to 1.464 (blue); (b) d_e; (c) d_i; (d) curvedness; (e) shapeindex.

(0.743), implying a more structured molecular surface and it is an oblate object (asphericity, 0.282). 2D-Fingerprint plots showing contributions from different contacts: (a) overall interactions (b) C···H/H···C (c) C···O/O···C (d) H···H (e) O···H/H···O (f) N···O/O···N are depicted in Fig. 4, and Fig. 5 (pie chart) clearly demonstrates that the O···H/H···O interactions dominate in the crystal.

5. Pharmacological activity

Epilepsy affects about 0.5% of the world's population. A seizure is caused by an asynchronous high-frequency discharge of a group of neurons, starting locally and spreading to a varying extent to affect other parts of the brain. 1,3-Dimethylbarbituric acid is the most significant compound
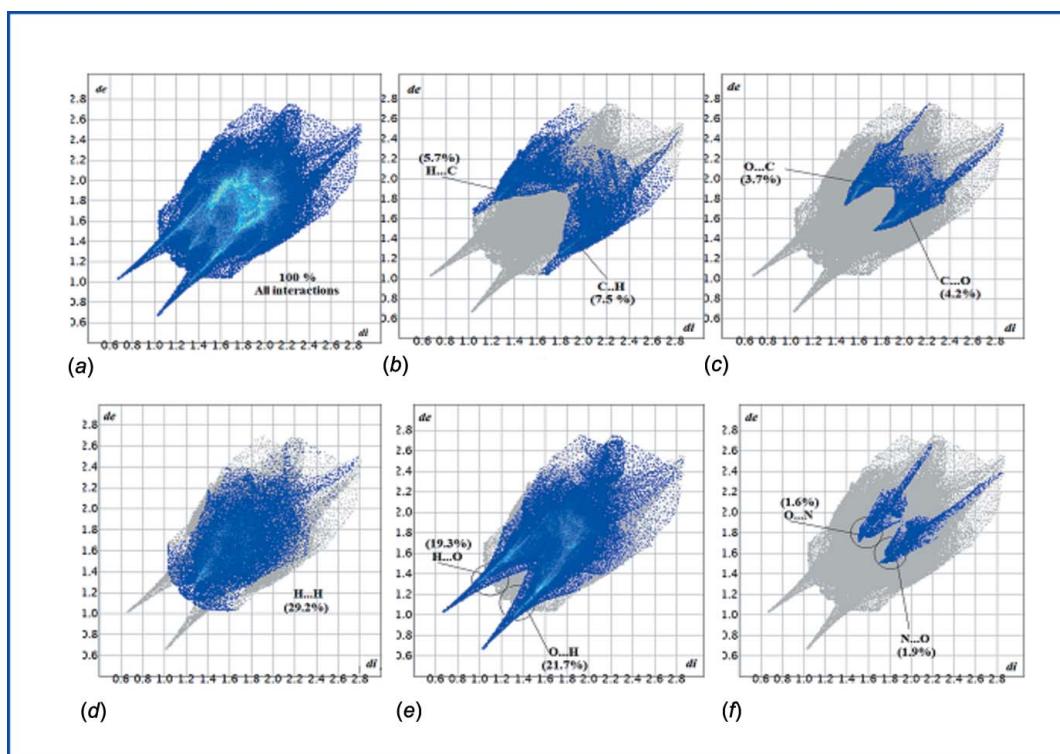
Figure 4
2D Fingerprint plots showing contributions from different contacts: (a) overall interactions; (b) C···H/H···C; (c) C···O/O···C; (d) H···H; (e) O···H/H···O and (f) N···O/O···N.
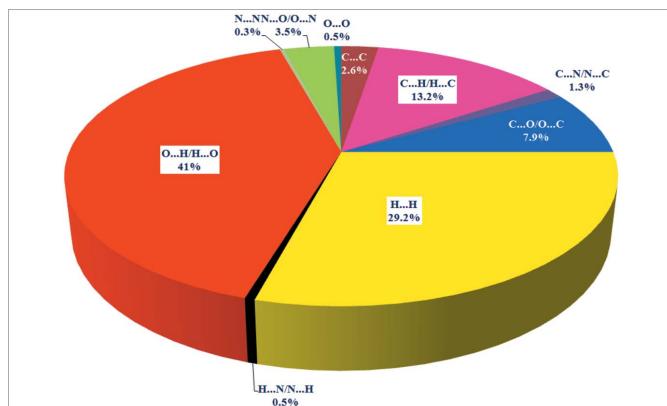
Figure 5
Pie chart showing the quantitative distribution of intermolecular interactions in (I).

