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The Crystal and Molecular Structure of 5-Ethyl-5-(1,3-dimethylbutyl)barbituric Acid (α-Methylamobarbital)

BY P. H. SMIT AND J. A. KANTERS

Laboratorium voor Structuurchemie, Transitorium 3, *Universiteitscentrum 'de Uithof', Padualaan* 8, *Utrecht, The Netherlands*

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Crystals of 5-ethyl-5-(1,3-dimethylbutyl)barbituric acid (α-methylamobarbital) are triclinic with lattice parameters $a=7{\cdot}758$ (3), $b=9{\cdot}084$ (3), $c=10{\cdot}438$ (3) Å, $\alpha=101{\cdot}95$ (10), $\beta=96{\cdot}67$ (9), $\gamma=107{\cdot}38$ (10)°, space group $P\bar{1}$ with two molecules in the unit cell. The structure was determined from the intensities of 1769 independent reflexions collected on an automatic four-circle Nonius diffractometer, using Cu $K\alpha$ radiation. The structure was solved by application of direct methods; a full-matrix least-squares refinement converged at $R=0{\cdot}12$. The positions of the isobutyl terminal carbon atoms are not well defined because of their unusually large amplitudes of thermal vibration that may partly be ascribed to rotational disorder. Except for a slight distortion, the trioxopyrimidine ring is planar. In the side chains, the carbon atoms of the ethyl group constitute a planar extended chain with two of the carbon atoms of the dimethylbutyl group, the remaining isobutyl chain being in a *gauche* position. The molecules are linked by N–H···O=C hydrogen bonds across centres of inversion, thus forming single ribbons along the **c** direction. The C(4)=O(4) carbonyl group is not involved in hydrogen bonding. The single ribbons are held together by weak van der Waals interactions.

Introduction

The crystal structure determination of 5-ethyl-5-(1,3-dimethylbutyl)barbituric acid [α-methylamobarbital or α-MAB, see Fig. 1(*a*)] was undertaken as part of a program for the study of the chemical and pharmacological properties of a series of barbituric acid derivatives (Sitsen, 1972). α-MAB is of special interest because of its convulsive rather than hypnotic activity. The crystal structures of a number of drug-active barbituric acid derivatives have recently been reported (see Table 1).

Crystal and experimental data

Single crystals of α-methylamobarbital were obtained from an ethanol solution by slow evaporation at room temperature. Oscillation and Weissenberg photographs showed the space group to be triclinic. Lattice parameters (Table 2) and X-ray intensity data were measured on an automatic four-circle Nonius diffractometer

Table 2. *Crystal data for α-methylamobarbital* ($C_{12}H_{20}N_2O_3$)

Melting point	173 °C
Crystal system	Triclinic
Crystal dimensions	0·3 × 0·3 × 0·5 mm
Space group	$P\bar{1}$
a	7·758 (3) Å
b	9·084 (3)
c	10·438 (3)
α	101·95 (10)°
β	96·67 (9)
γ	107·38 (10)
Z	2
D_m	1·184 g cm^{-3}
D_{calc}	1·188 g cm^{-3}
μ(Cu $K\alpha$)	7·08 cm^{-1}

Table 1. *5-R-5-Ethylbarbituric acids*

Generic name	R	Reference
Barbital	Ethyl	Polymorphs I, II: Craven, Vizzini & Rodrigues (1969) Polymorph IV: Craven & Vizzini (1971)
Barbital (in a 2:1 caffeine complex)	Ethyl	Craven & Gartland (1970)
Amobarbital (AB)	3-Methylbutyl	Craven & Vizzini (1969) (both polymorphs)
Vinbarbital	1-Methyl-1-butenyl	Craven & Cusatis (1969)
Sodium barbital	Ethyl	Berking & Craven (1971)
5-Ethylbarbituric acid	Hydrogen	Gatehouse & Craven (1971)
5-Hydroxybarbital	Hydroxyl	Gatehouse & Craven (1971)
γ-Methylamobarbital (γ-MAB)	3,3-Dimethylbutyl	Gartland & Craven (1971)
Barbituric acids with a methyl group at N(1)		
Sodium metharbital	Ethyl	Berking (1972)
Metharbital	Ethyl	Wunderlich (1973)

using Cu $K\alpha$ radiation ($\lambda = 1{\cdot}5418$ Å). Intensity measurements were made using the ω-scanning technique, measuring each reflexion and its background for two minutes or up to 1000 counts. Intensity data were collected for 1769 independent reflexions for which $\lambda^{-1} \sin\theta \leq 0{\cdot}59$ Å^{-1} ($\theta \leq 65°$). X-ray absorption corrections were neglected.

