Acta Cryst. (1974). B**30**, 980

Hydrogen Bonding NH···O=C of Barbiturates: The (1:1) Crystal Complex of Urea and 5,5-Diethylbarbituric Acid (Barbital)

BY G. L. GARTLAND* AND B. M. CRAVEN

Department of Crystallography, Univeristy of Pittsburgh, Pittsburgh, Pennsylvania 15260, *U.S.A.*

(*Received* 12 *October* 1973; *accepted* 10 *December* 1973)

The 1:1 complex of urea and barbital ($CH_4N_2O.C_8H_{12}N_2O_3$), m.p. 146–150°C, is orthorhombic with space group $P2_12_12_1$. Lattice translations are $a=10{\cdot}302$ (5), $b=10{\cdot}181$ (2), and $c=11{\cdot}627$ (3) Å. The crystal density ($D_m=1{\cdot}320$ g cm^{-3}) agrees with the calculated density ($D_x=1{\cdot}330$ g cm^{-3}) for four molecules of each component in the unit cell. The crystal structure has been determined from 1144 integrated intensities measured on a computer-controlled four-circle diffractometer with nickel-filtered Cu $K\alpha$ radiation (absorption coefficient, 9·05 cm^{-1}). The final R index is 0·037. In the crystal structure, barbital molecules hydrogen bond exclusively with urea molecules and *vice versa*. The NH···O=C hydrogen bonds in which barbital (NH) is donor are stronger (N···O distances 2·78 and 2·80 Å) than those in which it is acceptor (N···O distances 2·95, 3·16 Å). The minor role of urea as the hydrogen-bonding donor in this complex is confirmed by the isomorphous replacement of urea by acetamide. Thus we consider that the association in this complex is essentially that of a hydrogen-bonding acid (barbital) with a hydrogen-bonding base (urea).

Introduction

We have undertaken a series of crystal-structure determinations of molecular complexes of drug-active barbiturates such as barbital (Fig. 1) with other molecules which also contain the –NH–CO– amide grouping. Our particular interests are in the modes of NH···O=C hydrogen bonding, and the hydrogen-bonding distances in the crystal structures of the molecular complexes and of the component molecules. These crystal structures provide opportunities for NH···O=C hydrogen bonding of the types $A_d\cdots A_a$, $B_d\cdots B_a$, $A_d\cdots B_a$ and $B_d\cdots A_a$, where A and B are the component amide and barbiturate molecules respectively, and subscripts d and a refer to donor (NH) and acceptor (O=C) functions. We wish to determine whether any one of these is a preferred mode of hydrogen bonding, and whether there is any correlation between the N···O hydrogen-bonding distances and the mode of hydrogen bonding.

The results of nine crystal-structure determinations of barbiturate complexes, including those for the 1:1 barbital/urea complex which are presently reported, suggest that such relationships may exist. The barbiturate drugs appear to be more effective hydrogen-bonding donors than acceptors.

Experimental

The crystal complex was obtained as transparent prisms,† m.p. 146–150°C, from a solution of barbital (600 mg) and urea (300 mg) in an equal volume mixture of n-propanol and ethanol. The crystals are orthorhombic with space group $P2_12_12_1$ and lattice translations $a=10{\cdot}302$ (5), $b=10{\cdot}181$ (2) and $c=11{\cdot}627$ (3) Å. The crystal density (1·320 g cm^{-3}), which was determined by flotation in a mixture of ethyl acetate and tribromomethane, agrees with the calculated value (1·330 g cm^{-3}), assuming four molecules of each component in the unit cell. The lattice translations and X-ray intensity data were measured on a four-circle automatic diffractometer using nickel-filtered Cu $K\alpha$ radiation ($\lambda=1{\cdot}5418$ Å, $\mu=9{\cdot}05$ cm^{-1}). Integrated intensities were measured for 1144 symmetry-independent reflections in the range $\sin\theta/\lambda\le 0{\cdot}59$ Å^{-1} ($\theta\le 65°$) with the prism axis of the crystal (a) along the φ axis of the goniostat. The crystal dimensions were approximately 0·5 × 0·3 × 0·3 mm. Reflections were scanned in the θ:2θ mode at a rate of 2° min^{-1} with 20 s background counts being taken at each of the scan limits. The 2θ scan width was based on 1·4° and was varied to allow for spectral dispersion. There were 44 reflections for which the integrated intensity, I, was less than 1·2 $\sigma(I)$ as calculated from the counting statistics. These reflections were arbitrarily assigned intensities of $\sigma(I)/2$. No corrections were applied for X-ray absorption or extinction.