with a heterocyclic structure and exists in two tautomeric forms (keto and enol) due to the mobility of active methylene group hydrogen atoms in its molecule. Barbiturates are drugs that act as central nervous system depressants and can therefore produce a wide spectrum of effects from mild sedation to total anaesthesia. They are also effective as anxiolytics, hypnotics and anticonvulsants. As the molecular salt of the present investigation is a derivative of 1,3-dimethylbarbituric acid, it has been subjected to the Maximal Electro Shock method to evaluate its anticonvulsant activity (Misra *et al.*,1973; Kulkarni, 1999). It reduces all phases of convulsion (tonic-flexor, tonic-extensor, clonic-convulsion and stupor) even at low dosage (25 mg kg^{-1}) and the animals recovered after the experiment.

6. Synthesis and crystallization

1-Chloro-2,4-dinitrobenzene (2.02 g, 0.01 mol) in 40 mL of absolute alcohol was mixed with 1,3-dimethylbarbituric acid (1.56 g, 0.01 mol) in 30 mL ethanol. To this mixture, 0.02 mol of isoquinoline was added and the mixture was shaken well for 5 h and kept as such for 24 h. Excess ethanol was removed through evaporation. A maroon-red pasty mass was obtained. This paste was digested with hot ethanol to obtain a maroon-red solid. The solid deposited at the bottom of the flask was filtered, powdered well using an agate mortar, washed again with 20 mL of dry ether and recrystallized from absolute alcohol. Good quality single crystals suitable for X-ray diffraction analysis were obtained by slow evaporation of ethanol at room temperature (yield: 80%; m.p. 413 K).

7. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. The N-bound H atom was located in a difference Fourier map and refined isotropically. C-bound H atoms were positioned geometrically and refined as riding, with C—H = 0.93–0.96 Å and U_{iso}(H) = 1.2–1.5 U_{eq}(C).

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_9H_8N^+ \cdot C_{12}H_9N_4O_7^-$
M_r	451.40
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	296
a, b, c (Å)	7.5315 (3), 15.5640 (8), 17.3901 (8)
V (Å^3)	2038.47 (16)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.11
Crystal size (mm)	$0.35 \times 0.30 \times 0.25$
Data collection	
Diffractometer	Bruker Kappa APEXII CCD
Absorption correction	Multi-scan (*SADABS*; Bruker, 2004)
T_{min}, T_{max}	0.958, 0.984
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	27633, 3588, 2797
R_{int}	0.038
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.594
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.055, 0.164, 1.11
No. of reflections	3588
No. of parameters	302
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.29, −0.26
Absolute structure	Flack x determined using 1033 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter	0.5 (4)

Computer programs: *APEX2, SAINT* and *XPREP* (Bruker, 2004), *SIR92* (Altomare *et al.*, 1993), *SHELXL2014* (Sheldrick, 2015), *ORTEP-3 for Windows* (Farrugia, 2012) and *Mercury* (Macrae *et al.*, 2008).

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Isoquinolinium 5-(2,4-dinitrophenyl)-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate: crystal structure, Hirshfeld surface analysis and pharmacological evaluation

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Computing details

Data collection: *APEX2* (Bruker, 2004); cell refinement: *APEX2* and *SAINT* (Bruker, 2004); data reduction: *SAINT* and *XPREP* (Bruker, 2004); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1993); program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2015); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 2012) and *Mercury* (Macrae *et al.*, 2008); software used to prepare material for publication: *SHELXL2014* (Sheldrick, 2015).

