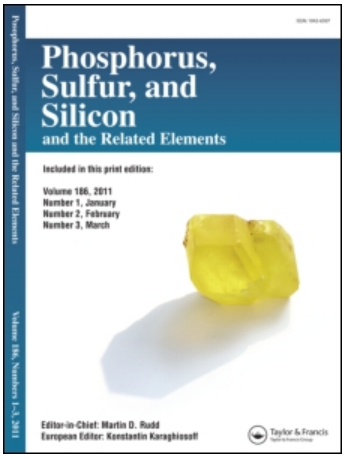


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

The Crystal and Molecular Structure of 3-Methyl-5-p-methylbenzylidene-2-selenohydantoin

E. Żesławska[a]; B. J. Oleksyn[b]; M. J. Korohoda[a]; K. Stadnicka[b]
[a] Pedagogical University, Kraków, Poland [b] Jagiellonian University, Kraków, Poland

Online publication date: 27 October 2010

To cite this Article Żesławska, E. , Oleksyn, B. J. , Korohoda, M. J. and Stadnicka, K.(2003) 'The Crystal and Molecular Structure of 3-Methyl-5-p-methylbenzylidene-2-selenohydantoin', Phosphorus, Sulfur, and Silicon and the Related Elements, 178: 2, 261 — 268
To link to this Article: DOI: 10.1080/10426500307936
URL: http://dx.doi.org/10.1080/10426500307936

Phosphorus, Sulfur and Silicon, 2003, Vol. 178:261–268

1042-6507/03 $12.00 + .00
DOI: 10.1080/10426500390170381

THE CRYSTAL AND MOLECULAR STRUCTURE OF 3-METHYL-5-p-METHYLBENZYLIDENE-2-SELENOHYDANTOIN

E. Żesławska,[a] *B. J. Oleksyn,*[b] *M. J. Korohoda,*[a] *and K. Stadnicka*[b]
Pedagogical University, Kraków, Poland[a] *and Jagiellonian University, Kraków, Poland*[b]

(Received May 10, 2002; accepted June 9, 2002)

The X-ray structure analysis of a single crystal of 3-methyl-5-p-methylbenzylidene-2-selenohydantoin was carried out. The crystals are monoclinic, space group $P2_1/c$, with $a = 5.244(1)$ Å, $b = 19.402(2)$ Å, $c = 11.606(1)$ Å, $\beta = 94.64(1)^\circ$, $Z = 4$. The molecule is a Z-isomer. The overall conformation is not exactly planar, the angle between the hydantoin and p-methylphenyl planes is 11.8(1)°. The packing of the molecules in the unit cell can be described as an arrangement of molecular chains which interact with each other via weak-hydrogen bonds, C—H···O. The chains consist of dimers in which molecules are linked together by two symmetry-equivalent hydrogen bonds, N—H···Se, that form accros inversion centres. The dimers interact also via weak hydrogen bonds, C—H···O, between methyl groups and carbonyls of molecules related by another inversion centres.

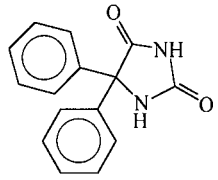
Keywords: Crystal structure; hydantoin; hydrogen bonding; selenoorganic compounds

INTRODUCTION

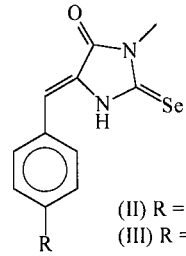
The molecule of 3-methyl-5-p-methylbenzylidene-2-selenohydantoin (**II**) is similar to that of anticonvulsant phenytoin (**I**) in which the substituents at C5 are replaced by paramethylbenzylidene. It has been reported recently that phenytoin can be also used for treatment of neuropathic pains[1] and as a mood stabilizing drug.[2]

As shown by Kolasa et al.,[3] the anticonvulsant activity of hydantoin is not abolished by the above change of the substituent at C5. On the

Address correspondence to B. J. Oleksyn, Faculty of Chemistry, Jagiellonian University, ul. R. Ingardena 3, Kraków 30 060, Poland. E-mail: oleksyn@chemia.uj.edu.pl



(I)



(II) R = CH_3
(III) R = Cl

other side, the activity depends remarkably on the electronegativity of the atom attached to C2, and it decreases in the order O, S, Se.[4,5]

The anticonvulsant activity of the phenytoin derivatives was found to depend on the kind of the components of the active molecules as well as on their mutual orientation.[6] Among these components the most important are one or two aromatic rings and one heterocyclic system, usually a cyclic imid. In particular, efficient binding of hydantoin derivatives to the neuronal voltage-dependent sodium channel requires a correct orientation of one of the phenyl rings to the hydantoin plane.[7] These rings should be approximately coplanar.

