3,6-Dithia-3,4,5,5-tetrahydrophthalimide

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Abstract. $C_6H_5NOS_2$, monoclinic, $P2_1/c$, $a = 7.186$ (2), $b = 12.200$ (2), $c = 8.632$ (2) Å, $\beta = 94.09°$, $V = 754.8$ (6) Å³, $M = 187.25$, $Z = 4$, $D_x = 1.647$ g cm⁻³. The refined atomic positions indicate a considerable strain within the molecule. The crystal is built up from molecules connected by hydrogen bonds forming infinite chains along **c**.

Introduction. Needle-shaped single crystals were crystallized from a glacial acetic acid solution. The crystal investigated was cut to dimensions of $0.3 \times 0.1 \times 0.3$ mm. Systematic absences of reflexions were observed for $0k0$ with k odd and $h0l$ with l odd. Reflexion intensity measurements were carried out in the $\theta–2\theta$ mode on an automatic Hilger & Watts four-circle diffractometer with Zr-filtered Mo $K\alpha$ radiation ($\lambda = 0.71069$ Å). The intensities of 3306 reflexions were measured resulting in a set of 1563 unique reflexions of which 373 were regarded as unobserved ($I < 3\sigma$). No absorption correction was applied ($\mu = 6.06$ cm⁻¹). The crystal structure was solved by use of the direct-method computer program *MULTAN* (Germain, Main & Woolfson, 1971). The sets of phases (200 E's) with the highest three combined figures of merit all fixed the positions of the heavy atoms. Refinement was carried out by full-matrix least-squares calculations using anisotropic temperature factors for the heavy atoms and a Cruickshank weighting scheme [$w = 29.7/(0.033|F_o|^2 - 2.26|F_o| + 68.0)$ for $|F_o| > 17.0$, $w = -0.00086|F_o|^2 + 0.59|F_o| + 0.01$ for $|F_o| < 17.0$]. The positions of the five hydrogen atoms were found from a difference electron density map. The atoms were allocated isotropic temperature factors and included in the final stage of refinement. Extinction was taken into account according to Zachariasen (1963) [$F_c = KF_o\{1 + \beta(2\theta)gI_o\}$] by including g in the list of variables (final value $g = 1.8 \times 10^{-6}$). The final R values obtained were $R(\text{overall}) = 0.049$ (0.034 omitting unobserved) and weighted $R(\text{overall}) = 0.030$ (0.029 omitting unobserved).[*]

Discussion. Thalidomide is well known as a hypnotic. Several years ago it received considerable attention because of its embryotoxic and teratogenic effects on the foetus leading to skeletal malformations when used during the sensitive phase of pregnancy. Since

Table 1. *The parameters and standard deviations (in parentheses) for the non-hydrogen atoms* ($\times 10^4$)

The expression for the anisotropic temperature factor is exp $[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + \beta_{12}hk + \beta_{13}hl + \beta_{23}kl)]$.
The positional parameters of the H atoms are $\times 10^3$.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C(1)	2647 (3)	195 (2)	4033 (2)	182 (5)	65 (2)	93 (3)	10 (3)	9 (3)	−2 (2)
C(2)	2304 (3)	−592 (2)	2974 (2)	185 (6)	66 (2)	89 (3)	6 (3)	17 (3)	−1 (2)
C(4)	2590 (5)	919 (2)	725 (3)	310 (9)	81 (2)	105 (4)	−6 (4)	−3 (5)	11 (2)
C(5)	4023 (5)	1467 (3)	1811 (9)	318 (9)	82 (3)	115 (4)	−21 (4)	3 (4)	16 (3)
C(7)	2228 (3)	−245 (2)	5580 (3)	185 (6)	78 (2)	96 (3)	23 (3)	10 (3)	−1 (2)
C(8)	1627 (3)	−1587 (2)	3767 (3)	202 (6)	68 (2)	111 (3)	9 (3)	18 (4)	−2 (2)
S(3)	2435 (1)	−564 (1)	−984 (1)	304 (2)	73 (1)	87 (1)	−8 (1)	27 (1)	−10 (1)
S(6)	3421 (1)	1515 (1)	3819 (1)	289 (2)	65 (1)	114 (1)	−12 (1)	6 (1)	−13 (1)
O(1)	2384 (3)	226 (2)	6824 (2)	292 (5)	101 (2)	87 (2)	20 (2)	12 (3)	−12 (2)
O(2)	1191 (3)	−2456 (1)	3199 (2)	350 (2)	65 (2)	139 (3)	−17 (2)	41 (3)	−8 (2)
N	1596 (3)	−1305 (2)	5319 (2)	256 (5)	77 (2)	96 (3)	−2 (3)	32 (3)	9 (2)

