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Structure of (+)-(*S*)-5-Phenyl-5-ethylhydantoin

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Abstract

The structure of (+)-(*S*)-5-phenyl-5-ethyl-2,4-imidazolidinedione or (+)-(*S*)-5-phenyl-5-ethylhydantoin (PHETHYD) is determined and compared with the structure of other related anticonvulsants. Among all the hydantoin derivatives previously described, the conformation of PHETHYD exhibits the smallest value (60°) of the dihedral angle between the phenyl ring and the hydantoin ring. The hydrogen-bond network suggests a particular stability of the homochiral packing. The two N—H and C═O bonds participate in the hydrogen-bond network which forms a flat ribbon parallel to the *a* axis. The nonpolar parts of the molecules are facing each other and are held together by van der Waals forces only.

Comment

The antiepileptic and/or sedative properties of 5,5-substituted hydantoin derivatives depend upon the nature of the substituents and the *R* or *S* configuration. This structure has been studied in order to compare its conformation with the conformation of other anticonvulsants such as methoin (Lisgarten & Palmer, 1980) and phenytoin (Camerman & Camerman, 1971).

The second aim of this study is to make a contribution to the knowledge of the way in which homochiral molecules crystallize as a conglomerate. These molecules include (+)-(*S*)-5-phenyl-5-ethylhydantoin (PHETHYD) and other 5-alkyl-5-arylhydantoin derivatives. Although a large majority of racemic mixtures (> 90%) crystallize as racemic compounds (Brock, Schweizer & Dunitz, 1991), the driving forces which lead either to this or to spontaneous resolution are not yet clear.

The racemic mixture, prepared in a good yield (> 90%) by Bucherer's reaction, was resolved *via* a new preparative route (Coquerel, Petit, Bouaziz & Depernet, 1992). Single crystals of *S* enantiomer were obtained by slow evaporation in ethanol at room temperature.

As expected, the hydantoin ring is almost planar, except for the slight deviation of the C(4) atom which is at 0.064 Å from the mean plane passing through the other four atoms. The dihedral angle between the phenyl and the heterocycle is 60°. This value is smaller than the angle observed in methoin (77°). It is in fact the smallest value of all alkyl/aryl or aryl/aryl disubstituted hydantoins and related barbiturates studied so far. Both N atoms are involved in hydrogen bonds: N(1)—H(1)···O(4)($1+x$, y, z) 2.28 Å, 170.3°; N(3)—H(3)···O(2)($0.5+x$, $1.5-y$, $-z$) 1.94 Å, 151.1°. The hydrogen-bonded molecules form an infinite ribbon, parallel to the *a* axis. These ribbons, possessing hydrophilic character, are held together only by means of van der Waals forces between the ethyl and phenyl groups which are in the vicinity of each other.

In a recent survey (Collet, 1990), it is shown that difficulties arise in dealing with the whole problem of homochiral *versus* heterochiral packing of enantiomers. Nevertheless, some special functional groups bring about a large increase in the proportion of conglomerates (usually between 5 and 10%). These

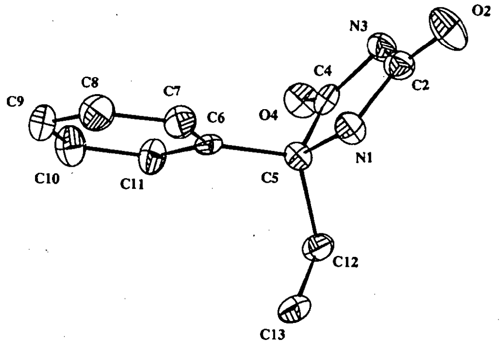

Fig. 1. *ORTEP* (Johnson, 1965) drawing with atom numbering.

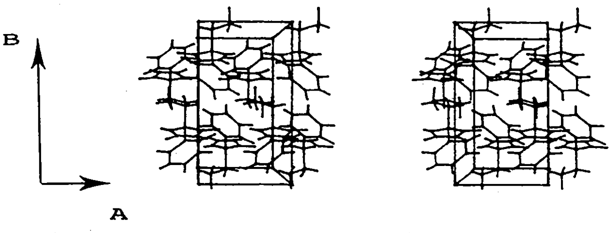

Fig. 2. Stereoscopic view down **c** of the crystal structure.

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functions allow non-centrosymmetric associations of the molecules which are thus predisposed to form stable conglomerates. For the enantiomers of 5-alkyl-5-arylhydantoin derivatives, we found the following analogies: a constant 6.3 Å axis in the direction of the strongest bonds, a great thermal stability (m.p. > 493 K) and a high proportion of conglomerates (5 out of 17). The packing of PHETHYD in which all the heteroatoms are involved in hydrogen bonds, could explain why all these similar structures have great stability and a predisposition to form conglomerates.

