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The Crystal Structure of the 1:1 Complex of Acetamide with 5,5-Diethylbarbituric Acid (Barbital)

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The 1:1 complex of acetamide and barbital ($C_2H_5NO.C_8H_{12}N_2O_3$), m.p. 116°C, is orthorhombic with space group $P2_12_12_1$. Lattice translations are $a=10{\cdot}615$ (2), $b=10{\cdot}568$ (2), $c=11{\cdot}243$ (2) Å. The crystal density (1·283 g cm^{-3}) agrees with the calculated density (1·281 g cm^{-3}) for four molecules of each component in the unit cell. The crystal structure has been determined from 1500 integrated intensities measured on a computer-controlled diffractometer with nickel-filtered Cu $K\alpha$ radiation. The final R index is 0·044. The crystal structure is isomorphous with the urea/barbital complex. The acetamide complex has slight differences in barbital conformation as well as in the relative translations and orientations of the component molecules, but is similar in having two strong hydrogen bonds (N···O, 2·84 Å) in which barbital is donor and the oxygen of the second component (acetamide) is acceptor.

Introduction

This crystal structure determination is one of a series involving NH···O=C hydrogen bonded complexes of drug-active barbiturates with various other amides. The crystal structure of the 1:1 complex of 5,5-diethylbarbituric acid (barbital, Fig. 1) with acetamide is of interest because it is isomorphous with the corresponding urea complex (Gartland & Craven, 1974). Thus the acetamide methyl group which does not hydrogen bond, replaces a urea amino group which does hydrogen bond, with only minor perturbation of the crystal structure.

Experimental

Transparent, prismatic crystals of the complex were grown from a saturated solution of barbital and acetamide in a solvent mixture of propanol and cyclohexane (4:1). The crystal density was determined by flotation in a mixture of benzene and carbon tetrachloride. Intensity data and unit-cell dimensions were measured on a four-circle computer-controlled diffractometer (Enraf–Nonius CAD-4) using nickel-filtered Cu $K\alpha$ radiation ($\lambda=1{\cdot}5418$ Å). The crystal data for the isomorphous complexes of barbital with acetamide and urea are given in Table 1.

Table 1. *Crystal data for the isomorphous* (1:1) *complexes barbital/acetamide and barbital/urea*

	Barbital/acetamide (This work)	Barbital/urea (Gartland & Craven, 1974)
	$C_8H_{12}N_2O_3.C_2H_5NO$	$C_8H_{12}N_2O_3.CH_4N_2O$
	Orthorhombic, space group $P2_12_12_1$	
m.p.	116°C	146–150°C
a	10·615 (2) Å	10·302 (5) Å
b	10·568 (2)	10·181 (2)
c	11·243 (2)	11·627 (3)
V	1261·2 Å^3	1219·5 Å^3
D_{meas}	1·283 g cm^{-3}	1·320 g cm^{-3}
D_x	1·281	1·330

1500 independent reflections were measured in the range $\theta \leq 75°$. The crystal, which had dimensions 0·3 × 0·2 × 0·2 mm, was mounted so that there was an angle of 15° between the crystal axis a and the φ axis of the goniostat. Reflections were scanned in the ω–2θ mode at different rates to obtain a minimum net count of 5000 within a specified maximum scan time (90 s). The background counts were taken at each of the scan limits for $\frac{1}{4}$ of the scan time. The 2θ scan width in degrees was $1{\cdot}2+0{\cdot}4\tan\theta$. There were 86 reflections for which the integrated intensity (I) was less than $2\sigma(I)$ as calculated from the counting statistics. These

reflections were assigned intensities of $\sigma(I)/2$. No corrections were made for X-ray absorption or extinction.

In retrospect this crystal structure could have been determined most readily from its isomorphism with the barbital/urea complex (Gartland & Craven, 1974). However, at the time, this relationship was not appreciated, and the crystal structure was determined by direct methods with the *MULTAN* program of Germain, Main & Woolfson (1971).