This article is a continuation of our studies of the crystal structures of the hydantoin derivatives in which we have investigated the effect of substituents on the molecular geometry. Assuming that the atom (O, S, Se) at C2 does not influence the conformation of the molecule, we decided to compare the molecular structure of (**II**) with that of (**III**).[5] This comparison should elucidate the role of geometrical changes introduced by *para* substituents in the benzylidene ring on the anticonvulsant activity. According to Kleinrok,[4] 3-methyl-5-parachlorobenzylidenehydantoin is more active than the paramethyl–derivative.

EXPERIMENTAL

The synthesis of 3-methyl-5-p-methylbenzylidene-2-selenohydantoin (MMBSH) was described previously.[8] Dark-yellow prismatic crystals were obtained from ethanol-DMSO by slow evaporation. One of them, with dimensions 0.23 × 0.18 × 0.10 mm, was mounted on a KM-4 automatic single crystal diffractometer (KUMA Diffraction, Poland) equipped with graphite monochromator. The intensity data collection was performed with CuKα radiation.

The lattice parameters and their standard deviations were determined by the least-squares analysis from the setting angles of 89 reflections, which were comprised in the Θ range of 1.5° to 60°. The

intensities of 2623 reflections in the theta range 1–80° for $0 \leq h \leq 6$, $0 \leq k \leq 24$, $-14 \leq l \leq 14$ were measured, from which 2157 had $I > 2\sigma(I)$. The set of unique reflections contained 2284 data with R(int) = 0.0583, R(sigma) = 0.0247.

Data reduction with corrections for Lorentz and polarization effects, but not for absorption, was perfomed using local KM-4 software. The linear absorption coefficient, μ, has a moderate value, but the anisotropy of the crystal size causes that the transmission factor changed in the range of 0.66–0.28. According to Jones,[9] this may lead to "the apparent highly anisotropic thermal motion of atoms," but "the atomic positions are not severely affected." At the same time, the accuracy of the final parameters may be overestimated, because of systematic errors introduced by uncorrected effects of absorption. Regrettably, the absorption correction could not be appplied for the investigated crystal, because of lack of the apropriate programs at our disposal. However, the neglect of absorption effects had probably not a very serious influence on structure parameters.

The phase problem was solved by the direct methods using SHELXS-97.[10] The positions of hydrogen atoms were found on subsequent difference Fourier maps after anisotropic refinement of all nonhydrogen atoms. The hydrogen atoms were refined isotropically in the idealized geometry using riding model according to SHELXL-97.[11] The whole refinement procedure was carried out on F_o^2. The weighting scheme was:

$$w^{-1} = \sigma^2(F_o^2) + (0.0729P)^2 + 1.27P, \quad \text{where} \quad P = 1/3[(F_o^2, 0) + 2F_c^2].$$

The F_c values were corrected also with the use of an extinction parameter, χ, according to the formula: $Fc' = k[1 + 0.001\chi Fc^2\lambda^3 \sin(2\theta)]^{1/4}$, where Fc′ is the corrected structure factor and k- the overall scale factor. χ refined to the value 0.0030(5).

The crystal data and details of measurments and refinement are listed in Table I.

RESULTS AND DISCUSSION

The final atomic coordinates for MMBSH together with other data have been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 180716. Selected bond lengths, bond angles are given in Table II.

The molecule, projected on the plane of methylbenzene ring, is depicted in Figure 1. The packing of the molecules in the unit cell is shown in Figure 2.