The crystal structure was determined by direct methods as reported in detail by Gartland (1971). Atomic parameters (Table 1) were refined by a block-diagonal least-squares procedure. The function minimized was $\sum_H w_H\Delta_H^2$, where $\Delta_H=|F_H^{\rm obs}|-|F_H^{\rm calc}|$. The weights were $w_H=1/\sigma^2(F_H)$, with $\sigma^2(F_H)=0{\cdot}16-0{\cdot}015\,|F_H|+0{\cdot}0024\,|F_H|^2$. The atomic scattering factors were those of Cromer & Waber (1965) for C, N, O and Stewart, Davidson & Simpson (1965) for H. All

---

* Present address: The University of Alabama Medical Center, Birmingham, Alabama 35233, U.S.A.

† Sekiguchi, Himuro, Horikoshi, Tsukuda, Okamoto & Yotsuyanagi (1969) describe the crystallization of this complex from n-propanol.

hydrogen-atom positions were obtained from difference Fourier syntheses which were calculated after refinement of anisotropic thermal parameters had been introduced for the non-hydrogen atoms. Hydrogen-atom positional parameters were subsequently included as variables in the refinement, but hydrogen-atom temperature parameters were fixed with values the same as those of the atoms to which they are covalently bonded. Before the last two cycles of least-squares refinement, 12 strong reflections for which $|F^{\text{calc}}| > |F^{\text{obs}}|$ were given zero weight. The calculated and observed structure amplitudes are listed in Table 2. The final overall R* index was 0·037. The r.m.s. displacements of atoms along the principal axes of their thermal ellipsoids are given in Table 1. In the barbital molecule, the largest atomic r.m.s. thermal displacements, excluding atoms of the ethyl groups, are approximately normal to the ring plane. Except for C(4) and C(5), which appear to have isotropic motion, the greatest deviations from this direction are about 20–25° for the carbonyl oxygen atoms. In the urea molecule, the largest thermal amplitudes are within 15° of being normal to the molecular plane, except for N(4), where the deviation from perpendicularity is 32°.

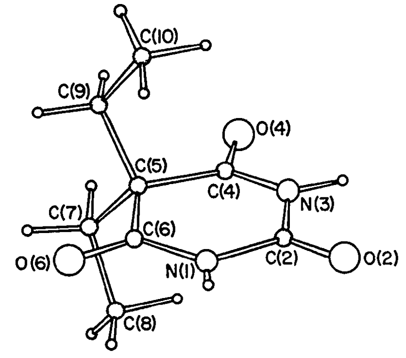

Fig. 1. Molecular structure of 5,5-diethylbarbituric acid (barbital).

---

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

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

Positional parameters are given as fractions of the unit-cell translations. Thermal parameters are given according to the expression: $T=\exp\left(-\sum_i \sum_j \beta_{ij} h_i h_j\right)$. The quantity U_k is the r.m.s. displacement (Å), derived from the components β_{ij}, along the direction of the kth principal axis of the thermal ellipsoid. The e.s.d.'s given in parentheses refer to the least significant figures in the parameter values. Non-hydrogen positional parameters and all thermal parameters are $\times 10^4$, hydrogen positional parameters are $\times 10^3$ and U_k parameters are $\times 10^2$.

(i) The barbital molecule

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}	U_1	U_2	U_3
N(1)	5754 (2)	4037 (2)	4891 (2)	93 (2)	70 (2)	60 (1)	3 (2)	25 (1)	3 (1)	17	19	25
H(1)	530 (2)	397 (2)	549 (2)									
C(2)	6588 (2)	3014 (2)	4688 (2)	108 (2)	62 (2)	52 (2)	0 (2)	9 (2)	2 (2)	18	19	24
O(2)	6704 (2)	2096 (2)	5348 (2)	185 (3)	87 (2)	71 (1)	25 (2)	32 (2)	27 (1)	18	23	33
N(3)	7285 (2)	3059 (2)	3684 (2)	101 (2)	65 (2)	48 (1)	21 (2)	10 (1)	6 (1)	17	18	25
H(3)	782 (3)	242 (2)	355 (2)									
C(4)	7199 (2)	4030 (2)	2864 (2)	66 (2)	85 (2)	55 (2)	2 (2)	−2 (1)	3 (2)	19	19	21
O(4)	7778 (2)	3896 (2)	1961 (1)	99 (2)	127 (2)	49 (1)	24 (2)	14 (1)	12 (1)	17	22	28
C(5)	6429 (2)	5255 (2)	3138 (2)	76 (2)	65 (2)	61 (2)	−1 (2)	1 (2)	8 (2)	18	20	21
C(6)	5626 (2)	5145 (2)	4232 (2)	86 (2)	71 (2)	71 (2)	1 (2)	13 (2)	−6 (2)	19	20	24
O(6)	4891 (2)	6006 (2)	4520 (2)	143 (2)	95 (2)	115 (2)	48 (2)	47 (2)	2 (2)	17	25	34
C(7)	5524 (3)	5591 (2)	2125 (2)	101 (3)	81 (2)	79 (2)	8 (2)	−18 (2)	7 (2)	19	22	26
H(71)	518 (3)	639 (2)	233 (2)									
H(72)	614 (3)	575 (3)	145 (2)									
C(8)	4563 (3)	4504 (3)	1814 (3)	92 (3)	131 (3)	102 (2)	1 (3)	−16 (2)	−12 (3)	21	25	28
H(81)	410 (3)	429 (3)	254 (2)									
H(82)	506 (3)	368 (3)	154 (3)									
H(83)	392 (3)	484 (3)	122 (2)									
C(9)	7427 (3)	6382 (2)	3301 (2)	109 (3)	84 (2)	76 (2)	−24 (2)	−3 (2)	10 (2)	19	23	26
H(91)	689 (3)	722 (3)	335 (2)									
H(92)	789 (3)	654 (2)	254 (2)									
C(10)	8372 (3)	6199 (3)	4282 (2)	108 (3)	130 (3)	75 (2)	−22 (3)	−2 (2)	−10 (2)	22	23	28
H(101)	786 (3)	605 (3)	500 (2)									
H(102)	894 (3)	539 (3)	419 (2)									
H(103)	902 (3)	696 (3)	423 (2)									

