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2-Cyanoimino-5,5-diphenyl-4-imidazolinone Monohydrate

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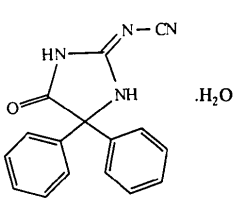
Abstract

The title compound has anticonvulsant properties. In crystals of $C_{16}H_{12}N_4O.H_2O$, its molecular structure is similar to that of phenytoin, an antiepileptic drug. The phenyl–phenyl angle is 101.05 (6)°. The imidazolinone cycle is planar and contains the cyanoimino moiety. The cohesion of the crystal is the result of van der Waals interactions and of four hydrogen bonds, three of which involve the water molecule.

Comment

The title compound, (I), is a bioisostere of phenytoin [diphenylhydantoin (DPH): 5,5-diphenyl-2,4-imidazolidinedione], an antiepileptic drug (Rogawski & Porter, 1990), the structure of which has been described previously (Camerman & Camerman, 1971). The molecule differs from DPH in that the urea moiety of the hydantoin ring is replaced with a cyanoguanidine function. Its synthesis and anticonvulsant properties will be published elsewhere.



(I)

The two phenyl rings are planar [maximum deviation of the ring atoms from the best plane through each ring is 0.003 (2) Å], as is the five-atom ring [maximum deviation −0.017 (1) Å] with O1 and N3 situated 0.075 (3) and 0.081 (3) Å from the plane through the five atoms. The conformation of $C_{16}H_{12}N_4O$ is similar to that of DPH. The angles between the normals to planes are: heterocycle–phenyl(C5–C10) 113.28 (7); heterocycle–phenyl(C11–C16) 125.28 (7); phenyl–phenyl 101.05 (6)° (the respective angles in DPH are 113, 114 and 90°). The geometric parameters that may be related to the biological activity according to Camerman & Camerman (1970) are the distances between the centroids of the phenyl rings (*X*) and the O-atom position: *X*1(C5–C10)···O1 4.041 (2), *X*2(C11–C16)···O1 4.216 (2), *X*1···*X*2 4.832 (2) Å. (3.968, 4.227 and 4.835 Å, respectively, in DPH). The 2-cyanoimino moiety is almost in the heterocyclic plane [N1—C1—N3—C2 −1.3 (3)°].

The 2-cyanoimino-5,5-diphenyl-4-imidazolinone and water molecules are linked by a system of four hydrogen bonds: N1—H1···O2^{i} [N1···O2^{i} 2.834 (2), H1···O2^{i} 1.99 Å, N1—H1···O2^{i} 165°; symmetry code: (i) $\frac{3}{2} - x, \frac{1}{2} + y, 1 - z$]; O2—H2*A*···N3 [O2···N3 2.949 (2), H2*A*···N3 2.02 Å, O2—H2*A*···N3 174°]; N2—H2···N4^{ii} [N2···N4^{ii} 3.017 (2), H2···N4^{ii} 2.18 Å, N2—H2···N4^{ii} 166°; symmetry code: (ii) $\frac{3}{2} - x, -\frac{1}{2} + y, 1 - z$]; O2—H2*B*···O1^{iii} [O2···O1^{iii} 2.861 (2), H2*B*···O1^{iii} 2.29 Å, O2—H2*B*···O1^{iii} 124°; symmetry code: (iii) $2 - x, -y, 1 - z$].

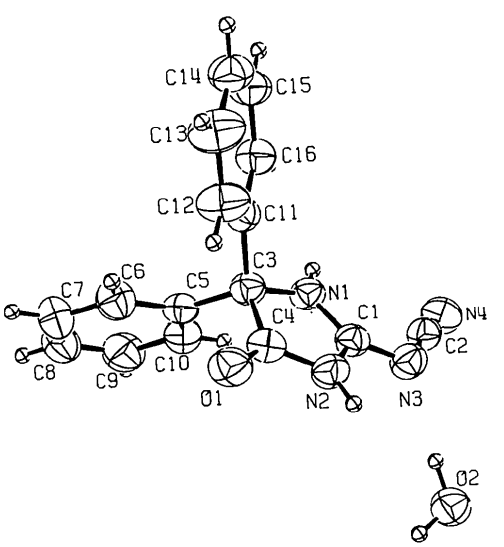


Fig. 1. Molecular structure of the title compound with atom-labelling scheme. Displacement ellipsoids are shown at the 50% probability level. H atoms are drawn as small circles of arbitrary radii.