	x	y	z	B
H1(C4)	122 (4)	125 (2)	83 (3)	3.7 (7)
H2(C4)	290 (4)	99 (2)	−28 (3)	2.9 (6)
H1(C5)	398 (3)	229 (2)	156 (3)	2.8 (6)
H2(C5)	523 (4)	106 (2)	176 (3)	3.2 (7)
H(N)	140 (5)	−174 (4)	596 (4)	2.2 (9)

then scientific interest in this compound has been concentrated on attempts to find a relationship between the chemical structure and the effects in animal tests. It seems that the embryotoxic and teratogenic effects are connected with the flat phthalimide moiety of the molecule. Several structural analogues of thalidomide have been synthesized and tested for embryotoxicity and teratogenicity. The important question is always whether the phthalimide analogue ring system of the molecule is planar or not. The title compound (Fig. 1) is related to the phthalimide moiety of thalidomide and has been found to cause embryotoxicity and teratogenicity in mice.

molecule is almost planar, though somewhat twisted. The average of the deviations from the least-squares plane A (Table 3) is 0·0127 Å, which is less than 4σ where $\sigma = 0·0035$ Å is the mean value of the e.s.d. for all heavy-atom distances. The S(3)–C(4) and S(6)–C(5) valences point to opposite sides of the plane. The distances of C(4) and C(5) from the plane are 0·518 and 0·300 Å respectively. There is a significant difference $(\varDelta = 0·218$ Å) which indicates a considerable strain within the molecule. Possibly this is the reason for the extraordinary similarity of the chemical behaviour of the title compound and the aromatic phthalimide. The five-membered imide ring itself is essentially planar with all deviations from the least-squares plane B, defined by the ring atoms, less than 3σ. The shortest distance between adjacent molecules

Table 2. *Interatomic distances* (Å) *and bond angles* (°)

Standard deviations are given in parentheses for the last significant digit.

