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REACTION OF 5,5-DIPHENYL-2-THIOHYDANTOIN WITH 1,3-DIBROMOPROPANE

CRYSTAL AND MOLECULAR STRUCTURE OF 2,3,4,5-TETRAHYDRO-6,6-DIPHENYLIMIDAZO [2,1-b]-THIAZINE-7 (6H)-ONE

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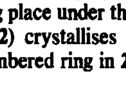
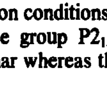
Abstract—The reaction between the potassium salt of 5,5-diphenyl-2-thiohydantoin (1) and 1,3-dibromopropane carried out in DME under anhydrous conditions has been found to give two isomeric diphenylimidazothiazines 2 and 3. When the reaction of 1 with 1,3-dibromopropane was performed in protic solvents (EtOH, HOH, NaOH) 2 and 3-(3-mercaptopropyl) - 5, 5 - diphenylthiohydantoin (4) were formed. The latter is the product of hydrolysis of 3 taking place under the reaction conditions. 2, 3, 4, 5 - Tetrahydro - 6, 6 - diphenylimidazo [2, 1-b] - thiazine - 7 (6H) - one (2) crystallises in space group $P2_1/n$ with a = 10.812(3), b = 14.905(7), c = 9.885(4) Å, β = 104.91(2)°. The 5-membered ring in 2 is planar whereas the 6-membered thiazine ring adopts the sofa conformation.

RECENTLY there has been considerable interest in the synthesis and properties of the derivatives of hydantoin. They are not only very useful synthetic intermediates but also have found an application as modern therapeutic agents possessing anticonvulsant properties.[1,2] It is interesting to note that a wide range of a new, biologically active compounds was prepared by N-alkylation of hydantoin and its sulphur analogue.[3] Alkylation of hydantoin and 2-thiohydantoin with the appropriate dihalogenoalkanes makes it possible to synthesise bicyclic compounds, derivatives of imidazooxazole and imidazothiazole.[4-6] For instance, Driscoll *et al.* have recently reported[6] the synthesis of two isomeric bicyclic compounds shown below which were formed upon treatment of 5, 5 - diphenyl - 2 - thiohydantoin (1) with 1 - bromo - 2 - chloroethane.





As part of our studies on the structure-activity relationship of 5, 5 - diphenyl - 2 - thiohydantoin (1)[7,8] derivatives the reaction of 1 with 1,3-dibromopropane was investigated.

RESULTS AND DISCUSSION

Reaction of 5,5-*diphenyl-2-thiohydantoin* (1) *with* 1,3-*dibromopropane*

Synthesis of 2,3,4,5-*tetrahydro*-6,6-*diphenylimidazo* [2,1-*b*]- *thiazine* -7 (6*H*) - *one* (2) *and* 2,3,4,5 - *tetrahydro* - 7,7 - *diphenylimidazo* - [2, 1-*b*] - *thiazine* - 6(6*H*) - *one* (3). The reaction of 1 with 1,3-dibromopropane was carried out under reflux in a solution of ethanol and water in the presence of equimolar quantity of sodium hydroxide as a base. In addition to some amounts of the unreacted 1 two main products were detected by tlc. Their separation by column chromatography afforded pure components having m.p. 158–160° and 198–199°, respectively, the structures of which have been assigned on the basis of spectroscopic data (MS, ^{1}H NMR, UV, IR) and independent synthesis. Since the mass spectrum of the first products having m.p. 158–160° showed the molecular peak at *m*/*e* 326, the bicyclic structures 2 or 3, which were expected to be formed as a result of the 1,2- or 2,3-dialkylation reaction, were excluded. The ^{1}H NMR spectrum of this product exhibited the one-proton reasonance signal at $\delta = 7,56$ ppm which can be ascribed, in accord with the literature,[6,9] to the proton connected with the N atom, N-1, of the hydantoin ring. These and other data suggest the structure of 3-(3-mercaptopropyl) - 5, 5 - diphenylhydatoin (4) for the product under consideration.

In order to get conclusive evidence for the proposed structure we decided to prepare 4 by a different route. Thus, 3-(3-bromopropyl) - 5, 5 - diphenylhydantoin (7)[7] was reacted with thiourea and the isothiouronium salt 8 formed was hydrolysed under alkaline conditions to give the desired compound 4, m.p. 158–160°. It should be noted that the spectroscopic properties of 4 obtained as described were identical in all respects with those of the product formed in the reaction of 1 with 1,3-dibromopropane.

The second product of the reaction having m.p. 198–199°, was identified as 2,3,4,5 - tetrahydro - 6,6 - diphenylimidazo [2, 1-b] - thiazine - 7 (6H) - one (2). The

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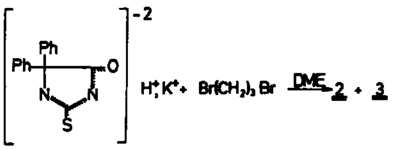
structural proof rests on the following facts. The first is that the mass spectrum of this compound showed the molecular peak at m/e 308. Secondly, in the UV spectrum there was no absorbtion characteristic for the thiocarbonyl group. Furthermore, alkaline hydrolysis of this product gave a compound, m.p. 221–223°, the mass spectrum of which showed the molecular peak at m/e 326. The ^{1}H NMR spectrum of the latter compound exhibited the one-proton resonance signal at $\delta = 9.19$ ppm which can be ascribed to the proton at N-3 of the hydantoin ring. Hence, all the spectroscopic data support the structure of 1-(3-mercaptopropyl) - 5,5 - diphenylhydantoin (**5**) for the alkaline hydrolysis product and consequently provide an additional proof for the bicyclic structure **2** of the second isolated product.

