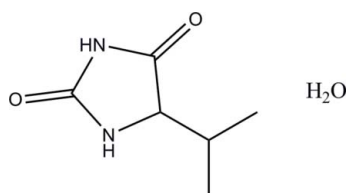# 5-Isopropylimidazolidine-2,4-dione monohydrate

Alaa A.-M. Abdel-Aziz,[a] Adel S. El-Azab,[a] Abdulrahman M. Al-Obaid,[a] Madhukar Hemamalini[b] and Hoong-Kun Fun[b]*‡

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In the title compound, $C_6H_{10}N_2O_2 \cdot H_2O$, the imidazole ring is essentially planar, with a maximum deviation of 0.012 (2) Å. In the crystal, molecules are connected *via* N—H⋯O and O—H⋯O hydrogen bonds, forming a supramolecular tape along the *a* axis.

Related literature

For details and applications of hydantoins, see: El-Deeb *et al.* (2010); Rajic *et al.* (2006); Carmi *et al.* (2006); Sergent *et al.*, (2008); Yu *et al.* (2004). For related structures, see: Delgado *et al.* (2007); Ciechanowicz-Rutkowska *et al.* (1994). For the synthetic procedure, see: Abdel-Aziz (2007). For a description of the Cambridge Structural Database, see: Allen (2002).

Experimental

Crystal data

$C_6H_{10}N_2O_2 \cdot H_2O$
$M_r = 160.18$
Orthorhombic, $P2_12_12_1$
$a = 6.2688$ (3) Å
$b = 9.2387$ (4) Å
$c = 14.8280$ (7) Å

$V = 858.77$ (7) Å^3
$Z = 4$
Cu $K\alpha$ radiation
$\mu = 0.84$ mm^{-1}
$T = 296$ K
$0.90 \times 0.21 \times 0.16$ mm

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Data collection

Bruker SMART APEXII CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2009)
$T_{min} = 0.518$, $T_{max} = 0.879$

5702 measured reflections
1497 independent reflections
1378 reflections with $I > 2\sigma(I)$
$R_{int} = 0.027$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.037$
$wR(F^2) = 0.098$
$S = 1.09$
1497 reflections
117 parameters
H atoms treated by a mixture of independent and constrained refinement

$\Delta\rho_{max} = 0.12$ e Å^{-3}
$\Delta\rho_{min} = -0.18$ e Å^{-3}
Absolute structure: Flack (1983), with 592 Friedel pairs
Flack parameter: 0.2 (3)

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

D—H⋯A	D—H	H⋯A	D⋯A	D—H⋯A
N1—H1N1⋯O2^i	0.81 (2)	2.12 (2)	2.927 (2)	174.0 (19)
N2—H1N2⋯O1W^{ii}	0.87 (3)	1.88 (3)	2.751 (2)	173 (2)
O1W—H1W1⋯O1	0.82 (4)	1.95 (4)	2.767 (2)	173 (3)
O1W—H2W2⋯O1^{iii}	0.86 (4)	1.98 (4)	2.839 (2)	171 (4)

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

Data collection: *APEX2* (Bruker, 2009); cell refinement: *SAINT* (Bruker, 2009); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 2008); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL* and *PLATON* (Spek, 2009).

References

Abdel-Aziz, A. A.-M. (2007). *Eur. J. Med. Chem.* **42**, 614–626.
Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Bruker (2009). *APEX2, SAINT* and *SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA.
Carmi, C., Cavazzoni, A., Zuliani, V., Lodola, A., Bordi, F., Plazzi, P. V., Alfieri, R. R., Petronini, P. G. & Mor, M. (2006). *Bioorg. Med. Chem. Lett.* **16**, 4021–4025.
Ciechanowicz-Rutkowska, M., Kieć-Kononowicz, K., Howard, S. T., Lieberman, H. & Hursthouse, M. B. (1994). *Acta Cryst.* B**50**, 86–96.
Delgado, G. E., Mora, A. J., Uzcátegui, J., Bahsas, A. & Briceño, A. (2007). *Acta Cryst.* C**63**, o448-o450.
El-Deeb, I. M., Bayoumi, S. M., El-Sherbeny, M. A. & Abdel-Aziz, A. A.-M. (2010). *Eur. J. Med. Chem.* **45**, 2516–2530.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Rajic, Z., Zorc, B., Raic-Malic, S., Ester, K., Kralj, M., Pavelic, K., Balzarini, J., De Clercq, E. & Mintas, M. (2006). *Molecules*, **11**, 837–848.
Sergent, D., Wang, Q., Sasaki, N. A. & Ouazzani, J. (2008). *Bioorg. Med. Chem. Lett.* **18**, 4332–4335.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Spek, A. L. (2009). *Acta Cryst.* D**65**, 148–155.
Yu, F.-L., Schwalbe, C. H. & Watkin, D. J. (2004). *Acta Cryst.* C**60**, o714–o717.

