

1,2,3,6-Tetrahydrophthalimide

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Abstract. $C_8H_9NO_2$, orthorhombic, $P2_12_12_1$, $a = 6.137$ (1), $b = 12.251$ (2), $c = 9.944$ (1) Å, $V = 747.7$ (2) Å³, $M = 151.17$, $Z = 4$, $D_x = 1.366$ g cm⁻³. The partially hydrogenated six-membered ring is in a tilted configuration and almost perpendicular to the five-membered planar ring. The crystal is built up of molecules connected by hydrogen bonds, forming infinite chains running along *a*.

Introduction. The title compound (Fig. 1) was synthesized by Professor K. Fickentscher (Pharmazeutisches Institut der Universität Bonn). A single crystal, $0.1 \times 0.2 \times 0.1$ mm, was obtained by recrystallization from an acetone solution. Intensity measurements were carried out in the θ - 2θ mode on an automatic Syntex P21 four-circle diffractometer using Mo $K\alpha$ radiation ($\lambda = 0.71069$ Å) monochromatized by a graphite crystal. 1993 reflexions were recorded resulting in a set of 1040 unique reflexions of which 289 were regarded as unobserved ($I < 3\sigma$). No absorption correction was applied ($\mu = 0.88$ cm⁻¹). The structure was solved by use of the direct-method computer program *MULTAN* (Germain, Main & Woolfson, 1971). The set of phases (200 E 's, 2000 Σ_2 relationships) with the highest combined figure-of-merit fixed the positions of the heavy atoms appearing in the E map. Structure refinement was carried out by full-matrix least-squares calculations with Cruickshank weights and anisotropic temperature factors for the heavy atoms. The positions of the H atoms were found from a difference electron density map. They were allocated isotropic temperature factors and included in the final stage of refinement. Secondary extinction was taken into account according

to Zachariasen (1963) $\{F_c = KF_o[1 + \beta(2\theta)gI_c]\}$ by including g in the list of variables (final value $g = 7.6 \times 10^{-5}$). The final R values obtained were $R(\text{overall}) = 0.058$ (0.038 omitting unobserved) and weighted $R(\text{overall}) = 0.041$ (0.035 omitting unobserved) [$w = 80.0/(0.01|F_o|^2 - 0.2|F_o| + 20.0)$ for $|F_o| > 10.0$ and $w = -0.0535|F_o|^2 + 1.07|F_o| + 0.001$ for $|F_o| < 10.0$].*

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31574 (7 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

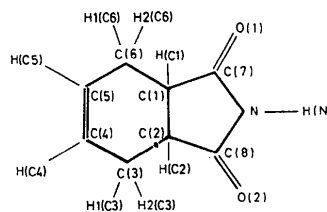


Fig. 1. Numbering scheme of atoms.



Fig. 2. Stereoscopic view of unit cell along *c*.

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 $\exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$.

	<i>x</i>	<i>y</i>	<i>z</i>	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C(1)	9315 (5)	4059 (2)	8528 (3)	255 (9)	64 (2)	69 (3)	13 (4)	-23 (4)	-14 (2)
C(2)	1165 (5)	4104 (3)	7506 (3)	186 (9)	74 (2)	118 (4)	25 (4)	-21 (5)	-26 (2)
C(3)	1802 (7)	5271 (3)	7059 (4)	305 (13)	98 (3)	161 (6)	-54 (6)	72 (7)	-42 (3)
C(4)	9796 (7)	5920 (3)	6765 (3)	510 (16)	58 (2)	112 (4)	-78 (6)	-30 (7)	-5 (3)
C(5)	8163 (6)	5870 (3)	7606 (4)	289 (11)	49 (2)	175 (5)	-6 (5)	-41 (7)	-17 (3)
C(6)	8328 (7)	5191 (3)	8842 (3)	355 (13)	65 (2)	120 (4)	2 (5)	45 (7)	-33 (2)
C(7)	7618 (5)	3330 (2)	7905 (3)	232 (10)	55 (2)	92 (3)	32 (4)	-17 (5)	-4 (2)
C(8)	308 (5)	3478 (2)	6305 (3)	305 (11)	44 (2)	93 (3)	32 (4)	11 (5)	-6 (2)
O(1)	5945 (3)	3006 (2)	8408 (2)	249 (7)	91 (2)	152 (3)	-10 (3)	26 (4)	-12 (2)
O(2)	1217 (4)	3350 (2)	5235 (2)	558 (11)	75 (2)	113 (2)	34 (4)	105 (5)	-22 (2)
N	8293 (4)	3076 (2)	6614 (2)	316 (9)	44 (1)	77 (2)	6 (3)	-35 (4)	-12 (2)

Table 1 (cont.)

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

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i>
H(C1)	972 (5)	369 (2)	937 (3)	2.2 (0.7)
H(C2)	234 (5)	364 (2)	778 (3)	2.6 (0.8)
H1(C3)	278 (7)	524 (3)	635 (4)	5.2 (1.1)
H2(C3)	265 (7)	561 (3)	781 (4)	6.8 (1.3)
H(C4)	997 (5)	635 (2)	599 (3)	2.1 (0.7)
H(C5)	692 (6)	627 (3)	751 (3)	3.4 (0.8)
H1(C6)	683 (7)	509 (3)	923 (3)	4.2 (0.9)
H2(C6)	928 (6)	560 (2)	953 (3)	3.6 (0.8)
H(N)	752 (6)	267 (3)	605 (3)	3.9 (0.9)

Table 2. *Interatomic distances* (Å) *and bond angles* (°)
Standard deviations are given in parentheses for the last significant digit.