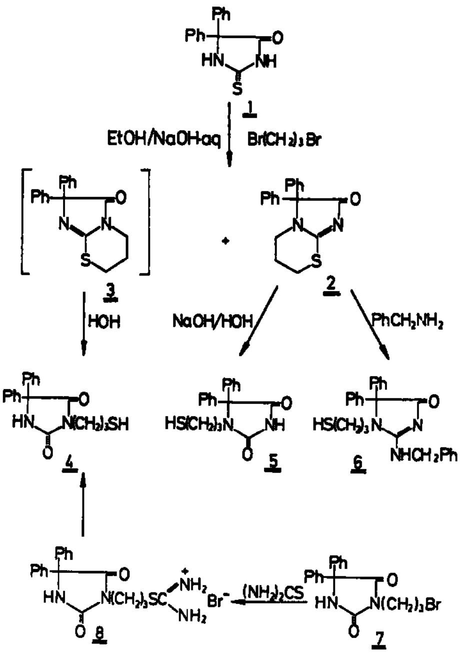
As expected, the reaction of benzylamine with **2** resulted in the formation of 1 - (3 - mercaptopropyl) - 2 - benzylamino - 5, 5 - diphenylhydantoin (**6**). Therefore, the results of alkaline hydrolysis and aminolysis indicate that **2** exhibits a typical reactivity of the isothiourea system[10] i.e. the nucleophilic attack is directed on the C atom, C-2, of the alkylated thiohydantoin ring.†

Finally, **4** and **5** are isomeric compounds in which the 3-mercaptopropyl group is attached to N-3 and N-1, respectively. In view of the fact that **5** was obtained by alkaline hydrolysis of **2** it is reasonable to assume that **3** is formed together with **2** during the reaction of **1** with 1,3 - dibromopropane but that it undergoes further hydrolysis under the reaction conditions to afford **4** as one of the two isolable reaction products. This is most probably due to the greater reactivity and smaller stability of **3** in comparison with its isomer **2** as a consequence of a better resonance stabilisation of the latter.

The above results prompted us to study the reaction between **1** and 1,3-dibromopropane under strictly anhydrous conditions. Thus, the freshly prepared and dry potassium salt of **1** was reacted with 1,3-dibromopropane in dimethoxyethane (DME) solution at 75–80° for 5 hr. In accord with our expectation this condensation resulted in the formation of both isomeric bicyclic products **2** and **3** in a ratio 1.75 : 1. The compound **3**, m.p. 227–227.5°, isolated in a pure state by column chromatography and crystallisation was characterised by mass, ^{1}H NMR and IR spectra.



The mass spectra of the isomeric thiazines **2** and **3** show distinct differences. Whereas in the mass spectrum of **2** an intense peak $[M-1]^+$ was observed it was not present in the mass spectrum of **3**. This observation is very easily to explain if one takes into account that proton elimination from **2** results in the formation of the cation **2a** and/or **2b** with the increased number of the conjugated double bonds. This situation is not possible for **3**. On the other hand, the characteristic fragmentation pathway for **3** is the HCO· elimination leading to the appearance in the mass spectrum of the peak at m/e 279 corresponding to the fragment $[M-29]^+$ (Scheme 2).



Scheme 1.

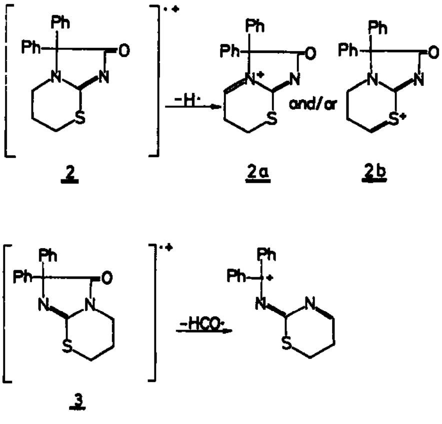
The exact mass fragmentation pathways for **2** and **3** are being investigated.

Crystal structure of 2,3,4,5 - *tetrahedro* - 6, 6 - *diphenylimidazo* - [2, 1-*b*] - *thiazine* - 7 (6*H*) - *one* (**2**). The X-ray analysis of **2** has been carried out in order to confirm the proposed molecular structure and to determine the conformation of the 6-membered ring condensed with the thiohydantoin moiety.

The atomic numbering in the molecule and packing of the molecules in the unit cell are given in Figs. 1 and 2. Tables 1 and 2 list the bond lengths and angles. The displacements of the atoms from various planes in **2** and some angles between them are shown in Table 3.

The molecule of **2** may be described in terms of four rings planes 1 to 4, Table 3). The hydantoin ring is planar with the experimental error ($X^2 = 10.24$). The angles between the plane of the hydantoin ring and the benzene rings are 98.5° and 110.3°, respectively.

As expected, the 6-membered thiazine ring is not planar. The torsion angles in this ring and the results of



Scheme 2.

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†All these reactions are summarised in Scheme 1.