Experimental

Crystals of the title compound were obtained at the Laboratory of Medicinal Chemistry, Liège; the synthesis will be reported elsewhere.

Crystal data

$C_{16}H_{12}N_4O.H_2O$
$M_r = 294.31$
Monoclinic
$P2_1/a$
$a = 11.576\ (2)$ Å
$b = 10.6933\ (7)$ Å
$c = 11.582\ (2)$ Å
$\beta = 101.448\ (9)°$
$V = 1405.1\ (3)$ Å^3
$Z = 4$
$D_x = 1.391$ Mg m^{-3}
Cu $K\alpha$ radiation
$\lambda = 1.5418$ Å
Cell parameters from 37 reflections
$\theta = 34.12–41.99°$
$\mu = 0.782$ mm^{-1}
$T = 293\ (2)$ K
Prism
0.42 × 0.38 × 0.27 mm
Colourless

Data collection

Stoe Siemens AED four-circle diffractometer
ω scans
Absorption correction: ψ scans (*EMPIR*; Stoe & Cie, 1987*b*)
$T_{min} = 0.709$, $T_{max} = 0.835$
2123 measured reflections
2012 independent reflections
1562 observed reflections $[I > 2\sigma(I)]$
$R_{int} = 0.0215$
$\theta_{max} = 58.94°$
$h = -12 \rightarrow 12$
$k = 0 \rightarrow 11$
$l = 0 \rightarrow 12$
2 standard reflections
frequency: 60 min
intensity decay: 5.0%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.0347$
$wR(F^2) = 0.1025$
$S = 1.192$
2012 reflections
202 parameters
H atoms constrained (riding) except water H atoms (fixed)
$w = 1/[\sigma^2(F_o^2) + (0.0553P)^2 + 0.2671P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.140$ e Å^{-3}
$\Delta\rho_{min} = -0.126$ e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.0142 (9)
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$

	x	y	z	U_{eq}
C1	0.7688 (2)	0.2279 (2)	0.3929 (2)	0.0456 (5)
C2	0.6520 (2)	0.3039 (2)	0.5130 (2)	0.0518 (5)
C3	0.8370 (2)	0.3021 (2)	0.2308 (2)	0.0468 (5)
C4	0.8933 (2)	0.1758 (2)	0.2736 (2)	0.0490 (5)
C5	0.9337 (2)	0.4023 (2)	0.2421 (2)	0.0483 (5)
C6	1.0054 (2)	0.4077 (2)	0.1595 (2)	0.0628 (6)
C7	1.0934 (2)	0.4968 (2)	0.1684 (2)	0.0709 (7)
C8	1.1111 (2)	0.5814 (2)	0.2594 (2)	0.0688 (7)
C9	1.0410 (2)	0.5768 (2)	0.3419 (2)	0.0694 (6)
C10	0.9528 (2)	0.4876 (2)	0.3336 (2)	0.0596 (6)
C11	0.7639 (2)	0.2945 (2)	0.1050 (2)	0.0464 (5)
C12	0.7886 (2)	0.2103 (2)	0.0234 (2)	0.0702 (7)
C13	0.7230 (3)	0.2087 (2)	−0.0902 (2)	0.0797 (7)
C14	0.6313 (2)	0.2903 (2)	−0.1230 (2)	0.0648 (6)
C15	0.6062 (2)	0.3739 (2)	−0.0429 (2)	0.0626 (6)
C16	0.6713 (2)	0.3765 (2)	0.0704 (2)	0.0550 (5)
N1	0.76165 (13)	0.32051 (15)	0.31717 (13)	0.0466 (4)
N2	0.84445 (14)	0.13960 (14)	0.36583 (14)	0.0517 (4)
N3	0.71989 (14)	0.21304 (15)	0.48504 (14)	0.0533 (5)
N4	0.5932 (2)	0.3777 (2)	0.5463 (2)	0.0643 (5)
O1	0.96777 (13)	0.11880 (14)	0.23558 (13)	0.0625 (4)
O2	0.84873 (14)	0.05654 (13)	0.67803 (13)	0.0628 (4)