Experimental

Crystal data

$C_{11}H_{12}N_2O_2$
$M_r = 204.23$
Orthorhombic
$P2_12_12_1$
$a = 6.230$ Å
$b = 10.701$ Å
$c = 15.550$ Å
$V = 1036$ (7) Å^3
$Z = 4$
$D_x = 1.31$ Mg m^{-3}
$D_m = 1.29$ Mg m^{-3}

Mo $K\alpha$ radiation
$\lambda = 0.71069$ Å
Cell parameters from 25 reflections
$\theta = 14$- 18°
$\mu = 0.086$ mm^{-1}
$T = 293$ (1) K
Acicular along **a**
0.45 × 0.12 × 0.08 mm
Colourless

Data collection

Enraf-Nonius CAD-4 diffractometer
θ-2θ scans
1089 measured reflections
1089 independent reflections
542 observed reflections [$I > 3\sigma(I)$]

$\theta_{\max} = 25°$
$h = 0 \rightarrow 7$
$k = 0 \rightarrow 12$
$l = 0 \rightarrow 18$
2 standard reflections
frequency: 60 min
intensity variation: none

Refinement

Refinement on F
Final $R = 0.037$
$wR = 0.039$
$S = 2.36$
542 reflections
137 parameters
Only coordinates of H atoms refined

$w = 1$
$(\Delta/\sigma)_{\max} = 0.05$
$\Delta\rho_{\max} = 0.14$ e Å^{-3}
$\Delta\rho_{\min} = -0.12$ e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

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

Equivalent isotropic $U_{\rm eq}$ is obtained from U_{ij} according to Pryor (1975):
$$U_{\rm eq} = \tfrac{1}{3}\textstyle\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	$U_{\rm eq}$
N(1)	0.8175 (8)	0.6788 (8)	0.1877 (3)	0.0387
C(2)	0.742 (1)	0.7092 (7)	0.1094 (4)	0.0402
O(2)	0.8468 (8)	0.7307 (5)	0.0451 (3)	0.0585
N(3)	0.5227 (9)	0.7143 (5)	0.1162 (3)	0.0381
C(4)	0.452 (1)	0.6812 (7)	0.1949 (4)	0.0337
O(4)	0.2674 (6)	0.6731 (6)	0.2190 (3)	0.0417
C(5)	0.648 (1)	0.6604 (6)	0.2509 (3)	0.0303
C(6)	0.659 (1)	0.7537 (5)	0.3244 (3)	0.0278
C(7)	0.828 (1)	0.8328 (7)	0.3361 (4)	0.0441
C(8)	0.829 (1)	0.9152 (7)	0.4046 (4)	0.0549
C(9)	0.658 (1)	0.9223 (7)	0.4596 (4)	0.0537
C(10)	0.491 (1)	0.8427 (8)	0.4483 (4)	0.0564
C(11)	0.488 (1)	0.7590 (7)	0.3818 (4)	0.0438
C(12)	0.647 (1)	0.5234 (6)	0.2840 (4)	0.0413
C(13)	0.843 (1)	0.4913 (6)	0.3386 (4)	0.0490

Table 2. *Geometric parameters* (Å, °)

N(1)—C(2)	1.345 (8)	N(1)—C(5)	1.456 (7)
C(2)—O(2)	1.215 (8)	C(2)—N(3)	1.374 (7)
N(3)—C(4)	1.349 (8)	C(4)—O(4)	1.213 (7)
C(4)—C(5)	1.514 (8)	C(5)—C(6)	1.519 (7)
C(5)—C(12)	1.554 (8)	C(6)—C(7)	1.365 (8)
C(6)—C(11)	1.388 (8)	C(7)—C(8)	1.382 (9)
C(8)—C(9)	1.37 (1)	C(9)—C(10)	1.36 (1)
C(10)—C(11)	1.369 (9)	C(12)—C(13)	1.527 (9)
C(5)—N(1)—C(2)	113.0 (5)	O(2)—C(2)—N(1)	127.3 (6)
N(3)—C(2)—N(1)	106.7 (6)	N(3)—C(2)—O(2)	126.0 (7)
C(4)—N(3)—C(2)	112.6 (6)	O(4)—C(4)—N(3)	127.5 (7)
C(5)—C(4)—N(3)	107.3 (5)	C(5)—C(4)—O(4)	125.2 (6)
C(4)—C(5)—N(1)	100.2 (4)	C(6)—C(5)—N(1)	112.7 (5)
C(6)—C(5)—C(4)	111.8 (5)	C(12)—C(5)—N(1)	110.6 (6)
C(12)—C(5)—C(4)	109.1 (6)	C(12)—C(5)—C(6)	111.8 (4)
C(7)—C(6)—C(5)	122.9 (6)	C(11)—C(6)—C(5)	118.5 (6)
C(11)—C(6)—C(7)	118.6 (6)	C(8)—C(7)—C(6)	120.2 (7)
C(9)—C(8)—C(7)	120.9 (7)	C(10)—C(9)—C(8)	118.9 (6)
C(11)—C(10)—C(9)	121.0 (7)	C(10)—C(11)—C(6)	120.3 (6)
C(13)—C(12)—C(5)	113.3 (6)		

The structure was solved by direct methods (Watkin, Carruthers & Betteridge, 1985) and refined by anisotropic full-matrix least squares on F. Corrections for absorption were made with *DIFABS* (Walker & Stuart, 1985). No anomalous contribution was considered; the absolute configuration has already been determined (Knabe & Wunn, 1980). Fig. 1 was drawn on a VAX station using *ORTEP* (Johnson, 1965). Fig. 2 is a stereoscopic view of the crystal structure.

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Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and complete geometry have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55765 (7 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: PA1028]

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