The Crystal and Molecular Structure of N-(4-Chlorophenyl)-3,6-dithiacyclohexene-1,2-dicarboximide

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Abstract

The crystal and molecular structure of the compound $C_{12}H_8ClNO_2S_2$ has been determined by three-dimensional X-ray analysis. The crystals are ortho-rhombic ($P2_12_12_1$) with $Z = 4$, $a = 12\cdot374$ (2), $b = 24\cdot445$ (3), $c = 4\cdot125$ (1) Å. The structure has been solved by direct methods with 1063 independent reflections collected on a Nonius CAD-4 diffractometer and has been refined by least-squares calculations to a final $R = 0\cdot038$. The molecule is not planar; the 3,6-dithiacyclohexene ring has a disordered half-chair conformation with the asymmetry parameter $\Delta C_2 = 9\cdot9°$, the imide ring is nearly planar and the dihedral angle between phenyl and imide rings is $50\cdot5°$. The differentiation of $C(sp^2)-S^{II}$ ($1\cdot734$ Å av.) and $C(sp^3)-S^{II}$ ($1\cdot823$ Å av.) bond lengths is observed. In the amide ring C—C single-bond distances average to $1\cdot489$ Å and the mean C—N distance is $1\cdot384$ Å indicating some π delocalization. Shortened $O\cdots H$—C distances are observed between adjacent molecules.

Introduction

The present structural investigation was undertaken as part of a study of the geometries and conformations of new heterocyclic molecules related to thalidomide (N-α-glutarimidophthalimide). A series of N-alkyl and N-aryl 3,6-dithia-3,4,5,6-tetrahydrophthalimides was synthesized by Hahn & Rybczyński (1971, 1976) in order to investigate the influence of the N-substituent on pharmacological activity. Preliminary pharmacological investigations have shown that imides in which the nitrogen atom is bound to phenyl or substituted phenyl groups are of slight toxicity and act depressively on the central nervous system.

Recently, two short papers dealing with the structure of partly hydrogenated derivatives of phthalimide, *i.e.* of 3,4,5,6-tetrahydrophthalimide (THP) (Kirfel, 1975) and 3,6-dithia-3,4,5,6-tetrahydrophthalimide (DTTHP) (Kirfel, Will & Fickentscher, 1975) have been published. The authors of the papers connect the observed deviations from a flat shape of the investigated molecules with their pharmacological activity.

The formula and atom-numbering scheme of the investigated compound are given below.
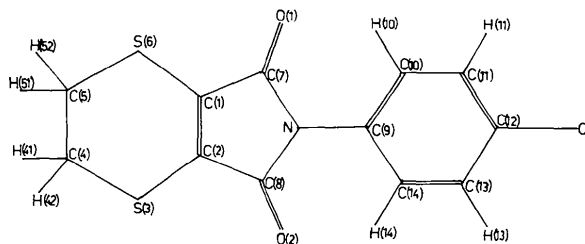
The aim of the work was to determine the conformation of the heterocyclic rings, the relative twists of the planes of the rings in the molecule, bond lengths and possible intermolecular interactions.

Experimental and crystal data

Crystals of the title compound were supplied by Professor W. Hahn and Dr B. Rybczyński from the Institute of Organic Chemistry of the University in Łódź. Single crystals were grown from anhydrous acetic acid as orange needles elongated along the c axis. The density was measured by flotation in aqueous KBr solution.

The space group was determined from Weissenberg photographs. The cell parameters and intensities were measured on a single crystal of $0\cdot225 \times 0\cdot200 \times 0\cdot175$ mm, at room temperature, on an automatic CAD-4 single-crystal diffractometer (Cu $K\alpha$, Ni-filtered

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Table 1. *Crystal data*

Formula: $C_{12}H_8ClNO_2S_2$ $D_x = 1·585$ Mg m^{-3}
$a = 12·374$ (2) Å $D_m = 1·57$
$b = 24·445$ (3) $Z = 4$
$c = 4·1254$ (10) $F(000) = 608$
$V = 1247·9$ Å^3 Space group $P2_12_12_1$
$M_r = 297·79$ $\mu(Cu\,K\alpha) = 5·646$ mm^{-1}

radiation), by θ–2θ scans. The reflections were measured within the interval $7° < 2\theta < 138°$. The intensities of 1422 symmetrically independent reflections were measured; of these, 359 for which $I < 3\sigma(I)$ were classed as unobserved. The unobserved reflections were omitted from the structure analysis. The intensities of two standard reflections were recorded after every 50 measurements during the data collection. The variation in intensity was observed to be less than 2·6% of the mean value. The intensities were measured in the Regional Laboratory of Physicochemical Analysis and Structural Research, Jagiellonian University of Kraków. The data were corrected for Lorentz and polarization factors. Correction for absorption was neglected in view of the low μr values for the crystal [$(\mu r)_{av.} = 0·6$]. The atomic scattering factors for non-hydrogen atoms were taken from Doyle & Turner (1968) and for H atoms from *International Tables for X-ray Crystallography* (1962). Crystal data are given in Table 1.

