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The 1:1 Crystal Complex of *N*-Methyl-2-pyridone and 5,5-Diethylbarbituric Acid (Barbital)

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The 1:1 crystal complex of *N*-methyl-2-pyridone (C_6H_7NO) and 5,5-diethylbarbituric acid (barbital, $C_8H_{12}N_2O_3$), m.p. 90°C, is monoclinic, with space group $P2_1/c$ and $a=7{\cdot}257$ (2), $b=19{\cdot}339$ (2), $c=11{\cdot}127$ (2) Å, $\beta=105{\cdot}20$ (1)°. The structure determination, by direct methods, was based on 3094 integrated intensities measured on an automatic diffractometer with graphite monochromated Cu $K\alpha$ radiation. Refinement by a full-matrix least-squares procedure gave a final R value of 0·053. Both NH···O=C hydrogen bonds, with N···O distances 2·86 and 2·89 Å, involve the pyridone oxygen atom as acceptor so that the barbital oxygen atoms are not hydrogen bonded.

Experimental

Crystals of the 1:1 complex of *N*-methyl-2-pyridone and 5,5-diethylbarbituric acid (barbital) were obtained by slow cooling of an ethanolic solution which was slightly supersaturated with respect to both components. The crystal density (1·292 g cm^{-3}), which was determined by flotation in a mixture of carbon tetrachloride and cyclohexane, agrees with the calculated value (1·293 g cm^{-3}) assuming four molecules of each component in the unit cell. The lattice constants and X-ray intensity data were measured on a four-circle computer-controlled diffractometer using graphite-monochromated Cu $K\alpha$ radiation ($\lambda=1{\cdot}5418$ Å). The crystal, which had dimensions of $0{\cdot}37\times0{\cdot}36\times0{\cdot}15$ mm, was coated with lacquer and mounted with the longest dimension (the c axis) along the φ axis of the goniostat. Integrated intensities were measured for 3094 independent reflections in the range $\theta\le75°$. Reflections were scanned in the $\theta/2\theta$ mode with a θ scan width of $(0{\cdot}6+0{\cdot}2\tan\theta)°$. There were 385 reflections for which the integrated intensity (I), was less than 2·0 $\sigma(I)$ as calculated from counting statistics. These reflections were assigned intensities of $\sigma(I)/2$. No corrections were applied for X-ray absorption or extinction.

The crystal structure was determined by direct methods (Germain, Main & Woolfson, 1971). Atomic parameters (Table 1) were refined by a full-matrix least-squares procedure. The function minimized was $\sum_H w_H\Delta^2_H$, where $\Delta_H=|F^o_H|-|F^c_H|$, and $w_H^{-1}=0{\cdot}1+0{\cdot}045|F_H|^2$. The atomic scattering factors were those of Cromer & Waber (1965) for carbon, nitrogen and oxygen, and Stewart, Davidson & Simpson (1965) for hydrogen. All hydrogen-atom positions were obtained from difference Fourier syntheses which were calculated after one cycle of refinement of anisotropic thermal parameters of the non-hydrogen atoms. Hydrogen-atom positional parameters were subsequently refined, but owing to computer limitations, hydrogen-atom temperature factors were fixed with values the same as those of the atoms to which they are covalently bonded. During the last cycles of refinement, six strong reflections for which $|F^c|>|F^o|$ and reflections with $I<2\sigma(I)$ were given zero weight.* The final R index† was 0·053 for all reflections and 0·045 for those with non-zero weight.

Discussion

(a) Barbital

The ring atoms are almost coplanar (Fig. 1) as found in a number of other crystal structures involving barbital (Craven, Cusatis, Gartland & Vizzini, 1973).

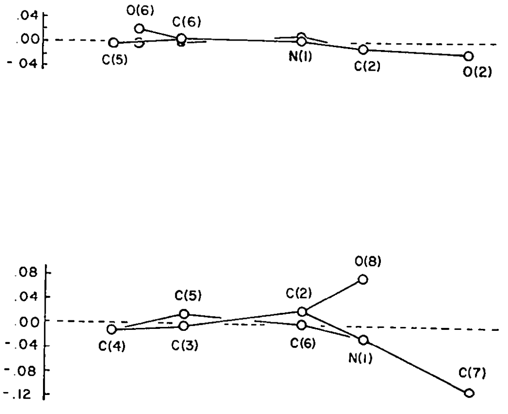

Fig. 1. The ring conformations of barbital (above) and *N*-methyl-2-pyridone (below). In each case, the dashed line is the trace of the best least-squares plane through the six ring atoms. The vertical scale (Å) is ten times the horizontal scale.