(ii) The urea molecule

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}	U_1	U_2	U_3
C	3894 (2)	4614 (2)	7596 (2)	67 (2)	92 (2)	60 (2)	−3 (2)	1 (2)	−11 (2)	19	19	23
O	4178 (2)	3786 (2)	6845 (1)	113 (2)	87 (2)	67 (1)	−31 (2)	30 (1)	−23 (1)	18	19	29
N(2)	4294 (2)	5858 (2)	7532 (2)	129 (2)	81 (2)	84 (2)	−3 (2)	18 (2)	−16 (2)	19	23	28
H(21)	470 (3)	596 (2)	698 (2)									
H(22)	425 (3)	644 (3)	816 (2)									
N(4)	3164 (2)	4292 (3)	8499 (2)	116 (2)	134 (3)	66 (2)	−13 (2)	23 (2)	−13 (2)	19	25	28
H(41)	300 (3)	356 (3)	856 (2)									
H(42)	295 (3)	488 (3)	904 (2)									

The molecular structures

(i) *Barbital*

The oxopyrimidine ring is almost planar, with C(5) and ethyl carbon atoms forming the spine of a hydrocarbon chain which extends nearly perpendicular to the ring. The slight twist conformation of the ring has already been shown and compared with similar conformations found in other barbiturate crystal structures (Craven, Cusatis, Gartland & Vizzini, 1973). Torsion angles C(8)–C(7) $\rightarrow$ C(5)–C(9) and C(10)–C(9) $\rightarrow$ C(5)–C(7) are 184·6 and 180·9° respectively, indicating that the extended hydrocarbon spine C(8)–C(7)–C(5)–C(9)–C(10) deviates slightly from twofold symmetry about the axis C(5)$\cdots$C(2). All carbon atoms of the hydrocarbon spine are coplanar to within 0·03 Å, and the best least-squares planes through these atoms and through atoms of the pyrimidine ring form a dihedral angle of 89·3°.

The bond lengths and angles (Table 3) are similar to those found in other barbiturates (Craven *et al.*, 1973). Within experimental error, the C=O and C–N bond lengths are symmetrical about the C(5)$\cdots$C(2) molecular axis. There is thus no evidence of the small (0·01 Å) C–N and C=O bond-length differences which consistently appear in barbiturate crystal structures

Table 2. *Observed and calculated structure amplitudes*

Successive columns are l, $10|F_H^{\text{obs}}|$, $10|F_H^{\text{calc}}|$. Reflections marked (*) were given zero weight in the final refinement cycles.