supplementary materials

5-Isopropylimidazolidine-2,4-dione monohydrate

A. A.-M. Abdel-Aziz, A. S. El-Azab, A. M. Al-Obaid, M. Hemamalini and H.-K. Fun

Comment

Hydantoins (imidazolidine-2,4-dione) are important classes of compounds which have long attracted attention, owing to their remarkable biological and pharmacological properties, such as antitumor activity, antiviral activity, insulinotropic properties and EGFR inhibitors (El-Deeb *et al.*, 2010; Rajic *et al.*, 2006; Carmi *et al.*, 2006; Sergent *et al.*, 2008). The crystal structures of (*S*)-5-Benzylimidazolidine-2,4-dione monohydrate (Delgado *et al.*, 2007) and diphenylhydantoin derivatives (Ciechanowicz-Rutkowska *et al.*, 1994) have been reported in the literature. The title compound was successfully obtained in an optical active form without racemization by dehydrative cyclization in one-pot reaction of L-valine and urea in the presence of DPPOX as catalyst (Abdel-Aziz, 2007).

The asymmetric unit contains one (*S*)-5-isopropylimidazolidine-2,4-dione molecule and one water molecule as shown in Fig. 1. The imidazole (N1,N2/C1–C3) ring is essentially planar, with maximum deviations of 0.012 (2) Å for atom C3. The N1—C1—O1 [128.32 (19)°] angle is greater than the N2—C1—O1 [124.05 (17)°] angle. This difference is also observed in the hydantoin molecule (Yu *et al.*, 2004) and 50 other hydantoin derivatives reported in the Cambridge Structural Database (Version 5.28; Allen, 2002) with both unsubstituted NH groups and sp^3-hybridization at C3. In the crystal structure (Fig. 2), the molecules are connected *via* N—H⋯O and O—H⋯O hydrogen bonds (Table 1), forming a supramolecular tape along the *a* axis.

Experimental

The DPPOX (1.5 equiv) was added to the equimolar solution of L-valine and urea in MeCN in addition to Et_3N (1.5 equiv) and the mixture was stirred at 50°C for 60 min. After removal of the solvent, the residue was taken up in organic solvent EtOAc, and washed successively with HCl aq and $NaHCO_3$ aq. Evaporation of the dried organic solvent gave the title compound. The colourless single-crystals suitable for X-ray analysis was obtained by recrystallization from ethanol (m.p. 145–147 °C; yield: 95%).

Refinement

Atoms H1N1, H1N2, H1W1 and H2W2 were located in a difference Fourier map and refined freely [N—H = 0.80 (2)–0.87 (3) Å; O—H = 0.82 (4)–0.87 (4) Å]. The remaining H atoms were positioned geometrically [C—H = 0.96 or 0.98 Å] and were refined using a riding model, with $U_{iso}(H) = 1.2$ or $1.5U_{eq}(C)$. A rotating group model was applied to the methyl groups. Even though there is sufficient anomalous dispersion to find the absolute configuration as the compound crystallize out in a chiral space group and Cu radiation was used, this was unsuccessful as the crystal is a inversion twin [BASF ratio of 0.8 (3):0.2 (3)].
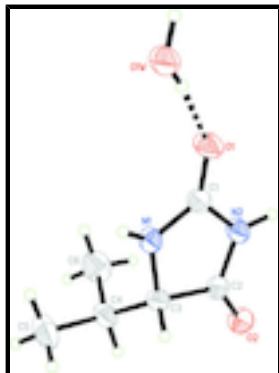
supplementary materials

Figures

Fig. 1. The asymmetric unit of the title compound, showing 50% probability displacement ellipsoids. The O—H···O hydrogen bond is shown by a dashed line.
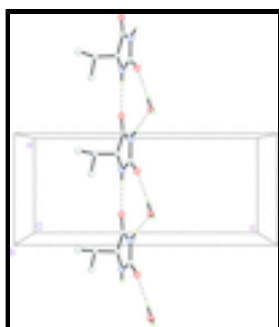

Fig. 2. A partial packing view of the title compound. The hydrogen bonds are shown by dashed lines.

