bonded chains with H(5) atoms in such positions are not observed.

A twist of the O(5)–H(5) bond in the opposite sense, *i.e.* away from the line of centres O(5)---O(5'), would weaken the hydrogen bond O(5)–H(5)---O(5'), but would strengthen the attractive interaction O(5)–H(5)---O(*W*) with the water oxygen atom at the bottom right of Fig. 2, by decreasing the H(5)---O(*W*) distance from 2·5 Å and increasing the angle at H(5) from 117°. The water molecule would then become involved in four, rather than three, hydrogen bonds, and these would be tetrahedrally disposed.

It appears that, within the observed range of twist of the O(5)–H(5) bond about the C(5)–O(5) bond, no one position is particularly favourable for intermolecular hydrogen bonding.

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The Crystal Structures of Two Polymorphs of 5,5'-Diethylbarbituric Acid (Barbital)

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Crystal morphological, X-ray and infrared spectral data are presented for the identification of three (I, II and IV) of the four reported polymorphs of 5,5'-diethylbarbituric acid (barbital). Three-dimensional X-ray crystal structure determinations of barbital I and II are reported. The crystal data are: I (trigonal, m.p. 190°C) $a = 26·921$, $c = 6·828$ Å (hexagonal lattice), space group $R\bar{3}$, with 18 molecules per cell; II (monoclinic, m.p. 183°C) $a = 7·120$, $b = 14·162$, $c = 9·810$ Å, $\beta = 89°14'$, space group $C2/c$ with 4 molecules per cell. For barbital I X-ray intensity data were collected from two different crystals and two independent structure determinations (I*a*, I*b*) were carried out. These agreed within experimental error. The X-ray intensity data (1526, 1617 and 840 reflections in I*a*, I*b* and II) were collected with a four-circle automatic diffractometer. Refinement of atomic positional and anisotropic thermal parameters was by full-matrix least-squares, resulting in final R values of 0·057, 0·041 and 0·062 for I*a*, I*b*, II, excluding the unobservably weak reflections. All hydrogen atoms were found. The molecule is in the 2·4,6-trioxo tautomeric form in both I and II. The molecular point symmetry is approximately 2 *mm*, but with distortions in the barbiturate ring and hydrocarbon chain which are most marked in I. Molecules are linked by NH···OC hydrogen bonds to form ribbons in which the barbiturate rings are almost coplanar, although the mode of hydrogen bonding is different in I and II. Van der Waals interactions are of greater importance in the stable form I. Variations of 0·014 Å in C–N ring bond lengths are near the limit of experimental error, but appear to be systematic and may be related to hydrogen bonding effects. The atomic thermal vibrational behaviour is strikingly similar in I and II.

Introduction

Since 1903 when Fischer and von Mering discovered the hypnotic action of 5,5'-diethylbarbituric acid (also known as barbital, veronal, or diemal, Fig. 1†), the relationship between chemical structure and drug action

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† The atomic nomenclature in the present work was chosen to conform as closely as possible to the chemical nomenclature. A twofold rotation axis of crystallographic symmetry passes through atoms O(2), C(2) and C(5) in the case of barbital II.

of barbiturates has been widely studied. Doran (1959) has reviewed the structures, physical and chemical properties, and pharmacological activity of several hundred different barbiturates.

In order to possess effective hypnotic activity, a barbiturate must be disubstituted at the C(5) ring position either by ethyl or by larger nonpolar groups, e.g. allyl, isoamyl, phenyl or cyclohexyl groups. Thus barbital is chemically the simplest hypnotic barbiturate. Hypnotic activity generally increases up to a total of about six to

Fig. 1. Molecular formula of barbital.

ten carbon atoms in the C(5) substituents. A second requirement for hypnotic action is that the barbiturate ring should have at least a minimum capability for hydrogen bonding, i.e. no more than one of the two ring imide groups may be methylated, and no more than two of the three carbonyl oxygen atoms may be replaced by sulfur.

In about 1900, Meyer & Overton correlated increased activity of anaesthetic agents with their increased lipid solubility. According to this theory, an anaesthetic (or barbiturate) with lipid solubility may pass from an aqueous biological medium and become associated with the lipids or lipoproteins of biological membranes, thus disrupting the normal metabolic process of the cell. Recently, progress has been made by Chance & Hollunger (1963) in determining the role of barbiturates in inhibiting the complex enzymatic processes of oxidative phosphorylation. It is perhaps significant that the enzymes concerned are believed to be either embedded in, or held in close proximity to, a mitochondrial membrane. The importance of a newly discovered specific hydrogen bonding of barbiturates to adenine derivatives has been stressed (Kyogoku, Lord & Rich, 1968; Kim & Rich, 1968). Although the detailed mechanism of barbiturate drug action at the molecular level is not understood, this must involve intermolecular interactions between barbiturate molecules and the drug acceptor site.

As a result of the chemical nature of the drug active barbiturates, these molecules are expected to exhibit
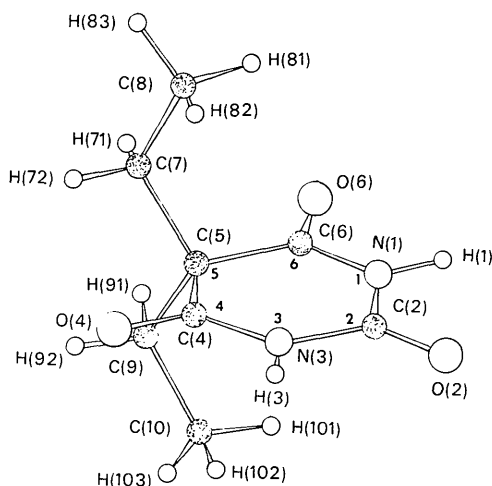
Table 1. *Crystal data for the polymorphs of barbital*

The lattice parameters are the result of the present work. These are in agreement with those previously reported for forms I (Ghose, Jeffrey, Craven & Warwicker, 1960) and II (Bertinotti, Bonamico, Braibanti, Coppola & Giacomello, 1959).

	I	II	III	IV
m.p.	190°C	183°C	181°C	176°C
Crystal system	Trigonal	Monoclinic	Monoclinic	Monoclinic*
Habit	Rhombohedral needles	Prisms	Needles	Twinned rectangular plates or flat pyramids
Space group†	$R\bar{3}$	$C2/c$	?	$P2_1$
a	26.921 ± 0.006 Å	7.120 ± 0.005 Å		12.585 ± 0.008 Å
b		14.162 ± 0.010 Å		22.083 ± 0.010 Å
c	6.828 ± 0.009 Å	9.810 ± 0.007 Å		6.788 ± 0.009 Å
β		$89°14 \pm 2'$		$90°55 \pm 2'$
Z	18	4		8
D_m	1.287 ± 0.007 g.cm^{-3}	1.238 ± 0.007 g.cm^{-3}		1.296 ± 0.007 g.cm^{-3}
D_x	1.284 g.cm^{-3}	1.242 g.cm^{-3}		1.303 g.cm^{-3}
Cleavage plane	$(10\bar{1}0)$	$(\bar{1}01)$		(010)

* Previously reported as triclinic (Huang, 1951; Köfler, 1948) and incorrectly as orthorhombic (Ghose, Jeffrey, Craven & Warwicker, 1960).
† By crystal structure determination.

Table 2. *Intensity data for barbital* I *and* II

	Barbital I		Barbital II
	1st data set	2nd data set	
Crystal dimensions (mm) (c given first)	0·3, 0·1, 0·1	0·46, 0·24, 0·16	0·3, 0·2, 0·2
Crystal axis parallel to diffractometer φ-axis	c	c	b
Number of independent reflections	1526	1617	840
Number of unobserved reflections	495	220	149
R value, including unobserved reflections	8·4%	4·7%	10·2%
R value, excluding unobserved reflections	5·7%	4·1%	5·2%
Standard deviation in observation of unit weight	0·6139	0·5141	0·7221

Table 3. *Observed and calculated structure factors*

Successive columns list k, $10|F_{obs}|$ and $10F_{calc}$. Reflections marked with an asterisk are either unobservably weak or very strong and considered to be affected by extinction. The latter were given zero weight in the least-squares refinement. The Table begins with the second data set for form I and continues with the data for form II at the top of the 11th column.

Table 3 (cont.)

considerable versatility in their intermolecular associations. Hydrogen bonding, van der Waals interactions between flat pyrimidine rings or between nonpolar hydrocarbon groups, dipole–dipole interactions between polar carbonyl groups and possibly charge-transfer interactions may be involved. Indeed, such versatility may eventually prove to be highly significant in determining the role of barbiturate molecules in their drug action.

