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6-Amino-5,5-diisopropyl-5*H*-pyrimidine-2,4-dione hemihydrate

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Key indicators

Single-crystal X-ray study
T = 163 K
Mean σ(C–C) = 0.002 Å
R factor = 0.035
wR factor = 0.098
Data-to-parameter ratio = 12.7

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

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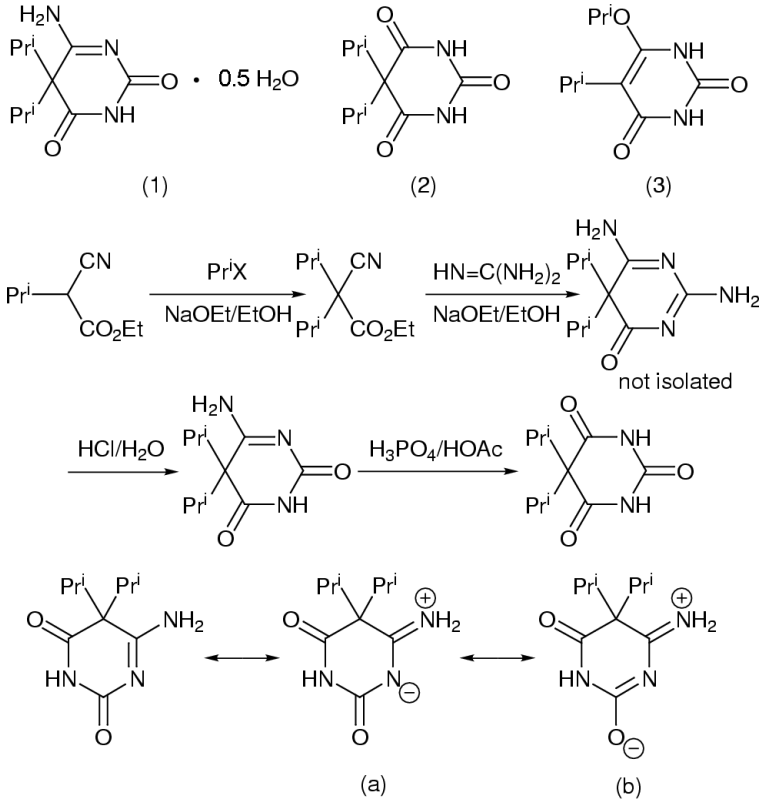
In the title compound, $C_{10}H_{17}N_3O_2\cdot0.5H_2O$, two 6-amino-5,5-diisopropyl-5*H*-pyrimidine-2,4-dione molecules and one molecule of water constitute the asymmetric unit in space group $P\overline{1}$. One molecule forms a one-dimensional hydrogen-bonded chain; the chains are cross-linked by hydrogen bonds to the second molecule and the water molecule.

Comment

5,5-Diisopropylbarbituric acid (2) is a pivotal structure for structure–reactivity and structure–activity relationship studies of barbituric acid derivatives (McKeown, 1980*a*, McKeown *et al.*, 1986, Wong & Mckeown, 1988, Prankerd & McKeown, 1990, 1992*a*,*b*, 1994). Although this structure had been reported (Preiswerk, 1923), the compound prepared had a different structure, *viz*. (3) (McKeown, 1980*b*). Attempts to prepare authentic (2) commenced with the synthetic route shown in the scheme, from which (1) was isolated as the penultimate product. The structure of (1) was initially determined using non-crystallographic methods, mainly ^{1}H-NMR.



Location of H atoms from the electron-density map indicated that (1) exists as the amino tautomer. However, due to

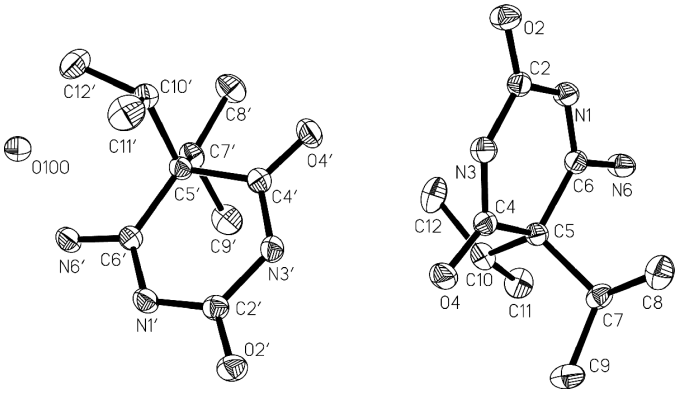


Figure 1
A view of the asymmetric unit of (1), showing displacement ellipsoids at the 50% probability level. H atoms are omitted for clarity.