Structure solution and refinement

The structure was solved by direct methods with the *MULTAN* program. The 178 E values greater than 1·3 were used to generate a starting set of phases ($R_{Karle} = 24·3$, absolute figure of merit of 1·26). An E map based on these phases yielded the positions of 15 atoms. A structure factor Fourier synthesis revealed the three remaining heavy atoms. The refinement of the structure was carried out by the block-diagonal least-squares method (program *CRYLSQ* of the XRAY system, Stewart, Kundell & Baldwin, 1970). Three cycles of least-squares calculations with isotropic temperature factors reduced R to 0·106. The next two cycles of least-squares calculations with anisotropic temperature factors reduced the value of R to 0·047. All hydrogen atoms were clearly revealed in a difference Fourier synthesis with reasonable bond lengths and angles. A further cycle of refinement including H atoms with isotropic temperature factors equal to those of the bonded atoms and changing only the parameters of the non-hydrogen atoms reduced R to 0·038. Unit weight was assigned for each reflection. The final atomic parameters are given in Table 2.

Results and discussion

Bond lengths and angles with estimated standard deviations are given in Table 3.* An *ORTEP* drawing of the molecule is shown in Fig. 1.

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* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33985 (8 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Atomic parameters*

(a) Positional parameters for non-hydrogen atoms ($\times 10^5$) with their estimated standard deviations

	x	y	z
C(1)	14418 (18)	31177 (7)	20322 (59)
C(2)	23161 (17)	33752 (8)	9751 (70)
C(4)	35816 (21)	25071 (9)	26265 (60)
C(5)	25558 (21)	21714 (8)	17801 (72)
C(7)	4999 (17)	34991 (8)	18349 (64)
C(8)	19797 (18)	39186 (9)	−2614 (71)
C(9)	2626 (17)	44632 (8)	−1556 (62)
C(10)	−6878 (18)	44212 (9)	−18800 (69)
C(11)	−12609 (20)	48962 (9)	−25693 (67)
C(12)	−8254 (19)	53965 (9)	−15518 (72)
C(13)	1115 (19)	54428 (10)	1563 (75)
C(14)	6897 (19)	49616 (9)	8902 (73)
O(1)	−4114 (11)	34071 (9)	26664 (50)
O(2)	25342 (14)	42617 (6)	−15710 (61)
S(3)	36475 (5)	31705 (2)	6153 (19)
S(6)	13005 (5)	24489 (2)	34114 (16)
N	8935 (14)	39774 (7)	4949 (55)
Cl	−15636 (6)	59923 (3)	−25054 (22)

(b) Positional parameters for the hydrogen atoms ($\times 10^3$)

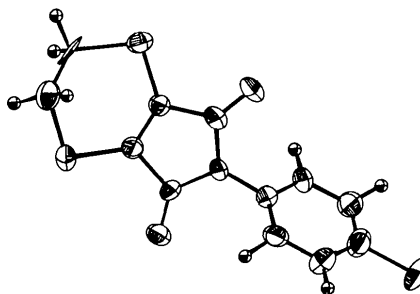|	x	y	z
H(10)	−113	404	−208
H(11)	−193	486	−375
H(13)	53	583	47
H(14)	142	499	233
H(41)	429	233	208
H(42)	371	253	542
H(51)	245	185	292
H(52)	242	219	−83

Fig. 1. An *ORTEP* drawing of the N-(4-chlorophenyl)-3,6-dithiacyclohexene-1,2-dicarboximide molecule.