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* The list of calculated and observed structure amplitudes has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30321 (20 pp., 1 microfiche). Copies may be obtained from the Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

† $R=\sum_H|\Delta_H|/\sum_H|F^o_H|$.

However, there is a slight displacement (0·02 Å) of atom C(2) from the plane of the other five ring atoms. The barbital ethyl groups and C(5) form a chain which is almost fully extended, with torsion angles C(7)–C(5)–C(9)–C(10) and C(8)–C(7)–C(5)–C(9) of −179·7° and 177·6° respectively, and e.s.d.'s of 0·14 Å. In other barbiturate crystal structures, slight differences in oxopyrimidine bond lengths and angles in the halves of the molecule on either side of C(2)···C(5) have been attributed to atom O(4) being hydrogen bonded while O(6) is not (Craven *et al.*, 1973). In the present complex, none of the barbital oxygen atoms are hydrogen bonded. Thus no significant bond length and angle differences of this kind are expected, and indeed none is observed (Fig. 2).

(*b*) *N-methyl-2-pyridone*

The molecule is almost planar (Fig. 1) but with a slight fold along C(2)···C(5), which increases the intramolecular distance (2·69 Å) of the carbonyl oxygen and *N*-methyl carbon atoms. There are significant differences among the C–C bond lengths. The alternating long and short bonds in the sequence C(2)–C(3)=C(4)–C(5)=C(6) are consistent with the formal single- and double-bond character of the expected principle valence-bond structure for the mole-

Table 1. *Atomic parameters and their e.s.d.'s*

Positional parameters are given as fractions of the unit cell translations ($\times 10^4$) for non-hydrogen atoms and ($\times 10^3$) for hydrogen atoms. Anisotropic thermal factors ($\times 10^5$) are given by the expression: $T=\exp[-\sum_i \sum_j (\beta_{ij}h_ih_j)]$. The e.s.d.'s are in brackets and refer to the least significant digit of the corresponding parameter.

(i) Barbital

(*a*) Non-hydrogen atom parameters

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N(1)	5990 (2)	2590 (1)	1160 (1)	1821 (25)	187 (3)	685 (10)	−115 (6)	230 (13)	32 (4)
N(3)	6179 (2)	1715 (1)	2637 (1)	1710 (23)	227 (3)	480 (9)	23 (6)	161 (11)	33 (4)
C(2)	6781 (2)	2356 (1)	2353 (1)	1544 (26)	218 (4)	638 (11)	−21 (7)	212 (13)	−40 (5)
C(4)	4838 (2)	1306 (1)	1872 (1)	1509 (24)	189 (3)	594 (10)	25 (7)	318 (13)	23 (4)
C(5)	3922 (2)	1559 (1)	556 (1)	1568 (25)	191 (3)	524 (10)	−74 (7)	199 (13)	6 (4)
C(6)	4641 (2)	2259 (1)	250 (1)	1482 (25)	188 (3)	574 (10)	20 (7)	242 (13)	31 (4)
C(7)	1750 (2)	1610 (1)	385 (2)	1465 (28)	362 (5)	835 (14)	−113 (9)	74 (16)	83 (7)
C(8)	1167 (3)	2096 (1)	1286 (2)	1921 (37)	487 (7)	1197 (20)	276 (13)	618 (22)	133 (10)
C(9)	4343 (3)	1026 (1)	−375 (2)	3265 (45)	219 (4)	726 (13)	−173 (10)	591 (19)	−83 (6)
C(10)	6442 (3)	926 (1)	−295 (2)	4043 (61)	243 (5)	1456 (24)	112 (13)	1601 (33)	−18 (8)
O(2)	7961 (2)	2687 (1)	3097 (1)	2392 (27)	325 (3)	819 (10)	−236 (7)	−14 (13)	−91 (5)
O(4)	4398 (2)	752 (1)	2235 (1)	2667 (28)	232 (3)	898 (11)	−113 (7)	322 (13)	134 (4)
O(6)	4051 (2)	2518 (1)	−771 (1)	2442 (25)	269 (3)	666 (9)	−30 (7)	107 (12)	130 (4)