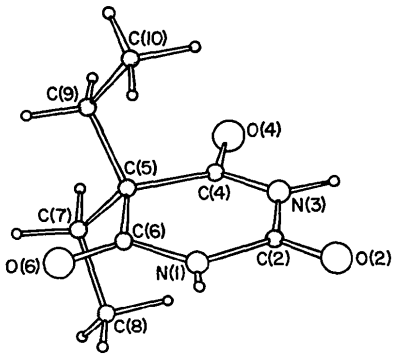


Fig. 1. Molecular structure of 5,5-diethylbarbituric acid (barbital).

Atomic parameters (Table 2) were refined by a full-matrix least-squares procedure. The function minimized was $\sum w_H \Delta_H^2$, where $\Delta_H = |F_H^{obs}| - |F_H^{calc}|$. The weights were assumed to be $w_H^{-1} = 0{\cdot}15 + 0{\cdot}002\ |F_H|^2$. The atomic scattering factors were those of Cromer & Waber (1965) for O, N, C, and of Stewart, Davidson & Simpson (1965) for H. All hydrogen atomic positions were obtained from a difference Fourier map which was calculated after refinement of anisotropic temperature factors had been applied for the non-hydrogen atoms. Hydrogen-atom positional and isotropic thermal parameters were subsequently refined. During the last three cycles of least-squares refinement, reflections with $I < 2\sigma(I)$ and 17 strong reflections for which $|F^{obs}| > |F^{calc}|$ were given zero weights. Refine-

Table 2. *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: $T = \exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$, or $T = \exp[-B\sin^2\theta/\lambda^2]$, and U_k is the r.m.s. displacement (Å) along the kth principal axis of the thermal ellipsoid. The parameters are listed $\times 10^4$, except for hydrogen atoms positional parameters ($\times 10^3$) and U_k ($\times 10^2$).

(i) The barbital molecule

				B (Å^2)								
	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}	U_1	U_2	U_3
N(1)	5757 (1)	4077 (1)	4916 (1)	88 (1)	59 (1)	55 (1)	−1 (1)	21 (1)	−2 (1)	17	18	24
H(1)	524 (2)	398 (3)	557 (2)	4·8 (5)								
C(2)	6551 (2)	3097 (2)	4653 (1)	106 (2)	54 (1)	55 (1)	6 (1)	11 (1)	1 (1)	17	18	25
O(2)	6584 (2)	2136 (1)	5245 (1)	200 (2)	73 (1)	88 (1)	26 (1)	43 (1)	30 (1)	17	23	36
N(3)	7313 (2)	3246 (1)	3677 (1)	94 (1)	57 (1)	57 (1)	18 (1)	17 (1)	2 (1)	16	18	25
H(3)	777 (2)	258 (2)	350 (3)	3·5 (4)								
C(4)	7318 (1)	4266 (2)	2920 (1)	61 (1)	64 (1)	46 (1)	−4 (1)	−2 (1)	−3 (1)	17	18	19
O(4)	7986 (1)	4259 (1)	2043 (1)	87 (1)	98 (1)	59 (1)	1 (1)	20 (1)	1 (1)	17	23	24
C(5)	6499 (1)	5390 (1)	3223 (1)	69 (1)	49 (1)	52 (1)	−3 (1)	−2 (1)	3 (1)	16	18	20
C(6)	5726 (2)	5230 (2)	4358 (1)	67 (1)	54 (1)	57 (1)	3 (1)	2 (1)	−7 (1)	17	20	20
O(6)	5071 (1)	6070 (1)	4744 (1)	103 (1)	78 (1)	96 (1)	28 (1)	19 (1)	−11 (1)	17	25	27
C(7)	5567 (2)	5634 (2)	2190 (2)	93 (2)	80 (2)	66 (1)	6 (1)	−17 (1)	4 (1)	19	22	24
H(71)	513 (2)	643 (2)	242 (2)	3·8 (4)								
H(72)	605 (2)	575 (2)	149 (2)	4·1 (5)								
C(8)	4677 (2)	4548 (2)	1930 (2)	89 (2)	127 (3)	88 (2)	−6 (2)	−22 (2)	−20 (2)	19	25	28
H(81)	417 (3)	432 (3)	263 (3)	5·5 (6)								
H(82)	511 (3)	378 (3)	168 (2)	5·6 (6)								
H(83)	414 (3)	473 (3)	127 (3)	6·5 (7)								
C(9)	7377 (2)	6550 (2)	3377 (2)	99 (2)	60 (1)	73 (1)	−21 (1)	−0 (1)	3 (1)	17	22	25
H(91)	690 (2)	736 (2)	349 (2)	4·2 (5)								
H(92)	777 (2)	672 (2)	256 (2)	4·0 (5)								
C(10)	8359 (2)	6385 (2)	4343 (2)	89 (2)	100 (2)	80 (2)	−28 (2)	−4 (1)	−19 (1)	18	23	27
H(101)	787 (3)	625 (3)	514 (3)	5·7 (6)								
H(102)	900 (3)	554 (3)	419 (3)	6·5 (7)								
H(103)	889 (3)	719 (4)	437 (3)	8·4 (9)								