TABLE I Crystallographic Parameters and Experimental Data for Compound (**II**)

Molecular formula	$C_{12}H_{12}N_2OSe$	
Formula weight	229.19	
Temperature	293 K	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 5.244(1) Å	$\alpha = 90.00^\circ$
	b = 19.402(2) Å	$\beta = 94.64(1)^\circ$
	c = 11.606(1) Å	$\gamma = 90.00^\circ$
Volume	1177.11 $Å^3$	
Z	4	
Density (calculated)	1.575 g/cm^3	
Wavelength	1.5418 Å	
Absorption coefficient	4.16 mm^{-1}	
F(000)	560	
2 Θ for data collection	2.0 to 160.0	
hkl range	$0 \le h \le 6$, $0 \le k \le 24$, $-14 \le l \le 14$	
Reference reflections		
Number	3	
Frequency	every 50 reflections	
Stability	0.85%	
Number of reflections		
Collected	2623	
Unique	2284 ($R_{int} = 0.0583$)	
Data/number of parameters	2284/120	
Final R(F)	0.0490 for Fo > 4σ(Fo)	
	0.0517 for all data	
wR(F^2)	0.1407	
S	1.127	
Shift/e.s.d.	0.000	
Max/min/e$Å^{-3}$	0.63/−0.88	

It is obvious from Figure 1 that MMBSH in the crystalline state is Z-isomer. The bond lengths and bond angles are comparable to within 3σ to those observed in 5-p-chlorobenzylidene-3-methyl-2-selenohydantoin (CMBSH),[5] with the exception of the angles C4-N3-C2 and C9-C10-C11. The decrease of C9-C10-C11 bond angle in the phenyl moiety MMBSH most probably is the effect of the exchange of the chlorine atom for the methyl group which is more bulky than Cl substituent. The value of the angle C9-C10-C11 is identical to that observed in 1-methyl-4-(p-methylbenzylidene-2-methyl-seleno-5-imidazolinone (MBMSI).[12] The bond angle C5-C6-C7 is large and similar to those in CMBSH and MBMSI which are also Z-isomers. Its value is a result of a stereoelectronic effect which leads to a compromise between the planarity of the conjugated system: hydantoin-benzylidene

TABLE II Bond Lengths [Å] and Angles [deg] for Nonhydrogen Atoms

Se(1)-C(2)	1.808(3)	C(6)-C(7)	1.440(5)
O(1)-C(4)	1.203(4)	C(7)-C(12)	1.396(5)
N(1)-C(2)	1.349(5)	C(7)-C(8)	1.396(5)
N(1)-C(5)	1.397(4)	C(8)-C(9)	1.385(5)
C(2)-N(3)	1.363(4)	C(9)-C(10)	1.385(6)
N(3)-C(4)	1.394(4)	C(10)-C(11)	1.394(7)
N(3)-C(13)	1.446(5)	C(10)-C(14)	1.492(6)
C(4)-C(5)	1.473(5)	C(11)-C(12)	1.374(6)
C(5)-C(6)	1.346(5)		
C(2)-N(1)-C(5)	111.0(3)	N(1)-C(5)-C(4)	105.2(3)
N(1)-C(2)-N(3)	108.0(3)	C(5)-C(6)-C(7)	131.6(3)
N(1)-C(2)-Se(1)	126.4(3)	C(12)-C(7)-C(8)	117.5(4)
N(3)-C(2)-Se(1)	125.6(3)	C(12)-C(7)-C(6)	118.6(3)
C(2)-N(3)-C(4)	111.0(3)	C(8)-C(7)-C(6)	123.9(3)
C(2)-N(3)-C(13)	125.8(3)	C(9)-C(8)-C(7)	120.9(3)
C(4)-N(3)-C(13)	123.2(3)	C(10)-C(9)-C(8)	121.3(4)
O(1)-C(4)-N(3)	125.5(3)	C(9)-C(10)-C(11)	117.7(4)
O(1)-C(4)-C(5)	129.7(3)	C(9)-C(10)-C(14)	121.2(5)
N(3)-C(4)-C(5)	104.7(3)	C(11)-C(10)-C(14)	121.1(4)
C(6)-C(5)-N(1)	131.9(3)	C(12)-C(11)-C(10)	121.3(4)
C(6)-C(5)-C(4)	122.9(3)	C(11)-C(12)-C(7)	121.3(4)

and a repulsion between hydrogen atoms bonded to N1 and C8. The distance between these atoms, 2.11 Å, is smaller than the sum of the van der Waals radii, i.e., 2.40 Å.