C(1)–C(2)	1·336 (3)	C(7)–N	1·384 (4)	
C(1)–C(7)	1·490 (3)	C(8)–O(2)	1·201 (3)	
C(1)–S(6)	1·718 (2)	C(8)–N	1·385 (3)	
C(2)–S(3)	1·728 (2)	C(4)–H1(C4)	1·07 (3)	
C(2)–C(8)	1·492 (3)	C(4)–H2(C4)	0·92 (3)	
C(4)–C(5)	1·499 (6)	C(5)–H1(C5)	1·03 (3)	
C(4)–S(3)	1·828 (3)	C(5)–H2(C5)	1·00 (3)	
C(5)–S(6)	1·817 (7)	N——H(N)	0·79 (3)	
C(7)–O(1)	1·216 (3)			
C(2)–C(1)–C(7)	108·3 (2)	H1(C4)–C(4)–S(3)	107 (2)	
C(2)–C(1)–S(6)	130·2 (2)	H1(C4)–C(4)–C(5)	112 (1)	
C(7)–C(1)–S(6)	121·5 (2)	H2(C4)–C(4)–S(3)	104 (2)	
C(1)–C(2)–C(8)	108·7 (2)	H2(C4)–C(4)–C(5)	110 (2)	
C(1)–C(2)–S(3)	130·2 (2)	H2(C4)–C(4)–H1(C4)	110 (2)	
C(8)–C(2)–S(3)	121·0 (2)	H1(C5)–C(5)–S(6)	99 (1)	
S(3)–C(4)–C(5)	114·2 (2)	H1(C5)–C(5)–C(4)	107 (1)	
S(6)–C(5)–C(4)	114·3 (3)	H2(C5)–C(5)–S(6)	109 (1)	
O(1)–C(7)–N	126·5 (2)	H2(C5)–C(5)–C(4)	108 (2)	
N——C(7)–C(1)	106·0 (2)	H2(C5)–C(5)–H1(C5)	120 (2)	
O(1)–C(7)–C(1)	127·5 (2)	H(N)——N——C(7)	126 (2)	
O(2)–C(8)–N	126·3 (2)	H(N)——N——C(8)	122 (2)	
O(2)–C(8)–C(2)	128·0 (2)			
N——C(8)–C(2)	105·7 (2)			
C(2)–S(3)–C(4)	98·6 (1)			
C(1)–S(6)–C(5)	100·0 (1)			
C(7)–N——C(8)	111·2 (2)			

Tables 1 and 2 summarize the atomic fractional coordinates, thermal parameters, bond distances, and angles. The bond distances and angles are normal. Fig. 2 shows the content of one half of the unit cell viewed along **a**. Since the six-membered ring with the *para*-standing sulphur atoms is partially hydrogenated, planarity of the whole molecule could not be expected. However, apart from C(4) and C(5) the rest of the
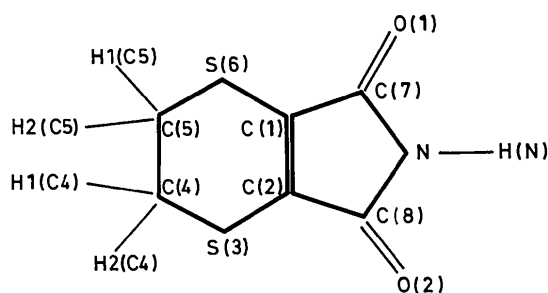

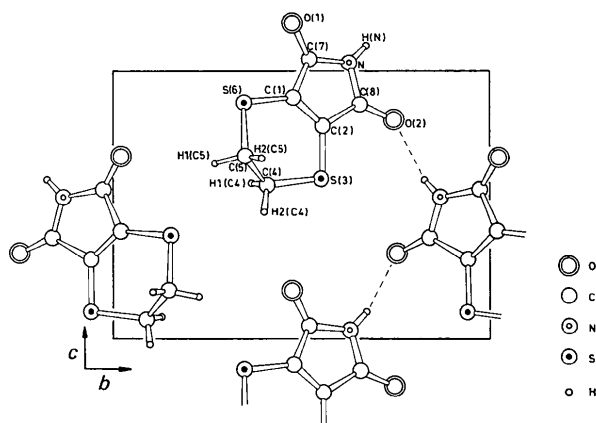Fig. 1. Numbering scheme of the atoms.

Fig. 2. Lower half of the unit cell in projection along **a**.

Table 3. *Atom to plane distances* (Å)

Atoms marked with an asterisk were not included in least-squares plane calculation.

Plane A

Atom	C(1)	C(2)	C(4)*	C(5)*	C(7)	C(8)	S(3)
Deviation	0·017	0·022	−0·518	0·300	−0·001	0·005	−0·026
Atom	S(6)	O(1)	O(2)	N			
Deviation	0·003	−0·002	0·016	−0·028			

Plane B

Atom	C(1)	C(2)	C(7)	C(8)	N
Deviation	−0·005	0·000	0·008	0·006	−0·010

is N···O(2^i)=2·94 Å. This clearly corresponds to a hydrogen bond with N–H(N) 0·79 Å and H(N)···O(2^i) 2·18 Å. Similar values were found between the glutarimido residuals in thalidomide (Allen & Trotter, 1970) where N···O is 2·93 Å, N–H(N) 0·82 Å and H(N)···O 2·12 Å. The molecules, connected by hydrogen bonds, form roof-like ribbons running along c. The average planes of the ribbons are parallel (100) and the packing distance of the ribbons is 3·38 Å.