Isoquinolinium 5-(2,4-dinitrophenyl)-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate

Crystal data

$C_9H_8N^+ \cdot C_{12}H_9N_4O_7^-$	$D_x = 1.471$ Mg m^{-3}
$M_r = 451.40$	Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Orthorhombic, $P2_12_12_1$	Cell parameters from 9400 reflections
$a = 7.5315$ (3) Å	$\theta = 2.3$–$24.0°$
$b = 15.5640$ (8) Å	$\mu = 0.11$ mm^{-1}
$c = 17.3901$ (8) Å	$T = 296$ K
$V = 2038.47$ (16) Å^3	Block, brown
$Z = 4$	$0.35 \times 0.30 \times 0.25$ mm
$F(000) = 936$	

Data collection

Bruker Kappa APEXII CCD diffractometer	27633 measured reflections
Radiation source: fine-focus sealed tube	3588 independent reflections
Graphite monochromator	2797 reflections with $I > 2\sigma(I)$
ω and φ scan	$R_{int} = 0.038$
Absorption correction: multi-scan (SADABS; Bruker, 2004)	$\theta_{max} = 25.0°$, $\theta_{min} = 2.3°$
	$h = -8 \rightarrow 8$
	$k = -18 \rightarrow 18$
$T_{min} = 0.958$, $T_{max} = 0.984$	$l = -20 \rightarrow 20$

Refinement

Refinement on F^2	Hydrogen site location: mixed
Least-squares matrix: full	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)] = 0.055$	
$wR(F^2) = 0.164$	$w = 1/[\sigma^2(F_o^2) + (0.0596P)^2 + 2.2423P]$
$S = 1.11$	where $P = (F_o^2 + 2F_c^2)/3$
3588 reflections	$(\Delta/\sigma)_{max} < 0.001$
302 parameters	$\Delta\rho_{max} = 0.29$ e Å^{-3}
0 restraints	$\Delta\rho_{min} = -0.26$ e Å^{-3}

Absolute structure: Flack *x* determined using
1033 quotients [(*I*⁺)-(*I*⁻)]/[(*I*⁺)+(*I*⁻)] (Parsons *et
al.*, 2013)
Absolute structure parameter: 0.5 (4)

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. The elements in the sample do not have sufficient anomalous scattering power for Mo(k*α*) radiation. Hence the Flack parameter and its standard deviation obtained from refinement have no physical significance.

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

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	1.0128 (8)	0.1849 (4)	0.6047 (3)	0.0420 (13)
C2	0.9775 (8)	0.1140 (3)	0.5603 (3)	0.0430 (13)
H2	0.9489	0.0617	0.5830	0.052*
C3	0.9850 (7)	0.1217 (3)	0.4818 (3)	0.0380 (12)
C4	1.0322 (7)	0.1979 (3)	0.4434 (3)	0.0360 (11)
C5	1.0660 (8)	0.2679 (3)	0.4922 (3)	0.0443 (13)
H5	1.0970	0.3204	0.4705	0.053*
C6	1.0549 (8)	0.2615 (4)	0.5715 (3)	0.0495 (14)
H6	1.0761	0.3094	0.6021	0.059*
C7	1.0594 (7)	0.2047 (3)	0.3605 (3)	0.0337 (11)
C8	1.1510 (7)	0.1402 (3)	0.3218 (3)	0.0357 (11)
C9	1.1333 (8)	0.2196 (3)	0.2030 (3)	0.0421 (13)
C10	1.0069 (7)	0.2807 (3)	0.3207 (3)	0.0388 (12)
C11	0.9855 (12)	0.3574 (4)	0.1982 (4)	0.072 (2)
H11A	0.9241	0.3963	0.2317	0.108*
H11B	1.0872	0.3856	0.1766	0.108*
H11C	0.9074	0.3396	0.1576	0.108*
C12	1.2891 (9)	0.0820 (4)	0.2065 (3)	0.0569 (16)
H12A	1.3142	0.0369	0.2426	0.085*
H12B	1.2236	0.0590	0.1639	0.085*
H12C	1.3985	0.1062	0.1884	0.085*
C13	1.4554 (8)	0.0032 (4)	0.5236 (3)	0.0486 (14)
H13	1.4114	0.0499	0.5511	0.058*
C14	1.5694 (7)	−0.0536 (3)	0.5585 (3)	0.0404 (12)
C15	1.6326 (7)	−0.1244 (4)	0.5152 (3)	0.0449 (13)
C16	1.5786 (8)	−0.1322 (4)	0.4383 (3)	0.0522 (15)
H16	1.6195	−0.1776	0.4084	0.063*
C17	1.4675 (8)	−0.0738 (4)	0.4083 (3)	0.0546 (15)
H17	1.4313	−0.0788	0.3573	0.065*
C18	1.6259 (8)	−0.0443 (4)	0.6357 (3)	0.0554 (15)
H18	1.5888	0.0026	0.6647	0.066*
C19	1.7348 (9)	−0.1043 (6)	0.6669 (4)	0.069 (2)
H19	1.7689	−0.0991	0.7181	0.083*