The crystal system is triclinic with two molecules in the unit cell. The ratio test of Ramachandran & Srinivasan (1959) yields a value of 0·806 and indicates the space group to be $P\bar{1}$, so both optical antipodes are present in the cell.

Structure analysis and refinement

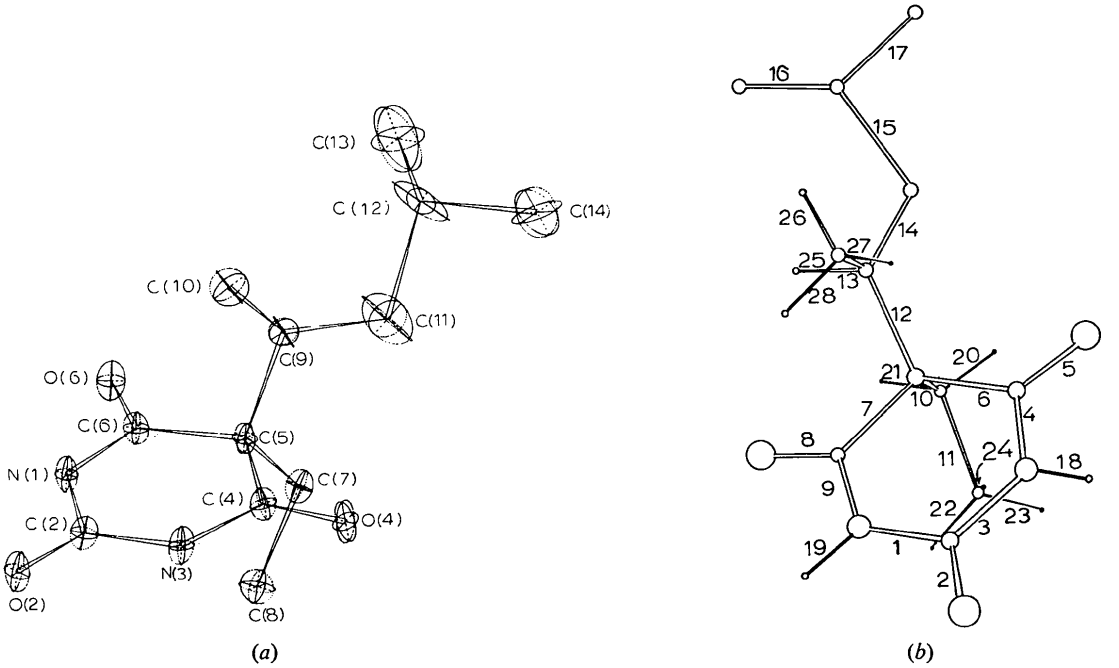
A direct method of phase determination was applied to 410 normalized structure factors, by the symbolic sign method of Spek (1972) from which eight sets of phases were obtained. For each set a reliability index, c, was calculated, where

$$c = \sum_{h,k} s_h s_k s_{h+k} (E_h E_k E_{h+k}) .$$

The set with the second highest reliability index proved to be the correct one. A three-dimensional electron-density Fourier synthesis with the normalized structure factors from this set as coefficients showed a recognizable part of the molecule. After several cycles of structure-factor and electron-density calculations all the non-hydrogen atoms were located. At this stage the R value was 0·24. Progressing along the isobutyl chain from C(9) to C(12) [see Fig. 1(*a*)] the electron density peaks became more diffuse, with indeed very diffuse peaks for atoms C(13) and C(14). In the block-diagonal matrix approximation a least-squares refinement of the carbon, nitrogen and oxygen positional parameters with anisotropic thermal parameters converged to an R value of 0·13. All the hydrogen atoms, with the exception of those bonded to the strongly vibrating carbon atoms C(11), C(12), C(13) and C(14), were located by comparing their calculated expected positions with the corresponding peaks in a three-dimensional difference electron-density synthesis. Keeping the hydrogen atoms at fixed positions, the structure was refined to an R value of 0·12 by a full-matrix least-squares refinement, applying the weighting scheme of Derissen, Endeman & Peerdeman (1968). The thermal parameters for the terminal isobutyl group carbon atoms are unusually large. The largest component of the β_{ij} tensor for atom C(11) corresponds to an r.m.s. amplitude of vibration of 0·59 Å [Fig. 1(*a*)]. Similar effects have been reported for the alkyl side chains in AB (amobarbital) and γ-MAB (γ-methylamobarbital).