The molecule as a whole is only approximately planar, with the torsion angles: C4-C5-C6-C7 = −179.7(3)°, C5-C6-C7-C8 = 11.7(6)°. These

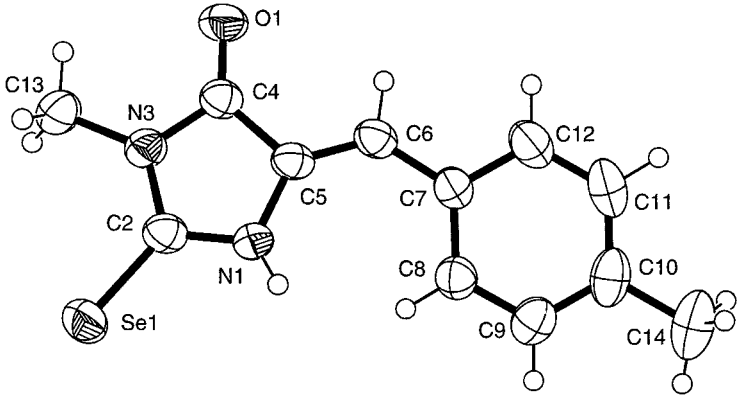


FIGURE 1 Atom numbering of the molecule of 3-methyl-5-p-methylbenzylidene-2-selenohydantoin.

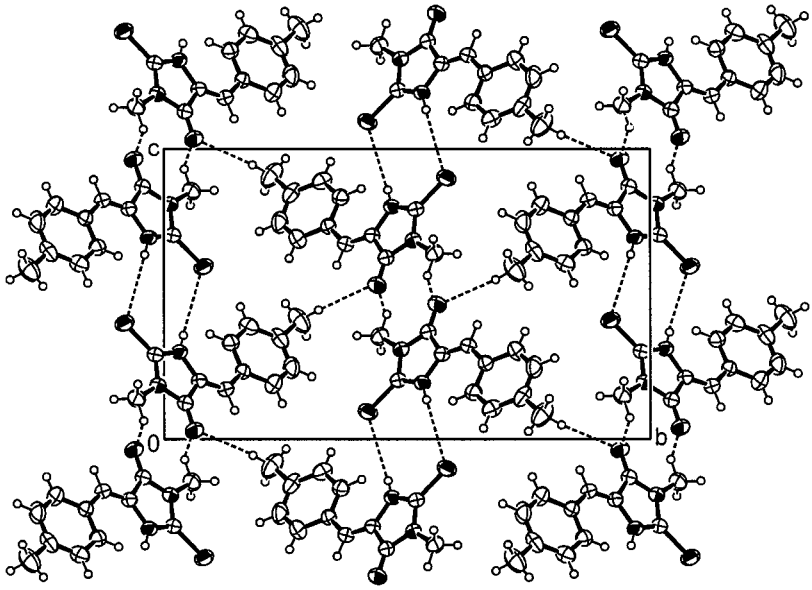


FIGURE 2 Packing of molecules in the unit cell of the crystalline 3-methyl-5-p-methylbenzylidene-2-selenohydantoin projected along the axis X. Hydrogen bonds are denoted by broken lines.

values are in agreement with the correlation between the bond angle C5-C6-C7 and the torsion angle C5-C6-C7-C8 which we observed earlier for similar molecules found in Cambridge Structural Database System.[5] On the other side, the planes of paramethylphenyl and hydantoin rings are less coplanar, with interplanar angle 11.8(1)°, than for parachlorophenyl derivative where this angle is 4.2(1)°.[5] Thus, one may expect that the anticonvulsant activity of molecules (**II**) should be lower than that of (**III**).