C20	1.7960 (10)	−0.1728 (5)	0.6242 (4)	0.074 (2)
H20	1.8716	−0.2126	0.6471	0.088*
C21	1.7487 (9)	−0.1835 (4)	0.5502 (4)	0.0642 (18)
H21	1.7926	−0.2298	0.5223	0.077*
N1	1.0035 (8)	0.1760 (4)	0.6875 (3)	0.0628 (15)
N2	0.9243 (7)	0.0456 (3)	0.4385 (3)	0.0496 (12)
N3	1.0427 (7)	0.2826 (3)	0.2415 (2)	0.0435 (11)
N4	1.1845 (6)	0.1485 (3)	0.2441 (2)	0.0389 (10)
N5	1.4081 (7)	−0.0079 (3)	0.4514 (3)	0.0508 (13)
O1	1.0316 (9)	0.2406 (4)	0.7261 (3)	0.0887 (18)
O2	0.9721 (10)	0.1063 (4)	0.7153 (3)	0.099 (2)
O3	0.8197 (6)	0.0553 (3)	0.3865 (3)	0.0632 (12)
O4	0.9781 (7)	−0.0246 (3)	0.4618 (3)	0.0690 (14)
O5	0.9298 (6)	0.3428 (3)	0.3499 (2)	0.0578 (11)
O6	1.1665 (7)	0.2254 (3)	0.1336 (2)	0.0643 (12)
O7	1.2084 (6)	0.0724 (2)	0.3535 (2)	0.0534 (11)
H5A	1.330 (8)	0.032 (4)	0.431 (3)	0.043 (15)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.050 (3)	0.052 (3)	0.025 (2)	0.002 (3)	0.002 (2)	−0.005 (2)
C2	0.053 (3)	0.039 (3)	0.037 (3)	−0.001 (3)	−0.001 (3)	0.005 (2)
C3	0.042 (3)	0.037 (3)	0.035 (3)	−0.002 (2)	0.000 (2)	−0.002 (2)
C4	0.036 (3)	0.039 (3)	0.034 (3)	0.002 (2)	−0.005 (2)	−0.003 (2)
C5	0.050 (3)	0.040 (3)	0.044 (3)	0.000 (3)	−0.004 (3)	0.002 (2)
C6	0.054 (3)	0.051 (3)	0.043 (3)	0.002 (3)	−0.010 (3)	−0.018 (3)
C7	0.041 (3)	0.030 (2)	0.030 (3)	−0.002 (2)	−0.004 (2)	0.000 (2)
C8	0.035 (3)	0.039 (3)	0.033 (3)	0.000 (2)	−0.004 (2)	0.002 (2)
C9	0.047 (3)	0.042 (3)	0.038 (3)	−0.013 (3)	0.001 (2)	0.006 (2)
C10	0.042 (3)	0.032 (3)	0.043 (3)	−0.004 (2)	−0.001 (2)	0.002 (2)
C11	0.108 (6)	0.053 (4)	0.054 (4)	0.004 (4)	−0.006 (4)	0.015 (3)
C12	0.059 (4)	0.065 (4)	0.047 (3)	0.008 (3)	0.012 (3)	0.000 (3)
C13	0.048 (3)	0.042 (3)	0.055 (4)	0.004 (3)	0.003 (3)	−0.004 (3)
C14	0.037 (3)	0.039 (3)	0.045 (3)	−0.002 (2)	0.002 (2)	0.004 (2)
C15	0.039 (3)	0.046 (3)	0.049 (3)	0.005 (3)	0.002 (3)	0.008 (3)
C16	0.051 (3)	0.052 (3)	0.054 (4)	0.007 (3)	0.002 (3)	−0.011 (3)
C17	0.055 (4)	0.064 (4)	0.045 (3)	−0.002 (3)	−0.006 (3)	0.004 (3)
C18	0.054 (4)	0.063 (4)	0.049 (4)	−0.006 (3)	−0.001 (3)	−0.004 (3)
C19	0.053 (4)	0.105 (6)	0.049 (4)	−0.014 (4)	−0.013 (3)	0.012 (4)
C20	0.066 (4)	0.082 (5)	0.073 (5)	0.019 (4)	−0.013 (4)	0.021 (4)
C21	0.062 (4)	0.057 (4)	0.074 (5)	0.020 (3)	−0.007 (4)	0.008 (3)
N1	0.070 (4)	0.081 (4)	0.037 (3)	0.018 (3)	−0.002 (3)	−0.004 (3)
N2	0.057 (3)	0.041 (3)	0.051 (3)	−0.010 (2)	0.009 (3)	−0.007 (2)
N3	0.062 (3)	0.033 (2)	0.036 (2)	0.002 (2)	−0.002 (2)	0.0105 (19)
N4	0.040 (2)	0.042 (2)	0.035 (2)	0.003 (2)	0.0034 (19)	0.0010 (19)
N5	0.051 (3)	0.048 (3)	0.054 (3)	0.008 (2)	−0.008 (2)	0.008 (3)
O1	0.122 (5)	0.099 (4)	0.045 (3)	0.009 (4)	−0.011 (3)	−0.026 (3)