	FOBS	CAL
H= 0 K= 0		
2	479*	648
4	432	467
6	307	297
8	221	221
10	21	23
12	19	19
H= 0 K= 1		
1	270	302
2	475*	601
3	323	347
4	533	606
5	186	190
6	41	38
7	145	141
8	122	112
9	126	126
10	57	52
11	91	93
12	88	85
13	51	51
H= 0 K= 2		
0	560*	860
1	135	136
2	579*	738
3	357	375
4	155	155
5	153	133
6	117	122
7	79	77
8	109	104
9	105	109
10	71	70
11	185	179
12	103	100
13	7	10
H= 0 K= 3		
1	525*	655
2	182	186
3	138	134
4	283	268
5	113	113
6	17	11
7	6	4
8	194	193
9	211	205
10	144	145
11	54	54
12	18	15
H= 0 K= 4		
0	548*	658
1	201	202
2	228	231
3	422	443
4	176	176
5	41	40
6	170	164
7	112	113
8	93	93
9	151	149
10	72	68
11	16	8
12	10	7
H= 0 K= 5		
1	24	22
2	277	275
3	163	160
4	140	136
5	19	18
6	86	89
7	38	34
8	38	36
9	18	17
10	7	2
11	31	30
12	77	77
H= 0 K= 6		
0	325	342
1	11	10
2	103	101
3	316	319
4	225	223
5	7	7
6	21	24
7	166	165
8	21	17
9	90	91
10	7	6
11	6	7
H= 0 K= 7		
1	54	54
2	63	65
3	94	97
4	61	59
5	96	91
6	47	43
7	14	13
8	112	113
9	7	10
10	116	115
H= 0 K= 8		
0	8	2
1	238	246
2	7	8
3	116	118
4	38	39
5	123	125
6	7	6
7	17	17
8	148	152
9	22	24
H= 0 K= 9		
1	186	185
2	55	54
3	16	15
4	128	133
5	73	75
6	94	96
7	17	18
8	6	2
H= 0 K= 10		
0	195	196
1	116	117
2	143	147
3	23	25
4	68	68
5	18	17
6	10	11
H= 0 K= 11		
1	32	33
2	45	48
3	33	31
4	6	7
H= 1 K= 0		
1	19	19
2	411	488
3	357	383
4	38	34
5	41	34
6	33	34
7	194	179
8	7	1
9	54	49
10	44	47
11	89	84
12	20	18
13	24	25
H= 1 K= 1		
0	416*	549
1	420	485
2	121	117
3	343	373
4	74	83
5	270	265
6	125	120
7	27	18
8	186	185
9	68	66
10	172	169
11	118	118
12	60	58
13	57	59
H= 1 K= 2		
0	154	166
1	205	206
2	174	190
3	241	245
4	195	190
5	153	148
6	313	313
7	254	247
8	31	30
9	196	194
10	93	91
11	146	144
12	65	63
13	51	50
H= 1 K= 3		
0	388	455
1	202	202
2	181	182
3	205	200
4	97	95
5	216	206
6	44	41
7	141	135
8	106	103
9	37	36
10	106	106
11	64	62
12	37	34
H= 1 K= 4		
0	66	67
1	316	319
2	90	81
3	93	86
4	113	106
5	198	185
6	165	162
7	35	35
8	50	49
9	153	146
10	13	6
11	31	29
12	52	49
H= 1 K= 5		
0	61	64
1	192	188
2	40	41
3	154	145
4	269	263
5	200	178
6	28	28
7	68	65
8	81	83
9	60	60
10	100	98
11	69	68
12	17	18
H= 1 K= 6		
0	94	85
1	149	143
2	181	176
3	250	249
4	40	42
5	46	47
6	56	60
7	55	60
8	87	84
9	33	30
10	81	78
11	59	57
H= 1 K= 7		
0	121	116
1	101	104
2	15	13
3	171	170
4	21	21
5	72	69
6	33	29
7	133	135
8	63	60
9	112	114
10	51	52
H= 1 K= 8		
0	16	21
1	75	77
2	80	81
3	75	78
4	69	66
5	57	58
6	97	100
7	63	63
8	21	21
9	47	44
H= 1 K= 9		
0	85	82
1	156	155
2	86	85
3	93	90
4	57	58
5	124	121
6	25	23
7	69	68
8	13	14
H= 1 K= 10		
0	17	19
1	110	111
2	85	86
3	104	108
4	38	36
5	66	68
6	23	21
H= 1 K= 11		
0	49	53
1	83	83
2	51	51
3	44	46
4	31	31
H= 2 K= 0		
0	166	168
1	517*	698
2	174	168
3	76	75
4	394	406
5	314	316
6	252	246
7	144	146
8	7	9
9	49	43
10	7	6
11	48	48
12	82	81
13	6	10
H= 2 K= 1		
0	319	348
1	615*	831
2	605*	764
3	391	413
4	530	575
5	216	219
6	108	110
7	80	77
8	86	87
9	94	89
10	52	53
11	124	124