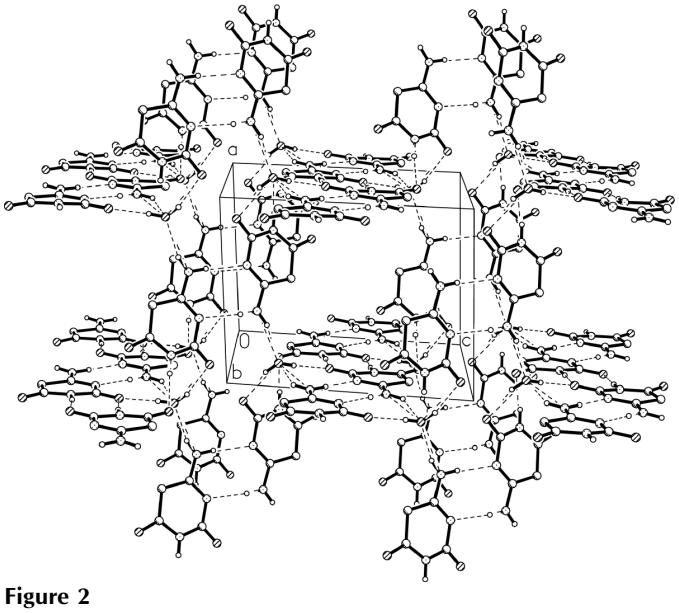


Figure 2
A packing diagram, showing the cross-linking (dashed lines) of chains by the second molecule of (1) and the water molecule. The isopropyl groups are omitted for clarity.

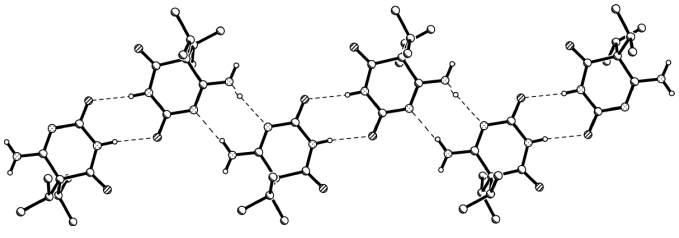


Figure 3
The one-dimensional hydrogen-bonded chain (dashed lines). H atoms not involved in hydrogen bonding are excluded for clarity.

considerable contribution from polar resonance contributors (*a*) and (*b*) (see Scheme), the amine bond is shortened [1.3162 (15) and 1.3252 (15) Å for molecules 1 and 2, respectively]. This phenomenon also contributes to the coplanarity of the amino H atoms, which deviate from the plane of the heterocyclic nucleus by 0.073 and 0.110 (H6*A* and H6*B*) and 0.258 and 0.138 (H6*D* and H6*E*) Å, for molecules 1 and 2, respectively. There is extensive delocalization around the barbiturate ring, exemplified by the bond distances between the ring atoms (see Table 1).

From the packing diagram (Fig. 2) it is apparent that (1) exists in a three-dimensional hydrogen-bonded network. A one-dimensional hydrogen-bonded ribbon (Fig. 3), generated by inversion centres, extends in the **b** direction. These ribbons are cross-linked by the second molecule of (1) and the water molecule, forming a three-dimensional network. All O—H and N—H H atoms are involved in hydrogen bonds, while only one potential hydrogen-bond acceptor (O4′) does not participate (Table 2).

Experimental

Ethyl diisopropylcyanoacetate (Marshall, 1930) (25.6 g, 0.13 mol), guanidinium carbonate (23.4 g, 0.13 mol) and sodium ethoxide (31.3 g, 0.46 mol) were refluxed for 23 h in dry ethanol (144 ml). Excess ethanol was then removed *in vacuo* and water (150 ml) was added. An oily layer (unreacted starting material) separated and was extracted with ether (4 × 20 ml). Concentrated hydrochloric acid was added to the aqueous phase until it was acid to Congo Red paper. An equal volume of concentrated hydrochloric acid was added and the solution refluxed for 24 h. The reaction mixture was then neutralized with ammonia solution and amphoteric (1) precipitated, was filtered off, washed with water, dried, and twice recrystallized from ethanol, providing crystals suitable for X-ray analysis, m.p. 536–539 K. Analysis. Found: C, 54.3; H, 8.1; N 19.0. Calc. for $C_{10}H_{17}N_3O_2\cdot0.5H_2O$: C, 54.5; H, 8.2; N, 19.1. ^{1}H NMR (500 MHz, d_6-DMSO): δ 10.48 (*s*, 1H, H3), 8.50 (*s*, 1H, H6*A*), 7.39 (*s*, 1H, H6*B*), 3.34 (*s*, 1H, $\frac{1}{2}$ H_2O), 2.35–2.41 (*m*, 2H, H7 & H10), 0.89–0.91 (*m*. 12H, H8, H9, H11 and H12). ^{13}C NMR (75 MHz, d_6-DMSO): δ 174.68 (C4), 173,32 (C6) 157.01 (C2), 56.47 (C5), 32.36 (C7, C10), 18.09 and 17.70 (C8, C9, C11 and C12).