O2	0.158 (6)	0.094 (4)	0.046 (3)	−0.004 (4)	0.003 (4)	0.015 (3)
O3	0.066 (3)	0.065 (3)	0.058 (3)	−0.014 (2)	−0.012 (2)	−0.016 (2)
O4	0.099 (4)	0.040 (2)	0.068 (3)	−0.005 (2)	0.012 (3)	−0.001 (2)
O5	0.076 (3)	0.044 (2)	0.054 (2)	0.010 (2)	−0.002 (2)	0.006 (2)
O6	0.086 (3)	0.063 (3)	0.044 (3)	−0.011 (3)	0.009 (2)	0.013 (2)
O7	0.060 (3)	0.055 (3)	0.045 (2)	0.017 (2)	0.003 (2)	0.007 (2)

Geometric parameters (Å, º)

C1—C6	1.362 (8)	C12—H12A	0.9600
C1—C2	1.372 (7)	C12—H12B	0.9600
C1—N1	1.448 (7)	C12—H12C	0.9600
C2—C3	1.372 (7)	C13—N5	1.316 (7)
C2—H2	0.9300	C13—C14	1.374 (8)
C3—C4	1.406 (7)	C13—H13	0.9300
C3—N2	1.476 (7)	C14—C18	1.415 (8)
C4—C5	1.404 (7)	C14—C15	1.418 (7)
C4—C7	1.460 (7)	C15—C16	1.402 (8)
C5—C6	1.385 (8)	C15—C21	1.408 (8)
C5—H5	0.9300	C16—C17	1.342 (8)
C6—H6	0.9300	C16—H16	0.9300
C7—C8	1.391 (7)	C17—N5	1.346 (8)
C7—C10	1.425 (7)	C17—H17	0.9300
C8—O7	1.267 (6)	C18—C19	1.357 (10)
C8—N4	1.381 (6)	C18—H18	0.9300
C9—O6	1.235 (6)	C19—C20	1.379 (10)
C9—N3	1.369 (7)	C19—H19	0.9300
C9—N4	1.373 (7)	C20—C21	1.346 (10)
C10—O5	1.236 (6)	C20—H20	0.9300
C10—N3	1.404 (7)	C21—H21	0.9300
C11—N3	1.452 (7)	N1—O2	1.211 (7)
C11—H11A	0.9600	N1—O1	1.228 (8)
C11—H11B	0.9600	N2—O3	1.209 (6)
C11—H11C	0.9600	N2—O4	1.234 (6)
C12—N4	1.455 (7)	N5—H5A	0.93 (6)
C6—C1—C2	120.6 (5)	N5—C13—C14	120.4 (5)
C6—C1—N1	121.1 (5)	N5—C13—H13	119.8
C2—C1—N1	118.3 (5)	C14—C13—H13	119.8
C3—C2—C1	118.9 (5)	C13—C14—C18	122.8 (6)
C3—C2—H2	120.6	C13—C14—C15	118.3 (5)
C1—C2—H2	120.6	C18—C14—C15	118.9 (5)
C2—C3—C4	123.8 (5)	C16—C15—C21	122.4 (6)
C2—C3—N2	115.1 (5)	C16—C15—C14	118.5 (5)
C4—C3—N2	120.9 (5)	C21—C15—C14	119.1 (6)
C5—C4—C3	114.5 (5)	C17—C16—C15	119.5 (6)
C5—C4—C7	121.0 (5)	C17—C16—H16	120.2
C3—C4—C7	124.4 (4)	C15—C16—H16	120.2

C6—C5—C4	122.3 (5)	C16—C17—N5	120.5 (6)
C6—C5—H5	118.9	C16—C17—H17	119.8
C4—C5—H5	118.9	N5—C17—H17	119.8
