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5-(1-Acetamido-3-methylbutyl)-5-methylimidazolidine-2,4-dione monohydrate

K. SethuSankar,[a] S. Thennarasu,[b] D. Velmurugan,[a]* S. Shanmuga Sundara Raj,[c] H.-K. Fun[c] and P. T. Perumal[b]

[a]Department of Crystallography and Biophysics, University of Madras, Guindy Campus, Chennai 600 025, India, [b]Organic Chemistry Division, CLRI, Chennai 600 020, India, and [c]School of Physics, Universiti Sains Malaysia, 11800 USM Penang, Malaysia

Correspondence e-mail: d_velu@yahoo.com

Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.003 Å
R factor = 0.057
wR factor = 0.166
Data-to-parameter ratio = 20.1

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

The single-crystal X-ray diffraction study of the title compound, *N*-[3-methyl-1-(4-methyl-2,5-dioxoimidazolidin-4-yl)buty]]acetamide monohydrate, $C_{11}H_{19}N_3O_3\cdot H_2O$, confirms that the imidazolidinedione ring is in a planar conformation, as evidenced by NMR studies. There are chains of intermolecular hydrogen bonds involving the imido carbonyl-O atom and the acetamido carbonyl-O atom as acceptors, and the water molecule as donor. The crystal packing is also stabilized by N—H···O intermolecular interactions.

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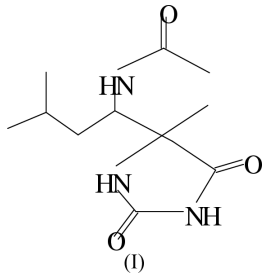
Comment

Hydantoins, well known for their central nervous system activity (Tunnicliff, 1996; Morkunas & Miller, 1997), have been reported to possess a variety of pharmacological properties. 5,5–Disubstituted hydantoins often exhibit narcotic and hypnotic activity and have been used for the treatment of chorea and epilepsy. Amino hydantoins are used in the treatment of urinary tract infections, as muscle relaxants and as bactericides. The structure consists of a 2,4-imidazolidinedione ring (commonly known as hydantoin) with a methyl group substituted at the 5 position. A number of 2,4-imidazolidinedione derivatives have been shown to act as inhibitors of metalloproteins (Kelly *et al.*, 1997) and exihibit anti-inflammatory and antifungal activities (Malhotra *et al.*, 1990). Recently 5,5-disubstituted hydantoins have been reported to possess potent inhibitory activity towards HIV protease (Comber *et al.*, 1992, 1997) and act as sodium channel blockers (Lang *et al.*, 1997; Wayne *et al.*, 1994). Also, hydantoins are attractive substrates for the synthesis of amino acids (Edward & Robert, 1994). In a continuation of our endeavour to design small antimicrobial peptidomimetics, the title compound, (I), was synthesized as an intermediate for an α,β-diamino acid. The structure was determined as a part of the characterization process. Of the two possible diastereomers, only one appears to have been selectively crystallized in our method. Preferential crystallization of hydantoin isomers has been reported in the literature (Ndzie *et al.*, 1997).



(I)

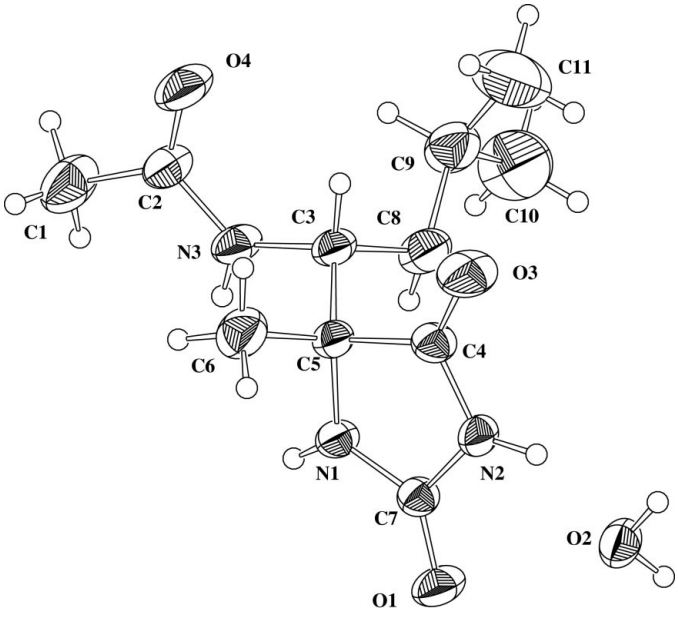


Figure 1
The molecular structure of (I) showing 50% probability displacement ellipsoids and the atom-numbering scheme.

Fig. 1 shows the *ZORTEP* plot (Zsolnai, 1997) of (I) along with the atom-numbering scheme. The five-membered ring is essentially planar. The NMR spectrum of the title compound in DMSO-d_6 shows two singlets at 10.67 and 7.62 p.p.m. corresponding to the imide and amide NH protons, respectively. This observation suggests a planar ring conformation, in agreement with a quasi-planar conformation proposal based on the existence of four-bond couplings between amide and imide protons in 1,3-positions of the imidazolidindione ring (Erzsebet *et al.*, 1998). The dihedral angle between the least-squares plane through atoms C3/C8/C9/C10/C11 and the imidazolidine ring is 81.9 (1)°. The dihedral angle between the least-squares planes through atoms C3/C8/C9/C10/C11 and C3/N3/C2/O4/C1 is 77.3 (1)°. The dihedral angle between the least-squares planes through atoms C3/N3/C2/O4/C1 and the five-membered ring is 4.59 (1)°. In the imidazolidine ring, the values of the N1—C5 and C4—C5 distances, and the N1—C5—C4 angle (see Table 1) are in agreement with the literature data (Camerman & Camerman, 1971; Florencio *et al.*, 1978; Verdier *et al.*, 1977, 1979; Fujiwara & Van der Veen, 1979; Koch *et al.*, 1975), the observed values for the above are in the ranges 1.45–1.48, 1.51–1.55 Å and 99–101°, respectively. The torsion angle C5—C3—C8—C9 of −159.2 (2)° describes the conformation of the portion of the side chain as (−)-antiperiplanar about C3—C8.

