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Acta Cryst. (1998). C**54**, 1168–1170

5,5-Diphenyl-2-thiohydantoin

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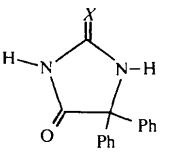
(*Received 16 June 1997; accepted 22 December 1997*)

Abstract

The molecular structure of the title compound, 5,5-diphenyl-2-thioxoimidazolidin-4-one, $C_{15}H_{12}N_2OS$, resembles that of 5,5-diphenylhydantoin (phenytoin). The C=S distance is 1.648 (2) Å. The crystal structure consists of ribbon-like infinite sheets of molecules bonded by N—H···O and N—H···S hydrogen bonds. The packing of sheets is governed by van der Waals forces only.

Comment

Phenytoin, 5,5-diphenylhydantoin, (I), is one of the main well established anti-epileptic drugs effective against various forms of partial and generalized seizures (Ramsay *et al.*, 1983). Although the mode of action of phenytoin is still not fully elucidated, it is believed to work mainly by blockade of sodium channels (McLean & Macdonald, 1983). Structure–activity relationship studies for some 80 hydantoin derivatives suggest that the –N3—C4(=O)—C5–phenyl segment of phenytoin (numbering as in Fig. 1) defines its anticonvulsant pharmacophore ('bioactive fragment'), while the –C2(=O)—N3(H)–amide 'face' of the imidazolidine-2,4-dione ring is most likely involved in its mutagenic and teratogenic effects (Weaver, 1992). It is postulated that alterations of this 'face' do not remove anticonvulsant activity, but may result in decreased toxicity in terms of mutagenic potential (Weaver, 1992). The 2-thio analog of phenytoin, 5,5-diphenyl-2-thiohydantoin, (II), was found to have the same spectrum of activity as phenytoin (Kozelka *et al.*, 1942); on the other hand, it was expected to display a different range of toxicity from phenytoin, namely, some undesired antithyroid effects (Gesler *et al.*, 1961). This reinforces the notion that the –C2(=O)—N3(H)–amide 'face' facilitates the differentiation of efficacy from toxicity. The crystal structure of (II) was solved as part of a program of structural analyses of phenytoin analogs with alterations in the 'biotoxic face' of the imidazolidinedione ring (Weaver, 1992) and of the metal complexes of phenytoin (Roszak *et al.*, 1995).



(I) X = O
(II) X = S

The molecular structure of (II) (Fig. 1) is very similar to the structure of 5,5-diphenylhydantoin, (I) (Camerman & Camerman, 1971; Chattopadhyay *et al.*, 1993), despite the different keto function at C2. The imidazolidine ring in (II) is planar, with the thioketone sulfur out of this plane by 0.036 (2) Å and the carbonyl oxygen by −0.013 (2) Å; the geometry of the ring equals that in (I) within 3σ. The spatial arrangement of the two phenyl rings *versus* the imidazolidine ring is slightly different in (I) and (II). The phenyl rings in 5,5-diphenyl-2-thiohydantoin form dihedral angles of 83.66 (7) (ring C51–C56) and 67.50 (7)° (ring C61–C66) with the plane of the five-membered ring, and an

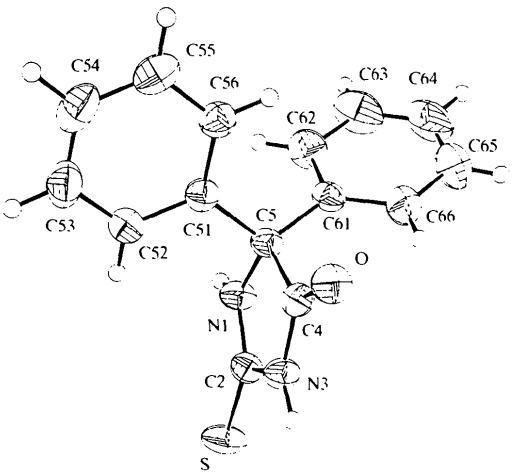


Fig. 1. The molecular structure of the title compound showing the atom-numbering scheme. Displacement ellipsoids are shown at the 50% probability level and H atoms are drawn as unlabelled spheres of arbitrary size.

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angle of 76.10 (7)° between themselves. Both phenyl rings in (I) form angles of about 66° with the hydantoin ring while being almost perpendicular to each other.