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Tetracyclo[5,2,1,0²˙⁶,0⁴˙⁹]decan-3-one-2,4-dinitrophenylhydrazone

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Abstract. Triclinic, $P\bar{1}$, $a=7·160$ (8), $b=11·066$ (7), $c=10·612$ (14) Å, $\alpha=81·77$ (5), $\beta=63·38$ (6), $\gamma=80·33$ (5)°, $C_{16}H_{16}O_4N_4$, $Z=2$, $D_o=1·473$ (14), $D_c=1·476$ g cm^{-3}. The compound contains a distorted boat cyclohexane ring with a short 1·90 (5) Å H···H contact. Endocyclic bond angles within the strained tetracyclo fragment (94·3 to 108·4°) are all less than the tetrahedral angle; C–C(cage) single-bond distances range from 1·497 to 1·583 Å (mean 1·541 Å).

Introduction. Crystals of the parent compound (VI, Fig. 1) (Sauers & Henderson, 1974) proved unacceptable for X-ray analysis. The 2,4-dinitrophenylhydrazone derivative was readily prepared and thin hexagonally shaped crystals were grown from ethanol/ethyl acetate solutions (m.p. 192–193·5°C). A single crystal, cut to 0·6×0·3×0·07 mm, was used. Preliminary Weissenberg photographs showed no systematic absences. Intensities were collected on a CAD-3 automated diffractometer (θ–2θ scan) with Ni-filtered Cu $K\alpha$ radiation. Of the 2499 unique reflections measured ($4<2\theta<130°$), 1734 with $F^2\geq2\sigma$ (counting statistics) were considered observed, and used in the structure solution and refinement. Absorption corrections were not applied (μ for Cu $K\alpha=9·19$ cm^{-1}).

The structure, assumed to be centrosymmetric, was solved by reiterative application of Sayre's equation using 312 reflections with $|E|\geq1·5$ and a program developed by Long (1965). In addition to the origin-defining reflections, the phases of five reflections were arbitrarily assigned, leading to 32 possible solutions. The true solution required the fewest iterations (two) for phase convergence, had approximately equal numbers of positive and negative phases (149+, 163−), and showed the second highest value of the consistency index $c=\langle|E_A\sum\limits_{A=B+C}E_BE_C|\rangle/\langle|E_A|\sum\limits_{A=B+C}|E_B|\,|E_C|\rangle$. All C, N and O atoms were located from an F map based on these 312 phases; the computer programs used have been described (Potenza, Giordano, Mastropaolo & Efraty, 1974). Scattering factors for H were taken from *International Tables for X-ray Crystallography* (1962) and for C, N and O from Cromer & Waber (1965). After five cycles of full-matrix refinement, the last two with anisotropic thermal parameters, 14 of the 16 H atoms were located on a difference map. After an ad-
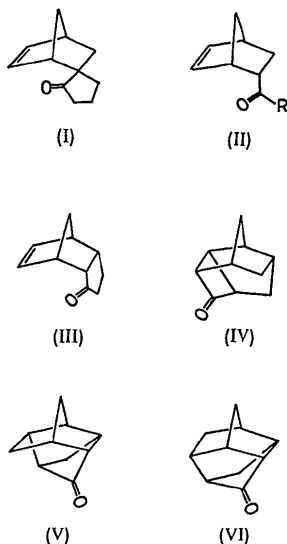
Fig. 1. Structures of compounds mentioned in the text.

(I)   (II)

(III)   (IV)

(V)   (VI)