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Dimorphism in 3′-aminocyclohexane-spiro-5′-hydantoin

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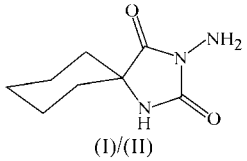
The title compound [systematic name: 1′-aminocyclohexane-spiro-4′-imidazole-2′,5′(3′*H*,4′*H*)-dione], $C_8H_{13}N_3O_2$, has been synthesized and was found to crystallize in two different structures, both monoclinic and both with the same $P2_1/c$ space group. In the first structure, there are two molecules in the asymmetric unit, one of which uses all of its hydrogen-bond donors and acceptors and forms undulating layers, while the other forms chains propagating perpendicular to the layers. In the second structure, there is only one independent molecule and the packing is based on a chain structure mediated by hydrogen bonding between the hydantoin moieties and further grouped into hydrophilic layers separated by layers of the hydrophobic cyclohexyl groups.

Comment

Hydantoins and cycloalkanespirohydantoins have been the subjects of extensive investigation due to their biological properties. As part of our research on the characterization of the biological activity of aminocycloalkanespiro-5-hydantoins and their metal complexes, the title compound was synthesized and its biological activity was investigated. The study shows very pronounced atropine-sensitive contractile effects on guinea pig ileum longitudinal muscles (Naydenova *et al.*, 2002). These results contrast with the anticonvulsive properties of hydantoins. The contractile effects are explained by the presence of the amino group at position 3 and are also related to the cycloalkane ring size (Avenado & Gonzalez, 1985).



(I)/(II)

Both structural modifications of the title compound, (I) and (II), are built up of molecules with almost identical geometry (Fig. 1). The hydantoin moieties are essentially planar, with r.m.s. deviations of 0.014, 0.003 and 0.017 Å for the two molecules in (I) and the molecule in (II), respectively. The bond distances and angles within the hydantoin units are comparable with those observed in other spiro-5-hydantoins (Gauthier *et al.*, 1997). The cyclohexane rings adopt chair conformations with similar endocyclic torsion angles (Tables 1 and 3). Analogous features are observed in the crystal structures of related heterocyclic molecules (Stasko *et al.*, 2002; Gauthier *et al.*, 1997).

The presence of a hydantoin ring, of which nearly all the atoms can be involved in hydrogen bonds, and a cyclohexane ring, acting as an impediment to hydrogen-bond formation, suggests a variety of possible hydrogen-bonding networks, resulting in different molecular packing in (I) and (II).

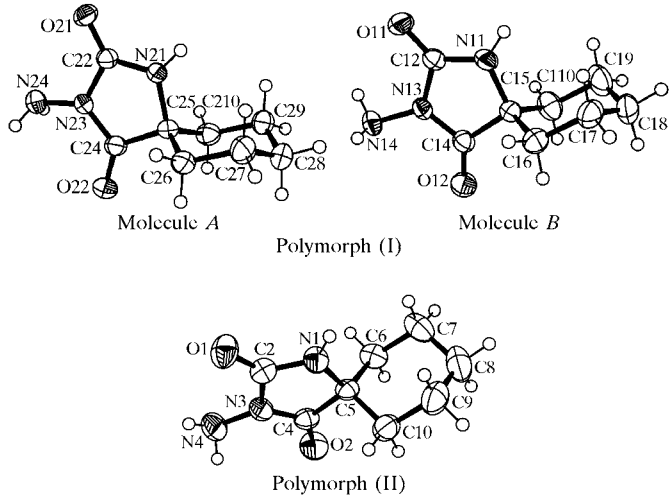


Figure 1
The structures of the two independent molecules, *A* and *B*, of (I) and of the molecule of (II), showing 50% probability displacement ellipsoids. H atoms are shown as small spheres of arbitrary radii, except for disordered atom H4*C* of (II), which has been omitted for clarity.

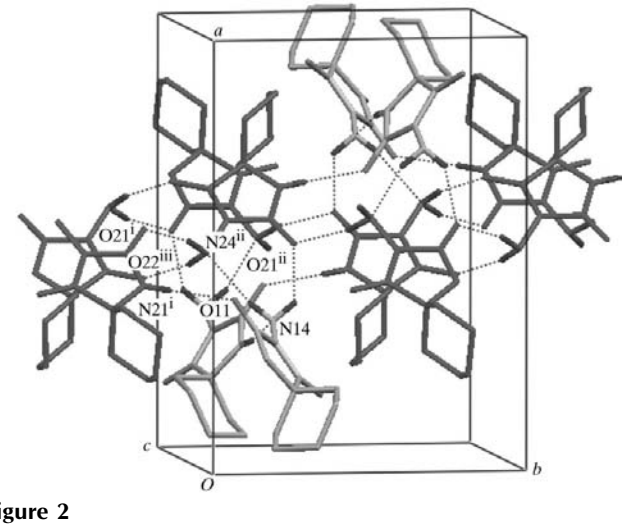


Figure 2
The packing in (I). Darker lines denotes *A* molecules. Hydrogen bonds are indicated by dotted lines. [Symmetry codes: (i) $x, y-1, z$; (ii) $1-x, y-\frac{1}{2}, \frac{3}{2}-z$; (iii) $x, \frac{1}{2}-y, \frac{1}{2}+z$.]