TABLE III Parameters of Intermolecular Hydrogen Bonds in the Unit Cell of MMBSH

Donor (D)	Hydrogen (H)	Acceptor (A)	D···A (Å)	D—H (Å)	H···A (Å)	D—H···A(°)
N1	H1	Se1[a]	3.652(3)	0.78(4)	2.89(4)	166(3)
C13	H13A	O1[b]	3.240	0.96	2.55	129
C14	H14C	O1[c]	3.483	0.96	2.57	160
C9	H9	Se1[d]	4.106	0.93	3.33	151

Coordinate codes: [a] −x, −y + 1, −z + 2; [b] −x + 1, −y + 1, −z + 1; [c] x−1, −y + 0.5, z + 0.5; [d] −x − 1, −y + 1, −z + 2.

The packing of the molecules in the unit cell can be characterized by intermolecular interactions listed in Table III.

Pairs of the molecules related by the inversion centres in positions 0.5, 0.5, 0.0 form a kind of dimers. The interactions which occur between the molecules in a dimer are short contacts between Se of one molecule and H1 at N1 of the other and vice versa. The selenium atom interacts also with the atom H9 of the other molecule. The weak intermolecular hydrogen bonds formed in this way, have the parameters shown in Table III. The dimers interact with each other via relatively short contacts. These contacts link pairs of molecules which are related by the inversion center in positions 0.5, 0.5, 0.5. The atom C13 of the methyl group of one molecule is a donor of the proton, H13A, which is accepted by O1 of the other molecule and vice versa. The chains of the molecules, formed in this way are parallel to z axis and related by the glide plane c perpendicular to y. They are interconnected with each other by weak hydrogen bonds between the methyl substituent, C14, at the benzene moiety of one chain and the oxygen atom, O1, of the other.

CONCLUSIONS

1. The crystal structure analysis of 3-methyl-5-p-methylbenzylidene-2-selenohydantoin revealed that the molecule is a Z-isomer and its conformation is not exactly planar, with the hydantoin and p-methylphenyl planes forming the angle of 11.8(1)°. The packing of the molecules is dominated by intermolecular hydrogen bonds of the types: C—H···O and N—H···Se.
2. It was found that the paramethyl substituent in compound (II) introduces a distortion from the coplanarity between the phenyl and hydantoin rings. This suggests that the reason for a lower anticonvulsant activity of 3-methyl-5-p-methylbenzylidene-2-selenohydantoin is the change of its conformation in comparison with that of the more active 3-methyl-5-p-chlorobenzylidene-2-selenohydantoin.

REFERENCES

[1] B. Nicholson, *Acta Neurol. Scand*., **101,** 359 (2000).
[2] P. Gareri, U. Falconi, P. De Fazio, and G. De Sarro, *Progress in Neurobiology*, **61,** 352 (2000).
[3] K. Kolasa, Z. Kleinrok, T. Pietrasiewicz, G. Czechowska, K. Kieć-Kononowicz, and A. Zejc, *Pol. J. Pharmacol*., **41,** 377 (1989).
[4] Z. Kleinrok, M. J. Korohoda, M. Kozicka, and A. Chodkowska, *Acta Polon. Pharm*., **XL**(4), 517 (1983).

[5] E. Żesławska, B. J. Oleksyn, M. J. Korohoda, and J. Sliwinski, *Phosphorus, Sulfur and Silicon*, **126,** 111 (1997).
[6] M. L. Brown, B. B. Brown, and W. J. Brouillette, *J. Med. Chem*., **40,** 602 (1997).
[7] M. G. Wong, G. B. Defina, and P. R. Andrews, *J. Med. Chem*., **29,** 562 (1997).
[8] M. J. Korohoda, *Polish J. Chem*., **55,** 359 (1981).
[9] P. G. Jones, *Chem. Soc. Rev*., **13,** 157 (1984).
[10] G. M. Sheldrick, *Acta Cryst*., **A46,** 467 (1990).
[11] G. M. Sheldrick, *SHELXL97*. Program for the Refinement of Crystal Structure. University of Gottingen, Germany, 1997.
[12] E. Żesławska, B. J. Oleksyn, M. J. Korohoda, and J. Śliwiński, *Polish J. Chem*., **74,** 751 (2000).