We are now reporting the first results of a program of crystal structure determinations of the drug-active barbiturates, in which our principal objective is the study of recurring features in the various modes of barbiturate molecular association. We hope to establish features which, although based on homomolecular assemblies, may, because of the presence of both polar and nonpolar moieties in the barbiturate molecule, be relevant to the likely structural relationships at heteromolecular barbiturate drug-acceptor sites.

Fig.2. Infrared spectra for barbital I, II and IV.

It is of interest that drug-active barbiturates are commonly polymorphous in their crystal structures and in the solid state readily form solutions and binary compounds with each other (Brandstätter-Kuhnert & Vlachopoulos, 1967; Cleverley & Williams, 1959). The molecular basis for polymorphism may depend on conformational variations when the C(5) substituents are flexible, but the results so far obtained for barbital and amobarbital (Craven & Vizzini, 1969) indicate that the major factor is in the interplay among the various types of molecular interaction, e.g. in barbital, van der Waals interactions appear to be more effective in polymorph I than in II. The crystal structure of polymorph II is dominated by hydrogen bonding.

Characterization of the polymorphs of barbital

Four polymorphs (I,II,III,IV) of barbital have been characterized by Köfler (1948) and Huang (1951) on the basis of crystal morphology, melting points and X-ray powder data. Cleverley & Williams (1959) have reported the infrared spectra of forms I, II and IV. More recently, Brandstätter-Kuhnert & Aepkers (1962) reported the existence of six (not four) polymorphs of barbital on the basis of thermal analyses of binary barbiturate systems. However, forms V and VI have not been isolated as single crystals. The melting points for these forms were obtained by extrapolation of the melting point curves for barbiturate solid solutions as a function of concentration.

Köfler and Huang also describe techniques for obtaining the various polymorphs both by sublimation and from solution. From studies on two-component systems, such as barbital–methylacetanilide, Köfler (1948) observed only one reversible phase transformation for barbital (III⇌IV at 135°C). Above 135°C, form I is most stable, followed by II, III, IV, in the order of decreasing melting points, while below 135°C, the order is I, II, IV, III.

Table 4. *Atomic parameters with e.s.d.'s*

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

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

The e.s.d.'s given in brackets refer to the least significant figures in the parameter values.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Barbital I (parameters obtained from second data set)									
N(1)	0·10452 (7)	0·48245 (7)	0·7215 (2)	0·00161 (3)	0·00207 (3)	0·0093 (3)	0·00120 (3)	−0·00008 (7)	−0·00006 (7)
H(1)	0·1032 (11)	0·4817 (12)	0·861 (4)						
C(2)	0·06321 (7)	0·48923 (7)	0·6293 (2)	0·00145 (3)	0·00147 (3)	0·0105 (4)	0·00083 (3)	0·00001 (8)	−0·00005 (8)
O(2)	0·02548 (6)	0·49129 (6)	0·7190 (2)	0·00162 (2)	0·00245 (3)	0·0133 (3)	0·00134 (3)	0·00056 (7)	0·00000 (7)
N(3)	0·06649 (6)	0·49317 (6)	0·4280 (2)	0·00144 (3)	0·00167 (3)	0·0099 (3)	0·00101 (3)	−0·00020 (7)	−0·00019 (7)
H(3)	0·0410 (12)	0·4991 (11)	0·368 (4)						
C(4)	0·10727 (8)	0·49143 (7)	0·3135 (2)	0·00159 (3)	0·00141 (3)	0·0103 (4)	0·00087 (3)	0·00010 (8)	−0·00002 (8)
O(4)	0·10697 (6)	0·49804 (6)	0·1382 (2)	0·00240 (3)	0·00254 (3)	0·0094 (3)	0·00162 (3)	0·00045 (7)	0·00041 (7)
C(5)	0·15065 (8)	0·47882 (8)	0·4109 (3)	0·00157 (4)	0·00189 (4)	0·0128 (4)	0·00114 (3)	−0·00047 (9)	−0·00009 (9)
C(6)	0·14719 (7)	0·47635 (8)	0·6324 (3)	0·00161 (4)	0·00188 (4)	0·0128 (4)	0·00111 (3)	−0·00028 (9)	−0·00020 (9)
O(6)	0·18018 (7)	0·46900 (8)	0·7316 (2)	0·00231 (5)	0·00370 (5)	0·0172 (4)	0·00222 (4)	−0·00111 (9)	−0·00011 (10)
C(7)	0·21165 (10)	0·52430 (11)	0·3486 (4)	0·00171 (4)	0·00269 (6)	0·0227 (6)	0·00119 (4)	−0·00135 (12)	0·00070 (13)
H(71)	0·2128 (13)	0·5273 (14)	0·210 (5)						
H(72)	0·2385 (13)	0·5089 (14)	0·385 (4)						
C(8)	0·23168 (12)	0·58369 (12)	0·4289 (5)	0·00208 (6)	0·00213 (5)	0·0407 (9)	0·00074 (5)	−0·00073 (17)	0·00131 (17)
H(81)	0·2032 (15)	0·5962 (15)	0·580 (6)						
H(82)	0·2354 (15)	0·5842 (15)	0·580 (6)						
H(83)	0·2743 (15)	0·6095 (14)	0·382 (6)						
C(9)	0·13795 (11)	0·41917 (10)	0·3346 (3)	0·00265 (5)	0·00218 (5)	0·0182 (5)	0·00173 (4)	−0·00026 (12)	−0·00094 (12)
H(91)	0·1715 (14)	0·4163 (13)	0·389 (4)						
H(92)	0·1417 (13)	0·4237 (13)	0·186 (4)						
C(10)	0·08089 (14)	0·36998 (11)	0·3947 (5)	0·00135 (7)	0·00175 (5)	0·0404 (9)	0·00133 (5)	−0·00031 (20)	−0·00072 (17)
H(101)	0·0734 (17)	0·3672 (15)	0·540 (6)						
H(102)	0·0466 (18)	0·3757 (15)	0·367 (6)						
H(103)	0·0763 (16)	0·3347 (15)	0·353 (6)						
Barbital II									
C(2)	0	0·3228 (3)	0·25	0·0134 (6)	0·00323 (18)	0·0067 (4)	0	−0·0023 (4)	0
O(2)	0	0·4073 (2)	0·25	0·0238 (7)	0·00235 (14)	0·0120 (4)	0	−0·0066 (4)	0
N(3)	−0·0971 (3)	0·2506 (1)	0·1551 (2)	0·0165 (5)	0·00284 (12)	0·0066 (2)	0·0005 (2)	−0·0053 (3)	0·00024 (12)
H(3)	−0·160 (5)	0·300 (2)	0·096 (3)						
C(4)	−0·1040 (3)	0·1744 (2)	0·1456 (2)	0·0130 (4)	0·00311 (13)	0·0059 (3)	0·0000 (2)	−0·0029 (3)	−0·00026 (14)
O(4)	−0·1925 (3)	0·1371 (1)	0·0543 (2)	0·0262 (5)	0·00341 (11)	0·0087 (2)	0·0003 (2)	−0·0100 (3)	−0·00072 (11)
C(5)	0	0·1160 (2)	0·25	0·0157 (7)	0·00221 (15)	0·0054 (3)	0	−0·0028 (4)	0
C(7)	0·1441 (4)	0·0536 (2)	0·1736 (3)	0·0216 (6)	0·00418 (16)	0·0082 (3)	0·0030 (3)	−0·0031 (4)	−0·00086 (17)
H(71)	0·210 (5)	0·012 (3)	0·242 (4)						
H(72)	−0·063 (5)	−0·003 (3)	0·119 (4)						
C(8)	0·2882 (6)	0·1066 (3)	0·0878 (4)	0·0247 (9)	0·00878 (29)	0·0152 (5)	0·0038 (4)	0·0063 (6)	−0·00052 (30)
H(81)	0·352 (7)	0·152 (4)	0·144 (5)						
H(82)	0·208 (6)	0·144 (3)	0·011 (5)						
H(83)	0·383 (6)	0·064 (3)	0·045 (5)						

