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A New Polymorph of 1-Acetyl-2-thiohydantoin

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The crystal structure of a new polymorph of 1-acetyl-2-thiohydantoin has been determined by X-ray diffraction. The crystal, $C_5H_6N_2O_2S$, belongs to space group $P\bar{1}$ with cell dimensions of a = 4.9865(7)Å, b = 5.5716(7)Å, c = 12.544(2)Å, α = 74.793(8)°, β = 80.413(9)°, γ = 85.001(10)°. The final $R1$ value is 0.036 for 1304 reflections ($I > 2.0\sigma(I)$). In the new polymorph, intermolecular hydrogen bonds are formed between the acetyl C=O and the amide N–H groups [N(1)···O(2)$^{(i)}$ 2.800(2)Å, N(1)–H···O(2)$^{(i)}$ 151.02°, symmetry codes: (i) x+1, y–1, z] to form an infinite chain structure. On the other hand, the hydrogen bonds in the known form are formed between the amide C=O and the amide N–H groups of the thiohydantoin rings.

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Polymorphism in crystal structures is a relatively common phenomenon in pharmaceutical solids. Since polymorphic crystals have different physicochemical properties such as melting point or solubility, the changes in polymorphic forms can influence the bioavailability and the chemical and physical stability of the drug. Thus, it is very important to control the crystal form of the pharmaceuticals. 2-Thiohydantoin derivatives provide useful synthetic intermediates with a wide range of applications such as therapeutics, fungicides and herbicides.[1,2] We have been studying the crystal structures and conformations of 5-substituted-2-thiohydantoins and their derivatives.[3,4] In the course of the crystallization experiment, we obtained a crystal modification of 1-acetyl-2-thiohydantoin different from the previously reported form.[5] This paper deals with the crystal structure of the new polymorph of 1-acetyl-2-thiohydantoin (I, see Figs. 1 and 2).

Compound I was prepared by reacting glycine with acetic anhydride and ammonium thiocyanate.[6] The crude product was washed with cold water several times and purified by repeated crystallization from methanol.

Single crystals of the new polymorph suitable for X-ray diffraction were obtained by slow evaporation of the ethanol solution. Table 1 gives the crystal and experimental data. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares methods and all hydrogen atoms were not refined. Selected bond distances, bond angles and torsion angles are listed in Table 2.

The new polymorph is crystallized in the triclinic form with two molecules in a unit cell. The thiohydantoin ring is

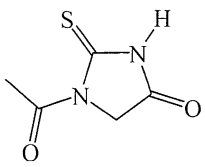

Fig. 1 Chemical formula of the title compound (I)

Table 1 Crystal and experimental data

Formula: $C_5H_6N_2O_2S$	
Formula weight: 158.17	
Crystal system: triclinic	
a = 4.9865(7)Å	α = 74.793(8)°
b = 5.5716(7)Å	β = 80.413(9)°
c = 12.544(2)Å	γ = 85.001(10)°
V = 331.27(8)Å^3	
Space group: $P\bar{1}$	Z = 2
D_{calc} = 1.586 g/cm^3	
F(0 0 0) = 164.00	
μ(Mo K_α) = 4.21 cm^{-1}	
T = 123 K	
$2\theta_{max}$ = 60.3° with Mo K_α (0.71070 Å)	
No. observations = 1304 ($I > 2.00\sigma(I)$)	
No. variables = 91	
$R1$ = 0.036	
Goodness-of-fit = 1.10	
$(\Delta/\sigma)_{max}$ = 0.001	
$(\Delta\rho)_{max}$ = 0.30 e/Å^3	
$(\Delta\rho)_{min}$ = –0.29 e/Å^3	
Diffractometer: Rigaku/MSC Mercury CCD	
Program system: teXsan ver. 1.11	
Structure determination: direct method (SIR92)	
Refinement: full-matrix least-squares	
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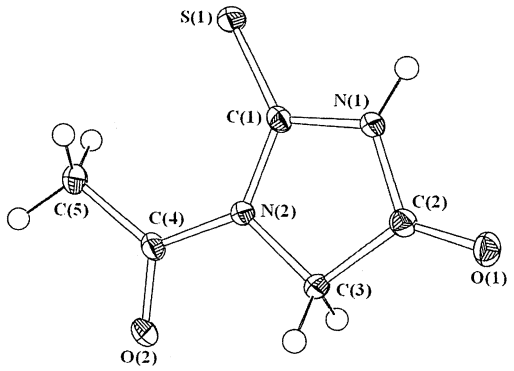

Fig. 2 Molecular structure of the title compound (I) with the labeling atoms. Thermal ellipsoids of non-H atoms are drawn at the 50% probability level. H atoms are indicated by small circles.