The 2-thiohydantoin ring in (II) displays differences when compared with unsubstituted 2-thiohydantoin (Walker *et al.*, 1969; Devillanova *et al.*, 1987), with the largest differences in the geometry about the C5 atom (an increase of the N1—C5 and C4—C5 bonds by about 0.02 and 0.03 Å, respectively, and a decrease in the N1—C5—C4 angle by *ca* 1.5°), caused by the 5,5-diphenyl substitution. Similar trends can be observed in 5,5-dimethylated 2-thiohydantoin derivatives due to the 5,5-dimethyl substitution (Cristiani *et al.*, 1992; Demartin *et al.*, 1992). The length of the C=S bond in (II), 1.648 (2) Å, is the same as observed in 2-thiohydantoin [1.642 (3) and 1.648 (2) Å in two determinations, respectively]; in 5,5-dimethyl-substituted 2-thiohydantoins, the C=S distances were 1.673 (3) and 1.650 (5) Å.

The 5,5-diphenyl substitution of 2-thiohydantoin produces dramatic changes in intermolecular interactions and in the crystal packing. Each molecule of (II) is involved in four intermolecular hydrogen bonds between N atoms and O and S atoms (Fig. 2). The geometry details of two hydrogen bonds are presented in Table 2; the third hydrogen bond is related to the first one by an inversion centre, while the fourth is related to the second by a 2_1 screw axis. Molecules connected by hydrogen bonds form ribbon-like infinite sheets running along the $(10\bar{1})$ planes of the crystal lattice. The distance between these sheets is *ca* 7.6 Å and the interaction between them is of van der Waals nature only. The shortest distance between the S atoms in (II) is 4.643 (1) Å and the density of the crystal structure is 1.351 g cm^{-3}. In contrast, the packing of molecules of 2-thiohydantoin (Walker *et al.*, 1969; Devillanova *et al.*, 1987) is much more compact (density of 1.62 g cm^{-3}), with the hydrogen-bonded infinite sheets lying 3.2 Å apart, and showing a partial π-stacking, and the S atoms in a close S···S contact (3.43 Å) and not involved in hydrogen bonding.

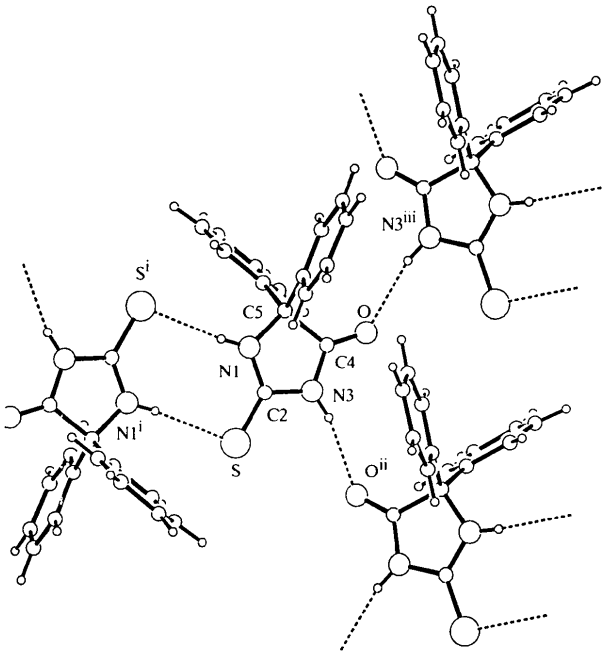

Fig. 2. The infinite network of hydrogen bonding in (II) with the hydrogen bonds represented by dashed lines; the symmetry codes are as in Table 2, with (iii) $x-\frac{1}{2}, -y+\frac{3}{2}, z-\frac{1}{2}$.

Experimental

The title compound was synthesized by the reaction of benzil with thiourea according to the method of Biltz (1909) as described elsewhere (Weaver, 1992). Suitable crystals were obtained from ethanol solution by slow evaporation.

Crystal data

$C_{15}H_{12}N_2OS$
M_r = 268.33
Monoclinic
$P2_1/n$
a = 8.890 (2) Å
b = 19.392 (2) Å
c = 8.704 (2) Å
β = 118.48 (2)°
V = 1318.9 (4) Å^3
Z = 4
D_x = 1.351 Mg m^{-3}
D_m not measured
Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 25 reflections
θ = 17.3–19.3°
μ = 0.238 mm^{-1}
T = 293 (2) K
Block
0.35 × 0.30 × 0.25 mm
Colorless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
3049 measured reflections
2872 independent reflections
1995 reflections with $I > 2\sigma(I)$
R_{int} = 0.025
θ_{max} = 26.97°
$h = 0 \rightarrow 11$
$k = 0 \rightarrow 24$
$l = -11 \rightarrow 9$
3 standard reflections
frequency: 60 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.112
S = 1.105
2872 reflections
221 parameters
All H atoms refined
$w = 1/[\sigma^2(F_o^2) + (0.055P)^2 + 0.2715P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.285 e Å^{-3}
$\Delta\rho_{min}$ = −0.259 e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.022 (3)
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °)*