Previous single-crystal X-ray studies have been concerned only with forms I, II and IV. The crystal structure of II has been determined in projection (Bertinotti, Bonamico, Braibanti, Coppola & Giacomello, 1959).
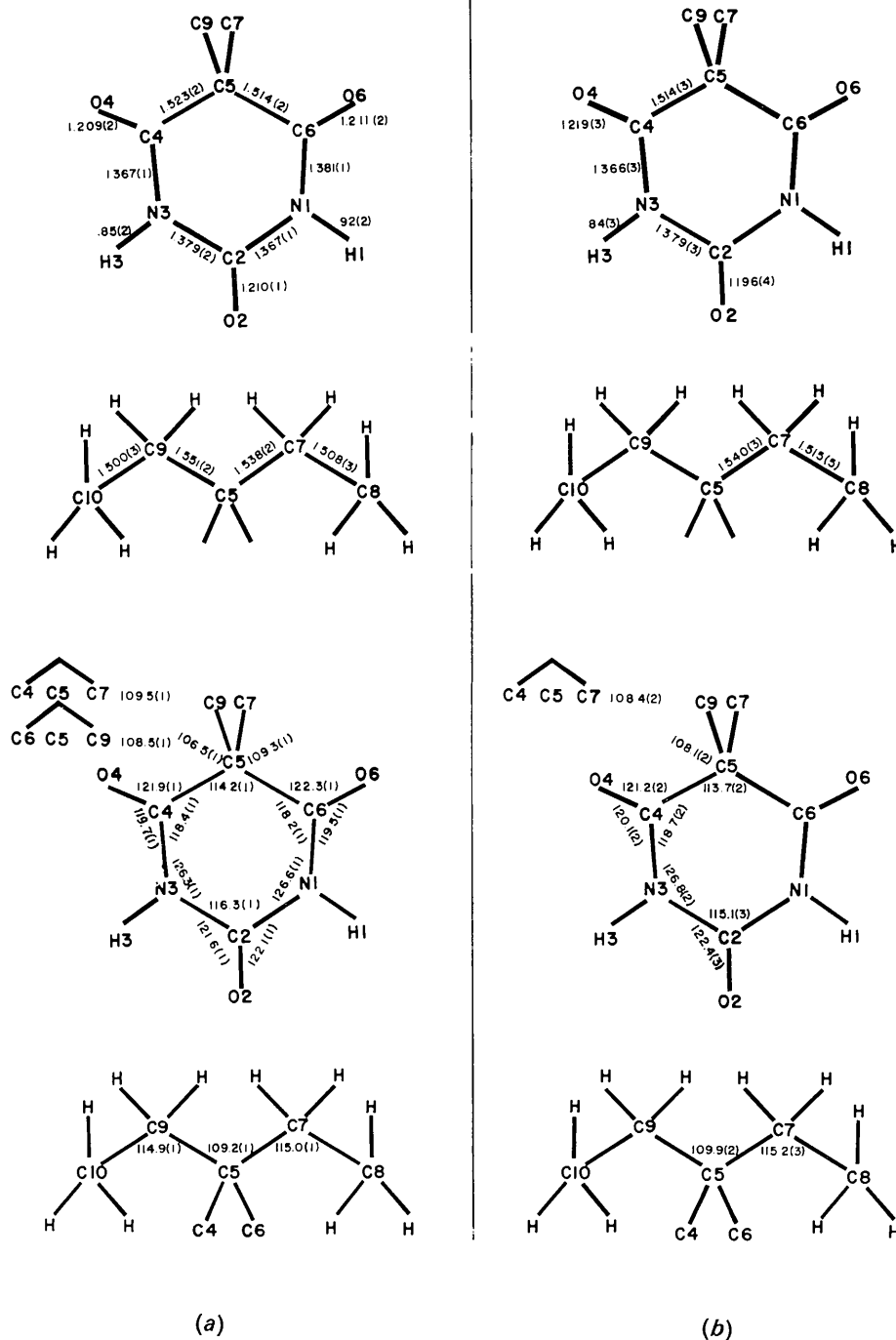

(a)

(b)

Fig. 3. Bond angles and bond lengths for barbital I and II. Bond lengths are in Å units, and are not corrected for the effect of anisotropic thermal motion. The e.s.d.'s in bond lengths and angles are given in brackets, and correspond to the least significant digits of the parameters involved. (a) The average values for the two independent structure determinations for barbital I. (b) Barbital II.

Approximate cell data and space groups have been reported for forms I and IV (Ghose, Jeffrey, Craven & Warwicker, 1960).

The present crystal data (Table 1) and infrared spectra (Fig. 2) for forms I and II agree with those previously reported. However, there are inconsistencies concerning form IV, which we assume to be the same 'rectangular' plates described by Köfler (1948) and subsequent workers. In Fig. 2, the infrared spectrum of IV is now shown to be different from that of II, whereas Cleverley & Williams (1959) found these spectra to be identical. Also, single-crystal X-ray data for form IV now show this to be monoclinic rather than triclinic, as previously reported by Huang (1951) and Köfler (1948) on crystal morphological evidence. It should be noted that form IV can be obtained either as 'rectangular' plates which are in fact monoclinic, but twinned on the well-developed (010) face, or occasionally as flattened-pyramidal crystals with morphological symmetry 2, (pseudo $m2m$). Only with the latter single crystals were the X-ray crystal data unambiguously determined for

this polymorph. Hence, the orthorhombic crystal data for form IV previously reported by Ghose, Jeffrey, Craven & Warwicker (1960) are incorrect, since these were obtained by the use of the pseudo-orthorhombic twinned crystals. Attempts to obtain form III, either from solution or by sublimation, were unsuccessful.

Experimental

Single crystals of polymorphs I, II and IV were obtained from the same ethanol solution by slow evaporation at room temperature. The infrared spectra (Fig. 2) were recorded with a Perkin-Elmer Model 137 spectrometer. Crystals were individually sorted according to their morphology, and for each polymorph a sample was prepared as a Nujol mull confined between rocksalt plates. Crystal densities were measured at room temperature by the flotation method. Lattice parameters (Table 1) and X-ray intensity data (Table 2) were measured with a Picker four-circle automatic diffractometer and Cu $K\alpha$ radiation. Intensity measurements

Table 5(a). *Interatomic distances and angles in barbital* I *determined from the second data set*

Atoms not in the crystal chemical unit (*i.e.* not listed in Table 4) are specified by a subscript. The four-digit subscript denotes how the atomic parameters can be derived from the corresponding atom in the crystal chemical unit. The first three digits code a lattice translation, *e.g.* 564 means a translation of $(5-5)a+(6-5)b+(4-5)c$ or $(b-c)$. The fourth digit refers to one of the following symmetry operations:

1: x, y, z
2: $\bar{y}, (x-y), z$
3: $\frac{1}{3}-y, \frac{2}{3}+(x-y), \frac{1}{3}+z$
4: $\frac{2}{3}+(y-x), \frac{1}{3}+(x-y), \frac{1}{3}+z$
5: $\frac{1}{3}+(y-x), \frac{1}{3}-x, \frac{1}{3}+z$
6: $\frac{2}{3}+y, \frac{1}{3}+(y-x), \frac{1}{3}-z$
7: $\frac{2}{3}+(x-y), \frac{1}{3}+y, \frac{1}{3}-z$

Interatomic distances and angles are expressed as follows:
1·379 (3) Å means a distance of 1·379 Å with an e.s.d. of 0·003 Å.
120·1 (2)° means an angle of 120·1° with an e.s.d. of 0·2°.

(i) Bond distances

Column (1) lists uncorrected distances,
    (2) lists distances with corrections based on the rigid body mode of molecular thermal motion.

	(1)	(2)
C(2)—O(2)	1·211 (2) Å	1·212 Å
C(2)—N(1)	1·368 (2)	1·372
N(1)—H(1)	0·95 (3)	
N(1)—C(6)	1·381 (2)	1·384
N(3)—H(3)	0·88 (3)	
C(2)—N(3)	1·378 (3)	1·384
C(6)—O(6)	1·210 (2)	1·212
C(6)—C(5)	1·514 (3)	1·521
C(5)—C(4)	1·523 (3)	1·528
C(4)—N(3)	1·370	1·371
C(4)—O(4)	1·211 (3)	1·213
C(5)—C(7)	1·538 (3)	1·545
C(5)—C(9)	1·555 (3)	1·562
C(7)—H(71)	0·96 (3)	
C(7)—H(72)	1·02 (3)	
C(9)—H(91)	1·01 (3)	
C(9)—H(92)	1·02 (3)	
C(7)—C(8)	1·512 (4)	1·517
C(9)—C(10)	1·499 (4)	1·504
C(8)—H(81)	1·01 (4)	
C(8)—H(82)	1·03 (4)	
C(8)—H(83)	1·04 (4)	
C(10)–H(101)	0·99 (4)	
C(10)–H(102)	1·01 (4)	
C(10)–H(103)	0·95 (4)	

Table 5(a) (cont.)

