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THE ANNULAR DESMOTROPY OF S-METHYL-5,5-DIPHENYL-2-THIOHYDANTOIN[a]

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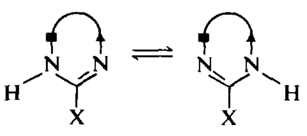
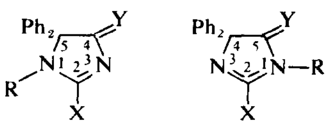
Abstract—The separate existence of two individual desmotropic forms (**2a** and **b**) of the S-Me derivative of 5,5-diphenylthiohydantoin which had been originally claimed on the basis of IR evidence, has been proved by X-ray molecular structure determination This is the first established case of annular desmotropy in the azole field.

Heterocyclic compounds of the general formula **1** (e.g. azoles, azolines and ring homologs) may theoretically exist in two annular tautomeric forms **1a** and **b**.[2,3] In spite of many claims in the literature of having isolated *both* individual tautomers, i.e. desmotrops of a given substance, no authenticated case of annular desmotropy was known prior to 1964, all claims of the contrary having been disproved.[4]



1a **1b**

The first established case of annular desmotropy of a compound of general structure **1**, *viz.* of (**2**) was reported from this laboratory in 1964.[5] Compound **2** was shown to be capable of existing in two different crystalline modifications (**2a** and **b**) whose structure assignments were based on their IR spectra. The "conjugated" form **2a** which was obtained on recrystallisation from ethanol or ethanol pyridine mixtures exhibited its νC=O and νC=N bands at 1700 (with a shoulder at 1685) and 1500 cm^{-1} (with a shoulder at 1515 cm^{-1}), respectively, while the non-conjugated form **2b** which was



a **b**

2-6

	R	X	Y
2	H	SMe	O
3	Me	SMe	O
4	H	SMe	S
5	H	Ph	O
6	H	Ph	S

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[a] Hydantoins, thiohydantoins and glycocyamidines, Part 35. For Part 34 see Ref 1 A preliminary account of part of the present work has been given in Ref 5

obtained either by recrystallization from chloroform and light petroleum or by sublimation *in vacuo*, had the same bands at 1725 and 1595+1580 (doublet) cm^{-1}; (both spectra in KBr pellets). These structure assignments were corroborated by comparison with the IR spectra of the N-Me derivatives **3a** and **b** of fixed structures, the νC=O and νC=N bands of the latter compounds appearing at 1720 and 1485, and 1740 and 1570 cm^{-1}, respectively (KBr pellets).[6] The desmotropic forms **2a** and **b** were found to be completely stable in the crystalline state, both being unchanged for periods of at least several years.

Several further cases of annular desmotropy of related compounds, *viz* **4**,[7] **5**[8] and **6**[9] were subsequently found.

In seeking corroboration for the desmotropy of compound **2** deduced solely by IR spectral evidence, the NMR[10] and UV spectra[11] of **2** were studied. Both types of spectra were, however, identical, irrespectively of which of the two crystalline modifications had been dissolved. Thus, in such solvents as DMSO,[10] ethanol[11] and chloroform[11] the tautomeric equilibrium between forms **2a** and **b** is rapidly established from both sides. By comparison of the UV spectra of **2a** (or **2b**) with those of the N-Me derivatives **3a** and **b*** the tautomeric mixture in ethanol was found to contain the conjugated and non-conjugated forms in a ratio of approximately 60:40 at room temperature and a total concentration of the order of 10^{-4} mole/l.[11]

Final proof for the separate existence of the individual desmotropic forms **2a** and **b** has been obtained by X-ray determination of the crystal and molecular structure of these compounds. The most important structural parameters are shown in Fig 1 and Tables 1 and 2.†

The hetero ring of **2a** is planar: with the exception of the atoms of the phenyl rings and of two hydrogens of the Me group, all other atoms of **2a** are situated on a mirror plane which corresponds to the mirror plane of the space group *Pnam*. The hetero ring of **2b**, on the other hand, is somewhat distorted from planarity: the greatest deviation from the best plane $[0{\cdot}572X - 0{\cdot}689Y - 0{\cdot}444Z + 8{\cdot}840 = 0]$ is 0·016 Å. The mirror plane related phenyl rings of **2a** make an angle of 66·6° with each other, and