3,6-Dithiacyclohexene ring

This ring has a deformed half-chair conformation. The torsion angles and asymmetry parameters (Duax & Norton, 1975) are given in Table 4 in comparison with those of the 3,6-dithiacyclohexene ring in DTTHP. The rings have similar geometries, but the ring in DTTHP is more symmetrical. $C(sp^3)$—S^{II} distances average 1·823 Å which agrees well with the data from other studies (Argay, Kálmán, Nahlovski & Ribár, 1975). The mean $C(sp^2)$—S^{II} distance is 1·734 Å while in the DTTHP structure it is somewhat shorter (1·723 Å). The shortest single $C(sp^2)$—S^{II} bond length suggested by Truter (1962) is 1·77 Å. Shortening of these bonds in the 3,6-dithiacyclohexene ring indicates some π delocalization proportional to the planarity of this part of the molecule. The determined $C(sp^3)$—$C(sp^3)$ (1·551 Å) and $C(sp^2)$—$C(sp^2)$ (1·326 Å) distances are typical for C—C single and double bonds. The presence of two heteroatoms in the ring and the condensation of the two rings result in a considerable increase in internal valency angles at the carbon atoms. The average S—C—C angles of $C(sp^3)$ and $C(sp^2)$ atoms are 114·3° and 130·7° respectively. Valency angles C—S—C average 99·1°, which agrees with literature data.

Imide ring

The data in Table 5 illustrate the puckering of the ring. The deviations of C(1) and C(2) atoms from the C(1)—C(2)—C(7)—C(8)—O(1)—O(2) plane are of the order of 10 σ and those of the N atom are of the order of 20 σ. The puckering of the imide ring in the investigated structure is similar to that in the thalidomide structure (Allen & Trotter, 1971) and is considerably greater than in DTTHP and THP (Kirfel, Will & Fickentscher, 1975; Kirfel, 1975). The C—C single-bond distances average to 1·489 Å and the mean C—N distance is 1·384 Å indicating some π delocalization.

Chlorophenyl ring

The Cl-phenyl ring is not rigorously planar within experimental errors ($\chi^2 = 34\cdot5$ which for four degrees of freedom gives a significance level $p < 0\cdot01$). The Cl atom is coplanar with the phenyl ring. The mean length of the C—C bonds is 1·389 Å, which agrees well with a typical bond length in an aromatic ring. The C—C—C angles at the non-substituted C atoms are contracted by ca 9σ to 118·6, 118·2, 118·3 and 118·0°, while the other two angles are expanded to a mean value of 123·5°. The dihedral angle between the mean plane of this ring and that of the imide is 50·5°.

Table 3. Bond lengths (Å) and angles (°) with estimated standard deviations in parentheses

Cl—C(12)	1·764 (2)	C(9)—C(10)	1·378 (4)
N—C(7)	1·382 (3)	C(9)—C(14)	1·396 (3)
N—C(8)	1·387 (3)	C(10)—C(11)	1·390 (3)
N—C(9)	1·446 (3)	C(11)—C(12)	1·401 (3)
C(1)—C(2)	1·326 (3)	C(12)—C(13)	1·361 (4)
C(1)—S(6)	1·740 (2)	C(13)—C(14)	1·410 (3)
C(1)—C(7)	1·495 (3)	C(4)—H(41)	1·00
C(2)—S(3)	1·728 (2)	C(4)—H(42)	1·16
C(2)—C(8)	1·483 (3)	C(5)—H(51)	0·92
S(3)—C(4)	1·823 (3)	C(5)—H(52)	1·09
C(4)—C(5)	1·551 (4)	C(10)—H(10)	1·08
C(5)—S(6)	1·824 (2)	C(11)—H(11)	0·96
C(7)—O(1)	1·200 (3)	C(13)—H(13)	1·09
C(8)—O(2)	1·211 (3)	C(14)—H(14)	1·08
C(7)—N—C(9)	125·36 (17)	N—C(7)—O(1)	127·16 (20)
C(7)—N—C(8)	110·10 (17)	C(1)—C(7)—O(1)	126·89 (21)
C(8)—N—C(9)	124·50 (18)	N—C(8)—C(2)	106·71 (19)
C(2)—C(1)—S(6)	129·49 (17)	N—C(8)—O(2)	125·28 (21)
C(2)—C(1)—C(7)	108·80 (18)	C(2)—C(8)—O(2)	127·95 (21)
S(6)—C(1)—C(7)	121·71 (16)	N—C(9)—C(10)	119·67 (19)
C(1)—C(2)—S(3)	131·97 (16)	N—C(9)—C(14)	117·05 (19)
C(1)—C(2)—C(8)	108·03 (19)	C(10)—C(9)—C(14)	123·20 (21)
S(3)—C(2)—C(8)	119·84 (16)	.C(9)—C(10)—C(11)	118·59 (20)
C(2)—S(3)—C(4)	100·13 (11)	C(10)—C(11)—C(12)	118·16 (20)
S(3)—C(4)—C(5)	113·87 (17)	Cl—C(12)—C(11)	117·06 (16)
C(4)—C(5)—S(6)	114·65 (17)	Cl—C(12)—C(13)	119·20 (17)
C(1)—S(6)—C(5)	98·24 (11)	C(11)—C(12)—C(13)	123·73 (22)
N—C(7)—C(1)	105·95 (17)	C(12)—C(13)—C(14)	118·29 (21)
		C(9)—C(14)—C(13)	118·01 (21)

