Acta Cryst. (1975). B31, 2494

3,4,5,6-Tetrahydrophthalimide

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(*Received* 6 *March* 1975; *accepted* 3 *May* 1975)

Abstract. $C_8H_9NO_2$, orthorhombic, *Pmca*, $a=6{\cdot}902$ (3), $b=12{\cdot}133$ (2), $c=8{\cdot}774$ (2) Å, $V=734{\cdot}7$ (7) Å^3, $M=151{\cdot}17$, $Z=4$, $D_x=1{\cdot}366$ g cm^{-3}. The molecule is not planar because of distortion of the partially hydrogenated six-membered ring. The crystal is built up of molecules connected by hydrogen bonds, forming infinite chains along **c**.

Introduction. The title compound (Fig. 1) was synthesized by Professor K. Fickentscher (Pharmazeutisches Institut der Universität Bonn). A single crystal, $0{\cdot}1\times0{\cdot}1\times0{\cdot}1$ mm, was obtained by recrystallization from a water–acetone solution. Intensity measurements were carried out in the θ–2θ mode on an automatic Hilger & Watts four-circle diffractometer with Zr-filtered Mo $K\alpha$ radiation ($\lambda=0{\cdot}71069$ Å). 2041 reflexions were measured resulting in a set of 963 unique reflexions of which 523 were regarded as unobserved ($I<3\sigma$). No absorption correction was applied ($\mu=0{\cdot}88$ cm^{-1}). The structure was solved with *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 appearing in the E maps. In space group *Pmca* with eight equivalent positions the four molecules per unit cell were expected in special positions with respect to the mirror planes at $x=\frac{1}{4},\frac{3}{4}$. In fact, the *MULTAN* results showed the molecule to lie on m except for C(4) and C(5), thus indicating the presence of either a partially disordered centrosymmetric structure or a non-centrosymmetric structure ($P2_1ca$) displaying pseudo-centrosymmetry. Accordingly, structure refinement was carried out for three different models by full-matrix least-squares calculations with Cruickshank weights and anisotropic temperature factors for the heavy atoms. The positions of the H atoms were calculated according to the model considered. They were allocated isotropic temperature factors and included in the final stage of refinement. Secondary 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. An ordered noncentrosymmetric model could be rejected at an early stage because of an unacceptable C(4)–C(5) distance of 1·38 Å. A disordered noncentrosymmetric model with C(4), C(5) occupancies of 0·5 could be refined to R (overall) = 0·12 and $R_w=0{\cdot}037$ (omitting unobserveds), but was dismissed because of C–C single bonds showing values between 1·44 and 1·65 Å. Finally, the refinement of a centrosymmetric disordered model with C(4) and C(5) out of the mirror plane led to reasonable bond distances and values of R (overall) = 0·116 (0·051 omitting unobserveds) and R (overall)$_w=0{\cdot}038$ (0·033 omitting unobserveds) [$w=56{\cdot}6/(0{\cdot}03|F_o|^2-0{\cdot}72|F_o|+24{\cdot}0)$ for $|F_o|>12{\cdot}0$, $w=-0{\cdot}0139|F_o|^2+0{\cdot}334|F_o|+0{\cdot}01$ for $|F_o|<12{\cdot}0$, $g=1{\cdot}6\times10^{-5}$]. Hence the last model was regarded as the correct one. An additional confirmation of the centrosymmetry of the structure was obtained from a second harmonic test performed by J. P. Dougherty (Philips Laboratories, Briarcliff Manor, N.Y., U.S.A., personal communication).*

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31116 (6 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 1. *Positional and thermal parameters*