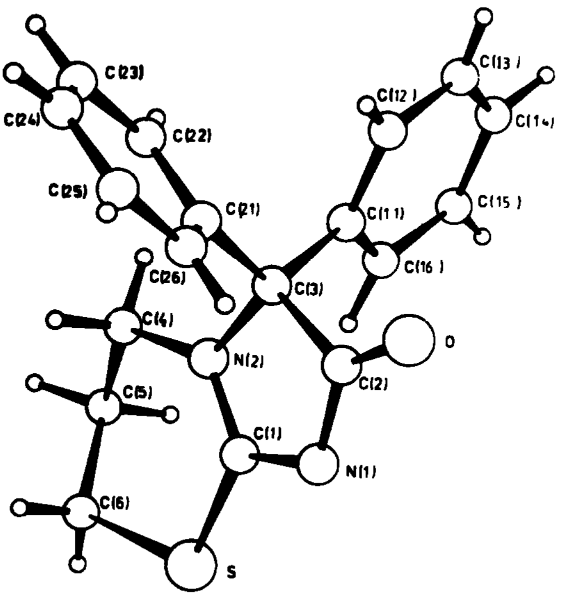


Fig. 1. Perspective view of the molecule of 2 with the numbering scheme.

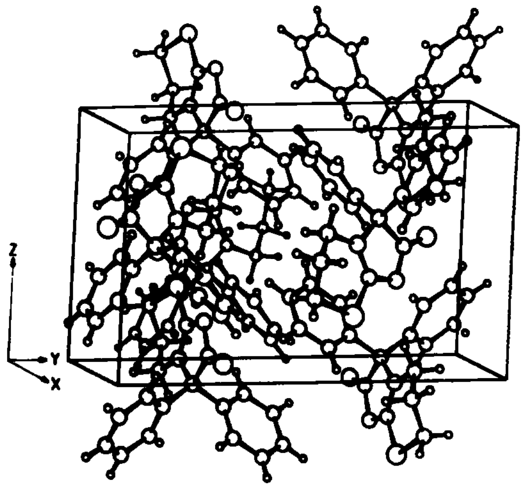
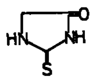


Fig. 2. The packing of the molecules of 2 in the unit cell.

test[11] are given in Table 4. Based on these results and the value of asymmetry parameters[12] $\Delta C_S = 7.3°$ one can define the conformation of this ring as a sofa. The plane of symmetry passes through atoms C(1) and C(5). The sofa conformation is clearly shown by the plane passing through the atoms C(1), N(2), C(4), C(6) and S. (plane 2, Table 3). The remaining atom C(5) of the thiazine ring is 0.655(17) Å off plane.

It should be noted that intermolecular packing forces do not appear to determine even the major features of the conformation of 2. There are no distances shorter than the sum of Van der Waals radii.

Since in 2 the hydantoin ring is fused to the thiazine ring it is interesting to compare the interatomic distances and angles in the hydantoin ring of 2 with those found for other related 2-thiohydantoin derivatives, i.e. (9), (10) and (11) (see Table 5).



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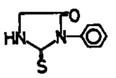

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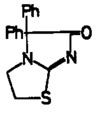

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Table 1.

Bond lengths (Å) in 2

C(1) -S	1.717(3)	C(6) -S	1.806(4)
C(2) -O	1.216(4)	C(1) -N(1)	1.333(4)
C(2) -N(1)	1.363(4)	C(1) -N(2)	1.330(3)
C(3) -N(2)	1.471(4)	C(4) -N(2)	1.459(4)
C(3) -C(2)	1.554(4)	C(11) -C(3)	1.527(4)
C(21) -C(3)	1.517(4)	C(5) -C(4)	1.509(6)
C(6) -C(5)	1.509(5)	C(12) -C(11)	1.380(5)
C(16) -C(11)	1.380(5)	C(13) -C(12)	1.378(5)
C(14) -C(13)	1.372(7)	C(15) -C(14)	1.354(6)
C(16) -C(15)	1.373(5)	C(22) -C(21)	1.388(4)
C(26) -C(21)	1.387(5)	C(23) -C(22)	1.372(5)
C(24) -C(23)	1.372(6)	C(25) -C(24)	1.366(5)
C(26) -C(25)	1.381(6)		
H(41) -C(4)	1.00 (4)	H(42) -C(4)	0.99 (4)
H(51) -C(5)	1.03 (4)	H(52) -C(5)	1.06 (3)
H(61) -C(6)	0.94 (4)	H(62) -C(6)	0.98 (4)
H(121)-C(12)	0.91 (4)	H(131)-C(13)	0.91 (4)
H(141)-C(14)	0.95 (3)	H(151)-C(15)	0.99 (4)
H(161)-C(16)	0.97 (4)	H(221)-C(22)	0.90 (4)
H(231)-C(23)	0.97 (3)	H(241)-C(24)	0.94 (4)
H(251)-C(25)	1.00 (4)	H(261)-C(26)	0.97 (3)

Table 2.