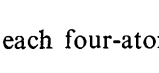
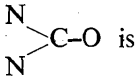
(ii) The acetamide molecule

C(1)	3793 (1)	4477 (2)	7644 (1)	62 (1)	77 (2)	57 (1)	−10 (1)	3 (1)	−10 (1)	18	19	22
O(1)	4048 (1)	3721 (1)	6832 (1)	122 (1)	88 (1)	74 (1)	−42 (1)	35 (1)	−29 (1)	18	19	32
N(2)	4191 (2)	5659 (2)	7620 (2)	104 (2)	69 (1)	88 (1)	−11 (1)	22 (1)	−17 (1)	19	21	27
H(21)	477 (3)	591 (3)	707 (3)	6·1 (7)								
H(22)	414 (2)	616 (3)	821 (2)	4·7 (5)								
C(3)	3041 (2)	4058 (2)	8699 (2)	102 (2)	103 (2)	67 (1)	−17 (2)	22 (1)	−11 (2)	19	22	27
H(31)	283 (3)	478 (3)	921 (3)	5·7 (6)								
H(32)	227 (3)	365 (3)	843 (2)	5·6 (6)								
H(33)	339 (3)	337 (4)	911 (3)	7·3 (9)								

ment was concluded when all parameter changes were less than $\sigma/3$. The final overall R index* is 0·044.†

The molecular structures

(i) *Barbital*

The oxopyrimidine ring is almost planar with C(5) and the ethyl carbon atoms forming the spine of a hydrocarbon chain which extends perpendicular to the ring. The slight ring puckerings, which occur in the barbital rings in both the acetamide and the urea complexes are shown in Fig. 2. In the acetamide complex the ring is skewed with respect to a twist about the C(2)···C(5) axis. In the urea complex, this feature is coupled with a displacement of atom C(5) from the mean plane of the remaining ring atoms. In both molecules, each four-atom group  and  is nearly planar. These puckering modes have both been noted in other barbiturate crystal structures (Craven, Cusatis, Gartland & Vizzini, 1973). Their occurrence presumably depends on the nature of the barbiturate molecular environment in the crystal structure. It is interesting that this conformational difference is now found to occur in a pair of isomorphous crystal structures as a result of substituting acetamide for urea.

Torsion angles C(8)–C(7)–C(5)–C(9) and C(10)–C(9)–C(5)–C(7) are 178·5 and 182·1°, corresponding to small twists of the hydrocarbon chain from the fully extended conformation. In the urea complex, these angles are 184·6 and 180·9° respectively, the greater difference being a twist of 5·9° about the C(5)–C(7) bond.

The bond lengths and angles in the oxopyrimidine ring (Table 3) are in excellent agreement with those reported for the urea complex. There is a small but significant difference (1·5°) in the bond angle C(6)–C(5)–C(7) which may be associated with the conformational differences in the two barbital molecules.

(ii) *Acetamide*

The carbon, oxygen and nitrogen atoms are nearly coplanar, with the central carbon atom C(1) only 0·008 Å from the plane through the other atoms. There appears to be a rotation of the methyl group about the C–CH_3 bond of about 5° from the configuration in which hydrogen atom H(31) is *anti* with respect to the carbonyl oxygen atom. The amide hydrogen atoms are displaced (0·13, 0·16 Å; e.s.d. 0·03 Å) from the molecular plane on the opposite side from H(31), so that the bonds at the amide nitrogen atom are possibly significantly non-coplanar.