The final atomic parameters are listed in Table 3.* In the block-diagonal matrix refinement atomic scat-

* The structure factor table is available from the authors and has also been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30272 (9 pp.). Copies may be obtained through the Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.



(*a*) (*b*)

Fig. 1. (*a*) 5-Ethyl-5-(1,3-dimethylbutyl)barbituric acid molecule with atomic labelling. Thermal-motion ellipsoids for non-hydrogen atoms are scaled for 66·7% probability. (*b*) Distance labelling as referred to in Table 5.

tering factors were taken from Doyle & Turner (1968), except those for C, which were taken from Allman (1967), and in the full-matrix refinement Moore's (1963) scattering factors were applied.

Molecular structure

In the crystal structure, α-MAB, like other 5,5-dialkyl-substituted barbitals, is in the 2,4,6-trioxo tautomeric form. The trioxopyrimidine ring is nearly planar. The ring puckering is very small (Table 4) compared to that reported for other 5,5-substituted barbitals (*e.g.* Gartland & Craven, 1971). In the crystal structure the ideal mirror-plane symmetry of the trioxopyrimidine ring is only disturbed by the tilting of the C(6)=O(6) carbonyl group (2·3°) from the least-squares plane, determined by the remaining barbiturate ring atoms that are very nearly coplanar (Table 4, plane 3; Fig. 2). This type of asymmetry has not been found in other barbituric acid derivatives, and is probably related to participation of the C(6)=O(6) group in hydrogen bonding.

Ring bond lengths and angles agree with those of other neutral 5,5-dialkyl-substituted barbitals, and partly confirm the conclusions of Craven, Cusatis, Gartland & Vizzini (1973) about systematic perturbations in the oxopyrimidine rings of those barbituric acid derivatives in which one of the carbonyl groups is not involved in hydrogen bonding.* The bond lengths and bond angles (Table 5) are not corrected for thermal motion.

The butyl and ethyl group carbon atoms including C(5) do not form an extended alkyl chain as is the case in the barbituric acid derivatives AB and γ-MAB. In α-MAB atoms C(7) and C(8) of the ethyl group constitute a planar extended chain with ring atom C(5) and atoms C(9) and C(10) of the dimethylbutyl chain, whereas the coplanarity of the atoms C(9), C(11), C(12) and C(14) is less pronounced (Table 4). The dihedral angle between the least-squares planes, determined by the chains as mentioned above is 60·4°, which corresponds to a *gauche* conformation about the C(5)–C(9) bond. In the terminal isobutyl group there is a torsion of 18° about the C(9)–C(11) bond.

The plane containing carbon atoms C(10), C(9), C(5), C(7), and C(8) is perpendicular (dihedral angle 89·3°) to the plane through the atoms of the trioxopyrimidine ring.

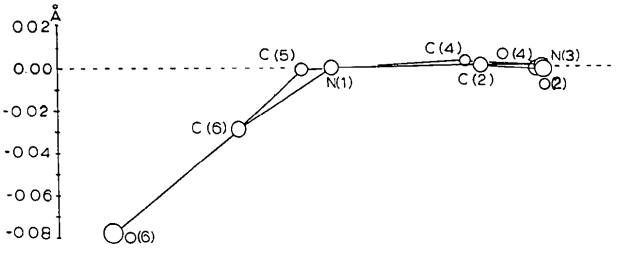


Fig. 2. Conformation of the trioxopyrimidine ring. Dotted line is the trace of the least-squares plane through all trioxopyrimidine ring atoms with the exception of atoms C(6) and O(6) (Table 4, plane 3). Scale in the vertical direction is 20 times that in the horizontal.

* In Fig. 1 of that paper the labelling of atoms is not consistent with that appearing in the previous articles (Table 1) on the crystal structures of barbiturates: the correct labelling is obtained by reflexion with respect to the line O(2)–C(5).