(*b*) Hydrogen atom parameters

	x	y	z		x	y	z
H(1)	648 (2)	298 (1)	98 (1)	H(83)	185 (3)	257 (1)	138 (2)
H(3)	669 (2)	158 (1)	338 (2)	H(91)	371 (3)	120 (1)	−123 (2)
H(71)	126 (2)	111 (1)	51 (2)	H(92)	378 (3)	56 (1)	−22 (2)
H(72)	120 (2)	181 (1)	−43 (2)	H(101)	698 (3)	133 (1)	−50 (2)
H(81)	−21 (3)	219 (1)	101 (2)	H(102)	664 (3)	59 (1)	−83 (2)
H(82)	161 (3)	191 (1)	210 (2)	H(103)	717 (3)	77 (1)	64 (2)

(ii) *N*-Methyl-2-pyridone

(*a*) Non-hydrogen atom parameters

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N(1)	10145 (2)	4369 (1)	1378 (1)	1676 (24)	217 (3)	595 (9)	−50 (6)	185 (11)	4 (4)
C(2)	9448 (2)	3927 (1)	390 (1)	1711 (27)	178 (3)	591 (10)	−82 (7)	209 (13)	21 (4)
C(3)	10736 (2)	3767 (1)	−344 (2)	2364 (36)	241 (4)	880 (14)	−57 (9)	581 (18)	−72 (6)
C(4)	1250 (2)	4057 (1)	−107 (2)	2026 (34)	306 (5)	1143 (17)	79 (10)	695 (20)	60 (7)
C(5)	13097 (2)	4530 (1)	871 (2)	1603 (30)	294 (5)	1154 (17)	−107 (9)	250 (18)	74 (7)
C(6)	11911 (2)	4669 (1)	1593 (1)	1838 (30)	245 (4)	800 (13)	−142 (9)	6 (15)	3 (6)
C(7)	8945 (3)	4507 (1)	2224 (2)	2486 (41)	377 (6)	761 (14)	−79 (12)	518 (20)	−101 (7)
O(8)	7778 (2)	3699 (1)	192 (1)	1943 (23)	281 (3)	734 (9)	−245 (6)	274 (11)	1 (4)

(*b*) Hydrogen atom parameters

	x	y	z		x	y	z
H(3)	1030 (3)	342 (1)	−103 (2)	H(71)	793 (3)	473 (1)	178 (2)
H(4)	1335 (3)	394 (1)	−62 (2)	H(72)	852 (3)	405 (1)	255 (2)
H(5)	1428 (3)	477 (1)	106 (2)	H(73)	960 (3)	481 (1)	287 (2)
H(6)	1220 (2)	500 (1)	230 (2)				

cule. Similar C–C bond-length variations were also observed in the crystal structure of 2-pyridone (Penfold, 1953). The most notable differences in the two molecules are in the C(2)–N(1) and C(6)–N(1) bond lengths, which are nearly the same in *N*-methyl-2-pyridone (1·379, 1·370 Å; e.s.d., 0·002 Å), but are significantly different in 2-pyridone (1·401, 1·335 Å; e.s.d., 0·01 Å).

(*c*) *The molecular association*

The crystal structure contains hydrogen-bonded ribbons which run parallel to **c** (Fig. 3). The ribbons are packed together with no unusual features, such as short intermolecular distances. The hydrogen bonds N(1)H· · ·O(8) and N(3)H· · ·O(8) have N· · ·O distances 2·86 and 2·89 Å, H· · ·O distances 2·01 and 2·04 Å and NH· · ·O angles 164 and 176°, respectively. There is also a short (3·03 Å) intraribbon N(3)· · ·O(6) distance between barbital molecules. However, this is not a hydrogen bond because the corresponding H(3)· · ·O(6) distance (2·92 Å) is long, even for a van der Waals interaction, and the N(3)H(3)· · ·O(6) angle is 89°.