12	34	34
13	51	53
H= 2 K= 2		
0	560*	718
1	230	221
2	380	391
3	334	336
4	58	60
5	204	208
6	318	313
7	119	117
8	25	23
9	83	82
10	51	51
11	154	154
12	62	64
H= 2 K= 3		
0	388	418
1	281	299
2	354	364
3	250	236
4	162	155
5	184	184
6	196	189
7	184	177
8	121	117
9	107	108
10	34	33
11	85	84
12	55	55
H= 2 K= 4		
0	5	0
1	253	250
2	292	289
3	193	180
4	179	171
5	122	118
6	19	16
7	132	128
8	146	140
9	176	178
10	77	79
11	26	25
12	17	16
H= 2 K= 5		
0	219	222
1	99	103
2	167	164
3	250	250
4	140	135
5	172	168
6	56	56
7	88	95
8	123	119
9	68	70
10	83	88
11	55	57
H= 2 K= 6		
0	141	141
1	46	45
2	116	108
3	143	141
4	170	173
5	60	57
6	30	25
7	88	86
8	109	105
9	108	111
10	104	106
11	17	18
H= 2 K= 7		
0	162	160
1	114	114
2	99	97
3	76	74
4	92	89
5	84	83
6	88	87
7	63	60
8	20	12
9	115	119
10	45	43
H= 2 K= 8		
0	27	23
1	121	124
2	172	173
3	32	34
4	66	63
5	38	41
6	110	116
7	105	108
8	57	58
9	27	26
H= 2 K= 9		
0	233	240
1	72	73
2	46	49
3	70	71
4	110	112
5	37	38
6	25	28
7	55	56
8	6	4
H= 2 K= 10		
0	35	37
1	90	91
2	74	74
3	70	73
4	11	11
5	55	57
6	14	17
H= 2 K= 11		
0	17	17
1	55	55
2	86	86
3	21	22
4	24	20
H= 3 K= 0		
1	358	393
2	189	184
3	304	323
4	9	10
5	222	222
6	183	186
7	94	95
8	63	62
9	18	18
10	150	166
11	66	65
12	117	129
H= 3 K= 1		
0	446	475
1	397	430
2	670*	832
3	366	358
4	124	125
5	294	294
6	33	30
7	138	139
8	39	35
9	68	68
10	27	30
11	59	62
12	27	30
H= 3 K= 2		
0	441	485
1	251	244
2	344	344
3	186	184
4	27	26
5	197	195
6	185	187
7	37	33
8	77	81
9	43	42
10	113	115
11	51	51
12	27	29
H= 3 K= 3		
0	465	495
1	325	328
2	399	411
3	275	271
4	209	200
5	152	144
6	180	178
7	72	70
8	126	129
9	94	92
10	57	58
11	41	38
12	46	48
H= 3 K= 4		
0	205	204
1	189	186
2	33	27
3	117	115
4	182	179
5	81	75
6	87	82
7	94	95
8	37	37
9	87	89
10	62	63
11	21	20
12	51	55
H= 3 K= 5		
0	261	260
1	301	301
2	292	278
3	63	61
4	81	80
5	91	94
6	107	109
7	113	116
8	201	208
9	105	104
10	30	31
11	17	17
H= 3 K= 6		
0	68	70
1	146	142
2	103	100
3	87	80
4	56	58
5	76	75
6	63	64
7	144	137
8	124	129
9	24	21
10	7	6
H= 3 K= 7		
0	7	12
1	28	27
2	63	64
3	158	161
4	18	15
5	111	109
6	151	157
7	98	97
8	58	57
9	46	46
10	33	37
H= 3 K= 8		
0	87	89
1	72	76
2	111	112
3	141	140
4	47	47
5	54	54
6	61	63
7	7	4
8	52	54
9	6	5
H= 3 K= 9		
0	31	30
1	146	151
2	130	129
3	117	118
4	42	43
5	20	24
6	33	37
7	53	56
H= 3 K= 10		
0	50	54
1	43	42
2	37	37
3	53	53
4	7	5
5	23	23
6	64	68
H= 3 K= 11		
0	16	14
1	6	5
2	34	36
3	43	43
H= 4 K= 0		
0	138	143
1	220	221
2	156	156
3	464	486
4	176	177
5	269	285
6	69	77
7	23	29
8	71	69
9	34	35
10	30	26
11	70	80
12	68	77
H= 4 K= 1		
0	255	237
1	278	269
2	117	113
3	190	196
4	117	117
5	358	351
6	92	93
7	85	75
8	88	88
9	102	114
10	17	18
11	55	60
12	59	65
H= 4 K= 2		
0	132	130
1	389	393
2	260	254
3	277	277
4	245	248
5	170	166
6	40	40
7	46	47
8	102	99
9	102	109
10	46	49
11	23	27
12	38	39
H= 4 K= 3		
0	229	223
1	159	164
2	303	294
3	192	193
4	214	207
5	147	144
6	92	85
7	104	99
8	111	121