Table 3. *Atomic parameters* ($\times 10^3$) *for α-methylamobarbital*

Positional parameters are given as fractions of the lattice translations. Thermal parameters are given according to the expression:

$$T=\exp\left[-(h^2\beta_{11}+k^2\beta_{22}+l^2\beta_{33}+2\beta_{12}hk+2\beta_{23}kl+2\beta_{31}hl)\right].$$

The e.s.d.'s given in parentheses refer to the least significant digit of the atomic parameters.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{23}	β_{31}
N(1)	70·5 (6)	35·1 (6)	188·5 (5)	9 (1)	21 (1)	5·1 (5)	8 (2)	7 (1)	4 (1)
C(2)	48·0 (8)	26·5 (8)	315·4 (6)	13 (1)	19 (1)	5·9 (7)	12 (2)	7 (2)	5 (2)
O(2)	−104·2 (5)	−25·8 (6)	341·2 (4)	11·1 (9)	30 (1)	7·8 (5)	11 (2)	15 (1)	8 (1)
N(3)	205·1 (6)	78·9 (6)	410·7 (4)	12 (1)	23 (1)	3·8 (5)	9 (2)	6 (1)	3 (1)
C(4)	384·3 (8)	140·4 (7)	390·2 (6)	13 (1)	14 (1)	5·9 (7)	6 (2)	2 (1)	3 (2)
O(4)	510·0 (5)	181·8 (5)	483·8 (4)	14 (1)	26 (1)	6·1 (5)	2 (2)	6 (1)	3 (1)
C(5)	411·6 (7)	150·4 (7)	249·1 (5)	10 (1)	14 (1)	5·7 (7)	8 (2)	5 (1)	4 (1)
C(6)	234·1 (8)	87·8 (7)	146·6 (6)	11·4 (6)	15 (1)	5·9 (7)	8 (2)	4 (1)	5 (1)
O(6)	235·0 (5)	83·6 (5)	30·7 (4)	13·4 (9)	28 (1)	5·3 (5)	1 (2)	11 (1)	6 (1)
C(7)	530·1 (8)	46·2 (7)	205·6 (6)	14 (1)	14 (1)	6·7 (7)	14 (2)	3 (1)	6 (2)
C(8)	435·7 (9)	−132·5 (8)	191·0 (7)	23 (2)	15 (1)	10·5 (9)	11 (2)	5 (2)	6 (2)
C(9)	505·3 (9)	327·2 (8)	250·2 (7)	15 (2)	12 (1)	18 (1)	7 (2)	6 (2)	6 (2)
C(10)	385·3 (10)	427·0 (8)	294·6 (8)	24 (2)	15 (1)	19 (1)	19 (3)	4 (2)	14 (2)
C(11)	69·4 (1)	39·6 (1)	30·8 (1)	36 (3)	23 (2)	66 (3)	17 (4)	23 (4)	38 (5)
C(12)	79·6 (2)	56·0 (1)	26·2 (2)	35 (3)	14 (2)	59 (4)	1 (4)	28 (4)	52 (6)
C(13)	81·7 (2)	55·9 (2)	11·4 (2)	58 (5)	38 (3)	38 (3)	9 (6)	−6 (5)	4 (6)
C(14)	99·1 (2)	61·8 (1)	36·1 (1)	41 (4)	48 (3)	48 (3)	34 (6)	53 (5)	35 (6)

	x	y	z
H(11)	−40 (10)	0 (10)	120 (10)
H(31)	190 (10)	70 (10)	500 (10)
H(71)	570 (10)	50 (10)	110 (10)
H(72)	650 (10)	70 (10)	270 (10)
H(81)	530 (10)	−190 (10)	150 (10)
H(82)	420 (10)	−160 (10)	280 (10)
H(83)	320 (10)	−190 (10)	120 (10)
H(91)	510 (10)	330 (10)	150 (10)
H(101)	420 (10)	540 (10)	300 (10)
H(102)	260 (10)	380 (10)	230 (10)
H(103)	340 (10)	430 (10)	380 (10)

As in other 5,5-dialkylsubstituted barbitals, the C(5)–C(7) and C(5)–C(9) bond lengths are somewhat longer than the accepted tetrahedral carbon–carbon distance [1·526 Å, Lide (1962)] which has been attributed to steric repulsion between the C(5) substituents (Craven, Vizzini & Rodrigues, 1969; Gartland & Craven, 1971).

The apparent deviation in the C–C bond lengths of the isobutyl group from the expected value of 1·53 Å (Bartell & Kohl, 1963) can be attributed partly to the high thermal motion of the side-chain atoms and partly to a certain degree of rotational disorder. This disordering is probably strongly related to packing effects.