N1—C2	1.326 (2)	C4—O	1.216 (2)
N1—C5	1.464 (2)	C4—C5	1.535 (2)
C2—N3	1.392 (2)	C5—C51	1.533 (2)
C2—S	1.648 (2)	C5—C61	1.525 (2)
N3—C4	1.363 (2)		

C2—N1—C5	114.11 (14)	N3—C4—C5	106.65 (13)
N1—C2—N3	106.79 (14)	N1—C5—C51	111.72 (13)
N1—C2—S	128.75 (13)	N1—C5—C61	109.64 (13)
N3—C2—S	124.46 (12)	C51—C5—C61	114.46 (13)
C2—N3—C4	112.51 (14)	N1—C5—C4	99.93 (12)
O—C4—N3	126.7 (2)	C4—C5—C51	107.29 (13)
O—C4—C5	126.66 (15)	C4—C5—C61	112.87 (14)
N1—C5—C51—C52	29.2 (2)	N1—C5—C61—C62	68.9 (2)
N1—C5—C51—C56	−156.2 (2)	N1—C5—C61—C66	−106.9 (2)
C4—C5—C51—C52	−79.4 (2)	C4—C5—C61—C62	179.3 (2)
C4—C5—C51—C56	95.2 (2)	C4—C5—C61—C66	3.5 (2)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···S^{i}	0.84 (2)	2.56 (2)	3.394 (2)	174 (2)
N3—H3···O^{ii}	0.87 (2)	2.25 (2)	3.094 (2)	165 (2)

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

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989). Cell refinement: *CAD*-4 *Software*. Data reduction: *Xtal*3.0 (Hall & Stewart, 1990). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1985). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *ORTEP*II (Johnson, 1976) and *PLUTON* (Spek, 1992). Software used to prepare material for publication: *SHELXL*93.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG1365). Services for accessing these data are described at the back of the journal.

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Acta Cryst. (1998). C**54**, 1170–1173

Racemic 2-Hydroxy-2-phenylpropanamidinium Chloride and (*S*)-2-Hydroxy-2-phenylbutanamidinium (*R*)-2-Hydroxy-2-phenylethanoate

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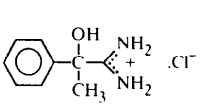
(*Received 26 September 1997; accepted 9 February 1998*)

Abstract

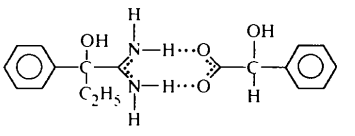
In 2-hydroxy-2-phenylpropanamidinium chloride, $C_9H_{13}N_2O^+.Cl^-$, the anion plays a central role in the hydrogen-bond network, chelating to one amidinium group and forming intermolecular links to neighbouring NH_2 and OH^- groups. The central feature in (*S*)-2-hydroxy-2-phenylbutanamidinium (*R*)-2-hydroxy-2-phenylethanoate, $C_{10}H_{15}N_2O^+.C_8H_7O_3^-$, is a ring linking the cation and anion through two hydrogen bonds. The structure is extended by intra- and intermolecular hydrogen bonds.

Comment

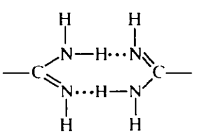
For almost 80 years, stereochemical studies of derivatives of mandelic (2-hydroxy-2-phenylethanoic) and atrolactic (2-hydroxy-2-phenylpropanoic) acids and the corresponding amidines have been carried out in what is now the University of Dundee (see *e.g.* McKenzie & Wren, 1919; Roger & Neilson, 1959). The supramolecular structures of the title compounds, (I) and (II), have now been investigated as part of a study of extended hydrogen-bond systems (Barnes & Barnes, 1996; Barnes *et al.*, 1998), using crystals from the original preparations (Roger & Neilson, 1959).



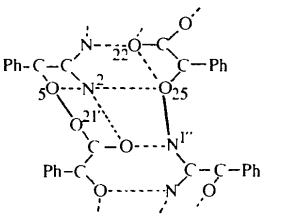
(I)



(II)



(III)



(IV)