Table 2. *Selected geometric parameters* (Å, °)

C1—N3	1.313 (2)	C5—C6	1.386 (3)
C1—N1	1.315 (2)	C6—C7	1.384 (3)
C1—N2	1.366 (2)	C7—C8	1.373 (3)
C2—N4	1.157 (3)	C8—C9	1.372 (3)
C2—N3	1.330 (3)	C9—C10	1.386 (3)
C3—N1	1.465 (2)	C11—C12	1.376 (3)
C3—C11	1.535 (3)	C11—C16	1.381 (3)
C3—C5	1.537 (3)	C12—C13	1.383 (3)
C3—C4	1.538 (3)	C13—C14	1.368 (3)
C4—O1	1.208 (2)	C14—C15	1.361 (3)
C4—N2	1.360 (2)	C15—C16	1.379 (3)
C5—C10	1.382 (3)		
N3—C1—N1	130.8 (2)	C7—C6—C5	120.7 (2)
N3—C1—N2	120.2 (2)	C8—C7—C6	120.4 (2)
N1—C1—N2	109.0 (2)	C9—C8—C7	119.5 (2)
N4—C2—N3	174.2 (2)	C8—C9—C10	120.4 (2)
N1—C3—C11	111.38 (15)	C5—C10—C9	120.7 (2)
N1—C3—C5	111.7 (2)	C12—C11—C16	118.2 (2)
C11—C3—C5	111.9 (2)	C12—C11—C3	122.4 (2)
N1—C3—C4	99.77 (15)	C16—C11—C3	119.4 (2)
C11—C3—C4	112.2 (2)	C11—C12—C13	120.8 (2)
C5—C3—C4	109.27 (15)	C14—C13—C12	120.4 (2)
O1—C4—N2	125.5 (2)	C15—C14—C13	119.2 (2)
O1—C4—C3	127.8 (2)	C14—C15—C16	120.8 (2)
N2—C4—C3	106.7 (2)	C15—C16—C11	120.6 (2)
C10—C5—C6	118.4 (2)	C1—N1—C3	112.8 (2)
C10—C5—C3	121.9 (2)	C4—N2—C1	111.6 (2)
C6—C5—C3	119.7 (2)	C1—N3—C2	118.7 (2)
N1—C3—C4—O1	−176.6 (2)	N2—C1—N1—C3	−1.2 (2)
N1—C3—C4—N2	2.2 (2)	C11—C3—N1—C1	118.0 (2)
C11—C3—C4—N2	−115.8 (2)	C5—C3—N1—C1	−116.1 (2)
C5—C3—C4—N2	119.5 (2)	C4—C3—N1—C1	−0.6 (2)
N1—C3—C5—C10	7.5 (2)	C3—C4—N2—C1	−3.2 (2)
C11—C3—C5—C10	133.2 (2)	N3—C1—N2—C4	−175.1 (2)
C4—C3—C5—C10	−101.9 (2)	N1—C1—N2—C4	2.9 (2)
N1—C3—C11—C12	−139.1 (2)	N1—C1—N3—C2	−1.3 (3)
C5—C3—C11—C12	95.0 (2)	N2—C1—N3—C2	176.2 (2)
C4—C3—C11—C12	−28.3 (3)	N4—C2—N3—C1	−168 (2)
N3—C1—N1—C3	176.5 (2)		

Data collection: *DIF*4 (Stoe & Cie, 1987*a*). Cell refinement: *DIF*4. Data reduction: *REDU*4 (Stoe & Cie, 1987*c*). 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). Software used to prepare material for publication: *SHELXL*93.