C(1)–C(2)	1.526 (4)	C(8)–O(2)	1.211 (4)
C(1)–C(6)	1.544 (4)	N—H(N)	0.89 (3)
C(1)–C(7)	1.505 (4)	C(1)–H(C1)	0.98 (3)
C(2)–C(3)	1.548 (5)	C(2)–H(C2)	0.97 (3)
C(2)–C(8)	1.513 (4)	C(3)–H1(C3)	0.92 (4)
C(3)–C(4)	1.495 (6)	C(3)–H2(C3)	1.00 (4)
C(6)–C(5)	1.488 (5)	C(4)–H(C4)	0.94 (3)
C(4)–C(5)	1.306 (6)	C(5)–H(C5)	0.91 (4)

Table 2 (cont.)

C(7)–N	1.384 (4)	C(6)–H1(C6)	1.00 (4)
C(8)–N	1.367 (4)	C(6)–H2(C6)	1.03 (3)
C(7)–O(1)	1.209 (4)		
C(2)–C(1)–C(6)	113.2 (3)	C(7)–C(1)–H(C1)	105 (2)
C(2)–C(1)–C(7)	105.2 (2)	C(2)–C(1)–H(C1)	113 (2)
C(6)–C(1)–C(7)	110.3 (3)	C(3)–C(2)–H(C2)	116 (2)
C(1)–C(2)–C(3)	114.3 (3)	C(1)–C(2)–H(C2)	110 (2)
C(1)–C(2)–C(8)	104.4 (2)	C(8)–C(2)–H(C2)	101 (2)
C(3)–C(2)–C(8)	109.2 (3)	C(2)–C(3)–H1(C3)	110 (2)
C(2)–C(3)–C(4)	109.8 (3)	C(4)–C(3)–H1(C3)	114 (3)
C(3)–C(4)–C(5)	118.8 (3)	H2(C3)–C(3)–H1(C3)	104 (4)
C(4)–C(5)–C(6)	120.2 (3)	C(2)–C(3)–H2(C3)	108 (2)
C(5)–C(6)–C(1)	111.2 (3)	C(4)–C(3)–H2(C3)	111 (3)
C(1)–C(7)–N	108.0 (2)	C(1)–C(6)–H1(C6)	109 (2)
C(1)–C(7)–O(1)	127.6 (3)	C(5)–C(6)–H1(C6)	109 (2)
O(1)–C(7)–N	124.4 (3)	H2(C6)–C(6)–H1(C6)	108 (3)
C(2)–C(8)–N	108.6 (2)	C(1)–C(6)–H2(C6)	110 (2)
C(2)–C(8)–O(2)	126.8 (3)	C(5)–C(6)–H2(C6)	109 (2)
O(2)–C(8)–N	124.6 (3)	C(3)–C(4)–H(C4)	111 (2)
C(7)–N–C(8)	113.5 (2)	C(5)–C(4)–H(C4)	129 (2)
C(7)–N–H(N)	123 (2)	C(4)–C(5)–H(C5)	124 (2)
C(8)–N–H(N)	123 (2)	C(6)–C(5)–H(C5)	116 (2)
		C(6)–C(1)–H(C1)	110 (2)

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

Plane <i>A</i>							
Atom	C(1)	C(2)	C(7)	C(8)	O(1)	O(2)	N
Deviation	–0.050	0.045	–0.008	0.006	0.039	0.000	–0.032
Plane <i>B</i>							
Atom	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	
Deviation	–0.148	–0.187	0.363	–0.181	–0.193	0.347	

Discussion. The investigation of the title compound (Fig. 1) was undertaken in continuation of the research on the relationships between the stereochemical properties and embryotoxic and teratogenic effects in animal tests of thalidomide and related compounds. Previous structural investigations are reported for 3,6-dithia-3,4,5,6-tetrahydrophthalimide (DTTHP) (Kirfel, Will & Fickentscher, 1975) and 3,4,5,6-tetrahydrophthalimide (THP) (Kirfel, 1975).

Tables 1 and 2 give the fractional coordinates, thermal parameters and bond distances and angles. Fig. 2 shows an *ORTEP* drawing (Johnson, 1965) of the unit cell from which it may be seen that the partially hydrogenated six-membered ring is almost perpendicular to the five-membered ring. Table 3 contains the results of least-squares planes calculations showing the five-membered ring to be essentially planar and the six-membered ring to be in a tilted configuration. The angle between the two ring planes is 108°. Thus the molecular structure is spacial whereas the molecular structures of DTTHP and THP can be characterized as planar. Taking into account that, contrary to DTTHP and THP, the title compound

causes only minimal teratogenic or embryotoxic effects in the animals tested, the structural result is in agreement with the intercalation hypothesis (Jönsson, 1972) since the molecule is too bulky to fit between two adjacent base pairs in the DNA helix.

In the crystal, adjacent molecules are connected through N–H(N)···O(2ⁱ) hydrogen bonds of 2.84 Å with N–H(N) 0.89 and H(N)···O(2ⁱ) 1.96 Å. The angle at H(N) is 171 (3)°. These values compare well with those found for DTTHP and THP. As in the latter compounds the molecules connected by hydrogen bonds form infinite chains, in this case running along *a*.

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