Bond angles (°) in **2**

C(6)	-S	-C(1)	101.1(2)	C(2)	-N(1)	-C(1)	105.7(2)
C(3)	-N(2)	-C(1)	108.4(2)	C(4)	-N(2)	-C(1)	127.8(3)
C(4)	-N(2)	-C(3)	123.8(2)	N(1)	-C(1)	-S	118.5(2)
N(2)	-C(1)	-S	124.8(2)	N(2)	-C(1)	-N(1)	116.6(3)
N(1)	-C(2)	-O	126.1(3)	C(3)	-C(2)	-O	123.5(3)
C(3)	-C(2)	-N(1)	110.4(3)	C(2)	-C(3)	-N(2)	98.9(2)
C(11)	-C(3)	-N(2)	111.2(2)	C(11)	-C(3)	-C(2)	106.7(2)
C(21)	-C(3)	-N(2)	110.8(2)	C(21)	-C(3)	-C(2)	113.5(2)
C(21)	-C(3)	-C(11)	114.6(2)	C(5)	-C(4)	-N(2)	111.2(3)
C(6)	-C(5)	-C(4)	112.4(3)	C(5)	-C(6)	-S	112.7(3)
C(12)	-C(11)	-C(3)	120.1(3)	C(16)	-C(11)	-C(3)	121.5(3)
C(16)	-C(11)	-C(12)	118.1(3)	C(13)	-C(12)	-C(11)	120.0(4)
C(14)	-C(13)	-C(12)	121.3(4)	C(15)	-C(14)	-C(13)	118.6(4)
C(16)	-C(15)	-C(14)	121.1(4)	C(15)	-C(16)	-C(11)	120.9(4)
C(22)	-C(21)	-C(3)	120.0(3)	C(26)	-C(21)	-C(3)	121.3(3)
C(26)	-C(21)	-C(22)	118.6(3)	C(23)	-C(22)	-C(21)	120.8(3)
C(24)	-C(23)	-C(22)	120.5(3)	C(25)	-C(24)	-C(23)	119.2(4)
C(26)	-C(25)	-C(24)	121.3(4)	C(25)	-C(26)	-C(21)	119.6(3).

Table 3. Some least-squares planes and displacements (Å) (with e.s.d.'s in parentheses) of atoms from these planes (in plane 1 and 2, atoms used in fitting the least-squares planes are denoted by asterisks)

Plane 1 $0.6360X - 0.7736Y + 0.0138Z = -0.3929$

Plane 2 $-0.6656X + 0.7280Y + 0.1639Z = 0.0871$

Plane 3 $0.5806X + 0.6754Y + 0.4479Z = 9.0700$

Plane 4 $0.3132X + 0.6939Y - 0.6510Z = -1.6640$

Plane 1		Plane 2	
C(3)*	-0.005(5)	C(1)*	0.048(5)
C(2)*	0.010(5)	N(2)*	-0.003(5)
N(2)*	-0.001(5)	C(4)*	-0.035(6)
N(1)*	-0.009(5)	C(5)	0.655(7)
C(1)*	0.007(5)	C(6)*	-0.047(7)
O	0.002(5)	S*	0.063(3)
C(11)	-1.335(5)		
C(21)	1.223(5)		
C(4)	0.057(6)		
S	-0.044(3)		
χ^2	10.24		

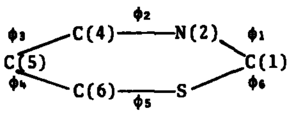
Plane 3		Plane 4	
C(11)	-0.006(6)	C(21)	-0.004(5)
C(12)	0.007(7)	C(22)	0.006(5)
C(13)	-0.004(8)	C(23)	-0.002(6)
C(14)	-0.002(8)	C(24)	-0.006(7)
C(15)	0.003(8)	C(25)	0.009(7)
C(16)	0.001(6)	C(26)	-0.003(6)
χ^2	2.25	χ^2	5.06

Some dihedral angles between planes

3∧4 69.0° 1∧3 98.5° 1∧4 110.3°

Table 4.

The torsion angles of thiazine ring:



$\phi_1 = -5.5^\circ$ $\phi_3 = -55.8^\circ$ $\phi_5 = -36.5^\circ$

$\phi_2 = 26.8^\circ$ $\phi_4 = 63.0^\circ$ $\phi_6 = 9.2^\circ$

The asymmetry parameter:

$$\Delta C_S = \sqrt{\sum_{i=1}^{m}(\phi_i + \phi_i')^2/3}$$

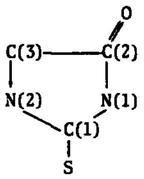
$$\Delta C_S^{C(1)} = 7.3^\circ$$

The test of conformation:

$$\mathrm{I} = \left\langle|\phi_i - \phi_{i+3}|\right\rangle = 65.6^\circ = \Sigma\mathrm{IV}/3$$
$$\mathrm{II} = \Sigma|\phi_i - \phi_{i+1}| = 393.6^\circ$$
$$\mathrm{III} = \Sigma|\phi_i| = 196.8^\circ$$
$$\mathrm{IV} = \Sigma|\phi_i - \phi_{i+3}| = 196.8^\circ = 3\mathrm{xI}$$
$$\mathrm{V} = \Sigma\big||\phi_i| - |\phi_{i+1}|\big| = 115^\circ$$

If $\mathrm{I} < 95^\circ$, $\mathrm{II} = 2\mathrm{III}$, $\mathrm{III} = \mathrm{IV}$ the ring adopts a half-chair or sofa conformation.