Table 3. *Bond lengths and angles for barbital and acetamide*

These values have not been corrected for the effects of anisotropic thermal motion. The e.s.d.'s are given in parentheses and refer to the least significant digit of the parameter. The C–H bond lengths in both barbital and acetamide range from 0·94 to 1·13 Å. The H–C–H and C–C–H bond angles range from 98 to 114°.

(*a*) Bond lengths (Å)

(*i*) Barbital

C(6)–N(1)	1·370 (2)	C(7)–C(8)	1·514 (3)
N(1)–C(2)	1·367 (2)	C(9)–C(10)	1·516 (3)
C(2)–N(3)	1·372 (2)	N(1)–H(1)	0·92 (3)
N(3)–C(4)	1·373 (2)	N(3)–H(3)	0·88 (2)
C(6)–O(6)	1·208 (2)		
C(2)–O(2)	1·214 (2)	(*ii*) Acetamide	
C(4)–O(4)	1·213 (2)	C(1)–O(1)	1·242 (2)
C(5)–C(4)	1·511 (2)	C(1)–N(2)	1·318 (2)
C(5)–C(6)	1·525 (2)	C(1)–C(3)	1·497 (3)
C(5)–C(7)	1·547 (3)	N(2)–H(21)	0·91 (3)
C(5)–C(9)	1·549 (2)	N(2)–H(22)	0·85 (3)

(*b*) Bond angles (°)

(*i*) Barbital

N(1)–C(2)–O(2)	122·2 (2)	C(6)—C(5)–C(7)	107·6 (1)
N(1)–C(2)–N(3)	116·7 (2)	C(7)—C(5)–C(9)	109·6 (1)
N(3)–C(2)–O(2)	121·1 (2)	C(5)—C(7)–C(8)	114·6 (2)
C(2)–N(3)–C(4)	126·0 (1)	C(5)—C(9)–C(10)	113·7 (2)
N(3)–C(4)–O(4)	120·1 (1)	C(6)—N(1)–H(1)	117 (2)
N(3)–C(4)–C(5)	118·3 (1)	C(2)—N(1)–H(1)	117 (2)
C(5)–C(4)–O(4)	121·6 (1)	C(4)—N(3)–H(3)	119 (1)
C(4)–C(5)–C(6)	114·3 (1)	C(2)—N(3)–H(3)	114 (1)
C(5)–C(6)–O(6)	121·9 (1)		
C(5)–C(6)–N(1)	117·9 (1)	(*ii*) Acetamide	
N(1)–C(6)–O(6)	120·1 (2)	N(2)—C(1)–O(1)	121·6 (2)
C(6)–N(1)–C(2)	126·1 (1)	O(1)—C(1)–C(3)	120·5 (2)
C(4)–C(5)–C(7)	109·3 (1)	C(3)—C(1)–N(2)	117·9 (2)
C(4)–C(5)–C(9)	107·5 (1)	C(1)—N(2)–H(21)	120 (2)
C(6)–C(5)–C(9)	108·5 (1)	C(1)—N(2)–H(22)	124 (2)
		H(21)–N(2)–H(22)	113 (3)

The bond lengths and angles (Table 3) agree with those reported in the two crystal forms of acetamide itself [rhombohedral, Senti & Harker (1940) and Denne & Small (1971); orthorhombic, Hamilton (1965)] although in the latter structure determinations, the e.s.d.'s are greater (0·05, 0·005 and 0·016 Å respectively in bond lengths).*

Differences between the isomorphous complexes

There are both intra- and intermolecular differences between the isomorphous complexes of acetamide and urea with barbital. The intramolecular differences consist of the obvious difference between acetamide and urea, and the small conformational differences in the barbital molecule which have already been described. The intermolecular differences will be de-

* $R=\sum_H|\Delta_H|/\sum_H|F_H^{obs}|$.

† A list of structure amplitudes has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30318 (10 pp., 1 microfiche). Copies may be obtained through the Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

* The present results should be compared with those of Denne & Small (1971) before correction for molecular librations.

scribed in terms of the relative translations and orientations of the two components in each complex.