Table 2 Selected bond lengths (Å), bond angles (°) and torsion angles (°)

Atom	Atom	Atom	Atom	
S(1)	C(1)			1.643(2)
O(1)	C(2)			1.206(2)
O(2)	C(4)			1.223(2)
N(1)	C(1)			1.370(2)
N(1)	C(2)			1.384(2)
N(2)	C(1)			1.389(2)
N(2)	C(3)			1.475(2)
N(2)	C(4)			1.393(2)
C(2)	C(3)			1.502(2)
C(4)	C(5)			1.493(2)
C(1)	N(1)	C(2)		114.0(1)
C(1)	N(2)	C(3)		110.9(1)
C(1)	N(2)	C(4)		131.1(1)
C(3)	N(2)	C(4)		118.0(1)
S(1)	C(1)	N(1)		123.6(1)
S(1)	C(1)	N(2)		130.1(1)
N(1)	C(1)	N(2)		106.3(1)
O(1)	C(2)	N(1)		125.7(1)
O(1)	C(2)	C(3)		128.5(1)
N(1)	C(2)	C(3)		105.9(1)
N(2)	C(3)	C(2)		102.5(1)
O(2)	C(4)	N(2)		116.4(1)
O(2)	C(4)	C(5)		122.7(1)
N(2)	C(4)	C(5)		120.9(1)
S(1)	C(1)	N(1)	C(2)	-178.1(1)
S(1)	C(1)	N(2)	C(3)	174.0(1)
S(1)	C(1)	N(2)	C(4)	-7.2(2)
O(1)	C(2)	N(1)	C(1)	-177.0(1)
O(1)	C(2)	C(3)	N(2)	174.2(1)
O(2)	C(4)	N(2)	C(1)	174.4(1)
O(2)	C(4)	N(2)	C(3)	-6.8(2)
N(1)	C(1)	N(2)	C(3)	-5.6(2)
N(1)	C(1)	N(2)	C(4)	173.3(1)
N(1)	C(2)	C(3)	N(2)	-5.8(1)
N(2)	C(1)	N(1)	C(2)	1.5(2)
C(1)	N(1)	C(2)	C(3)	2.9(2)
C(1)	N(2)	C(3)	C(2)	7.1(2)
C(1)	N(2)	C(4)	C(5)	-6.8(2)
C(2)	C(3)	N(2)	C(4)	-171.9(1)
C(3)	N(2)	C(4)	C(5)	171.9(1)

essentially planar. The S(1)-C(1)-N(2) angle [130.1(1)°] is greater than the S(1)-C(1)-N(1) angle [123.6(1)°] due to the bulky acetyl group. The acetyl group is almost coplanar with the thiohydantoin ring [O(2)-C(4)-N(2)-C(1) 174.4(1)° and O(2)-C(4)-N(2)-C(3) –6.8(2)°]. Similar molecular geometries are reported for the known polymorph.[5] For the two polymorphic forms, neighboring molecules are linked through intermolecular hydrogen bonds to form an infinite chain structure. However, the hydrogen bonding pattern is entirely different between the forms. In crystals of the new polymorph,

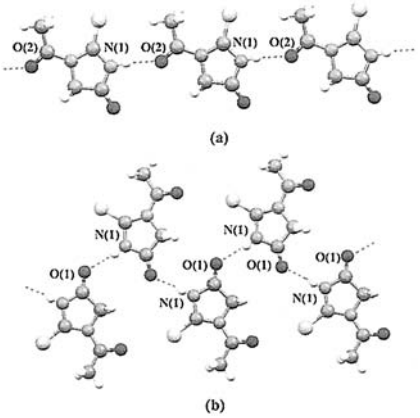

Fig. 3 Perspective views of intermolecular hydrogen bonds in (a) the new polymorph (b) the known form.

the hydrogen bonds are formed between the acetyl C=O and the amide NH groups [N(1)···O(2)$^{(i)}$ 2.800(2)Å, N(1)–H···O(2)$^{(i)}$ 151.02°, symmetry codes: (i) x+1, y–1, z], whereas they are formed between the amide C=O and the amide NH groups in the known form. Due to the different hydrogen bond pattern, the acetyl and the amide C=O bonds of the new polymorph are longer and shorter, respectively, than those of the known form [C(4)-O(2) and C(2)-O(1) are 1.223(2) and 1.206(2)Å for the new polymorph, and 1.208(3) and 1.218(3)Å for the known form]. In the IR spectra, the $\nu_{C=O}$ frequencies of the acetyl group and the amide groups are observed at 1668 and 1763 cm^{-1}, respectively, in the new polymorph, whereas the corresponding bands are observed at higher and lower frequencies (1704 and 1740 cm^{-1}) in the known form. These $\nu_{C=O}$ frequencies also reflect the difference in the hydrogen bonding pattern. A separate experiment showed that the ground sample of the new polymorph transformed into the known form in a week. Thus the new polymorph is considered to be a meta stable form.

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