C1—C6—C5	120.0 (5)	C19—C18—C14	119.5 (6)
C1—C6—H6	120.0	C19—C18—H18	120.3
C5—C6—H6	120.0	C14—C18—H18	120.3
C8—C7—C10	120.1 (4)	C18—C19—C20	121.2 (6)
C8—C7—C4	119.6 (4)	C18—C19—H19	119.4
C10—C7—C4	120.0 (4)	C20—C19—H19	119.4
O7—C8—N4	116.1 (4)	C21—C20—C19	121.5 (7)
O7—C8—C7	124.1 (4)	C21—C20—H20	119.3
N4—C8—C7	119.8 (4)	C19—C20—H20	119.3
O6—C9—N3	121.8 (5)	C20—C21—C15	119.9 (7)
O6—C9—N4	120.8 (5)	C20—C21—H21	120.1
N3—C9—N4	117.5 (4)	C15—C21—H21	120.1
O5—C10—N3	118.4 (5)	O2—N1—O1	123.3 (6)
O5—C10—C7	125.4 (5)	O2—N1—C1	119.5 (6)
N3—C10—C7	116.1 (5)	O1—N1—C1	117.2 (6)
N3—C11—H11A	109.5	O3—N2—O4	124.8 (5)
N3—C11—H11B	109.5	O3—N2—C3	118.9 (5)
H11A—C11—H11B	109.5	O4—N2—C3	116.2 (5)
N3—C11—H11C	109.5	C9—N3—C10	124.1 (4)
H11A—C11—H11C	109.5	C9—N3—C11	117.9 (5)
H11B—C11—H11C	109.5	C10—N3—C11	118.0 (5)
N4—C12—H12A	109.5	C9—N4—C8	122.3 (4)
N4—C12—H12B	109.5	C9—N4—C12	119.4 (4)
H12A—C12—H12B	109.5	C8—N4—C12	118.2 (4)
N4—C12—H12C	109.5	C13—N5—C17	122.8 (5)
H12A—C12—H12C	109.5	C13—N5—H5A	117 (3)
H12B—C12—H12C	109.5	C17—N5—H5A	121 (3)
C6—C1—C2—C3	−0.1 (9)	C13—C14—C18—C19	178.2 (6)
N1—C1—C2—C3	179.7 (5)	C15—C14—C18—C19	−1.8 (9)
C1—C2—C3—C4	1.9 (9)	C14—C18—C19—C20	2.1 (10)
C1—C2—C3—N2	−172.9 (5)	C18—C19—C20—C21	−0.8 (12)
C2—C3—C4—C5	−2.1 (8)	C19—C20—C21—C15	−0.8 (11)
N2—C3—C4—C5	172.5 (5)	C16—C15—C21—C20	−180.0 (7)
C2—C3—C4—C7	173.1 (5)	C14—C15—C21—C20	0.9 (9)
N2—C3—C4—C7	−12.4 (8)	C6—C1—N1—O2	−177.3 (7)
C3—C4—C5—C6	0.5 (8)	C2—C1—N1—O2	2.9 (10)
C7—C4—C5—C6	−174.8 (6)	C6—C1—N1—O1	1.3 (9)
C2—C1—C6—C5	−1.4 (9)	C2—C1—N1—O1	−178.4 (6)
N1—C1—C6—C5	178.9 (5)	C2—C3—N2—O3	131.3 (5)
C4—C5—C6—C1	1.2 (9)	C4—C3—N2—O3	−43.7 (8)
C5—C4—C7—C8	132.9 (5)	C2—C3—N2—O4	−44.6 (7)
C3—C4—C7—C8	−41.9 (8)	C4—C3—N2—O4	140.4 (5)
C5—C4—C7—C10	−41.3 (7)	O6—C9—N3—C10	−177.7 (5)
C3—C4—C7—C10	143.8 (5)	N4—C9—N3—C10	3.2 (8)