5-Isopropylimidazolidine-2,4-dione monohydrate

Crystal data

$C_6H_{10}N_2O_2 \cdot H_2O$	$F(000) = 344$
$M_r = 160.18$	$D_x = 1.239$ Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Cu $K\alpha$ radiation, $\lambda = 1.54178$ Å
Hall symbol: P 2ac 2ab	Cell parameters from 2281 reflections
$a = 6.2688$ (3) Å	$\theta = 5.6–65.9°$
$b = 9.2387$ (4) Å	$\mu = 0.84$ mm^{-1}
$c = 14.8280$ (7) Å	$T = 296$ K
$V = 858.77$ (7) Å^3	Needle, colourless
$Z = 4$	$0.90 \times 0.21 \times 0.16$ mm

Data collection

Bruker SMART APEXII CCD area-detector diffractometer	1497 independent reflections
Radiation source: fine-focus sealed tube	1378 reflections with $I > 2\sigma(I)$
graphite	$R_{int} = 0.027$
φ and ω scans	$\theta_{max} = 67.3°$, $\theta_{min} = 5.6°$
Absorption correction: multi-scan (*SADABS*; Bruker, 2009)	$h = -7 \rightarrow 5$
$T_{min} = 0.518$, $T_{max} = 0.879$	$k = -11 \rightarrow 10$

5702 measured reflections $l = -17 \rightarrow 17$

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.037$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.098$	$w = 1/[\sigma^2(F_o^2) + (0.0552P)^2 + 0.0813P]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.09$	$(\Delta/\sigma)_{max} = 0.001$
1497 reflections	$\Delta\rho_{max} = 0.12$ e Å^{-3}
117 parameters	$\Delta\rho_{min} = -0.18$ e Å^{-3}
0 restraints	Absolute structure: Flack (1983), 592 Friedel pairs
Primary atom site location: structure-invariant direct methods	Flack parameter: 0.2 (3)

Special details

Experimental. ^{1}H NMR (DMSO–d$_6$): 10.54 (s, 1H, NH), 7.87 (s, 1H, NH), 3.89 (s, 1H), 2.01–1.97 (m, 1H), 0.94–0.92 (d, 3H, J = 7.0 Hz), 0.80–0.78 (d, 3H, J = 6.5 Hz). ^{13}C NMR (DMSO–d$_6$): 175.87, 158.28, 63.22, 30.01, 18.93, 16.31.

Geometry. All s.u.'s (except the s.u. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell s.u.'s are taken into account individually in the estimation of s.u.'s in distances, angles and torsion angles; correlations between s.u.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell s.u.'s is used for estimating s.u.'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 $F^2 > 2\sigma(F^2)$ 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}
O1	0.6583 (2)	0.56794 (15)	0.46328 (11)	0.0679 (5)
O2	1.2150 (2)	0.27203 (15)	0.39487 (11)	0.0590 (4)
N1	0.6703 (3)	0.34173 (17)	0.39871 (11)	0.0472 (4)
N2	0.9719 (2)	0.44507 (16)	0.43611 (11)	0.0503 (4)
C1	0.7524 (3)	0.46070 (19)	0.43523 (13)	0.0481 (4)
C2	1.0337 (3)	0.31526 (19)	0.40226 (13)	0.0440 (4)
C3	0.8324 (3)	0.23514 (18)	0.37618 (12)	0.0436 (4)
H3A	0.8156	0.1507	0.4156	0.052*
C4	0.8317 (3)	0.1851 (2)	0.27789 (14)	0.0534 (5)
H4A	0.9533	0.1196	0.2701	0.064*
C5	0.6312 (4)	0.0986 (3)	0.25796 (19)	0.0828 (8)
H5A	0.6202	0.0197	0.2998	0.124*