9	115	118
10	78	80
11	53	57
12	19	22
H= 4 K= 4		
0	323	324
1	172	166
2	269	260
3	326	327
4	108	108
5	69	68
6	79	76
7	149	142
8	162	159
9	28	28
10	58	62
11	24	26
H= 4 K= 5		
0	14	14
1	211	210
2	53	44
3	144	140
4	48	47
5	136	131
6	182	176
7	125	125
8	67	65
9	66	66
10	20	19
11	67	68
H= 4 K= 6		
0	63	67
1	74	74
2	23	14
3	120	118
4	161	155
5	61	57
6	19	15
7	113	111
8	111	112
9	49	49
10	48	49
H= 4 K= 7		
0	156	157
1	121	121
2	40	41
3	191	188
4	77	79
5	61	60
6	29	30
7	88	89
8	74	74
9	15	13
H= 4 K= 8		
0	44	38
1	112	109
2	48	50
3	76	77
4	101	99
5	99	99
6	68	64
7	31	29
8	17	15
H= 4 K= 9		
0	63	58
1	46	45
2	25	25
3	93	93
4	30	29
5	57	57
6	50	53
7	34	35
H= 4 K= 10		
0	14	9
1	43	44
2	49	47
3	46	47
4	63	64
5	27	25
H= 4 K= 11		
0	79	78
H= 5 K= 0		
1	200	188
2	167	168
3	175	169
4	52	60
5	89	93
6	126	121
7	65	64
8	89	92
9	55	63
10	38	37
11	19	20
12	6	7
H= 5 K= 1		
0	120	121
1	88	82
2	143	136
3	125	125
4	238	235
5	29	29
6	35	33
7	141	136
8	93	93
9	75	74
10	23	23
11	75	80
12	21	21
H= 5 K= 2		
0	153	154
1	139	131
2	107	102
3	195	197
4	179	172
5	188	182
6	88	84
7	53	53
8	84	87
9	59	61
10	57	58
11	38	35
H= 5 K= 3		
0	106	102
1	120	124
2	170	177
3	114	110
4	220	221
5	61	59
6	194	189
7	97	93
8	38	36
9	84	83
10	48	53
11	47	48
H= 5 K= 4		
0	45	40
1	98	96
2	65	59
3	46	47
4	203	200
5	175	177
6	20	17
7	116	111
8	78	76
9	30	30
10	40	36
11	39	40
H= 5 K= 5		
0	21	21
1	143	135
2	62	60
3	68	68
4	82	78
5	47	48
6	174	168
7	168	163
8	35	34
9	32	30
10	63	62
H= 5 K= 6		
0	123	120
1	37	35
2	53	49
3	212	219
4	89	89
5	166	168
6	131	130
7	28	24
8	64	66
9	31	28
10	46	41
H= 5 K= 7		
0	17	12
1	72	66
2	21	20
3	47	45
4	130	132
5	87	86
6	54	53
7	66	67
8	58	58
9	52	47
H= 5 K= 8		
0	34	31
1	67	68
2	120	122
3	68	66
4	7	6
5	32	36
6	85	86
7	43	43
H= 5 K= 9		
0	14	15
1	7	11
2	37	36
3	60	63
4	40	43
5	7	13
6	41	39
H= 5 K= 10		
0	61	64
1	30	30
2	43	48
3	27	26
4	18	16
H= 6 K= 0		
0	206	212
1	178	178
2	379	392
3	202	193
4	50	46
5	24	19
6	24	23
7	22	23
8	49	43
9	27	24
10	90	92
11	12	8
H= 6 K= 1		
0	19	15
1	64	62
2	147	147
3	138	138
4	69	66
5	38	39
6	108	106
7	63	70
8	80	82
9	39	40
10	59	56
11	12	12
H= 6 K= 2		
0	159	159
1	86	88
2	156	147
3	66	60
4	241	246
5	92	92
6	186	184
7	74	72
8	102	98
9	42	43
10	51	53
11	35	34
H= 6 K= 3		
0	19	15
1	300	301
2	58	56
3	114	117
4	185	187
5	139	136
6	158	153
7	8	13
8	54	52
9	43	42
10	36	33
11	11	9
H= 6 K= 4		
0	161	156
1	82	80
2	164	164
3	103	103
4	137	132
5	172	173
6	257	256
7	119	114
8	68	63
9	63	66
10	67	64
H= 6 K= 5		
0	26	19
1	26	26
2	116	114
3	143	144
4	61	60
5	82	81
6	58	57
7	52	51
8	44	44
9	30	30
10	61	64
H= 6 K= 6		
0	17	20
1	15	15
2	76	72
3	94	95
4	143	140
5	228	230
6	29	28
7	18	14
8	32	32
9	44	43
H= 6 K= 7		
0	25	28
1	130	130
2	61	58
3	110	115
4	50	49
5	44	44
6	24	21
7	27	25
8	64	65
H= 6 K= 8		
0	52	50
1	65	62
2	21	27
3	45	43
4	35	37
5	44	44
6	80	80
7	66	63
H= 6 K= 9		
0	44	45
1	22	20
2	40	43
3	38	37
4	30	27
5	32	31