The parameters and standard deviations (in parentheses) for the non-hydrogen atoms $\times 10^4$. The expression for the temperature factor is $\exp[-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+2\beta_{12}hk+2\beta_{13}hl+2\beta_{23}kl)]$.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C(1)	2500	7756 (3)	6731 (4)	226 (12)	65 (3)	99 (5)			2 (3)
C(2)	2500	6911 (3)	5777 (4)	256 (11)	66 (3)	99 (5)			3 (3)
C(3)	2500	6999 (4)	4076 (4)	415 (20)	85 (5)	106 (5)			3 (4)
C(4)	2000 (13)	8181 (6)	3626 (6)	409 (48)	102 (5)	100 (6)	0 (11)	1 (10)	27 (5)
C(5)	3090 (11)	9014 (5)	4577 (7)	340 (38)	79 (4)	153 (8)	3 (8)	7 (11)	25 (5)
C(6)	2500	8929 (4)	6262 (5)	355 (18)	62 (3)	121 (7)			−2 (3)
C(7)	2500	7323 (3)	8319 (4)	223 (12)	73 (3)	93 (5)			−4 (3)
C(8)	2500	5869 (3)	6669 (4)	287 (13)	74 (3)	101 (5)			−1 (3)
O(1)	2500	7830 (2)	9494 (3)	339 (10)	89 (2)	101 (3)			−16 (2)
O(2)	2500	4930 (3)	6197 (3)	573 (12)	61 (2)	139 (5)			−7 (2)
N	2500	6183 (3)	8191 (4)	326 (11)	63 (3)	101 (4)			9 (3)

Table 1 (*cont.*)

The positional parameters of the hydrogen atoms $\times 10^3$

	x	*y*	*z*	*B*
H1(C3)	162 (8)	638 (3)	362 (5)	1·5 (1·0)
H2(C3)	398 (7)	680 (4)	383 (5)	1·6 (1·0)
H1(C4)	211 (9)	830 (3)	253 (4)	2·1 (0·8)
H2(C4)	36 (9)	823 (5)	383 (7)	4·2 (1·0)
H1(C5)	295 (6)	976 (3)	421 (4)	0·8 (0·8)
H2(C5)	459 (8)	888 (4)	445 (5)	1·6 (0·9)
H1(C6)	322 (9)	936 (4)	670 (5)	1·7 (1·0)
H2(C6)	107 (8)	929 (5)	649 (6)	2·5 (1·0)
H(N)	250	571 (3)	894 (4)	1·5 (0·7)

Discussion. The investigation of the title compound THP (Fig. 1) was undertaken within the framework of research on the relationships between the stereochemical properties and embryotoxic and teratogenic effects in animal tests of thalidomide and related compounds. THP has been found to cause embryotoxicity and teratogenicity only when applied in large doses. Tables 1 and 2 give the fractional coordinates, thermal parameters and bond distances and angles. Fig. 2 shows a projection of the unit cell along **a**. All heavy atoms except C(4) and C(5) lie on the mirror planes, and the C(3)–C(4) and C(6)–C(5) valences point in opposite directions. As in the recently investigated compound 3,6-dithia-3,4,5,6-tetrahydrophthalimide (DTTHP) (Kirfel, Will & Fickentscher, 1975) the deviations from the plane are significantly different, C(4) = 0·345 and C(5) = 0·407 Å, indicating some strain within the molecule. However, the difference of the distances (0·062) is smaller than in DTTHP (0·218 Å). Since the embryotoxic and teratogenic effects of THP are much smaller than those of DTTHP, there may be a connexion between the different distortions of the six-membered rings of THP and DTTHP and their teratological effects.

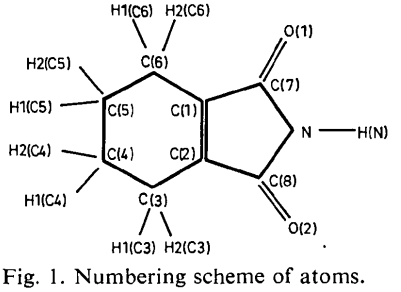

Fig. 1. Numbering scheme of atoms.

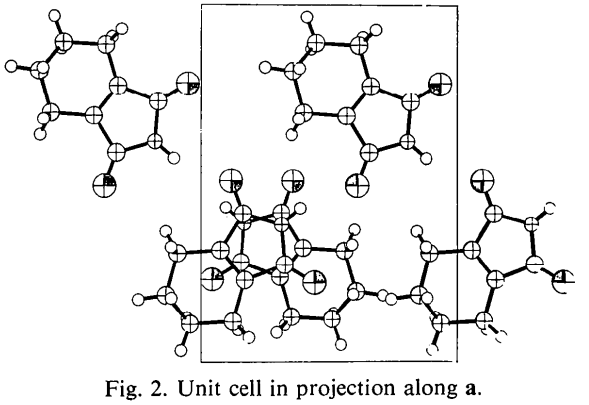

Fig. 2. Unit cell in projection along **a**.