H5B	0.6381	0.0613	0.1976	0.124*
H5C	0.5086	0.1602	0.2639	0.124*
C6	0.8624 (5)	0.3102 (3)	0.21256 (16)	0.0810 (7)
H6A	0.9926	0.3600	0.2266	0.122*
H6B	0.7446	0.3760	0.2177	0.122*
H6C	0.8694	0.2736	0.1520	0.122*
H1N1	0.543 (4)	0.329 (2)	0.3981 (13)	0.045 (5)*
H1N2	1.059 (5)	0.509 (3)	0.4591 (17)	0.078 (8)*
O1W	0.2489 (3)	0.63212 (17)	0.52044 (13)	0.0665 (4)
H1W1	0.374 (6)	0.617 (3)	0.507 (2)	0.096 (11)*
H2W2	0.214 (6)	0.721 (4)	0.531 (3)	0.122 (13)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0438 (9)	0.0566 (8)	0.1033 (12)	0.0068 (6)	−0.0017 (7)	−0.0302 (8)
O2	0.0292 (8)	0.0607 (8)	0.0871 (11)	0.0039 (6)	−0.0030 (6)	−0.0086 (7)
N1	0.0246 (8)	0.0507 (8)	0.0662 (10)	−0.0020 (6)	−0.0013 (6)	−0.0127 (7)
N2	0.0309 (9)	0.0475 (8)	0.0725 (11)	−0.0035 (6)	−0.0045 (7)	−0.0147 (8)
C1	0.0372 (10)	0.0474 (9)	0.0597 (12)	0.0028 (8)	−0.0024 (8)	−0.0079 (8)
C2	0.0312 (9)	0.0468 (9)	0.0541 (10)	−0.0018 (7)	−0.0011 (7)	−0.0001 (8)
C3	0.0323 (9)	0.0394 (8)	0.0591 (10)	−0.0025 (6)	0.0003 (7)	−0.0028 (7)
C4	0.0443 (11)	0.0491 (9)	0.0667 (12)	−0.0016 (8)	0.0028 (8)	−0.0161 (8)
C5	0.0645 (16)	0.0895 (17)	0.0945 (18)	−0.0206 (13)	−0.0049 (14)	−0.0376 (14)
C6	0.098 (2)	0.0838 (16)	0.0617 (14)	−0.0079 (15)	0.0041 (13)	−0.0044 (12)
O1W	0.0438 (10)	0.0557 (8)	0.1000 (12)	−0.0042 (7)	−0.0067 (8)	−0.0203 (8)

Geometric parameters (Å, °)

O1—C1	1.226 (2)	C4—C5	1.518 (3)
O2—C2	1.210 (2)	C4—C6	1.520 (3)
N1—C1	1.329 (2)	C4—H4A	0.9800
N1—C3	1.454 (2)	C5—H5A	0.9600
N1—H1N1	0.80 (2)	C5—H5B	0.9600
N2—C2	1.357 (2)	C5—H5C	0.9600
N2—C1	1.383 (3)	C6—H6A	0.9600
N2—H1N2	0.87 (3)	C6—H6B	0.9600
C2—C3	1.513 (2)	C6—H6C	0.9600
C3—C4	1.529 (3)	O1W—H1W1	0.82 (4)
C3—H3A	0.9800	O1W—H2W2	0.87 (4)
C1—N1—C3	112.51 (15)	C5—C4—C3	110.30 (17)
C1—N1—H1N1	120.6 (15)	C6—C4—C3	112.16 (16)
C3—N1—H1N1	126.2 (15)	C5—C4—H4A	107.2
C2—N2—C1	111.89 (15)	C6—C4—H4A	107.2
C2—N2—H1N2	124.4 (19)	C3—C4—H4A	107.2
C1—N2—H1N2	123.6 (19)	C4—C5—H5A	109.5
O1—C1—N1	128.32 (19)	C4—C5—H5B	109.5
O1—C1—N2	124.05 (17)	H5A—C5—H5B	109.5

N1—C1—N2	107.63 (16)	C4—C5—H5C	109.5
O2—C2—N2	126.42 (17)	H5A—C5—H5C	109.5
O2—C2—C3	126.79 (16)	H5B—C5—H5C	109.5
N2—C2—C3	106.79 (15)	C4—C6—H6A	109.5
N1—C3—C2	101.12 (13)	C4—C6—H6B	109.5
N1—C3—C4	114.95 (15)	H6A—C6—H6B	109.5
C2—C3—C4	113.19 (15)	C4—C6—H6C	109.5
N1—C3—H3A	109.1	H6A—C6—H6C	109.5
C2—C3—H3A	109.1	H6B—C6—H6C	109.5
C4—C3—H3A	109.1	H1W1—O1W—H2W2	116 (3)
C5—C4—C6	112.4 (2)		

Hydrogen-bond geometry (Å, °)

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N1—H1N1$\cdots$O2[i]	0.81 (2)	2.12 (2)	2.927 (2)	174.0 (19)
N2—H1N2$\cdots$O1W[ii]	0.87 (3)	1.88 (3)	2.751 (2)	173 (2)
O1W—H1W1$\cdots$O1	0.82 (4)	1.95 (4)	2.767 (2)	173 (3)
O1W—H2W2$\cdots$O1[iii]	0.86 (4)	1.98 (4)	2.839 (2)	171 (4)

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

Fig. 1

Fig. 2