(ii) Bond angles

C(2)——N(3)—C(4)	126·3 (2)°
N(3)—C(2)—N(1)	116·4 (2)
N(3)—C(2)—O(2)	121·6 (2)
C(2)——N(3)—H(3)	116 (2)
H(3)—N(3)—C(4)	117 (2)
N(1)—C(2)—O(2)	122·0 (2)
C(2)——N(1)—H(1)	116 (2)
C(2)——N(1)—C(6)	126·4 (2)
C(6)——N(1)—H(1)	118 (2)
N(1)——C(6)—O(6)	119·7 (2)
N(1)——C(6)—C(5)	118·2 (2)
C(5)——C(6)—O(6)	122·2 (2)
C(6)——C(5)—C(4)	114·1 (2)
C(6)——C(5)—C(9)	108·2 (2)
C(6)——C(5)—C(7)	109·2 (2)
C(5)——C(4)—N(3)	118·4 (2)
C(5)——C(4)—O(4)	121·8 (2)
C(4)——C(5)—C(7)	109·5 (2)
N(3)——C(4)—O(4)	119·8 (2)
C(4)——C(5)—C(9)	106·6 (2)
C(9)——C(5)—C(7)	109·0 (2)
C(5)——C(7)—C(8)	114·6 (2)
C(5)——C(9)—C(10)	114·8 (2)
H(71)—C(7)—H(72)	107 (3)
H(81)—C(8)—H(82)	110 (3)
H(82)—C(8)—H(83)	103 (3)
H(83)—C(8)—H(81)	117 (3)
H(91)—C(9)—H(92)	110 (2)
H(101)-C(10)-H(102)	92 (3)
H(102)-C(10)-H(103)	114 (3)
H(103)-C(10)-H(101)	107 (3)

(iii) Hydrogen-bond distances and angles

N(3)···O(2)$_{4552}$	2·888 (4) Å	N(1)···O(4)$_{5561}$-C(4)$_{5561}$	163·4 (1)°
H(3)···O(2)$_{4552}$	2·02 (4)	H(1)···O(4)$_{5561}$-C(4)$_{5561}$	160 (1)
		N(1)—H(1)····O(4)$_{5561}$	173 (1)
N(1)···O(4)$_{5561}$	2·871 (4)	N(3)···O(2)$_{4552}$-C(2)$_{4552}$	129·2 (2)
H(1)···O(4)$_{5561}$	1·94 (3)	H(3)···O(2)$_{4552}$-C(2)$_{4552}$	132·1 (7)
		N(3)—H(3)····O(2)$_{4552}$	170 (2)
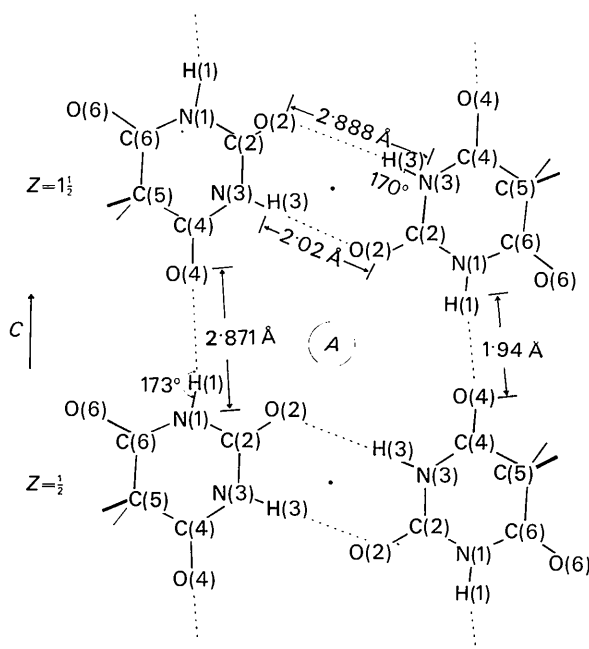
Fig. 4. The hydrogen bonding in barbital I.

were made by scanning reflections in the θ:2θ mode at a rate of 2° min⁻¹ with scans of 2° and a background count of 20 seconds at each of the scan limits. Data were collected for which 2θ was less than 130° (sin θ/λ <0·59 Å⁻¹). An integrated intensity, I, was assumed to be unobservably weak if I was less than $1\cdot5\sigma(I)$, where $\sigma(I)$ is the estimated standard deviation in I as determined from counting statistics. These reflections were assigned an intensity of $0\cdot5\sigma(I)$. X-ray absorption corrections were neglected.

For form I, two sets of intensity data were obtained, each from a different crystal, and independent structure determinations were carried out (Table 2).

Determination of the crystal structures

(a) Barbital I

The observed Laue symmetry, $(\overline{3})$, and the systematic spectral absences for form I indicated that the space group was either $R3$ or $R\overline{3}$. The space group was initially assumed to be $R\overline{3}$, which was subsequently confirmed by detailed structure determination.

In the three-dimensional Patterson function for the space group $R\overline{3}$ the Harker vectors at $w=0$ arising from

Table 5(a) (cont.)

(iv) Other close intermolecular approaches

The atom listed at the left of each pair belongs to the crystal chemical unit (i.e. has the parameters listed in Table 4). Intermolecular distances marked v lie within 0·2 Å of the sum of the appropriate van der Waals radii (Pauling, 1960).

C(2)·····O(6)$_{5556}$	3·115 (4)v Å
C(10)····C(10)$_{4555}$	3·981 (4)v
····H(102)$_{4555}$	3·09 (4)v
····O(4)$_{4555}$	3·635 (4)
····C(4)$_{4555}$	3·937 (4)v
····O(2)$_{4554}$	3·539 (4)v
H(101)···H(102)$_{4555}$	2·41 (6)v
···C(10)$_{4555}$	2·81 (4)v
H(102)···H(102)$_{5543}$	3·07 (5)
···H(103)$_{5543}$	3·04 (6)
H(103)···O(4)$_{4555}$	2·81 (4)
C(8)·····C(8)$_{5556}$	4·120 (7)v
·····C(8)$_{4556}$	4·369 (7)
·····C(7)$_{4556}$	3·879 (5)v
·····H(71)$_{4557}$	3·17 (3)v
C(7)·····C(7)$_{5557}$	4·364 (3)
·····H(81)$_{5557}$	3·16 (4)v
H(71)····H(81)$_{5557}$	2·37 (4)v
H(72)····O(4)$_{5557}$	2·83 (3)
H(81)····C(7)$_{4556}$	3·16 (4)v
····H(71)$_{4556}$	2·37 (5)
····H(72)$_{4556}$	3·15 (5)
O(4)·····H(72)$_{4556}$	2·83 (3)
·····H(91)$_{4556}$	2·88 (3)
·····C(2)$_{5541}$	3·639 (5)

Table 5(b). *Interatomic distances and angles in barbital* II

Atomic subscripts are as above, except that the fourth digit specifies one of the following symmetry operations:

1	x, y, z	5	$\frac{1}{2}+x, \frac{1}{2}+y, z$
2	$-x, y, \frac{1}{2}-z$	6	$\frac{1}{2}-x, \frac{1}{2}+y, -z$
3	$-x, -y, -z$	7	$\frac{1}{2}+x, \frac{1}{2}-y, \frac{1}{2}+z$
4	$x, -y, \frac{1}{2}+z$	8	$\frac{1}{2}-x, \frac{1}{2}+y, \frac{1}{2}-z$

Thus the atom C(4)$_{5552}$ has fractional coordinates (0·10398, 0·17440, 0·35437) and is related to C(4) by the crystallographic (and molecular) twofold rotation axis at ($x=0$, $z=\frac{1}{4}$).

(i) Bond distances
Column (1) lists uncorrected distances,
(2) lists distances with corrections based on the rigid body mode of molecular thermal motion.