Hydrogen bonding and molecular packing

In the crystal structure every molecule is connected to two neighbouring molecules by pairs of hydrogen

Table 4. *Least-squares planes and dihedral angles*

Atoms defining the plane

Plane 1: N(1), C(2), N(3), C(4), C(5) and C(6)
Plane 2: N(1), C(2), N(3), C(4), C(5), C(6), O(2), O(4) and O(6)
Plane 3: N(1), C(2), N(3), C(4), C(5), O(2) and O(4)
Plane 4: O(2), C(2), C(5), C(7) and C(9)
Plane 5: C(8), C(7), C(5), C(9) and C(10)
Plane 6: C(9), C(11), C(12) and C(14)
Plane 7: N(1), C(6), O(6), N(1), C(6^{i}) and O(6^{i})
Plane 8: C(2), O(2), N(3), C(2^{ii}), O(2^{ii}) and N(3^{ii})

The symbols i and ii denote the symmetry operations i: $\bar{x}$, $\bar{y}$, $\bar{z}$ and ii: $\bar{x}$, $\bar{y}$, $1-z$, which generate the positional parameters of atoms not belonging to the crystal asymmetric unit as listed in Table 3.

(i) Equations of planes

The equations of the planes referred to the crystallographic axes, with X, Y, Z in Å units, are in the form $AX+BY+CZ=D$.

Plane	A	B	C	D
1	0·1000	−0·9765	−0·1909	0·0892
2	0·0978	−0·9780	−0·1842	0·0645
3	0·1016	−0·9749	−0·1982	0·1130
4	−0·2481	0·1437	−0·9580	3·0348
5	−0·2283	0·1682	−0·9590	2·9630
6	0·4423	0·5410	−0·7153	0·9817
7	0·1090	−0·9838	−0·1426	0·0000
8	0·1159	−0·9642	−0·2385	0·2662

(ii) Distances of atoms to planes in Å units. Atoms marked with an asterisk do not constitute the plane.

Plane 1								
N(1)	C(2)	N(3)	C(4)	C(5)	C(6)	O(2)*	O(4)*	O(6)*
−0·010	−0·001	0·006	−0·001	−0·008	0·014	0·006	0·009	0·053
Plane 2								
N(1)	C(2)	N(3)	C(4)	C(5)	C(6)	O(2)	O(4)	O(6)
−0·022	−0·003	0·008	−0·004	−0·022	−0·004	0·008	0·012	0·027
Plane 3								
N(1)	C(2)	N(3)	C(4)	C(5)	O(2)	O(4)	C(6)*	O(6)*
0·000	0·001	0·000	0·003	−0·001	−0·001	−0·001	−0·029	−0·078
Plane 4								
O(2)	C(2)	C(5)	C(7)	C(9)	C(8)*	C(10)*		
0·009	−0·009	−0·011	0·006	0·006	0·115	−0·022		
Plane 5								
C(8)	C(7)	C(5)	C(9)	C(10)	O(2)*	C(2)*		
−0·034	0·029	0·038	−0·027	−0·006	0·112	0·103		
Plane 6								
C(9)	C(11)	C(12)	C(14)	C(13)*				
0·055	−0·067	−0·034	0·045	−1·152				
Plane 7								
N(1)	C(6)	O(6)	N(1^{i})	C(6^{i})	O(6^{i})	H(11)*	H(11^{i})*	
0·005	−0·008	0·007	−0·006	0·009	−0·007	0·066	−0·065	
Plane 8								
C(2)	O(2)	N(3)	C(2^{ii})	O(2^{ii})	N(3^{ii})	H(31)*	H(31^{ii})*	
−0·015	0·012	0·009	0·015	−0·012	−0·009	0·036	−0·036	

(iii) Dihedral angles

∠(1)–(5)	88·99°	∠(1)–(4)	89·77°
∠(2)–(5)	89·33	∠(2)–(4)	89·42
∠(3)–(5)	89·84	∠(3)–(4)	88·59
∠(5)–(6)	60·40		

bonds across centres of symmetry, thus constituting single ribbons along the **c** direction with a periodicity of 10·44 Å (Figs. 3 and 4). The pyrimidine rings lie in planes close to the crystallographic planes ($1\bar{3}0$). This type of hydrogen bonding has often been called 'cyclic dimer': for examples see Gartland & Craven (1971). The N(1)–H(11)···O(6^{i}) and N(3)–H(31)···O(2^{ii}) hydrogen bonds have very similar interatomic distances and angles (Table 6). Both cyclic hydrogen-bond configurations are planar within 0·015 Å (Table 4, planes 7 and 8) with the two pyrimidine rings that are related by the centre of inversion I (Fig. 3) at a perpendicular distance of 0·078 Å, and the two pyrimidine rings related by the centre of inversion II at a perpendicular distance of 0·251 Å. The least-squares planes through the two pairs of hydrogen bonds nearly coincide. The C(4)=O(4) carbonyl group is not involved in hydrogen bonding. When comparing the crystal structure of α-MAB with that of AB it appears that the single ribbons in these two structures differ in the direction in which the side chains project. In the latter structure the isoamyl groups project on the same side of the ribbon, whereas in the former the dimethylbutyl chains alternate their projection direction in the ribbon, thus ex-