Table 1. Interatomic distances with their e.s.d.'s

Bond	**2a**	**2b**
S—C(4)	1·770 (7) Å	1·782 (5) Å
S—C(2)	1·732 (5) Å	1·740 (4) Å
C(2)—N(1)	1·312 (6) Å	1·396 (5) Å
C(2)—N(2)	1·328 (6) Å	1·278 (5) Å
C(1)—N(1)	1·389 (6) Å	1·357 (5) Å
C(1)—O	1·210 (6) Å	1·221 (4) Å
C(1)—C(3)	1·554 (7) Å	1·548 (5) Å
C(3)—N(2)	1·461 (7) Å	1·494 (4) Å
C(3)—C(5)	1·540 (6) Å	1·533 (5) Å
C(5)—C(6)	1·372 (5) Å	1·386 (5) Å
C(6)—C(7)	1·402 (6) Å	1·386 (5) Å
C(7)—C(8)	1·374 (6) Å	1·391 (6) Å
C(8)—C(9)	1·390 (6) Å	1·376 (6) Å
C(9)—C(10)	1·386 (6) Å	1·389 (6) Å
C(5)—C(10)	1·399 (6) Å	1·380 (5) Å
C(3)—C(11)	—	1·534 (5) Å
C(11)—C(12)	—	1·382 (5) Å
C(12)—C(13)	—	1 393 (5) Å
C(13)—C(14)	—	1·384 (6) Å
C(14)—C(15)	—	1·370 (6) Å
C(15)—C(16)	—	1·390 (6) Å
C(11)—C(16)	—	1·387 (5) Å
N(2)—H	0·96 (7) Å	—
N(1)—H	—	0·93 (5) Å
C_{ar}—H(av)	1·03 (6) Å	0·97 (4) Å
C(4)—H(av.)	1·07 (7) Å	0·97 (4) Å
N(2) . . . O″	2·749 (6) Å	—
N(1) . . . O′	—	2·873 (5) Å
[N(2)—]H . . . O″	1·81 Å	—
[N(1)—]H . . . O′	—	1·96 Å

Table 2. Bond angles with their e.s.d 's

Bond angles	**2a**	**2b**
C(4)—S—C(2)	101·6 (3)°	100·9 (2)°
S—C(2)—N(1)	123·0 (4)°	115·9 (3)°
N(1)—C(2)—N(2)	117·3 (4)°	115·8 (3)°
S—C(2)—N(2)	119·6 (4)°	128·2 (3)°
C(2)—N(2)—C(3)	108·9 (4)°	106·3 (3)°
C(2)—N(1)—C(1)	105·1 (4)°	108·8 (3)°
N(1)—C(1)—O	125·7 (5)°	126·4 (3)°
N(1)—C(1)—C(3)	110·0 (4)°	105·3 (3)°
C(3)—C(1)—O	124·3 (4)°	128·3 (3)°
C(1)—C(3)—N(2)	98·7 (4)°	103·7 (2)°
C(1)—C(3)—C(5)	111·0 (4)°	112·4 (3)°
C(1)—C(3)—C(11)	—	109·9 (3)°
N(2)—C(3)—C(5)	111·4 (4)°	108·0 (3)°
N(2)—C(3)—C(11)	—	111·6 (3)
C(5)—C(3)—C(5′)	112·5 (4)°	—
C(5)—C(3)—C(11)	—	110·9 (2)°
C(3)—C(5)—C(6)	121·0 (3)°	117·4 (3)°
C(3)—C(5)—C(10)	119·6 (3)°	123·2 (3)°
C(6)—C(5)—C(10)	119·4 (3)°	119·4 (3)°
C(5)—C(6)—C(7)	120·4 (3)°	120·8 (3)°
C(6)—C(7)—C(8)	120·7 (4)°	119·4 (3)°
C(7)—C(8)—C(9)	118·6 (4)°	119·7 (4)°
C(8)—C(9)—C(10)	121·4 (4)°	120·7 (4)°
C(9)—C(10)—C(5)	119·5 (4)°	119·9 (3)°
C(3)—C(11)—C(12)	—	121·7 (3)°
C(3)—C(11)—C(16)	—	118·8 (3)°
C(12)—C(11)—C(16)	—	119·5 (4)°
C(11)—C(12)—C(13)	—	119·9 (4)°
C(12)—C(13)—C(14)	—	120·3 (4)°
C(13)—C(14)—C(15)	—	119·7 (4)°
C(14)—C(15)—C(16)	—	120·5 (4)°
C(15)—C(16)—C(11)	—	120·1 (4)°