	(1)	(2)
C(2)–O(2)	1·196 (4) Å	1·197 Å
C(2)–N(3)	1·379 (3)	1·384
N(3)–H(3)	0·84 (3)	
N(3)–C(4)	1·366 (3)	1·370
C(4)–O(4)	1·219 (3)	1·222
C(4)–C(5)	1·514 (3)	1·520
C(5)–C(7)	1·540 (3)	1·548
C(7)–H(71)	1·01 (4)	
C(7)–H(72)	1·07 (4)	
C(7)–C(8)	1·515 (5)	1·521
C(8)–H(81)	0·96 (5)	
C(8)–H(82)	1·09 (5)	
C(8)–H(83)	0·99 (5)	

(ii) Bond angles

N(3)–C(2)–N(3)$_{5552}$	115·1 (3)°	C(5)—C(7)–H(71)	109 (2)°
C(2)–N(3)–C(4)	126·8 (3)	C(5)—C(7)–H(72)	106 (2)
N(3)–C(4)–C(5)	118·7 (2)	C(8)—C(7)–H(71)	110 (2)
C(4)–C(5)–C(4)$_{5552}$	113·7 (2)	C(8)—C(7)–H(72)	115 (2)
N(3)–C(2)–O(2)	122·4 (3)	H(71)–C(7)–H(72)	102 (3)
C(2)–N(3)–H(3)	118 (2)	C(7)—C(8)–H(81)	110 (3)
C(4)–N(3)–H(3)	115 (2)	C(7)—C(8)–H(82)	105 (3)
N(3)–C(4)–O(4)	120·1 (2)	C(7)—C(8)–H(83)	112 (3)
C(5)–C(4)–O(4)	121·2 (2)	H(81)–C(8)–H(82)	109 (4)
C(4)–C(5)–C(7)	108·4 (2)	H(81)–C(8)–H(83)	109 (4)
C(4)–C(5)–C(7)$_{5552}$	108·1 (2)	H(82)–C(8)–H(83)	112 (4)
C(7)–C(5)–C(7)$_{5552}$	109·9 (2)		
C(5)–C(7)–C(8)	115·2 (3)		

Table 5(b) (cont.)

(iii) Hydrogen bond distances and angles

N(3)$\cdots$C(4)$_{4556}$	2·867 (3) Å	N(3)—H(3)$\cdots\cdots$O(4)$_{4555}$	117 (3)°
H(3)$\cdots$O(4)$_{4556}$	2·03 (3)	H(3)$\cdots$O(4)$_{4556}$—C(4)$_{4556}$	128 (1)
		N(3)$\cdots$O(4)$_{4556}$—C(4)$_{4556}$	127·2 (2)
		C(4)—N(3)$\cdots\cdots$O(4)$_{4556}$	112·8 (2)

(iv) Other close intermolecular approaches

The atom listed at the left of each pair belongs to the crystal chemical unit (i.e. has parameters listed in Table 4). Since atoms C(2) and O(2) lie on a twofold rotation axis, the close approaches to these atoms occur in symmetry-related pairs, only one of which is listed.

Intermolecular distances marked v lie within 0·2 Å of the sum of the appropriate van der Waals radii (Pauling, 1960).

C(2)$\cdots$C(8)$_{5556}$	3·745 (4)v Å	H(72)$\cdots$H(72)$_{5553}$	2·50 (5)v Å	
$\cdots$H(83)$_{5556}$	3·40 (5)	$\cdots$O(4)$_{5553}$	2·76 (4)v	
$\cdots$H(71)$_{4555}$	3·39 (4)	$\cdots$H(82)$_{5553}$	3·12 (6)	
O(2)$\cdots$C(7)$_{4555}$	3·365 (4)v	C(8)$\cdots$C(2)$_{5556}$	3·745 (5)v	
$\cdots$H(71)$_{4555}$	2·55 (4)v	$\cdots$O(2)$_{5556}$	3·615 (5)	
$\cdots$C(8)$_{4555}$	3·580 (5)v	$\cdots$N(3)$_{5556}$	3·654 (5)	
$\cdots$H(83)$_{4555}$	3·11 (5)	$\cdots$O(2)$_{5455}$	3·580 (5)	
$\cdots$C(8)$_{5556}$	3·615 (5)	$\cdots$C(8)$_{6552}$	4·404 (6)	
$\cdots$H(83)$_{5556}$	3·02 (5)	$\cdots$C(8)$_{5556}$	4·445 (7)	
O(4)$\cdots$C(7)$_{5553}$	3·514 (4)v	H(81)$\cdots$H(81)$_{6552}$	2·97 (7)	
$\cdots$H(72)$_{5553}$	2·76 (4)v			
		H(82)$\cdots$C(2)$_{5556}$	3·30 (5)	
C(7)$\cdots$O(2)$_{5455}$	3·365 (4)v	$\cdots$O(2)$_{5556}$	3·35 (5)	
$\cdots$O(4)$_{5553}$	3·514 (4)v			
$\cdots$C(7)$_{5553}$	4·265 (5)	H(83)$\cdots$C(2)$_{5556}$	3·40 (5)	
		$\cdots$O(2)$_{5455}$	3·11 (5)	
H(71)$\cdots$O(2)$_{5455}$	2·55 (4)v	$\cdots$O(2)$_{5556}$	3·02 (5)	
$\cdots$C(2)$_{5455}$	3·39 (4)	$\cdots$H(83)$_{6553}$	2·61 (7)	
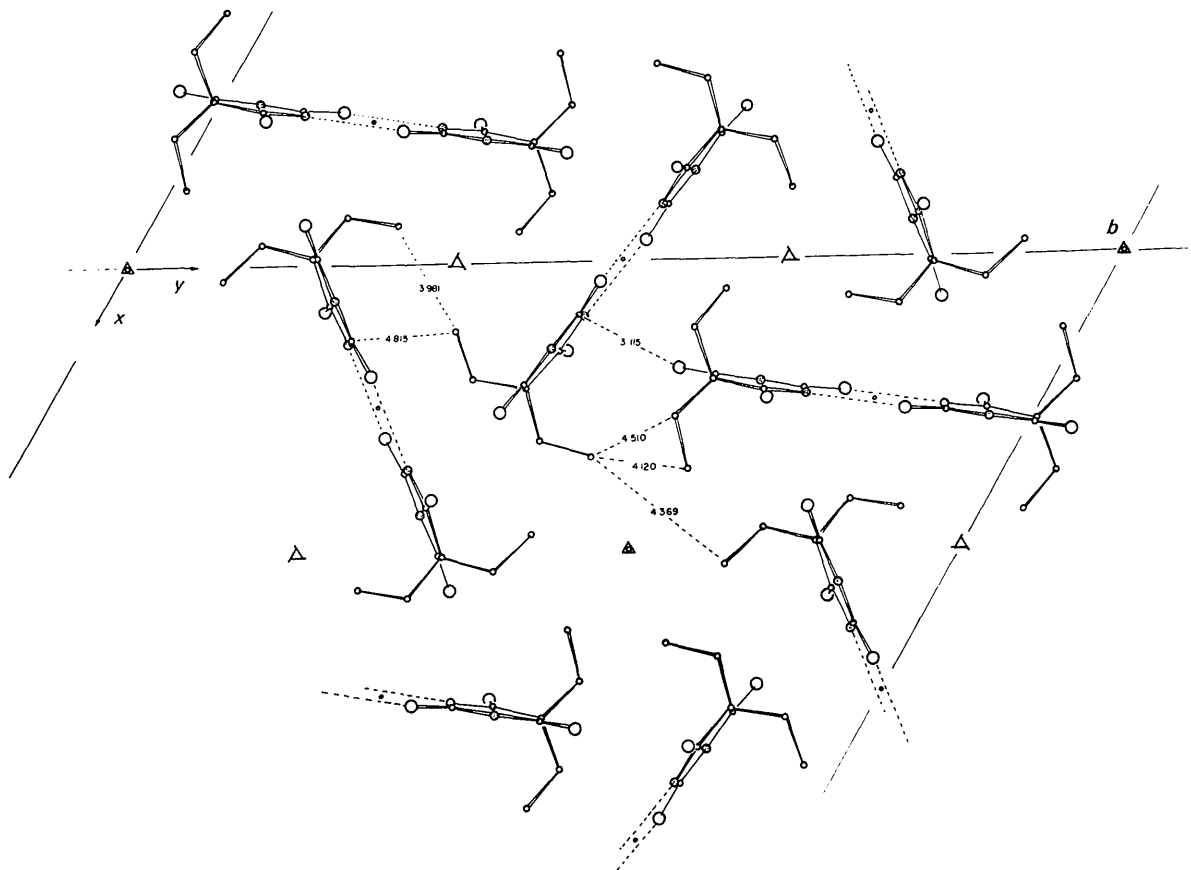
Fig. 5. The crystal structure of barbital I viewed down the c axis.