Table 5. Comparison of selected distances (Å) and angles (°) in some thiohydantoins (the labeling of the atoms refers to the diagram shown below)



Bond (Å)	**2**	**9**	**10**	**11**
N(2)-C(1)	1.330(3)	1.322(4)	1.337(5)	1.314(4)
N(1)-C(1)	1.333(4)	1.393(3)	1.395(5)	1.326(4)
N(2)-C(3)	1.471(4)	1.448(3)	1.446(6)	1.462(4)
N(1)-C(2)	1.363(4)	1.349(3)	1.401(5)	1.374(4)
C(2)-C(3)	1.554(4)	1.508(3)	1.522(6)	1.566(4)
C(1)-S	1.717(3)	1.642(3)	1.717(4)	1.705(3)
Angle (°)				
N(1)-C(1)-N(2)	116.6(3)	106.3(2)	107.0(3)	118.0(3)
C(3)-N(2)-C(1)	108.4(2)	113.4(2)	113.4(3)	108.3(2)
N(2)-C(3)-C(2)	98.9(2)	101.1(2)	102.5(3)	98.5(2)
C(3)-C(2)-N(1)	110.4(3)	106.5(2)	104.9(3)	110.3(3)
C(2)-N(1)-C(1)	105.7(2)	112.6(2)	112.2(3)	104.8(3)

Table 6. Positional parameters ($\times 10^4$) for the nonhydrogen atoms

	x	y	z
S	5921(1)	2196(1)	13300(1)
O	7869(2)	3743(2)	9999(2)
N(1)	7159(2)	3101(2)	11778(3)
N(2)	5514(2)	2278(2)	10485(2)
C(1)	6210(3)	2524(2)	11744(3)
C(2)	7147(3)	3252(2)	10414(3)
C(3)	6031(3)	2728(2)	9424(3)
C(4)	4456(3)	1640(3)	10151(4)
C(5)	3793(4)	1584(3)	11319(4)
C(6)	4704(4)	1352(3)	12707(4)
C(11)	5096(3)	3427(2)	8615(3)
C(12)	5206(4)	3730(2)	7332(3)
C(13)	4414(4)	4403(3)	6648(4)
C(14)	3526(4)	4797(3)	7229(4)
C(15)	3432(4)	4507(3)	8497(4)
C(16)	4203(3)	3832(2)	9191(4)
C(21)	6476(3)	2045(2)	8513(3)
C(22)	5589(3)	1617(2)	7439(3)
C(23)	5965(4)	958(2)	6661(4)
C(24)	7229(4)	717(3)	6920(4)
C(25)	8112(4)	1146(3)	7957(5)
C(26)	7754(3)	1801(2)	8768(4)

Table 7. Hydrogen atom positional parameters ($\times 10^4$) with isotropic temperature factors ($\text{Å}^2 \times 10^3$)

	x	y	z	U
H(41)	3891(36)	1838(26)	9237(39)	83(5)
H(42)	4764(36)	1025(26)	10054(40)	83(5)
H(51)	3386(36)	2196(26)	11438(40)	83(5)
H(52)	3141(28)	1044(18)	11054(37)	83(5)
H(61)	4312(34)	1388(24)	13452(41)	83(5)
H(62)	5120(36)	780(26)	12626(39)	83(5)
H(121)	5792(32)	3476(23)	6943(36)	68(3)
H(131)	4538(32)	4564(23)	5806(36)	68(3)
H(141)	3068(32)	5281(23)	6705(36)	68(3)
H(151)	2838(31)	4824(23)	8953(34)	68(3)
H(161)	4107(30)	3594(23)	10077(37)	68(3)
H(221)	4761(34)	1779(24)	7241(24)	68(3)
H(231)	5367(31)	632(23)	5933(35)	68(3)
H(241)	7498(32)	252(23)	6425(36)	68(3)
H(251)	9034(34)	972(22)	8208(36)	68(3)
H(261)	8405(33)	2092(22)	9498(36)	68(3)

Table 8. Anisotropic temperature factors ($Å^2 \times 10^3$) in the form: $\exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{23}klb^*c^* + 2U_{13}lhc^*a^* + 2U_{12}hka^*b^*)]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S	63(1)	86(1)	40(1)	13(1)	20(1)	7(1)
O	44(1)	56(1)	58(1)	-4(1)	18(1)	-12(1)
N(1)	42(1)	57(2)	39(1)	-4(1)	9(1)	1(1)
N(2)	40(1)	43(1)	37(1)	3(1)	15(1)	- 3(1)
C(1)	41(2)	51(2)	39(2)	2(1)	16(1)	8(2)
C(2)	35(2)	41(2)	47(2)	-2(1)	14(1)	2(1)
C(3)	37(2)	43(2)	37(1)	3(1)	16(1)	- 3(1)
C(4)	54(2)	55(2)	53(2)	2(2)	23(2)	-14(2)
C(5)	68(3)	82(3)	66(2)	2(2)	36(2)	-18(2)
C(6)	85(3)	81(3)	59(2)	17(2)	39(2)	- 7(2)
C(11)	36(2)	42(2)	41(2)	-1(1)	9(1)	- 7(1)
C(12)	69(2)	52(2)	48(2)	7(2)	25(2)	2(2)
C(13)	93(3)	56(2)	50(2)	16(2)	15(2)	- 8(2)
C(14)	72(3)	48(2)	68(3)	12(2)	4(2)	7(2)
C(15)	61(2)	54(2)	74(3)	3(2)	17(2)	15(2)
C(16)	55(2)	54(2)	53(2)	2(2)	24(2)	6(2)
C(21)	42(2)	41(2)	37(2)	3(1)	16(1)	0(1)
C(22)	54(2)	52(2)	43(2)	-1(2)	11(2)	- 3(2)
C(23)	81(3)	51(2)	44(2)	-4(2)	18(2)	2(2)
C(24)	95(3)	51(2)	56(2)	-1(2)	37(2)	14(2)
C(25)	64(2)	63(2)	78(3)	-1(2)	30(2)	19(2)
C(26)	48(2)	55(2)	58(2)	-4(2)	16(2)	5(2)