The packing is stabilized by O—H···O and N—H···O intermolecular hydrogen bonds. The solvent molecule plays a major role in the packing of the molecule. Packing shows that each molecule is bound to its neighbours through hydrogen bonds to form chains running parallel to one another in the crystal.

Experimental

Potassium cyanide (1.3 g, 0.02 mol) and ammonium carbonate (6.283 g, 0.04 mol) were dissolved in aqueous ethanol (200 ml) and 3-acetamido-5-methylhexan-2-one (1.7 g, 0.01 mol) was added. The clear reaction mixture was heated at 333–343 K for 9 h and the solvent was removed by distillation. The solid obtained was extracted with ethyl acetate. Evaporation of the ethyl acetate gave a colourless solid which was recrystallized from 0.1 *N* hydrochloric acid. Crystallization: 750 mg of the title compound was dissolved in 7.0 ml methanol and 3.0 ml of 3 *N* HCl, and the solution was refluxed on a water bath for 1 h and filtered using Whatmann filter paper. The hot solution was allowed to cool to room temprature while methanol was allowed to evaporate. When the volume of the solution was about 5.0 ml, 3–5 drops of concentrated HCl were added along the sides of the container. Needle-like crystals were seen after 16 h. The supernatant was transfered to another beaker and the crystals were dried..

Crystal data

$C_{11}H_{19}N_3O_3\cdot H_2O$
M_r = 259.31
Monoclinic, $P2_1/c$
a = 6.2770 (1) Å
b = 19.7080 (4) Å
c = 11.9399 (1) Å
β = 101.64 (1)°
V = 1446.67 (4) Å^3
Z = 4
D_x = 1.191 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 6646 reflections
θ = 1.5–28.3°
μ = 0.09 mm^{-1}
T = 293 (2) K
Block, white
0.40 × 0.30 × 0.26 mm

Data collection

Siemens SMART CCD area-detector diffractometer
ω scans
10 168 measured reflections
3536 independent reflections
2418 reflections with $I > 2\sigma(I)$
R_{int} = 0.063
θ_{max} = 28.2°
$h = -8 \rightarrow 8$
$k = -26 \rightarrow 26$
$l = -15 \rightarrow 9$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.057
$wR(F^2)$ = 0.166
S = 0.94
3536 reflections
176 parameters
H atoms: see below
$w = 1/[\sigma^2(F_o^2) + (0.1P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.065
$\Delta\rho_{max}$ = 0.34 e Å^{-3}
$\Delta\rho_{min}$ = −0.36 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.006 (4)

Table 1
Selected geometric parameters (Å, °).

O1—C7	1.222 (2)	N2—C4	1.356 (2)
O3—C4	1.225 (2)	N2—C7	1.393 (2)
O4—C2	1.227 (2)	N3—C2	1.348 (2)
N1—C7	1.354 (2)	N3—C3	1.458 (2)
N1—C5	1.464 (2)	C4—C5	1.533 (2)
C7—N1—C5	112.1 (1)	O3—C4—N2	126.7 (2)
C4—N2—C7	111.8 (1)	O3—C4—C5	125.9 (2)
C2—N3—C3	125.0 (1)	N2—C4—C5	107.4 (1)
O4—C2—N3	122.2 (2)	N1—C5—C4	100.7 (1)
O4—C2—C1	122.4 (2)	N1—C5—C3	112.2 (1)
N3—C2—C1	115.3 (2)	O1—C7—N1	128.1 (1)
N3—C3—C5	109.5 (2)	O1—C7—N2	124.4 (1)
N3—C3—C8	110.3 (2)	N1—C7—N2	107.5 (1)
C3—N3—C2—O4	3.7 (3)	N3—C3—C5—N1	69.7 (2)
C3—N3—C2—C1	−176.5 (2)	C5—N1—C7—N2	−6.9 (2)
C7—N2—C4—O3	178.4 (2)	C4—N2—C7—O1	−175.4 (2)
O3—C4—C5—N1	177.7 (2)		

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N2—H2···O2	0.86	2.03	2.809 (2)	151
N1—H1···O3^{i}	0.86	2.31	3.122 (2)	157
N3—H3···O3^{i}	0.86	2.12	2.964 (2)	166
O2—H1O···O4^{ii}	0.83 (3)	1.99 (3)	2.820 (2)	177 (3)
O2—H2O···O1^{iii}	0.91 (3)	1.89 (3)	2.796 (2)	176 (3)

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

All H atoms, except for the water H atoms, were included at calculated positions and refined using a riding model. The water H atoms were found from difference Fourier syntheses and were refined isotropically.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ZORTEP* (Zsolnai, 1997); software used to prepare material for publication: *SHELXL*97 and *PARST* (Nardelli, 1983, 1995).

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