The atoms which are close to the center of mass of each component are C(5) in barbital and the carbonyl carbon of acetamide and urea. The C(5)···C distance between these atoms (Table 1) is almost the same in both complexes (5·82 and 5·84 Å). However, the components of the C → C(5) intermolecular vector differ by 0·25 Å, 0·31 Å and 0·21 Å along the crystal axes x, y and z respectively, corresponding to a relative translation of 0·45 Å between these atoms in the two complexes.

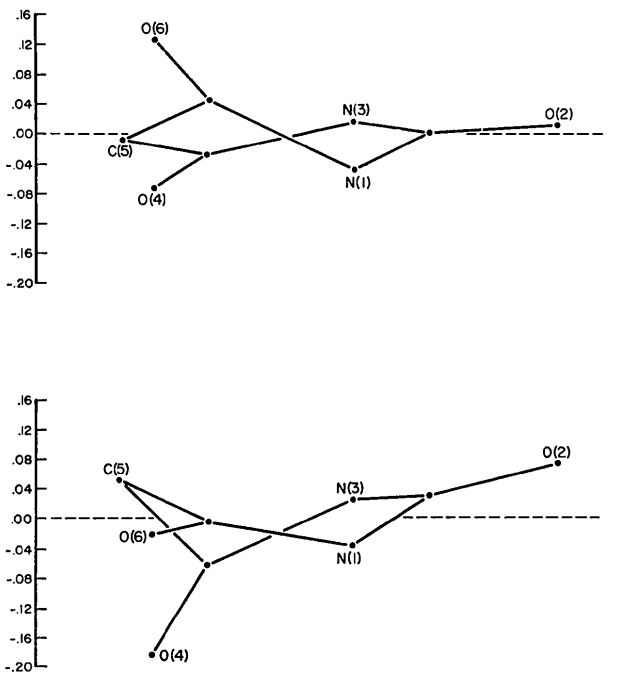


Fig. 2. Conformations of the barbiturate trioxopyrimidine ring in the complex with acetamide (above) and urea (below). The dashed lines are the traces of the best least-squares plane through the six ring atoms. The vertical scale (Å) is seven times that of the horizontal.

Molecular orientations are given in Table 4 in terms of the direction cosines of the normals to the molecular planes with respect to crystal axes, and the direction cosines of a selected C=O bond which lies in each of these molecular planes. In each case, the molecules chosen are those for which atomic parameters are given [see Table 1 in this paper, and in Gartland & Craven (1974)]. These molecules are shown as the central acetamide (or urea) and the barbital at the bottom right in Fig. 3. The angle between the plane normals of the barbiturate ring and acetamide in one complex is different by only 1·4° from the angle between the plane normals of the barbiturate ring and urea in the other. Similarly the angle between the directions of the C(2)=O(2) barbital bond and the carbonyl bond in acetamide differ by only 2·3° from the corresponding angle in the urea complex. The greatest differences in molecular orientation in the two complexes are in the normals to the barbiturate rings (5·9°) and the direction of the barbital C(2)=O(2) carbonyl group (7·1°). It is noteworthy that these differences in intramolecular and intermolecular configuration have little effect on the N···O distances in corresponding NH···O=C hydrogen bonds in the two complexes.

The hydrogen bonding

The important molecular interactions in this crystal structure are the NH···O=C hydrogen bonds (Table 5). Both NH groups from barbital are hydrogen

Table 4. *Molecular orientations in the isomorphous complexes of barbital with acetamide and urea*

Molecular orientations are expressed as best least-squares planes, $Lx+My+Nz=D$, or as directions (L,M,N) where L,M,N are direction cosines with respect to the crystal axes, and D is in Å. The appropriate angle is listed underneath each direction cosine.