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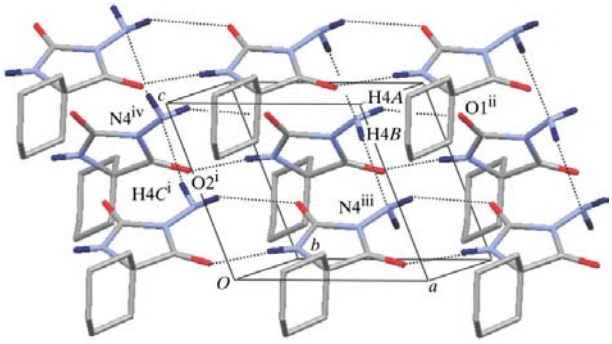

Figure 3
The molecular packing in (II). Hydrogen bonds are indicated by dotted lines. [Symmetry codes: (i) $x-1, y, z$; (ii) $x+1, y, z$; (iii) $x, \frac{1}{2}-y, z-\frac{1}{2}$; (iv) $x, \frac{1}{2}-y, z+\frac{1}{2}$.]

The two independent molecules in (I) participate in hydrogen bonding in quite different manners. All possible hydrogen-bond donors and acceptors in the first molecule (*A*) are involved in a total of six intermolecular hydrogen bonds (two of which are weak), while the second molecule (*B*) participates in only four hydrogen bonds and atom O12 is not involved in any such interactions (Table 2). Two N—H···O bonds involving the H atoms of the amino group at N24 link neighbouring *A* molecules to form undulating layers parallel to (100). In contrast, *B* molecules are linked through N11···N14($x, \frac{1}{2}-y, z-\frac{1}{2}$) hydrogen bonds and form infinite chains threaded through the troughs of the undulating layers. The remaining three hydrogen bonds connect *A* and *B* molecules and also stabilize the structural motif (Fig. 2).

Details of the hydrogen-bonding network for the second polymorph, (II), are given in Table 4. The molecules form chains *via* two hydrogen bonds, *viz*. N1···O2($x-1, y, z$) and N4···O1($x+1, y, z$), the first being significantly stronger than the second. An additional weak hydrogen bond, *viz*. N4···N4($x, \frac{1}{2}-y, \frac{1}{2}+z$), mediates two-dimensional packing of the chains into infinite layers parallel to (010) (Fig. 3). Due to positional disorder of one of the N4 amino H atoms, there are two mutually exclusive congeners for this interaction. Both cases are shown in Fig. 3; the first case, N4—H4*B*···N4($x, \frac{1}{2}-y, \frac{1}{2}-z$), includes the more populated disorder component (H4*B*), while the second case, shown as N4($x-1, y, z$)—H4*C*($x-1, y, z$)···N4($x, \frac{1}{2}-y, \frac{1}{2}+z$) in Fig. 2, is mediated by H4*C*.

We note the similar hydrogen-bonding contributions of the amino groups, which are simultaneously donors of two and acceptors of one hydrogen bond each in both (I) and (II). Another analogy between the polymorphs is that they contain layers based on hydrogen bonding of the hydantoin moieties, with cyclohexyl groups which block the formation of strong non-covalent interactions in the direction perpendicular to the plane of the layers.

Experimental

The compound 3′-aminocyclohexanespiro-5′-hydantoin was prepared according to the method of Naydenova *et al.* (2002). The first polymorph, (I), was obtained by recrystallization from methanol. The second polymorph, (II), pecipitated from a methanol solution containing (I) and $B(OH)_3$ (1:1) during an attempt to obtain a borate compound.