Table 4. Comparison of torsion angles (°) and asymmetry parameters (°) of 3,6-dithiacyclohexene rings in the present structure and DTTHP

	Present structure	DTTHP
S(6)—C(1)—C(2)—S(3)	−1·7	−2·5
C(1)—C(2)—S(3)—C(4)	−7·1	−9·3
C(2)—S(3)—C(4)—C(5)	41·7	45·0
S(3)—C(4)—C(5)—S(6)	−69·3	−70·8
C(4)—C(5)—S(6)—C(1)	51·1	49·1
C(5)—S(6)—C(1)—C(2)	−16·9	−13·6
$\Delta C_2(1–2) = 9\cdot9°$		$\Delta C_2(1–2) = 4\cdot2°$

Table 5. Least-squares planes

The equations for the planes in the standard orthogonal system are $AX + BY + CZ = D$.

Plane	A	B	C	D
I C(1)—C(2)—C(7)—C(8)—O(1)—O(2)	0·2043	0·3872	0·8991	4·1076
II Cl-phenyl ring	0·5062	0·0841	−0·8583	1·1368

The perpendicular distances (Å) from each atom to the planes. Atoms marked (*) were not included in the least-squares calculation.

Plane I				Plane II	
Atom		Atom		Atom	
C(1)	−0·0382	C(4)*	0·1452	C(9)	0·0001
C(2)	0·0345	C(5)*	−0·7458	C(10)	0·0068
C(7)	0·0115	C(9)*	0·1259	C(11)	−0·0105
C(8)	0·0052	C(10)*	−0·7938	C(12)	0·0048
O(1)	0·0025	C(11)*	−0·7446	C(13)	0·0036
O(2)	−0·0155	C(12)*	0·2164	C(14)	−0·0002
N*	0·0668	C(13)*	1·1306	Cl	0·0025
S(3)*	0·0438	C(14)*	1·0935		
S(6)*	−0·1954	Cl*	0·2400		

The acute angle between planes I and II is 50·5°.

The rotation of the phenyl-ring plane relative to the imide-ring plane is conditioned by van der Waals contacts $O(1)-H(10) = 2.768$ Å and $O(2)-H(14) = 2.649$ Å.

Geometry of the molecule and intermolecular interactions

Hindered rotation of the chlorophenyl ring around the C—N bond allows the formation of rotational isomers. It follows from the deviations of the remaining atoms from the mean central plane of the molecule (plane I in Table 5) that the Cl-phenyl-ring plane is approximately parallel to the direction of the C(4)—C(5) bond. The deviations of this bond from the

central plane of the molecule and the rotation of the Cl-phenyl ring around the C—N bond determine the degree of non-planarity of the molecule.

The molecular packing is shown in Fig. 2. A clear shortening of $O(2)-H(14) = 2.286$ Å between two molecules connected by a 2_1 axis can be observed. The H(14) atom does not lie precisely on the $O(2)-C(14)$ line; the $O(2)-H(14)-C(14)$ angle is $141.1°$. Table 6 presents interatomic contacts smaller than the sum of the van der Waals radii.

Table 6. *The shortened intermolecular distances* (Å)

Key to symmetry operations

(i) $x, \quad y, \quad 1 + z$
(ii) $\frac{1}{2} - x, 1 - y, -\frac{1}{2} + z$
(iii) $\frac{1}{2} + x, \frac{1}{2} - y, \quad 1 + z$

A	H	B	$A\cdots B$	$A\cdots H$
S(3)	H(42^i)	C(4^i)	3.674	2.66
O(2)	H(14^{ii})	C(14^{ii})	3.087	2.29
O(1)	H(42^{iii})	C(4^{iii})	3.212	2.66

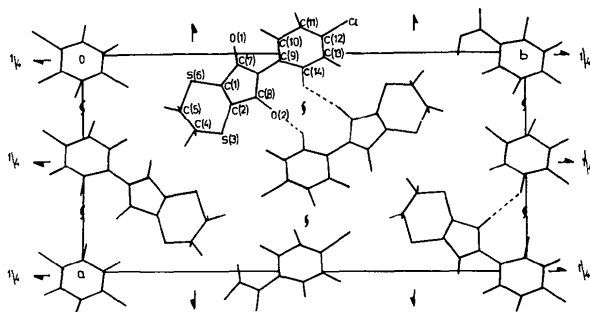
Fig. 2. The molecular packing.

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