	Barbital/acetamide				Barbital/urea			
	L	*M*	*N*	*D*	*L*	*M*	*N*	*D*
(1)	0·7295	0·3858	0·5648	9·2874	0·7524	0·4464	0·4843	9·0873
	43·2°	67·3°	55·6°		41·2°	63·5°	61·0°	
(2)	0·8398	−0·2670	0·4726	6·1860	0·8244	−0·2407	0·5123	6·6990
	32·9°	105·5°	61·8°		34·5°	103·9°	59·2°	
(3)	0·0292	−0·8364	0·5481	–	0·0984	−0·7692	0·6316	–
	88·3°	146·8°	56·8°		84·4°	140·3°	50·8°	
(4)	0·2175	−0·6428	−0·7351	–	0·2345	−0·6755	−0·6997	–
	77·4°	130·0°	137·3°		76·4°	132·5°	134·4°	

(1) Plane of pyrimidine ring
(2) Plane of acetamide or urea
(3) Direction cosines for barbital C(2)=O(2) bond
(4) Direction cosines for acetamide or urea C=O bond

Angles between plane normals, or between bond directions. Subscripts a and u refer to the acetamide and urea complexes respectively.

$(1)_a \wedge (2)_a$	39·1°	$(1)_a \wedge (1)_u$	5·9°
$(1)_u \wedge (2)_u$	40·5	$(2)_a \wedge (2)_u$	2·9
$(3)_a \wedge (4)_a$	81·9	$(3)_a \wedge (3)_u$	7·1
$(3)_u \wedge (4)_u$	84·2	$(4)_a \wedge (4)_u$	1·8

bonded to the acetamide oxygen atom, with N···O distances (2·84 Å) slightly longer than the corresponding distances (2·80 and 2·78 Å) in the barbital/urea complex. Only one of the acetamide amide hydrogen atoms H(22), forms a normal hydrogen bond, and this is with the barbital O(2) atom. The N···O distance is rather long (2·98 Å). The remaining amide hydrogen atom appears (Fig. 3) as if it might be hydrogen bonded to a barbital O(4) atom, with N···O distance 3·07 Å. However, the N(2)–H(21)···O(4) angle is 131° and the H···O distance is 2·39 Å, indicating that this is at most a very weak interaction.* The acetamide methyl hydrogen atom H(31), which corresponds to the amine hydrogen atom in the urea complex, is at a normal van der Waals distance (2·64 Å) from the barbital O(2) atom. This hydrogen atom is not considered to be involved in C–H···O hydrogen bonding.

* In barbital/urea, the corresponding interaction is even weaker, with N···O distance 3·10 Å, H···O distance 2·60 Å and N–H···O angle of 123°.

Table 5. *Hydrogen-bonding distances and angles*

Parameters for atoms not in the crystal chemical unit (Table 1) may be derived by operations which are specified by subscripts *i*, *j*, where *i* is $(\frac{1}{2}+x, \frac{1}{2}-y, 1-z)$ and *j* is $(1-x, \frac{1}{2}+y, \frac{3}{2}-z)$. The e.s.d.'s given in parentheses refer to the least significant figures in the distances and angles.

N(1)···O(1)	2·841 (2) Å
H(1)···O(1)	1·92 (3)
N(3)···O(1)$_i$	2·836 (2)
H(3)···O(1)$_i$	1·96 (3)
N(2)···O(2)$_j$	2·980 (3)
H(22)···O(2)$_j$	2·16 (3)
N(1)···O(1)——C(1)	127·7 (1)°
N(1)——H(1)···O(1)	175 (2)
N(3)···O(1)$_i$——C(1)$_i$	118·6 (1)
N(3)——H(3)···O(1)$_i$	170 (2)
N(2)···O(2)$_j$——C(2)$_j$	150·6 (1)
N(2)——H(22)···O(2)$_j$	161 (3)

In the crystal structures of simple aliphatic amides both amide hydrogen atoms are usually involved in NH···O=C hydrogen bonds. Often, the amide molecules form cyclic dimers linked by pairs of hydrogen bonds which involve the hydrogen atom *cis* to the carbonyl oxygen atom. The hydrogen atom which is *trans* to the oxygen atom forms hydrogen bonds which further link dimers to give ribbons. Table 6 lists the