Table 6. *Least squares planes and dihedral angles*

Barbital I	Barbital II
Plane 1: Least-squares plane through the six pyrimidine ring atoms, all atoms being equally weighted.	The best least-squares plane through the six pyrimidine ring atoms, all atoms being equally weighted.
Plane 2: The plane passing through the atoms N(1), C(2), N(3) and C(4).	The plane parallel to the crystallographic plane (10$\bar{1}$) and passing through the crystallographic twofold rotation axis which contains atoms O(2), C(2), C(5); *i.e.* the idealized plane of an extended ribbon of hydrogen bonded oxypyrimidine rings.
Plane 3: The plane passing through the atoms N(1), C(4), C(5) and C(6).	The plane passing through atoms C(2), C(5) and the α-carbon atom, C(7), of the ethyl group substituents.

(i) Equations of planes

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

Plane	A	B	C	D	A	B	C	D
1	0·13059	0·79136	0·06670	10·95041	−0·80050	0	0·58854	1·43722
2	0·08971	0·81540	0·07226	11·20009	−0·80292	0	0·58526	1·42921
3	0·16654	0·76879	0·06496	10·78306	0·59226	0	0·81360	1·98683

(ii) Distances $d(i)$ of atoms from the ith plane
(The e.s.d.'s given in brackets refer to the least significant digit of the distances quoted.)

	Atoms forming the plane				Atoms not forming the plane		
	$d(1)$	$d(2)$	$d(3)$		$d(1)$	$d(2)$	$d(3)$
Barbital I							
N(1)	0·024 (2) Å	−0·001 (2) Å	−0·009 (3) Å	O(2)	−0·067 (2) Å	0·001 (2) Å	
C(2)	−0·019 (2)	0·002 (2)		O(4)	0·099 (3)	0·059 (3)	
N(3)	−0·015 (2)	−0·002 (2)		O(6)	−0·015 (3)	−0·133 (3)	
C(4)	0·039 (2)	0·001 (2)	0·008 (2)	C(5)		−0·123 (2)	
C(5)	−0·033 (2)		−0·015 (2)	C(6)		−0·076 (2)	
C(6)	0·003 (2)		0·016 (2)	Center at			
				(0,½,½)		0·022	
				C(2)			−0·095 (2) Å
				N(3)			−0·088 (2)
				H(3)	0·03 (3)	0·03 (3)	
				N(3)		0·013 (2)	
Barbital II				C(4)		−0·002 (2)	
C(2)	0			O(4)	−0·028 (2)	−0·018 (2)	
N(3)	0·008 (2)			H(71)			0·83 (4)
C(4)	−0·007 (2)			H(72)			−0·78 (4)
C(5)	0			C(8)			−0·074 (4)
				H(81)			0·64 (5)
				H(82)			−1·03 (5)
				H(83)			−0·01 (5)

(iii) Dihedral angles

Barbital I
(2) ∧ (3)   4·5° fold along the C(4)–N(1) line.

Barbital II (These angles are positive for an anticlockwise twist when viewing the molecule along the axis from atom C(5) to C(2).)

(1) ∧ (2)   0·23°   (1) ∧ (3)   90·5 (2)°   (2) ∧ (3)   90·3 (2)°
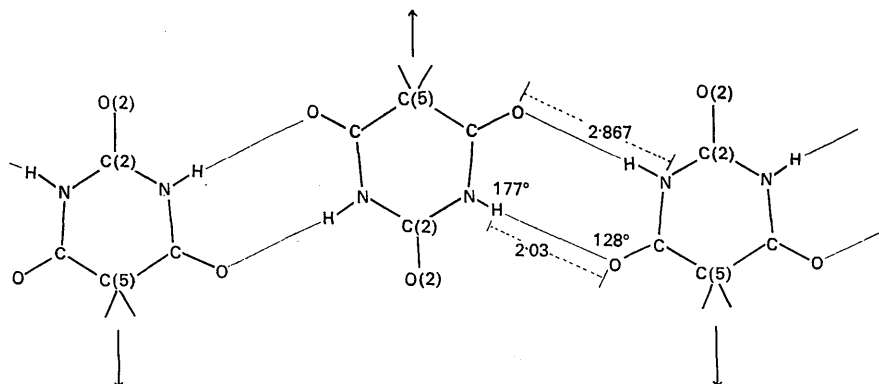

Fig. 6. The hydrogen bonding in barbital II.

Table 7. *Comparison of rigid body vibrational tensors* ($\mathbf{T},\omega$) *for barbital I and II*

The tensors $\mathbf{T}$ and ω are referred to right handed orthogonal molecular axes directed with
  (1) along the vector from atoms C(5) to C(2),
  (2) the normal to the pyrimidine ring on the side of atom C(9),
  (3) in the plane of the pyrimidine ring, approximately parallel to the vector from atoms C(5) to O(6).

The origin is at the molecular center of mass.

the 3̄-axial symmetry constitute the **c** projection of the crystal structure transformed by a rotation of 30° and magnified by a factor of $\sqrt{3}$ (Buerger, 1959). The correct interpretation of the Harker section $w=0$ for barbital I was not immediately obvious, because of the presence of what subsequently proved to be non-Harker peaks. However, after the determination of the orientation of the barbiturate ring from the characteristic pattern of the intra-ring atom vectors near the three-dimensional Patterson origin, the **c** projected structure was recognized in the Harker section $w=0$. The atomic z parameters were obtained from a consideration of the molecular packing and the hydrogen bonding.

(b) Barbital II

Approximate atomic positional parameters were derived by inspection of the three-dimensional sharpened Patterson function. These agreed satisfactorily with the parameters determined by the two-dimensional structure analysis of Bertinotti *et al.* (1959).

The refinement of parameters

The refinement procedure was very similar for both crystal structures. Several cycles of structure factors and three-dimensional Fourier syntheses of the electron density were calculated in order to confirm the initial trial structures. X-ray atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1962). The atomic positional and isotropic thermal parameters were refined by full-matrix least-squares procedures to give R values of 0·15 and 0·11 for forms I and II, respectively. A three-dimensional difference Fourier synthesis revealed all hydrogen atom positions in both crystal structures. Subsequent least-squares refinement involved the positional parameters of all atoms and anisotropic thermal parameters only for non-hydrogen atoms. The hydrogen atoms were assumed to have the same thermal parameters as the atoms to which they were covalently bonded.

The least-squares calculations were based on structure amplitudes, F, with the e.s.d. in a structure amplitude assumed to be given by the expression

$$\sigma(F)=\sigma+0\cdot05|F|,$$

where σ is the e.s.d. derived from counting statistics. In the final two cycles of least-squares refinement, the largest structure amplitudes were assigned zero weight when it became apparent that, with increasing magnitude of structure amplitude, the observed structure amplitudes were systematically less than the calculated values, indicating extinction effects. The results of the refinement for both crystal structures are given in Tables 3, 4 and 5. The observed and calculated structure factors for barbital I (Table 3) are those of the second of the two data sets. The corresponding atomic parameters with e.s.d.'s are listed in Table 4. Final R values are given in Table 2.

The molecular structure of barbital

In the crystal structures of both polymorphs I and II, molecules of barbital are in the trioxopyrimidine tautomeric form (Fig. 1). There are no significant differences between the values obtained for the two independent structure determinations of barbital I (Vizzini, 1968). In Fig. 3, the weighted average values of bond lengths and angles for barbital I are shown together with the values obtained for barbital II. In Table 5, distances and angles are given only for the more precise second structure determination of barbital I and for barbital II. In Tables 5(a)(i) and 5(b)(i) the bond lengths are shown with corrected values obtained by assuming rigid body thermal motion according to Cruickshank (1956, 1961).

In both barbital I and II, the C–N bond lengths alternate between values close to 1·384 and 1·370 Å around the pyrimidine rings. These differences (0·014 Å) have an e.s.d. of 0·004 Å and so are probably real. In barbital I, there are no significant differences in the C–O bond lengths, but in barbital II, the bond lengths of the hydrogen bonded carbonyl groups are longer than the other C–O bond lengths (1·222 vs. 1·97 Å, with e.s.d. of 0·005 Å in the difference). The evidence for a correlation between C–N and C–O bond length variations and the mode of hydrogen bonding in barbital and other 5,5-dialkylbarbiturates is discussed by Craven, Cusatis, Gartland & Vizzini (1969).