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

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

C(1)–C(2)	1·324 (5)	C(8)–O(2)	1·212 (5)
C(1)–C(6)	1·481 (6)	N—H(N)	0·88 (3)
C(1)–C(7)	1·489 (5)	C(3)–H1(C3)	1·05 (5)
C(2)–C(3)	1·497 (5)	C(3)–H2(C3)	1·07 (6)
C(2)–C(8)	1·486 (5)	C(4)–H1(C4)	0·98 (4)
C(3)–C(4)	1·527 (8)	C(4)–H2(C4)	1·15 (7)
C(6)–C(5)	1·537 (7)	C(5)–H1(C5)	0·97 (4)
C(4)–C(5)	1·511 (9)	C(5)–H2(C5)	1·05 (6)
C(7)–N	1·387 (5)	C(6)–H1(C6)	0·91 (5)
C(8)–N	1·389 (5)	C(6)–H2(C6)	1·10 (5)
C(7)–O(1)	1·201 (4)		
C(2)–C(1)–C(6)	124·6 (3)	H1(C3)–C(3)–C(2)	109 (2)
C(2)–C(1)–C(7)	108·6 (3)	H1(C3)–C(3)–C(4)	116 (3)
C(6)–C(1)–C(7)	126·8 (3)	H1(C3)–C(3)–H2(C3)	109 (4)
C(1)–C(2)–C(3)	125·1 (4)	H2(C3)–C(3)–C(2)	101 (3)
C(1)–C(2)–C(8)	109·0 (3)	H2(C3)–C(3)–C(4)	112 (3)
C(8)–C(2)–C(3)	125·9 (4)	H1(C4)–C(4)–C(3)	112 (3)
C(2)–C(3)–C(4)	108·9 (4)	H1(C4)–C(4)–C(5)	114 (3)
C(1)–C(6)–C(5)	109·4 (4)	H1(C4)–C(4)–H2(C4)	103 (4)
C(3)–C(4)–C(5)	111·9 (5)	H2(C4)–C(4)–C(3)	103 (3)
C(4)–C(5)–C(6)	110·8 (5)	H2(C4)–C(4)–C(5)	112 (3)
C(1)–C(7)–N	106·0 (3)	H1(C5)–C(5)–C(4)	113 (2)
C(1)–C(7)–O(1)	128·5 (4)	H1(C5)–C(5)–C(6)	111 (2)
O(1)–C(7)–N	125·5 (3)	H1(C5)–C(5)–H2(C5)	102 (4)
C(2)–C(8)–N	105·9 (3)	H2(C5)–C(5)–C(4)	109 (3)
C(2)–C(8)–O(2)	128·3 (3)	H2(C5)–C(5)–C(6)	111 (3)
O(2)–C(8)–N	125·9 (4)	H1(C6)–C(6)–C(1)	112 (3)
C(7)–N—C(8)	110·5 (3)	H1(C6)–C(6)–C(5)	114 (3)
C(7)–N—H(N)	127 (2)	H1(C6)–C(6)–H2(C6)	99 (5)
C(8)–N—H(N)	123 (2)	H2(C6)–C(6)–C(1)	109 (3)
		H2(C6)–C(6)–C(5)	113 (3)

On the mirror planes adjacent molecules are connected through N–H(N)···O(2^{i}) hydrogen bonds of 2·96 Å with N–H(N) 0·88 and H(N)···O(2^{i}) 2·12 Å. The angle at H(N) is 160 (3)°. These values compare well with those found for DTTHP (2·94, 0·79 and 2·18 Å). As in DTTHP the molecules connected by hydrogen bonds form infinite chains running along **c**. The packing distance between the chains is $a/2 = 3{\cdot}45$ Å (3·38 Å in DTTHP).

The author thanks Professor M. M. Woolfson, University of York, England, and Professor G. Will, Universität Bonn, Germany (BRD) for their interest in and support of this work. The receipt of a European Program fellowship provided by the Deutsche Forschungsgemeinschaft is gratefully acknowledged.

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