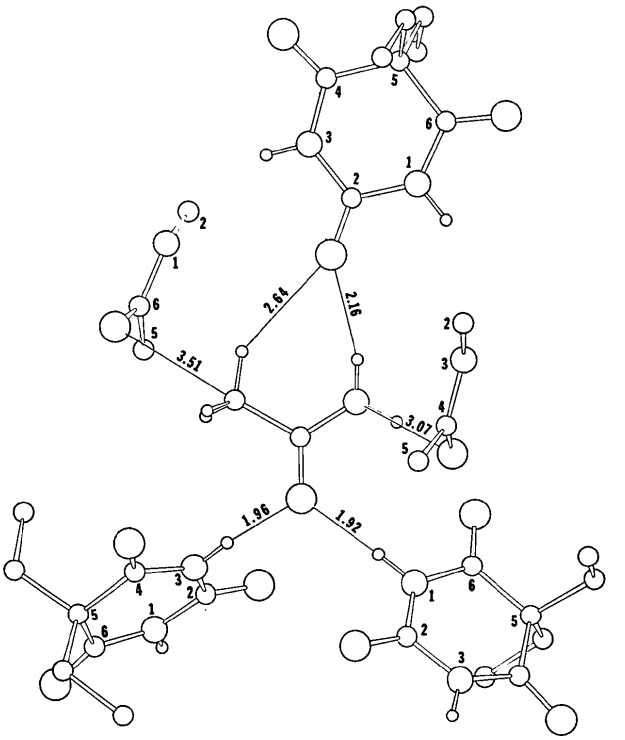


Fig. 3. The environment of the acetamide molecule, viewed normal to the plane of the amide group.

Table 6. *Distances* N···O *in* NH···O=C *hydrogen bonds in the crystal structures of aliphatic amides*

Amide*	N···O distances N–H *trans* to C=O	N–H *cis* to C=O
Formamide (Ladell & Post, 1954)	2·88 Å	2·94 Å
Acetamide, orthorhombic (Hamilton, 1965)	2·87, 2·94	2·97, 3·01
Acetamide, rhombohedral (Denne & Small, 1971)	2·91	2·95
Chloroacetamide, α-form (Penfold & Simpson, 1956)	2·95	2·99
Chloroacetamide, β-form (Katayama, 1956)	3·05	–
Fluoroacetamide (Hughes & Small, 1962)	2·88	2·96
Cyanoacetamide (Chieh & Trotter, 1970)	–	2·96, 2·94
Decanamide (Brathovde & Lingafelter, 1958)	2·90	2·88
Tetradecanamide (Turner & Lingafelter, 1955)	2·93	2·99
Oxamide (Ayerst & Duke, 1954)	2·94	2·95
Malonamide (Chieh, Subramanian & Trotter, 1970)	2·89, 2·92 2·95, 2·95	2·89, 2·94 3·04, 3·14
Dichloromalonamide (Leibscher, Krishna Rao & Trotter, 1971)	3·05	2·96
Succinamide (Davies & Pasternak, 1956)	2·94	2·94
Glutaramide (Hospital & Housty, 1966*a*)	2·94	2·97
Adipamide (Hospital & Housty, 1966*b*)	2·93	2·94
Suberamide (Hospital & Housty, 1966*c*)	2·97	2·91
Azelamide (Hospital, 1971)	2·97	2·99

* This tabulation was compiled from the bibliography of Kennard & Watson (1970, 1971).

N···O distances for the two kinds of hydrogen bonds in amide crystal structures. The distributions of these two kinds of hydrogen bonds are very similar, with the 20 *cis* N···O distances ranging from 2·88 to 3·14 Å with an average value of 2·97 Å and the 21 *trans* distances ranging from 2·87 to 3·05 Å with an average value of 2·94 Å. The combined average distance is 2·95 Å.

The N···O distances for the NH···O=C hydrogen bonds in which barbital provides the donor (NH) and acetamide the acceptor (O=C) group are shorter (2·84 and 2·84 Å) than any of the distances in Table 6. They are also shorter than all but four of the 49 N···O distances in which a barbiturate is both donor and acceptor [see Table 5 in Gartland & Craven (1974)].

The N···O distance (2·98 Å) for the hydrogen bond in which acetamide provides the donor and barbital the acceptor is near the average value (2·95 Å) of the distances in Table 6, but is longer than all but one of the 49 barbiturate–barbiturate N···O distances.

These results are consistent with the conclusion (Gartland & Craven, 1974) that in NH···O=C hydrogen bonds the drug-active barbiturates are more effective as donor than acceptor. Analogous conclusions regarding the hydrogen bonding properties of acetamide and other simple amides must await crystal structure determinations of other complexes in which they are involved.

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