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Lists of structure factors, anisotropic displacement parameters, least-squares-planes data, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: PA1170). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Stoe & Cie (1987*c*) *REDU*4. *Data Reduction Program*. Version 6.2. Stoe & Cie, Darmstadt, Germany.

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3-Benzamido-4*H*-pyrido[4,3-*e*]-1,2,4-thiadiazine 1,1-Dioxide

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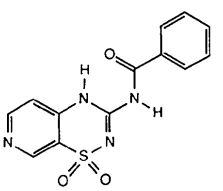
Abstract

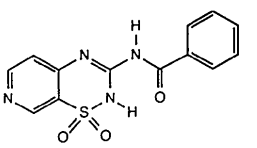
The title compound, $C_{13}H_{10}N_4O_3S$, is an original drug developed as a structural analogue of the anti-inflammatory agent piroxicam. It is also structurally related to diazoxide, an antihypertensive compound. The crystal structure determination shows that the 4*H* (rather than 2*H*) tautomeric form is preferentially adopted by this pyridothiadiazine derivative in the solid state.

Comment

3-Benzamido-4*H*-pyrido[4,3-*e*]-1,2,4-thiadiazine 1,1-dioxide is an original drug developed as a structural analogue of the anti-inflammatory agent piroxicam (4-hydroxy-2-methyl-*N*-(2-pyridyl)-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide). Moreover, the compound may be regarded as an acyl derivative of recently reported 3-alkylaminopyridothiadiazine dioxides (Pirotte *et al.*, 1993), known to be strong activators of the pancreatic ATP-sensitive potassium channel and structurally related to diazoxide [7-chloro-3-methyl-2*H*(or 4*H*)-1,2,4-benzothiadiazine 1,1-dioxide]. The particular interest of the present crystallographic study is to demonstrate which is the preferential tautomeric form adopted by the acyl derivative in the solid state: the 4*H* form (1) or the 2*H* form (2).



(1)



(2)

The values of the torsion angles show that the molecule is almost planar except for the phenyl moiety which is twisted by *ca* 40° [N11—C12—C13—C14 −141.0 (2)°] with respect to the rest of the molecule. There is an intramolecular hydrogen bond: N4···O3 2.643 (2), H4···O3 1.92 Å, N4—H4···O3 132°. The cohesion of the crystal is the result of van der Waals interactions and of one intermolecular hydrogen bond: N11···N8^{i} 2.908 (2), H11···N8^{i} 1.99 Å, N11—H11···N8^{i} 175° [symmetry code: (i) $-\frac{1}{2}+x, \frac{3}{2}-y, \frac{1}{2}+z$]. The N2—C3 and N4—C3 bond lengths, the location of the H atom on N4 rather than on N2, and the hydrogen-bonding scheme, including the N4—H4···O3 intramolecular hydrogen bond, indicate that the 4*H* form rather than the 2*H* form is favoured in the crystal, confirming previous results obtained for the diazoxide (Bandoli & Nicolini, 1977) and for other thiadiazine derivatives, for example, 3-amino- and 3-*tert*-butyl-4*H*-pyrido[4,3-*e*]-1,2,4-thiadiazine 1,1-dioxide (Dupont, Pirotte, de Tullio, Masereel & Delarge, 1995).

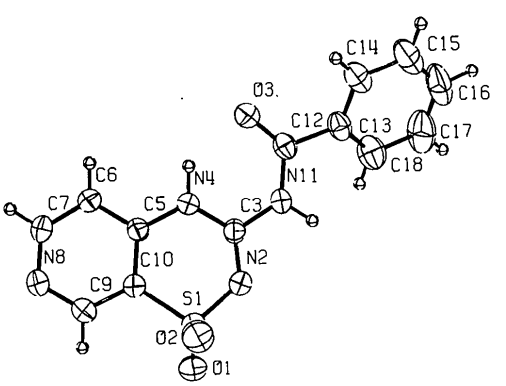


Fig 1. Molecular structure with atom-labelling scheme. Displacement ellipsoids are shown at the 50% probability level. H atoms are drawn as small circles of arbitrary radii.