H= 6 K= 10		
0	13	9
1	52	50
H= 7 K= 0		
1	92	98
2	119	121
3	126	116
4	51	47
5	14	12
6	36	37
7	105	105
8	54	54
9	25	26
10	26	23
H= 7 K= 1		
0	52	51
1	117	116
2	63	58
3	20	19
4	115	110
5	36	35
6	138	137
7	34	32
8	31	31
9	43	47
10	53	55
H= 7 K= 2		
0	107	109
1	67	62
2	83	85
3	154	152
4	26	27
5	126	124
6	107	107
7	18	20
8	16	19
9	78	80
10	27	24
H= 7 K= 3		
0	93	94
1	86	87
2	80	76
3	222	223
4	54	52
5	135	137
6	137	138
7	15	14
8	30	34
9	54	55
10	46	45
H= 7 K= 4		
0	29	10
1	113	115
2	95	90
3	86	86
4	77	80
5	20	20
6	82	88
7	17	19
8	43	45
9	41	41
H= 7 K= 5		
0	39	37
1	78	74
2	42	43
3	101	101
4	85	82
5	161	159
6	34	37
7	48	46
8	7	8
9	28	26
H= 7 K= 6		
0	28	22
1	19	20
2	55	60
3	49	51
4	81	78
5	12	7
6	42	44
7	31	29
8	11	9
H= 7 K= 7		
0	45	51
1	46	47
2	52	52
3	25	22
4	46	50
5	7	14
6	68	67
7	61	60
H= 7 K= 8		
0	27	36
1	62	60
2	73	75
3	36	33
4	29	28
5	57	54
H= 7 K= 9		
0	7	3
1	40	40
2	47	46
3	47	46
H= 8 K= 0		
0	126	125
1	36	32
2	28	25
3	41	42
4	41	43
5	7	7
6	13	11
7	78	78
8	16	15
9	74	78
H= 8 K= 1		
0	71	70
1	106	98
2	54	53
3	26	27
4	119	120
5	100	101
6	70	73
7	36	32
8	88	87
9	19	18
H= 8 K= 2		
0	63	63
1	40	39
2	50	51
3	120	117
4	168	169
5	99	95
6	7	4
7	47	49
8	28	27
9	58	61
H= 8 K= 3		
0	7	5
1	62	62
2	50	48
3	21	22
4	86	90
5	112	115
6	52	54
7	27	24
8	53	54
9	54	50
H= 8 K= 4		
0	7	8
1	91	93
2	67	65
3	45	44
4	60	55
5	69	70
6	54	58
7	63	59
8	53	52
H= 8 K= 5		
0	73	80
1	46	49
2	48	45
3	51	52
4	50	54
5	87	86
6	72	70
7	65	68
8	54	55
H= 8 K= 6		
0	78	77
1	48	47
2	67	66
3	56	59
4	57	55
5	64	64
6	104	104
7	53	50
H= 8 K= 7		
0	45	45
1	62	68
2	37	39
3	30	29
4	89	86
5	18	19
H= 8 K= 8		
0	28	26
1	21	20
2	39	40
3	54	58
H= 9 K= 0		
1	30	32
2	58	54
3	67	69
4	63	63
5	34	33
6	24	24
7	28	28
8	36	34
H= 9 K= 1		
0	69	73
1	57	57
2	115	118
3	108	106
4	82	84
5	95	95
6	29	29
7	48	49
8	46	49
H= 9 K= 2		
0	29	31
1	102	98
2	88	90
3	17	16
4	90	86
5	27	28
6	52	54
7	54	52
8	62	63
H= 9 K= 3		
0	49	49
1	99	106
2	13	12
3	34	35
4	91	92
5	66	65
6	53	50
7	71	74
8	66	70
H= 9 K= 4		
0	29	29
1	82	82
2	76	77
3	7	13
4	89	88
5	65	65
6	73	75
7	39	38
H= 9 K= 5		
0	16	13
1	58	59
2	58	61
3	27	30
4	34	37
5	53	54
6	17	19
H= 9 K= 6		
0	113	118
1	25	27
2	18	22
3	36	36
4	7	11
5	48	47
H= 9 K= 7		
0	35	33
1	25	24
2	34	34
3	50	49
H= 10 K= 0		
0	69	68
1	21	23
2	8	9
3	160	162
4	21	23
5	66	63
6	15	15
7	55	60
H= 10 K= 1		
0	21	21
1	34	30
2	45	46
3	54	57
4	67	65
5	7	6
6	11	13
7	45	47
H= 10 K= 2		
0	19	16
1	22	21
2	36	35
3	16	18
4	43	48
5	52	53
6	17	17
H= 10 K= 3		
0	17	18
1	24	26
2	21	20
3	57	59
4	33	30
5	28	26
6	6	8
H= 10 K= 4		
0	36	38
1	26	25
2	26	25
3	49	50
4	7	7
5	34	32
H= 10 K= 5		
0	7	7
1	57	54
2	39	36
3	25	21
4	31	31
H= 10 K= 6		
0	49	53
1	32	32
2	27	27
H= 11 K= 0		
1	123	125
2	70	70
3	7	13
4	27	30
H= 11 K= 1		
0	83	84
1	40	38
2	44	45
3	49	51
4	13	15
H= 11 K= 2		
0	35	35
1	57	58
2	28	29
3	55	58
4	13	13
H= 11 K= 3		
0	34	35
1	72	72
2	45	44
3	30	33
H= 11 K= 4		
0	44	47
1	22	20