The C–C bonds in barbital are of three types, i.e. the ring bonds at C(5), each between a tetrahedrally and a trigonally bonded carbon atom, the bonds between atom C(5) and the α-carbon atoms of the ethyl groups and the bonds between α- and β-carbon atoms of the ethyl groups. Averaging over both barbital I and II, these have bond lengths of 1·52, 1·55 and 1·51 Å respectively, after correction for rigid body motion. The

C(α)–C(β) bond length average becomes 1·53 Å assuming the riding motion correction (Busing & Levy, 1964). In either case, there are significant variations in this bond length sequence. A comparison of the barbital ring C–C bond lengths with the C–C bond length in acetaldehyde (1·501 Å from microwave spectra; Kilb, Lin & Wilson, 1957) and the ethyl C–C bond lengths with those in normal hydrocarbons (1·532 Å from electron diffraction; Bartell & Kohl, 1963) shows a lengthening of the bonds in barbital involving atom C(5). This is attributed to the non-bonded repulsive effects between the substituents at the C(5) position.

The internal angles at barbiturate ring atoms in barbital are very similar to those observed in the crystal structure of barbituric acid (Bolton, 1963). In particular the steric requirements of ring formation lead to an opening of the angle at the tetrahedrally bonded atom C(5) from the tetrahedral angle (109·4°) to 114°, for both barbital I and II and for barbituric acid. In the ethyl groups of barbital, a comparison with the average C–C–C angles in normal hydrocarbons (112·6°; Bartell & Kohl, 1963) shows that the steric repulsion between the terminal methyl groups and the ring atoms has given rise to a small increase in the angle at the α-carbon atoms (115°) with a corresponding decrease of the C(α)–C(5)–C(α) angle (109·0° and 109·9° in barbital I and II, respectively.).

The differences in molecular conformation in barbital I and II are small but real. The pyrimidine ring in barbital I is slightly folded along the line C(4)–N(1). Atoms N(1), C(2), N(3) and C(4) are coplanar, while atoms C(4), C(5), C(6) and N(1) are almost coplanar. The dihedral angle between the best least-squares planes of the halves of the pyrimidine ring is 4·5° (Table 6). However, in barbital II the pyrimidine ring is planar within experimental error (Table 6). The
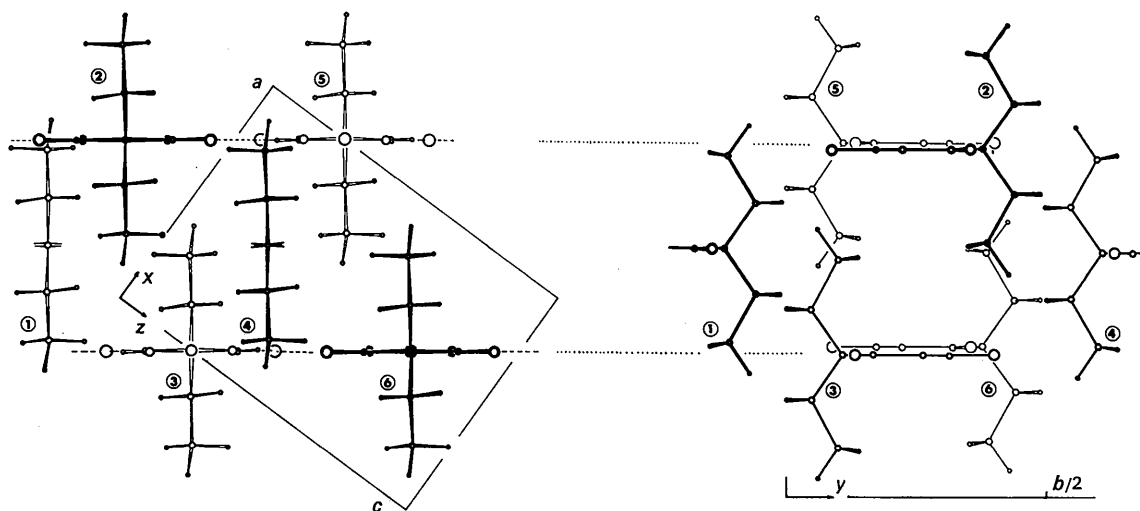

Fig. 7. The crystal structure of barbital II. The projection on the left is down the crystallographic b axis. The projection at the right is down [101]. In the latter projection, molecules which actually superimpose are shown slightly displaced. Molecules are numbered in the same way in both projections.

hydrocarbon chains are distorted from the idealized all *trans* conformation by twists about the C(5)–C(α) bonds of 5·2°, 4·3° in barbital I and 3·7° in barbital II. In barbital I, the spine of the hydrocarbon chain as viewed down the line C(5)→C(2) is slightly bowed, bringing the terminal atoms C(10) and C(8) both closer to O(6) than to O(4). The twofold rotation axis

relating the ethyl groups in barbital II gives the hydrocarbon spine a slight 'S' shape. For Newman projections including the hydrogen atoms, see Vizzini (1968). It should be noted that the deviations from an idealized geometry with molecular point symmetry 2*mm* are greater in barbital I than in barbital II, as might be expected from the crystal environments discussed below.

The crystal structures

(a) Barbital I

The hydrogen bonds in barbital I link barbiturate rings to form approximately planar ribbons running parallel to **c**, as shown in Fig. 4.

In Fig. 5, the packing of hydrogen bonded barbiturate ribbons is viewed down the trigonal *c* axis. In this mode of packing there are a number of van der Waals interactions between ethyl groups, as shown by the C···C (Fig. 5) and H···H distances listed in Table 5(*a*). The C(7)–C(8) ethyl groups are arranged about the threefold inversion axes, and the C(9)–C(10) ethyl groups are arranged about the threefold screw axes, but there are no van der Waals interactions between the two crystallographically distinct ethyl groups.

The carbonyl group C(6)–O(6), which is not hydrogen bonded, is directed towards the C(2) atom of a carbonyl group in an adjacent molecule, so that the angle C(6)–O(6)···C(2') is 137°. The O(6)···C(2') distance (3·12 Å) corresponds to a normal van der Waals interaction. Bolton (1964) has drawn attention to a number of crystal structures, including barbiturates, in which there appear to be dipole–dipole intermolecular interactions between carbonyl groups. These are characterized by C···O distances as much as 0·3 Å less than the van der Waals distance and C–O···C angles near 160°. Although the carbonyl–carbonyl interaction in barbital I is weak, as indicated by the larger C···O distance, it is believed that it does have some structure determining influence. It should be noted that the molecules which interact with a given hydrogen bonded ribbon in this way (Fig. 5) are arranged so that their C(9)–C(10) ethyl groups approach the ribbon on either side of the open area labelled '*A*' in Fig. 4.

An inspection of a model of the crystal structure of barbital I shows that the observed molecular distortions from idealized geometry result in closer intermolecular packing than would otherwise be the case. For example, the 4·5° 'folding' of the pyrimidine ring about the C(4)–N(1) axis, which is almost parallel to the *c* axis of projection in Fig. 6, leads to closer approaches by about 0·3 Å among both of the two sets of terminal methyl groups. The observed distances are C(8)···C(8') at 4·1 Å and C(10)···C(10') at 4·0 Å.