Polymorph (I)

Crystal data

$C_8H_{13}N_3O_2$
$M_r = 183.21$
Monoclinic, $P2_1/c$
$a = 14.0813\ (13)$ Å
$b = 10.2094\ (19)$ Å
$c = 12.372\ (3)$ Å
$\beta = 91.621\ (14)^\circ$
$V = 1777.9\ (6)$ Å^3
$Z = 8$
$D_x = 1.364$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 22 reflections
$\theta = 16.7$–17.7°
$\mu = 0.10$ mm^{-1}
$T = 290\ (2)$ K
Prism, white
0.24 × 0.21 × 0.12 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
Non-profiled $\omega/2\theta$ scans
7138 measured reflections
3509 independent reflections
1946 reflections with $I > 2\sigma(I)$
$R_{int} = 0.076$
$\theta_{max} = 26.0^\circ$
$h = -17 \rightarrow 17$
$k = -12 \rightarrow 12$
$l = -15 \rightarrow 0$
3 standard reflections
every 500 reflections
intensity decay: 3%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.050$
$wR(F^2) = 0.118$
$S = 0.99$
3509 reflections
253 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0418P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.17$ e Å^{-3}
$\Delta\rho_{min} = -0.22$ e Å^{-3}

Table 1
Selected torsion angles (°) for (I).

C25—C26—C27—C28	54.2 (3)	C15—C16—C17—C18	54.7 (3)
C26—C27—C28—C29	−56.6 (3)	C16—C17—C18—C19	−55.4 (3)
C27—C28—C29—C210	57.3 (3)	C17—C18—C19—C110	55.9 (4)

Table 2
Hydrogen-bond geometry (Å, °) for (I).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N11—H11*A*···N14^{i}	0.83 (3)	2.26 (3)	3.083 (3)	170 (3)
N21—H21*A*···O11^{ii}	0.83 (3)	2.14 (3)	2.970 (3)	179 (3)
N14—H14*A*···N24^{iii}	0.89 (3)	2.49 (3)	3.247 (3)	144 (2)
N14—H14*B*···O21^{iii}	0.90 (3)	2.29 (3)	2.865 (3)	121 (2)
N24—H24*A*···O21^{iii}	0.94 (3)	2.04 (3)	2.970 (3)	167 (2)
N24—H24*B*···O22^{iv}	0.86 (3)	2.43 (3)	3.264 (3)	166 (2)

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

Polymorph (II)

Crystal data

$C_8H_{13}N_3O_2$
$M_r = 183.21$
Monoclinic, $P2_1/c$
$a = 6.1743\ (12)$ Å
$b = 26.765\ (3)$ Å
$c = 6.0257\ (12)$ Å
$\beta = 111.425\ (11)^\circ$
$V = 927.0\ (3)$ Å^3
$Z = 4$
$D_x = 1.313$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 22 reflections
$\theta = 18.0$–19.0°
$\mu = 0.10$ mm^{-1}
$T = 290\ (2)$ K
Prismatic, pale yellow
0.21 × 0.18 × 0.12 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
Non-profiled $\omega/2\theta$ scans
4768 measured reflections
2218 independent reflections
1178 reflections with $I > 2\sigma(I)$
$R_{int} = 0.100$
$\theta_{max} = 28.0°$
$h = -8 \rightarrow 7$
$k = -35 \rightarrow 35$
$l = 0 \rightarrow 7$
3 standard reflections
every 500 reflections
intensity decay: 1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.055$
$wR(F^2) = 0.138$
$S = 1.04$
2218 reflections
120 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.05P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.19$ e Å^{-3}
$\Delta\rho_{min} = -0.20$ e Å^{-3}

Table 3
Selected torsion angles (°) for (II).

C5—C6—C7—C8	54.6 (3)	C7—C8—C9—C10	56.3 (3)
C6—C7—C8—C9	−55.5 (3)		

Table 4
Hydrogen-bond geometry (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O2^{i}	0.86	1.98	2.833 (3)	174
N4—H4A···O1^{ii}	0.89	2.64	3.325 (3)	135
N4—H4B···N4^{iii}	0.89	2.42	3.2127 (14)	148
N4—H4C···N4^{iv}	0.89	2.35	3.2127 (14)	165

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

H atoms attached to N atoms in polymorph (I) and the amino N atom of polymorph (II) were placed in positions found from an electron-density map. For the amino N atom of (II), three possible H-atom positions were identified. After refinement, one of the positions (N4*A*) was found to be fully occupied, while the other two (N4*B* and N4*C*) were partialy occupied in an approximate 4:1 ratio. The remainder of the H atoms were placed in idealized positions (C—H = 0.97 Å and N—H = 0.86 Å). All the H atoms were constrained to ride on their parent atoms, with $U_{iso}(H) = 1.2U_{eq}(C,N)$.

For both compounds, data collection: *CAD-4 EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD-4 EXPRESS*; data reduction: *XCAD4* (Harms & Wocadlo, 1995); structure solution: *SHELXS97* (Sheldrick, 1997); structure refinement: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); publication software: *WinGX* (Farrugia, 1999).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FA1115). Services for accessing these data are described at the back of the journal.

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