This structure determination is one of a series of crystal complexes of drug-active barbiturates with other amides such as urea (Gartland & Craven, 1974), acetamide (Hsu & Craven, 1974*a*) and salicylamide (Hsu & Craven, 1974*b*). The aim is to see whether the modes of NH· · ·O=C hydrogen bonding and the hydrogen bonding N· · ·O distances are suggestive of differences in the inherent hydrogen-bonding affinities of the various NH and O=C groups involved. Gartland & Craven (1974) have pointed out that the N· · ·O distances in NH· · ·O=C hydrogen bonds involving barbiturates tend to be short (2·75 to 2·82 Å) when barbiturate is donor and a non-barbiturate oxygen atom is acceptor. The N· · ·O distances are of intermediate length (2·82 to 2·98 Å) when barbiturate is both donor and acceptor, and longer (2·95 to 3·39 Å) when barbiturate is acceptor and a non-barbiturate is donor. This pattern of N· · ·O distances suggests that barbiturates are more effective as hydrogen-bonding donors than as acceptors.

The hydrogen bonds in the complex of barbital with *N*-methyl-2-pyridone have longer N· · ·O distances than the others in which barbiturate is involved as donor. The range of such distances must thus be extended (2·75 to 2·89 Å) so as to overlap the range for hydrogen bonds in which barbiturates hydrogen bond with each other (2·82 to 2·98 Å).

It must be noted that both hydrogen bonds involve the 2-pyridone oxygen atom as acceptor, so that none of the three barbital oxygen atoms is hydrogen bonded. Similarly, in the complex of barbital with urea (Gartland & Craven, 1974) and acetamide (Hsu & Craven, 1974*a*), the barbital NH groups hydrogen bond only

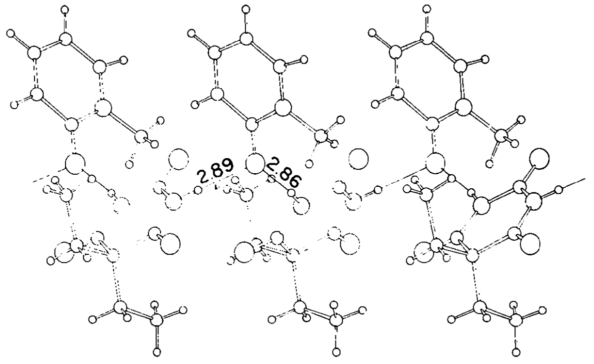

Fig. 3. A hydrogen-bonded ribbon in the projection down **b**. The hydrogen bond distances N· · ·O are in Å.