Table 5. *Bond lengths* (Å) *and angles* (°)

Bond lengths and angles are not corrected for thermal motion. The e.s.d.'s are given in parentheses and refer to the least significa nt digit of the molecular parameters. The numbers of the distances refer to Fig. 1(*b*).

1	1·371 (8)	9	1·373 (8)	17	1·60 (2)	25	1·1 (1)
2	1·218 (8)	10	1·545 (9)	18	0·9 (1)	26	1·1 (1)
3	1·370 (8)	11	1·535 (9)	19	1·0 (1)	27	1·1 (1)
4	1·395 (8)	12	1·549 (9)	20	1·0 (1)	28	1·0 (1)
5	1·206 (8)	13	1·53 (1)	21	1·1 (1)		
6	1·529 (9)	14	1·41 (1)	22	1·1 (1)		
7	1·517 (9)	15	1·66 (2)	23	1·0 (1)		
8	1·203 (8)	16	1·58 (3)	24	1·0 (1)		

∠1–2	121·4 (6)	∠ 7—9	118·6 (5)	∠12–13	110·8 (6)	∠ 3–18	116 (5)
2–3	122·1 (6)	9—1	126·8 (5)	12–14	116·9 (7)	4–18	118 (5)
1–3	116·5 (5)	8—9	120·1 (5)	13–14	115·4 (7)	22–23	111 (7)
3–4	126·0 (5)	10—6	107·3 (5)	14–15	113 (1)	22–24	103 (7)
4–5	118·7 (6)	10—7	107·3 (5)	15–16	123 (1)	23–24	110 (7)
5–6	123·2 (6)	10–12	112·2 (5)	15–17	99 (1)	12–25	105 (4)
4–6	118·1 (5)	12—6	109·1 (5)	16–17	112 (1)	26–27	101 (7)
6–7	114·0 (5)	12—7	107·2 (5)	1–19	117 (5)	26–28	99 (8)
7–8	121·3 (5)	10–11	114·1 (5)	9–19	116 (5)	27–28	101 (8)

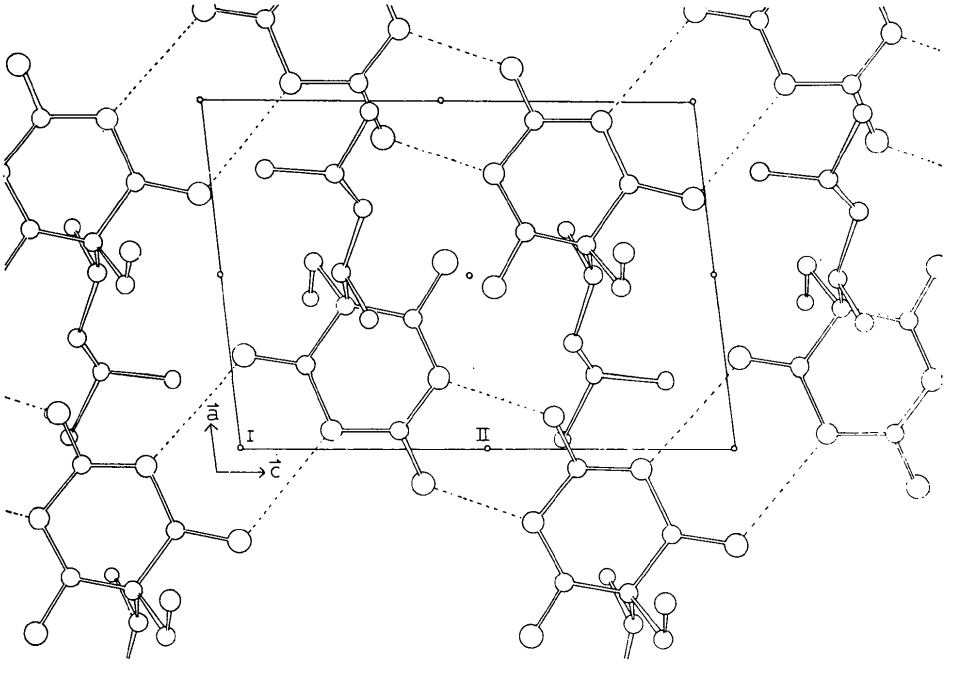


Fig. 3. Hydrogen-bonded molecules in single ribbons as viewed down the *b* axis.