(b) Barbital II

In this crystal structure, the molecules are hydrogen bonded N(3) H(3)···O(4') in ribbons in which the barbiturate rings are very nearly parallel to the crystal-
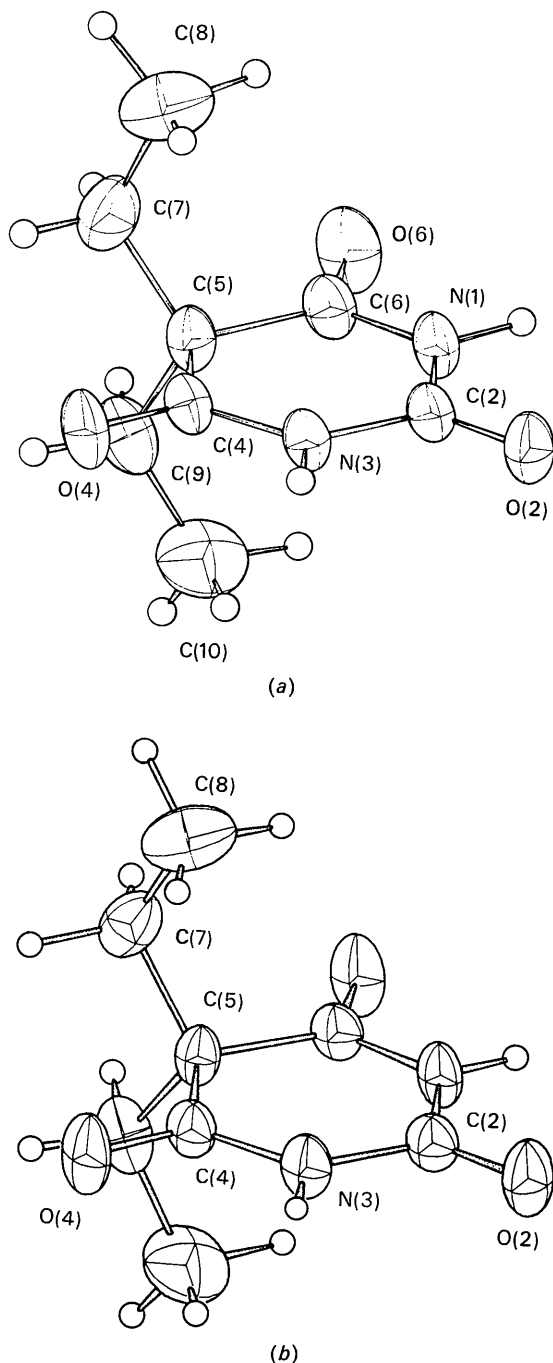

(a)

(b)

Fig. 8. The ellipsoidal representation of anisotropic thermal parameters (*a*) barbital I, (*b*) barbital II.

lographic plane (10$\bar{1}$). One such ribbon is shown in Fig. 6.

The carbonyl oxygen atom O(2) is not hydrogen bonded, nor is it involved in a carbonyl–carbonyl interaction similar to that of the non-hydrogen bonded carbonyl group in barbital I. However, the hydrogen bonded ribbons pack so that atom O(2), lying on a twofold rotation axis, is in van der Waals contact with an ethyl group from each of two symmetry related molecules. The van der Waals distances are listed in Table 5(*b*).

It is of particular interest that there are so few close intermolecular approaches between the ethyl group atoms in this crystal structure. The only intermolecular distance involving these atoms which lies within 0·2 Å of the sum of the appropriate van der Waals radii (1·2 Å for hydrogen, 2·0 Å for methyl or methylene carbon atoms; Pauling, 1960) is the distance H(72)$\cdots$H(72') of 2·50 Å, for which the corresponding C(7)$\cdots$C(7') distance is 4·27 Å. Thus the mode of molecular packing in this crystal structure is dominated by the hydrogen bonding requirements of the barbiturate rings, the attractive interactions between the non-polar ethyl groups being of little importance.

Adjacent parallel ribbons of hydrogen-bonded barbiturate rings are separated by 5·72 Å. These ribbons form the 'walls' of tunnels parallel to the [101] direction and running through the structure, with spanning ethyl groups forming the 'floor' and 'roof' (Fig. 7). The closest intermolecular approach between floor and roof is the H(82)$\cdots$H(82') distance of 3·08 Å, with corresponding C(8)$\cdots$C(8') distance of 4·445 Å.

Relationship between barbital I and II

In both barbital I and II, there are NH$\cdots$OC hydrogen bonds involving the two imine groups and two of the three carbonyl groups. These hydrogen bonds link the barbiturate rings to form almost planar ribbons. However, in barbital II, these are simple ribbons in which each molecule is hydrogen bonded to only two adjacent molecules, while in barbital I, a more complex double ribbon is formed in which each molecule is hydrogen bonded to three others.

In forming a crystal structure, the hydrogen bonded ribbons in barbital I pack more efficiently than those of barbital II. This can be seen in the appreciable difference in crystal densities (1·29 *vs.* 1·24 g.cm^{-3} in barbital I and II respectively), as well as from a consideration of the detailed intermolecular structural features. It is concluded that barbital I is the more stable structure because of the more effective van der Waals interactions, particularly those between ethyl groups.

In spite of environmental differences, the molecular thermal vibrational behaviour in both crystal structures is similar. This can be seen from the ellipsoidal representation of atomic thermal parameters in Fig. 8(*a*) and (*b*) and a comparison of the molecular rigid body translational and librational tensor components (Table 7). The rigid body model is invoked not because this is claimed to be the true description of the molecular vibrational behaviour, but rather as a convenient description of the similarity of this behaviour in the two crystal structures.* The close correspondence in rigid body parameters for the two molecules, however, does provide evidence that this model is a useful approximation.

The two translational tensors (**T**) correspond to almost isotropic motions of similar amplitudes. The principal values of the librational tensors (ω) are in directions which are close to the chosen molecular axes. Furthermore, the librational amplitudes about corresponding molecular axes are almost the same. The librational motion is markedly anisotropic, such that the amplitude of libration about the molecular axis which is normal to the pyrimidine ring (and hydrogen bonded ribbon of molecules) is smaller than the libration about the other two axes. The larger amplitudes of libration correspond to flexing motions within a hydrogen bonded ribbon of molecules.

It is concluded that the molecular vibrational behaviour in the two crystal structures is largely determined by the hydrogen bonding of molecules to form ribbons. The amplitude of flexing motions in these ribbons seems to be insensitive to the precise structure of the ribbons, and to the manner in which these are packed together to form the crystal structure.

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* Schomaker & Trueblood's (1968) recent treatment of rigid body motion is more appropriate for a barbital molecule with point symmetry 2*mn*, since it does not require the present assumption of librational axes intersecting at the molecular center of mass. For *comparison* of the two crystal structures, Cruickshank's procedure (1956, 1961) is adequate.

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The Crystal Structures of Two Polymorphs of 5-Ethyl-5-isoamylbarbituric Acid (Amobarbital)

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Two crystalline forms of 5-ethyl-5-isoamylbarbituric acid (amobarbital) are known. Three-dimensional X-ray crystal structure determinations of these are reported. The crystal data are: I (monoclinic, m.p. 154–156°C) $a=21\cdot480$, $b=11\cdot590$, $c=10\cdot370$ Å, $\beta=97°4'$, space group $C2/c$ with 8 molecules per cell; II (monoclinic, m.p. 160–162°C) $a=10\cdot281$, $b=22\cdot601$, $c=11\cdot679$ Å, $\beta=109°6'$, space group $P2_1/c$ with 8 molecules per cell. The X-ray intensity data (1861 and 4139 reflections in I and II) were collected with a four-circle automatic diffractometer and Cu $K\alpha$ radiation. Refinement of atomic positional and anisotropic thermal parameters was by a least-squares procedure, resulting in final R values of 9·6 and 7·2 per cent for all reflections or 6·9 and 7·1 per cent excluding unobserved and extinction affected reflections. The positions of the three isoamyl terminal atoms are not well-defined in either I or II because of unusually large amplitudes of thermal vibration and possibly some degree of conformational disorder. Hydrogen atoms were found except for those associated with the isoamyl terminal groups. The molecules are in the 2,4,6-trioxo tautomeric form. Variations of 0·012 Å in C–N ring bond lengths are observed which appear to be systematic and may be correlated with the effects of hydrogen bonding. The main difference between I and II is in the mode of assembly of the same structural unit, the so-called double ribbon. A single ribbon is formed from (NH···OC) hydrogen bonded barbiturate rings with all isoamyl groups projecting on one side and all ethyl groups on the other. In the double ribbon, the two component ribbons are interlocked with their ethyl group surfaces in close contact.

Introduction

A study of polymorphism in drug-active barbiturates has been undertaken in this laboratory.* In this paper, the crystal structure determinations of the two polymorphs of 5-cthyl-5-isoamyl barbituric acid, or amobarbital (Fig. 1) are reported.

Experimental

Single crystals of amobarbital I and II were obtained

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* See the previous paper (Craven, Vizzini & Rodrigues, 1969).

from the same aqueous ethanol solution by slow evaporation at room temperature. The melting points, crystal morphology, and infrared spectra of these two forms as presently observed are in agreement with those previously reported (Williams, 1959; Cleverley & Williams, 1959; Brandstätter-Kuhnert & Aepkers, 1962). The crystal data are listed in Table 1.

The intensity data were collected in the same way as for barbital (Craven, Vizzini & Rodrigues, 1969). For both forms I and II, the crystals were oriented with the symmetry axis b along the φ axis of the diffractometer. X-ray absorption corrections were applied only to the data for amobarbital I.