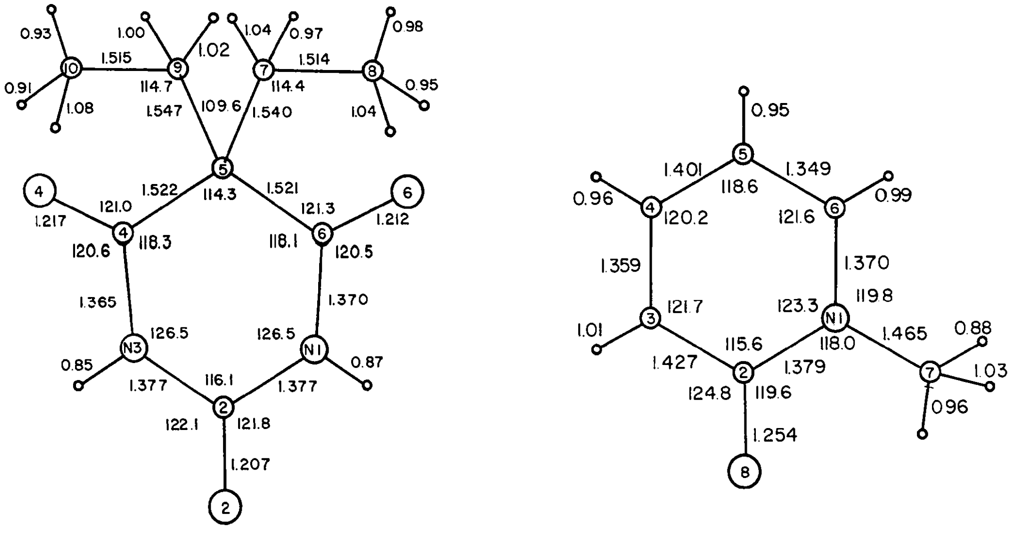

Fig. 2. Bond lengths and angles in barbital (left) and *N*-methyl-2-pyridone (right). The C–H and N–H bond lengths have e.s.d.'s of 0·02 Å. The e.s.d.'s are 0·002 Å in other bond lengths and 0·1° in bond angles.

with the urea or acetamide oxygen atoms. There are also weak hydrogen bonds involving the amide amino group as donor and barbital oxygen atoms as acceptor, but these have no counterpart in the *N*-methyl-2-pyridone complex because of *N*-methylation. Thus, the mode of hydrogen bonding in each of these complexes is consistent with the barbital oxygen atoms being relatively poor hydrogen-bonding acceptors.

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The Crystal and Molecular Structure of Methyl 3,3,4-Trichloro-5-methoxyindolenine-2-carboxylate

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The structure of a trichlorinated intermediate in the synthesis of isatin compounds by a new pathway has been determined by X-ray crystallography. The compound crystallizes in the orthorhombic system with $a=22{\cdot}450$, $b=13{\cdot}292$, $c=8{\cdot}558$ Å, space group $Pna2_1$, and two molecules of $C_{11}H_8NO_3Cl_3$ in the asymmetric unit. The structure was solved by the symbolic addition method, the phases of the 150 strongest $|E|$'s being found close to 0 or π. This is probably due to the near centrosymmetric distribution of the chlorine atoms. The structure, based on 1297 diffractometer intensities, has been refined to $R=0{\cdot}036$.

Introduction

Recent investigations of the products and mechanism of attack by the positive chlorine ion (Cl^+) on indole-2-carboxylic acid (Hinman & Bauman, 1964; Foglio & Swern, 1968; Muchowski, 1970) have provided a novel route for the synthesis of substituted isatins. R. J. Bass of Pfizer (U.K.) Ltd., who aroused our interest in this matter, proposed a reaction sequence (Fig. 1) involving an unstable 'intermediate compound' [Fig. 1 (I)]. Later, Muchowski (1970) suggested that this intermediate consists rather of a sequence of reactions (Fig. 2) leading to the formation of a trichloro species [Fig. 2 (7)] which subsequently loses the elements of hydrogen chloride and carbon dioxide before tautomerizing to an oxindole [Fig. 2 (8)]. Attack by a further Cl^+ ion then yields the 3,3,4-trichloro-oxindole shown in Fig. 2 (2).

Bass found that treatment of the intermediate with diazomethane yielded a more stable and isolable com-

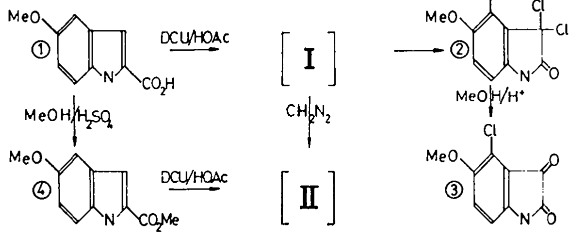

Fig. 1. Reaction sequence for synthesis of substituted isatins.

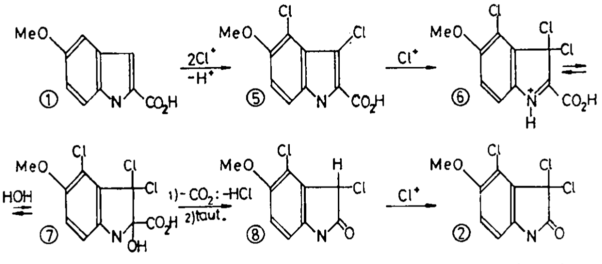

Fig. 2. Sequence of reactions comprising intermediate in Fig. 1 (I).

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