C10—C7—C8—O7	177.1 (5)	O6—C9—N3—C11	0.2 (9)
C4—C7—C8—O7	2.9 (8)	N4—C9—N3—C11	−179.0 (6)
C10—C7—C8—N4	−2.6 (7)	O5—C10—N3—C9	177.3 (5)
C4—C7—C8—N4	−176.8 (5)	C7—C10—N3—C9	−4.4 (8)
C8—C7—C10—O5	−177.8 (5)	O5—C10—N3—C11	−0.5 (8)
C4—C7—C10—O5	−3.6 (8)	C7—C10—N3—C11	177.7 (5)
C8—C7—C10—N3	4.0 (7)	O6—C9—N4—C8	179.4 (5)
C4—C7—C10—N3	178.2 (5)	N3—C9—N4—C8	−1.4 (8)
N5—C13—C14—C18	179.4 (6)	O6—C9—N4—C12	4.0 (8)
N5—C13—C14—C15	−0.6 (8)	N3—C9—N4—C12	−176.8 (5)
C13—C14—C15—C16	1.2 (8)	O7—C8—N4—C9	−178.5 (5)
C18—C14—C15—C16	−178.8 (5)	C7—C8—N4—C9	1.2 (7)
C13—C14—C15—C21	−179.7 (5)	O7—C8—N4—C12	−3.1 (7)
C18—C14—C15—C21	0.4 (8)	C7—C8—N4—C12	176.7 (5)
C21—C15—C16—C17	179.9 (6)	C14—C13—N5—C17	−0.3 (9)
C14—C15—C16—C17	−0.9 (9)	C16—C17—N5—C13	0.6 (9)
C15—C16—C17—N5	0.1 (9)		

Hydrogen-bond geometry (Å, °)

D—H···A	D—H	H···A	D···A	D—H···A
N5—H5A···O7	0.93 (6)	1.74 (6)	2.592 (6)	150 (5)
C13—H13···O5[i]	0.93	2.40	3.260 (7)	153
C16—H16···O6[ii]	0.93	2.33	3.187 (7)	154
C17—H17···O2[iii]	0.93	2.61	3.424 (8)	146

Symmetry codes: (i) $x+1/2, -y+1/2, -z+1$; (ii) $-x+3, y-1/2, -z+1/2$; (iii) $-x+5/2, -y, z-1/2$.