The N(2)–C(1) bond length of 1.330(3) Å is in good agreement with those reported for other hydantoins and 2-thiohydantoins.[13,14,16–18] The bond N(1)–C(1) = 1.333(4) Å is much shorter than those found in **9** and **10**. However, it is very close to the value of 1.326(4) Å observed in a bicyclic structure **11**. This comparison shows that the variations of bond lengths reflect the electron charge delocalisation within the ring.

The another significant difference concerns the carbon–carbon bond involving the tetrahedral carbon in the hydantoin ring. The value for the C(2)–C(3) bond in **2** was found to be 1.554(4) Å. This value is higher than the value usually observed for a sp^2–sp^3 carbon–carbon single bond of 1.501 Å. The elongation of the C–C bond observed in our case may be due to the presence of a bulky substituents on the tetrahedral carbon atom. Similar phenomenon was also observed in DL-allantoin[13] and N-methylgranantoine-3-spiro-5′-hydantoin.[16]

The both carbon–sulphur distances, i.e. C(1)–S and C(6)–S are 1.717(9) Å and 1.806(9) Å, respectively. They are in good agreement with the values usually observed for the C_{sp^2}–S and C_{sp^3}–S bond lengths (1.74 and 1.81 Å).

The other bond length and angles agree with the literature data.

EXPERIMENTAL

M.ps were determined on a Boetius hot stage microscope and are uncorrected. Infrared spectra were measured with Specord 71 IR (VEB Carl Zeiss Jena) using KBr discs (concentration 1:300 mg KBr), and are reported in cm^{-1}. ^1H NMR spectra were recorded on a Perkin–Elmer R 12B spectrometer at 60 MHz and chemical shifts are given in parts per million from tetramethylsilane. ^{13}C NMR spectra were recorded on a Bruker HX 90 spectrometer at 90 MHz using TMS as internal standard. The mass spectra were obtained using an GCMS 2091 LKB mass spectrometer operating at an ionising energy of 70 eV. The samples were introduced into source via direct inlet system. Ultraviolet spectra were taken on a Specord UV-Vis (VEB Carl Zeiss Jena). Developed tlc plates were visualized by spraying with 0.1 n I_2 in 10% HCl.

2,3,4,5-Tetrahydro-6,6-diphenylimidazo[2,1-*b*]-*thiazine-7(6H)-one* (**2**) *and 3-(3-mercaptopropyl)-5,5-diphenylhydantoin* (**4**). A boiling solution of 5,5-diphenyl-2-thiohydantoin (5,36 g, 0.02 mol) and 1,3-dibromopropane (4.02 g, 0.02 mol) in 40 ml of 96% ethanol was treated dropwise with a solution of NaOH (0.8 g, 0.02 mol) in 40 ml of 50% ethanol. The mixture was refluxed for the next 3 h, evaporated to 60–70% of the volume and refrigerated; 5.8 g of a white solid was collected. Tlc analysis showed mainly 3 spots [Kiesel gel; benzene:acetone (20:1.5)]. The components were separated on a glass column packed with silica gel, Merck 100/200 mesh. The first fraction separated with benzene:acetone (20:1.5) elution was evaporated to dryness affording 3.43 g of a white solid which on crystallisation from 96% ethanol gave **4** [R_f – 0.50, kiesel gel, benzene:acetone (20:1.5)], m.p. 152–154°. One recrystallisation from ethanol gave 2.08 g (31.9%) of the analytically pure product, m.p. 158–160° (lit.[8] m.p. 160–161°).

The ethanol filtrates were combined and evaporated to dryness. According to tlc analysis [R_f – 0.62 kiesel gel, benzene:acetone (20:1.5)] it was the starting material **1**, 1.1 g (21%), UV (EtOH) λ_{max} 270 nm.

Elution of a second fraction with ethanol gave **2** which was recrystallised from *n*-propanol to give 1.86 g (30.2%) of a white crystals, m.p. 198–199° [R_f – 0.71, kiesel gel, *n*-butanol:formic acid:water (7:2:2)]. IR: 1685, 1590 broad weak, 1490, 1430, 1370, 1210, 960, 860, 830, 690. UV (EtOH) λ_{max} 240 nm, logϵ 4.21, λ_{max} 266 nm, log ϵ 3.96. ^1H NMR ($CDCl_3$; δ[ppm]: J[Hz]):2.19(2H, m, $-CH_2-C\underline{H}_2-CH_2-$); 3.04(2H, m, $-S-C\underline{H}_2-$); 3.23(2H, m, $>N-C\underline{H}_2-$); 7.11–7.40(10H, m, $C_6\underline{H}_5$). ^{13}C NMR (CD_3SOCD_3; δ[ppm]): 21.78 ($-CH_2-\underline{C}H_2-CH_2-$); 25.81($-S(\underline{C}H_2-$); 44.75($>N-\underline{C}H_2$); 77.16(Ph$\underline{C}$): 127.60, 128.19, 128.51 and 136.44 (aromatic carbons);

178.96 and 185.56$\left(>\underline{\mathrm{C}}=\mathrm{O}\ \text{and}\ >\underline{\mathrm{C}}=\mathrm{N}-\right)$. MS [*m/e* (rel intensity)]: 308(100), 307(14), 266(11), 261(15), 248(10), 206(17), 165(72), 128(15), 103(23), 91(19), 77(21). *Anal.* Calc. for $C_{18}H_{16}N_2OS$: C, 70.10; H, 5.22; N, 9.08. Found: C, 69.88; H, 5.12; N, 8.78%.