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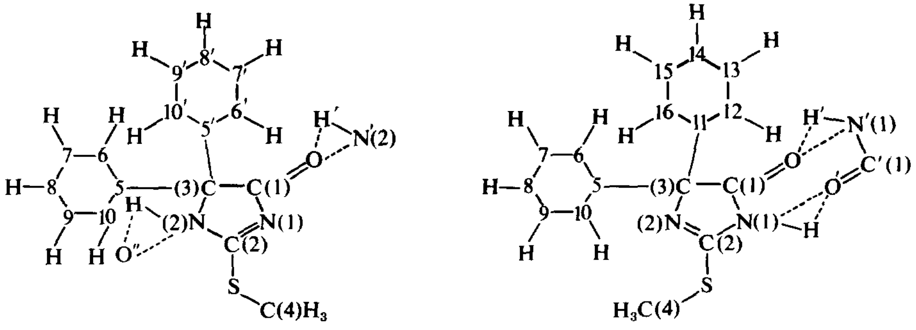
*These UV spectra will be published in Ref 12.

†A detailed account on the crystal and molecular structure of compounds **2a** and **b** will be published elsewhere.[13 14]



2a 2b

Fig 1. Chemical formulae of compounds **2a** and **b**, showing atomic numbering used in Tables 1 and 2, and the H-bonds.

two equivalent angles of 56·7° with the plane of the hetero ring. The phenyl rings are almost completely planar, the greatest deviation from their best planes $[-0{\cdot}728X+0{\cdot}409Y-0{\cdot}549Z-4{\cdot}830=0$ and $-0{\cdot}728X+0{\cdot}409Y+0{\cdot}549Z-1{\cdot}185=0$, respectively] is less than 0·002 Å. The dihedral angles between the best planes $[0{\cdot}288X+0{\cdot}254Y+0{\cdot}923Z-7{\cdot}384=0$ and $0{\cdot}326X+0{\cdot}934Y-0{\cdot}147Z-9{\cdot}319=0]$ of the two non-equivalent and independent phenyl rings and of the hetero ring of **2b** are 78·7°, 65·2° and 66·9°, respectively. The mean deviations from the planes of these phenyl rings are 0·006 and 0·007 Å, respectively. The mean bond lengths of the phenyl rings for both molecules, 1·387 (2X), 1·385 and 1·384 Å, respectively, are comparable with the corresponding data found in the literature. Similarly, the S—C, C—O, C(sp^3)—C(sp^2) bond lengths agree, within experimental error, with each other and with other experimental data reported in the literature. The bond distances between the individual atoms of the C(1)—N(1)—C(2)—N(2)* moiety of **2a** and **2b** exhibit, as expected, significant differences, their average values, however, are identical (1·343 Å).

The C(2)—N(1) and N(1)—C(1) bonds of **2b** are, according to their lengths, very similar to the corresponding bonds of 2-thiohydantoin (1·393 and 1·349 Å, respectively[15]). The former constitutes a weak and the latter a strong multiple bond. The N(2)—C(2) bond of 2-thiohydantoin is an even stronger multiple bond, (d = 1·322 Å),[15] while the corresponding bond of **2b** is an essentially pure double bond. (Compare its length—1·278 Å—with the average value of 1·29 Å found for the C═N bond of oximes.) A similar short C═N double bond has been found in 2-(2,6-dimethylphenylimino)-3 (2-chlorobenzoyl)thiazolidine.[16] The case of compound **2a** is rather different. Here, as shown by the closely similar lengths of the two CN bonds involving C(2), the lone pair of N(2) strongly interacts with the C(2)—N(1) double bond and, as a result, the CN double bond becomes almost completely delocalized. On the other hand, since the lone pair of N(1) in **2a** does not occupy a p_Z-orbital, there can be no strong interaction with the CO group, and the N(1)—C(1) bond, therefore, is considerably longer than the corresponding bonds of **2b** and thiohydantoin, its double bond character being, consequently, less expressed.

The conformations of the two desmotrops are shown on the two stereoscopic diagrams (Figs 2 and 3). The S-Me groups are, in both cases, arranged *trans* with respect to the N-hydrogen atoms.

While an infinite chain of *inter*molecularly H-bonded molecules if formed in the case of **2a**, **2b** forms cyclic dimeric associates linked by two O . . . H—N hydrogen bonds, each, *cf* Ref 6. Similar dimeric molecular associates maintained by intermolecular N—H . . . O hydrogen bonds have been

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*According to the numbering shown in Fig 1.