Crystal data

$C_{10}H_{17}N_3O_2\cdot0.5H_2O$
M_r = 220.27
Triclinic, $P\overline{1}$
a = 9.250 (3) Å
b = 10.701 (3) Å
c = 12.135 (4) Å
α = 74.918 (4)°
β = 89.738 (4)°
γ = 85.213 (4)°
V = 1155.6 (6) Å^3
Z = 4
D_x = 1.266 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4571 reflections
θ = 4.4–54.8°
μ = 0.09 mm^{-1}
T = 163 (2) K
Block, colourless
0.55 × 0.55 × 0.30 mm

Data collection

Bruker SMART CCD diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 1999)
T_{min} = 0.831, T_{max} = 0.970
15159 measured reflections
4935 independent reflections
4326 reflections with $I > 2\sigma(I)$
R_{int} = 0.025
θ_{max} = 27.6°
$h = -11 \rightarrow 11$
$k = -7 \rightarrow 13$
$l = -15 \rightarrow 15$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.098
S = 1.05
4935 reflections
389 parameters
Only coordinates of H atoms refined
$w = 1/[\sigma^2(F_o^2) + (0.0536P)^2 + 0.2578P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.38 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}
Extinction correction: *SHELXTL*
Extinction coefficient: 0.009 (2)

Table 1
Selected bond lengths (Å).

N1—C6	1.3309 (14)	N1′—C6′	1.3314 (14)
N1—C2	1.3600 (14)	N1′—C2′	1.3621 (14)
C2—O2	1.2390 (14)	C2′—O2′	1.2360 (14)
C2—N3	1.3917 (14)	C2′—N3′	1.3928 (14)
N3—C4	1.3675 (14)	N3′—C4′	1.3764 (14)
C4—O4	1.2217 (13)	C4′—O4′	1.2164 (13)
C4—C5	1.5293 (15)	C4′—C5′	1.5365 (15)
C5—C6	1.5310 (14)	C5′—C6′	1.5303 (14)
C6—N6	1.3162 (15)	C6′—N6′	1.3252 (15)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3—H3*A*···O2^{i}	0.835 (15)	2.172 (16)	3.0031 (15)	172.8 (13)
N6—H6*A*···N1^{ii}	0.925 (15)	2.027 (16)	2.9498 (15)	174.9 (13)
N6—H6*B*···O100^{iii}	0.885 (16)	2.123 (15)	2.8519 (14)	139.2 (13)
N3′—H3*D*···O4	0.885 (15)	2.122 (15)	2.9595 (14)	157.6 (13)
N6′—H6*D*···N1′^{iv}	0.884 (15)	2.055 (16)	2.9353 (16)	173.3 (13)
N6′—H6*E*···O100	0.897 (15)	2.082 (16)	2.9535 (16)	163.6 (13)
O100—H102···O2^{v}	0.901 (17)	2.030 (17)	2.9281 (14)	174.2 (15)
O100—H101···O2′^{vi}	0.855 (18)	1.970 (18)	2.7995 (14)	163.3 (15)

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

All H atoms were located in a difference map and then coordinates were freely refined. Atomic displacement parameters were set as $U_{iso}(H) = 1.5U_{eq}(X)$ where X is a methyl C or O atom and $U_{iso}(H) = 1.2U_{eq}(X)$ where X is any other bonded carrier atom.

Data collection: *SMART* (Bruker, 1999); cell refinement: *SAINT-Plus* (Bruker, 1999); data reduction: *SAINT-Plus*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 2001); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

Richard A. Robson (1972), Margaret A. Telford (1973), Peter A. Barron (1974) and Rosalie J. Nicolson (1974) all prepared large-scale batches of (1), for which *B. Pharm.* research reports entitled 'Synthesis of 5,5-Diisopropylbarbituric Acid' are held in the archives of the Health Sciences Library, School of Medicine, University of Otago, PO Box 913, Dunedin, New Zealand.

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