3-(3-*Mercaptopropyl*)-5,5-*diphenylhydantoin* (**4**). A suspension of 3-(3-bromopropyl)-5,5-diphenylhydantoin[7] (3.73 g, 0.01 mol) and thiourea (0.76 g, 0.01 mol) in 96% ethanol (15 ml) was refluxed for 4 h. Removal of the solvent *in vacuo* gave **8** as a white solid. Then NaOH (1 g, 0.025 mol) in H_2O (30 ml) was added. The suspension was refluxed for 2 h. The reaction mixture was filtered and a small amount (0.3 g) of a solid substance was discarded. Acidification of the solution with 10% H_2SO_4 gave the product which was recrystallised from ethanol to give 2.0 g (61%) of **4** m.p. 158–160°. The IR, mass spectral, ^1H NMR, tlc properties were identical with those of the material obtained as described above. IR: 3340–3110, 1745, 1680, 1430, 1345, 1245, 1095, 745, 690. ^1H NMR ($CDCl_3$, δ[ppm]): 1.57(1H, t, J = 7.96, $-CH_2-S\underline{H}$); 1.93(2H, qt, J = 6.75; $-CH_2-C\underline{H}_2-CH_2-$); 2.47(2H, q, J = 7.34, $-C\underline{H}_2-S-$); 3.68(2H, t, J = 6.75, $>N-C\underline{H}_2-$); 7.35(10H, s, $C_6\underline{H}_5$); 7.56(1H, s, $>NH$). MS [*m/e* (relative intensity)]: 326(52), 293(35), 208(28), 194(22), 180(100), 165(27), 118(4), 104965), 77(41). *Anal.* Calc. for $C_{18}H_{18}N_2O_2S$: C, 66.23; H, 5.54; N, 8.58. Found: C, 66.46; H, 5.57; N, 8.49%.

1-(3-*Mercaptopropyl*)-5,5-*diphenylhydatoin* (**5**). A suspension of **2** (0.308 g, 0.001 mol) in a solution (10 ml) of 2% NaOH was refluxed for 2 h. Upon cooling H_2O (40 ml) was added and the reaction mixture was acidified with 10% H_2SO_4. The resulting solid was filtered, washed with water and recrystallised from 96% ethanol to give 2.44 g (75%) of **5** m.p. 221–223°. IR: 3400 broad, 2960, 1760, 1705, 1450, 1415, 1270, 1140, 1025, 980, 925, 760, 700. ^1H NMR ($CDCl_3$; δ[ppm]; J[Hz]): 1.1(1H, t, J = 8.07, $-CH_2-S\underline{H}$); 1.16(2H, qt, J = 7.34, $-CH_2-C\underline{H}_2-CH_2-$); 2.21(2H, q, J = 7.94, $-C\underline{H}_2-S-$); 3.47(2H, m, $N-C\underline{H}_2-$); 7.23–7.46(10H, m, C_6H_5), 9.19(1H, s, $>NH$). MS [*m/e* (rel intensity)]: 326(48), 254(12), 222(10), 208(40), 194(100), 165(40), 117(4), 104(20), 90(22), 77(32). *Anal.* Calc. for $C_{18}H_{18}N_2O_2S$: C, 66.23; H, 5.54; N, 8.58. Found: C, 66.10; H, 5.76; N, 8.38%.

Attempt at acid hydrolysis of **2**. **2** (0.308 g, 0.001 mol) was refluxed in 10% HCl (10 ml) for 0.5 h. The product crystallised from 96% ethanol yielded a hydrochloride of **2** m.p. 248–250°, soluble in water. Heating for 3 h gave also unreacted starting material.

1-(3-*Mercaptopropyl*)-2-*benzylamino*-5,5-*diphenylhydantoin* (**6**). A solution of **2** (0.308 g, 0.001 mol) and benzylamine (0.107 g, 0.001 mol) in 10 ml of toluene was refluxed for 10 h. The solvent was removed and the residue was recrystallised from 96% ethanol to give 0.28 g (67%) of **6** m.p. 166–168°. IR: 3400 broad, 1700, 1610, 1510, 1415, 1275, 1210, 1025, 775, 710. UV (EtOH) λ_{max} 218 nm, logϵ 4.48, λ_{max} 246.2 nm, logϵ 3.94. MS [*m/e* (rel intensity)]: 415(18), 414(29), 413(100), 412(10), 382(26), 381(76), 380(36), 379(62), 341(11), 340(12), 322(39), 308(19), 288(24), 254(14), 252(17), 207(23), 194(13), 162(14), 110(12), 104(11), 91(19), 78(14), 78(19), 64(52), 44(19), 43(12), 42(11), 41(11), 36(13). *Anal.* Calc. for $C_{25}H_{25}N_3OS$: C, 72.25; H, 6.06; N, 10.10. Found: C, 72.40; H, 5.91; N, 9.91%.