cluding the formation of 'double ribbons'. As Table 7 shows, only a few and weak van der Waals interactions are involved in the packing of the single ribbons of α-MAB molecules. The reason for the adoption of this type of ribbon packing may well be found in the 'bulkiness' of the alkyl side chain. As was indicated in the cases of AB and γ-MAB, the cross-sectional area of the side chain is probably one of the important factors in determining the ribbon structure. In our case the *gauche* conformation in the α-methylisoamyl chain implies a larger cross-sectional area than the extended one, thus rendering the side chain more 'bulky' and therefore the ribbon stacking less compact.

Table 6. *Hydrogen-bond distances and angles*

The positions of atoms not belonging to the crystal asymmetric unit are specified by the operations i: $\bar{x}, \bar{y}, \bar{z}$ or ii: $\bar{x}, \bar{y}, 1-z$. The e.s.d.'s given in parentheses refer to the least significant figures in the tabulated values.

N(1)···O(6^{i})	2·865 (7) Å
H(11)···O(6^{i})	1·9 (1)
N(3)···O(2^{ii})	2·883 (7)
H(31)···O(2^{ii})	2·0 (1)
N(1)—H(11)···O(6^{i})	171 (8)°
H(11)–N(1)···O(6^{i})	5·8 (6)
C(6)—O(6)···N(1^{i})	128·6 (4)
C(6)—O(6)···H(11^{i})	131 (2)
N(3)—H(31)···O(2^{ii})	168 (8)
H(31)–N(3)···O(2^{ii})	8·6 (8)
C(2)—O(2)···N(3^{ii})	129·4 (4)
C(2)—O(2)···H(31^{ii})	133 (2)

The suggestion that the distortion of the pyrimidine ring is largely determined by the packing mode (Voet, 1972) fits the observation that the pyrimidine ring in α-MAB is very nearly planar.

The packing as described above leaves a relatively high degree of freedom to the atoms of the side chain. In terms of the van der Waals repulsive and attractive interactions the potential curve for the different side-chain atoms should have a rather 'flat bottom' and thus allow quite large amplitudes of vibration.

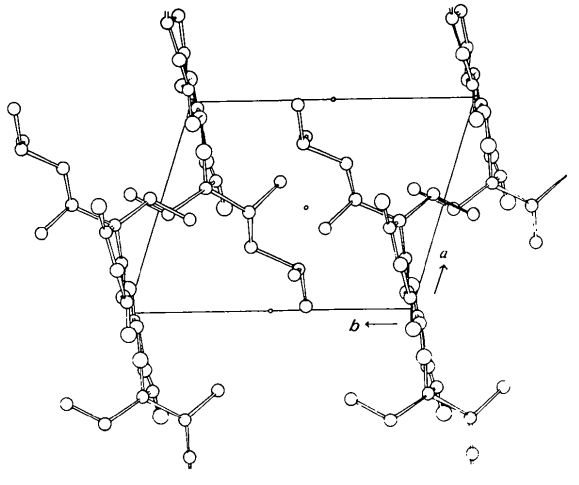


Fig.4. Crystal structure viewed down the *c* axis.

Table 7. *Intermolecular distances*

All intermolecular distances between non-hydrogen atoms within 0·2 Å of the sum of the appropriate van der Waals radii (Pauling, 1960) are listed. Parameters for atoms not in the crystal asymmetric unit (as listed in Table 3) may be derived from those in Table 3 by operations specified by the subscripts *i*, *j*, *k*, *l*. The first three digits code a lattice translation of $(i-5)\mathbf{a}+(j-5)\mathbf{b}+(k-5)\mathbf{c}$. The last digit denotes one of the two following operations: $l=1$: x, y, z; $l=2$: $\bar{x}, \bar{y}, \bar{z}$. E.s.d.'s given in parentheses refer to the least significant figures in tabulated values.

C(8)···O(2)$_{6552}$	3·485 (9) Å
C(8)···O(4)$_{6662}$	3·509 (9)
C(7)···O(6)$_{6552}$	3·452 (7)
C(7)···O(2)$_{6551}$	3·323 (8)
C(14)···C(14)$_{7662}$	3·97 (2)
C(14)···C(2)$_{6651}$	3·74 (1)
C(14)···O(2)$_{6651}$	3·56 (1)
C(12)···O(2)$_{6651}$	3·50 (1)

To arrive at more quantitative and less intuitive conclusions it will be necessary to calculate detailed potential functions and to analyse the crystal structures of these and related compounds at low temperature.