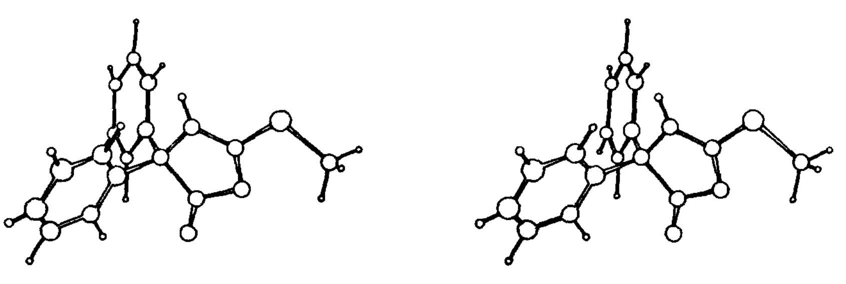

Fig 2. Stereoscopic diagram of the molecule **2a**.

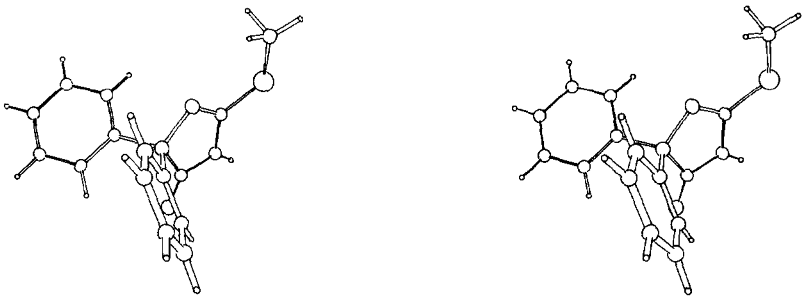

Fig 3. Stereoscopic diagram of the molecule **2b**

frequently described in the literature; e.g. in the case of 3-phenylpyrrolidine-2,5-dione[17] where the N—H . . . O distance was found to be 2·86 Å.

EXPERIMENTAL

Compound **2** has been prepared by methylation of 5,5-diphenyl-2-thiohydantoin as described in the literature [18] Crystals of the desmotropic forms **2a** and **b** for the X-ray analysis were obtained by allowing an aqueous-methanolic solution of **2** to cool very slowly and by keeping a saturated solution of **2** in chlofoform-light petroleum prepared at room temp for several weeks in a refrigerator, respectively. Both desmotropic forms had identical m.ps (210–211°)

The IR spectra were obtained with the aid of a UR-10 double-beam spectrometer (Carl Zeiss, Jena, GDR) in KBr pellets.

The crystals of **2a** are orthorhombic with the following lattice parameters (measured from precession photographs): a = 17·539 (10), b = 6·024 (5), c = 13·271 (8) Å. The systematic absences allowed two space groups, either $Pna2_1$ or *Pnam*. Since Z = 4, the space group was initially assumed to be $Pna2_1$. 1044 independent reflexions were collected from the layers $h0l$ to $h5l$ on a Stoe-Güttinger automatic off-line Weissenberg goniometer system using CuK_α ($\bar{\lambda}$ = 1·5418 Å) at *CRIC* (Budapest). The phase problem was solved for the acentric space group, $Pna2_1$ by the direct method,[19] using 224 reflexions of $E \geqslant 1{\cdot}25$. The E-map computed from the set of the best figures of merit gave the positions of all the 20 non-hydrogen atoms with an unambiguous indication of the fact that the molecule has been fixed to a mirror plane. Thus the actual space group is *Pnam*, and the asymmetric unit is only the half of the molecule The blockdiagonal least-squares refinement of the fractional atomic coordinates for the 14 heavy and 8 H atoms of the asymmetric unit with anisotropic and isotropic vibrational parameters, respectively, resulted in the final residual R of 8·5%. All calculation were performed on a *CDC*-3300 computer using the atomic scattering factors taken from *International Tables for X-ray Crystallography*.[20]

The very thin needles of compound **2b** are monoclinic. The space group is $P2_1/c$, Z = 4. The cell dimensions [a = 6·571 (3), b = 15·878 (7), c = 13·577 (5), β = 95·55 (1)° and 1512 independent reflexions (with $\vartheta \leqslant 51°$) were measured on a computer controlled Enraf-Nonius 4-circle kappa diffractometer (CAD-4) at *LKRU* (Utrecht) using CuK_α radiation. The structure was solved by the direct method using the program AUDICE written by Dr. A. L. Spek.[21] The solution of the greatest probability was used for the Fourier calculation from which the atomic positions were found automatically. The block-diagonal least squares refinement of the positional and vibrational parameters (anisotropic for the heavy and isotropic ones for the hydrogen atoms) gave the final structure factor agreement of R = 4·2%. The calculations were performed by the complex program system STRUCTAN-1972[22] (including AUDICE) assembled by Mr. D. Kaas using the atomic scattering factors of Cromer and Mann.[23]

The interatomic distances and bond angles for both structures are given in Tables 1 and 2. Other parameters will be published elsewhere.[13] [14]

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