2,3,4,5-*Tetrahydro*-6,6-*diphenylimidazo* [2,1-*b*] *thiazine*-7(6*H*)-*one* (**2**) *and* 2,3,4,5-*tetrahydro*-7,7-*diphenylimidazo*[2,1-*b*]*thiazine*-6(7*H*)-*one* (**3**). A suspension of the potasium salt of 5,5-diphenyl-2-thiohydantoin (1.53 g, 0.005 mol) and 1,3-dibromopropane (1.01 g, 0.005 mol) in dry DME (50 ml) was vigorously stirred and heated of 75–80° for 5 h. The reaction mixture was filtered and potassium bromide (0.57 g, 96%) was discarded. The filtrate was evaporated to dryness and 1.58 g of a white solid was obtained. Tlc analysis showed mainly 3 spots [kiesel gel, benzene : acetone (20 : 1.5)]. The components were separated by column chromatography on silica gel (Merck 100/200 mesh). The first fraction separated with benzene : acetone (20 : 1.5) elution was evaporated to dryness affording 0.73 g of a white solid which on crystallisation from benzene (10 ml), gave as a first fraction 0.24 g of the unreacted **1**. The benzene filtrate was evaporated to 50–60% of the volume and the second crop of **1** (0.04 g) was collected (0.28 g, 21%). The filtrate was evaporated to dryness affording 0.44 g of **3** m.p. 224–6°. One recrystallisation from benzene gave 0.403 g (26.2%) of the analytically pure product, m.p. 227–227.5°. IR: 3640–3200, 3050 broad weak, 2940 broad weak, 2884 weak, 1720, 1580, 1560, 1486, 1470, 1447, 1380, 1345, 1330, 1296, 1242, 1148, 1039, 1030, 1020, 913, 752, 702, 693, 655. ^1H NMR ($CDCl_3$, δ[ppm], J[Hz]): 2.19(2H, m, $-CH_2-C\underline{H}_2-CH_2-$); 3.05(2H, m, $-S-C\underline{H}_2-$); 3.65(2H, t, J = 5.87, $>N-C\underline{H}_2-$); 7.19–7.62(10H, m, $C_6\underline{H}_5$) ^{13}C NMR (C_6D_6, δ[ppm]): 22.09($-CH_2-\underline{C}H_2-CH_2-$); 24.69($-S-\underline{C}H_2-$); 39.76$\left(>N-\underline{C}H_2-\right)$; 77.06($Ph_2\underline{C}$); 141.38($\underline{C}_\alpha$ in aromatic ring); 155.81 and 179.45$\left(>\underline{\mathrm{C}}=\mathrm{N}-\ \text{and}\ >\underline{\mathrm{C}}=\mathrm{O}\right)$. MS *m/e*, (rel intensity): 308(100), 279(51), 233(11), 224(28), 180(10), 177(53), 176(86), 165(59), 130(20), 121(17), 104(21), 77(36), 72(16), 51(16). *Anal.* Calc. for $C_{18}H_{16}N_2OS$: C, 70.10; H, 5.22; N, 9.08. Found: C, 70.28; H, 5.41; N, 8.87%. Elution of a second fraction with ethanol gave **2** which was recrystallised from *n*-propanol to give 0.705 g (45.8%) of a white crystals, m.p. 198–199°.

X-Ray structure determination of **2**. The compound was crystallised from DMSO. Intensity data were collected for a grinded crystal on a Syntex $P2_1$ diffractometer by the use of graphite monochromated Mo-K_α radiation. Intensity data were collected in the θ–2θ mode ($2\theta < 50°$). A Lorentz polarisation correction was applied but no absorption [$\mu(MoK_\alpha) = 1.70\ cm^{-1}$] correction was applied. After application of the acceptance criterion $F > 4.0\sigma(F)$, 1764 of the 2710 unique reflections measured were considered to be observed.

Crystal data. $C_{18}H_{16}ON_2S$, M = 308.40. Monoclinic, a = 10.812(3), b = 14.905(7), c = 9.885(4) Å, β = 104.91(2)°; V = 1538.63(57) Å^3, Z = 4, D_c = 1.338, D_m = 1.315 g · cm^{-3}. Space group $P2_1/n$ from systematic absences: OKO with K = 2n and hO1 with 1 + t = 2n.

The structure was solved by direct methods. The initial coordinates of five atoms [S, C(1), N(2), C(2) and C(3)] were obtained from the E map calculated from phases developed for direct methods program for centrosymmetric structures (SHEL-X-76; G. M. Sheldrick). Several difference syntheses were carried out to find the positions of other non-hydrogen atoms (R = 0.1380).

Refinement by blocked full-matrix least squares with anisotropic temperature factors for all the non-hydrogen atoms converged to an R factor 0.089. The positions of hydrogens were located from a difference map. 8 cycles of blocked full-matrix least-squares refinement with anisotropic temperature factors for all non-H atoms reduced the R value to 0.050 [R_w = 0.052, R_G − 0.061‖, w = 1.6364/| sigma**2 (F) + 0.001288F*F]. The largest parameter shift in the final cycle of refinement was less than 0.2 of its standard deviation. The highest residual electron density in the final difference map. was 0.21 eÅ^{-3}. Final atomic coordinates for the non-H atoms and isotropic temperature factors with atomic coordinates for H atoms are given in Tables 6–8.

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