The study of the crystal structures of the barbituric acid derivatives which have a strongly convulsive activity *in vivo* may shed light on the similarity in the detailed architecture of convulsive barbituric acid derivatives. The comparison of conformational characteristics with those found in a number of anticonvulsiva, investigated by Camerman & Camerman (1971), as suggested by Sitsen (1972), might introduce new and interesting features in the relationship between structure and drug action of barbituric acid derivatives.

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Polymorphisme du Radical Libre Nitroxyde Tétraméthyl-2,2,6,6 Piperidinone-4 Oxyl-1. Affinement de la Structure de la Phase Orthorhombique

PAR D. BORDEAUX ET J. LAJZÉROWICZ

Laboratoire de Spectrométrie Physique (associé au CNRS), Université Scientifique et Médicale, B.P. n° 53, 38041 Grenoble Cedex, France

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Three crystalline forms have been found for the title compound, $C_9H_{16}NO_2$: orthorhombic, monoclinic and hexagonal. The orthorhombic structure as determined by Shibaeva, Atovmian, Nejgauz, Novakoskaia & Ginzberg [*Zh. Strukt. Khim.* (1972). **13**, 887] has been refined using data from a four-circle diffractometer (space group $Pca2_1$; $a=7{\cdot}924$ (3), $b=11{\cdot}859$ (5), $c=10{\cdot}386$ (5) Å; $Z=4$; $R=0{\cdot}06$). The piperidinone ring has a symmetric twist conformation.

Introduction

La structure de la phase orthorhombique du radical nitroxyde tétraméthyl-2,2,6,6 piperidinone-4 oxyl-1 (Fig. 1), a été déterminée, à partir de clichés photographiques par Shibaeva, Atovmian, Nejgauz, Novakoskaia & Ginzburg (1972) (dans la suite nous désignerons ce travail par la référence SANNG et nous appellerons TANO ce composé).

Nous avons identifié trois formes cristallines du TANO et affiné la phase orthorhombique afin de connaître avec plus de précision la forme croisée du cycle et la géométrie du groupement $\begin{matrix}C\\C\end{matrix}\!\!>\!\!NO$. Ce travail entre dans le cadre des études de structures et de certaines propriétés physiques que nous effectuons sur les radicaux libres nitroxydes (Lajzérowicz-Bonneteau, 1972).

Partie expérimentale

Le composé a été synthétisé au laboratoire de chimie organique du Centre Nucléaire de Grenoble (Brière, Lemaire & Rassat, 1965). Trois formes ont été identifiées sur monocristaux: monoclinique, orthorhombique et hexagonale. Une analyse chimique précise conduit à la même formule pour ces trois formes, leurs spectres infrarouge sont identiques. Les caractéristiques des mailles cristallines obtenues à partir de clichés de Weissenberg sont données dans le Tableau 1. Il existe une relation entre les mailles orthorhombique et hexagonale puisque:

$$|\mathbf{a}'| = |3\mathbf{c}_{ort} + 2\mathbf{a}_{ort}| \simeq a_{hex}$$
$$|\mathbf{c}'| = |3\mathbf{c}_{ort} - 2\mathbf{a}_{ort}| \simeq b_{hex}$$
$$(\mathbf{a}', \mathbf{c}') \simeq 120°$$
$$b_{ort} \simeq 2c_{hex}\,.$$

Une relation existe également entre la maille monoclinique et la maille hexagonale, deux des paramètres étant égaux. Les cristaux hexagonaux se présentent sous forme d'aiguilles très fines accolées les unes aux autres, et il est difficile d'obtenir des clichés corrects; des extinctions supplémentaires aux extinctions classiques des groupes hexagonaux sont observées.

Nous avons quelques difficultés à préciser les domaines d'existence de ces trois formes. Les cristaux orthorhombiques obtenus à partir de solutions dans différents solvants (acétone, chloroforme) ou par sublimation sont stables, leur température de fusion est 38 °C. Les cristaux monocliniques obtenus par sublimation à basse température (10 °C) par recristallisation dans d'autres solvants (eau, hexane, éther) ou par fusion de la forme hexagonale, se transforment assez rapidement en un mélange de cristaux orthorhombiques et hexagonaux. Cette transformation se produit aussi