where the O(4) oxygen atom is hydrogen bonded but O(6) is not. In barbital/urea, the barbital O(4) and O(6) oxygen atoms are both at most weakly hydrogen bonded.

(ii) *Urea*

The urea molecule is planar except possibly for the hydrogen atom H(22) which is 0·19 Å (6σ) from the plane. The bond lengths and angles (Table 3) are in good agreement with those found in the crystal structures of urea itself (Caron & Donohue, 1964; Pryor & Sanger, 1970) and the 1:1 glucose/urea complex (Snyder & Rosenstein, 1971). The bonds N(2)–H(22) and N(4)–H(42), which are *trans* to the urea oxygen atom, may be significantly longer (0·94 and 0·89 Å) than the other two urea N–H bonds (0·77 Å). The longer bonds involve the hydrogen atoms which are weakly hydrogen bonded to barbital oxygen atom O(2).

Table 3. *Bond lengths and angles for the barbital and urea molecules*

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 digits in the tabulated quantities.

(*a*) Bond lengths

(i) Barbital

C(6)–N(1)	1·370 (3) Å	N(1)—H(1)	0·84 (2) Å
N(1)–C(2)	1·370 (3)	N(3)—H(3)	0·87 (2)
C(2)–N(3)	1·371 (3)	C(7)—H(71)	0·92 (2)
N(3)–C(4)	1·376 (3)	C(7)—H(72)	1·02 (3)
C(6)–O(6)	1·205 (3)	C(9)—H(91)	1·02 (3)
C(2)–O(2)	1·215 (3)	C(9)—H(92)	1·01 (2)
C(4)–O(4)	1·215 (3)	C(8)—H(81)	0·99 (3)
C(5)–C(4)	1·511 (3)	C(8)—H(82)	1·04 (3)
C(5)–C(6)	1·522 (3)	C(8)—H(83)	1·02 (3)
C(5)–C(7)	1·540 (3)	C(10)–H(101)	1·00 (3)
C(5)–C(9)	1·552 (3)	C(10)–H(102)	1·02 (3)
C(7)–C(8)	1·528 (4)	C(10)–H(103)	1·03 (3)
C(9)–C(10)	1·511 (4)		

(ii) Urea

C——O	1·238 (3)	N(2)—H(21)	0·77 (2)
C——N(2)	1·344 (3)	N(2)—H(22)	0·94 (3)
C——N(4)	1·332 (3)	N(4)—H(41)	0·77 (3)
		N(4)—H(42)	0·89 (3)

(*b*) Bond angles

(i) Barbital

N(1)–C(2)–O(2)	122·5 (2)°
N(1)–C(2)–N(3)	116·7 (2)
N(3)–C(2)–O(2)	120·8 (2)
C(2)–N(3)–C(4)	125·5 (2)
N(3)–C(4)–O(4)	119·1 (2)
N(3)–C(4)–C(5)	118·7 (2)
C(5)–C(4)–O(4)	122·1 (2)
C(4)–C(5)–C(6)	113·6 (2)
C(5)–C(6)–O(6)	121·3 (2)
C(5)–C(6)–N(1)	118·4 (2)
N(1)–C(6)–O(6)	120·2 (2)
C(6)–N(1)–C(2)	126·1 (2)
C(4)–C(5)–C(7)	109·8 (2)
C(4)–C(5)–C(9)	106·8 (2)
C(6)–C(5)–C(9)	108·2 (2)
C(6)–C(5)–C(7)	109·1 (2)

Table 3 (*cont.*)

C(7)——C(5)—C(9)	109·3 (2)°
C(5)——C(7)—C(8)	114·3 (2)
C(5)——C(9)—C(10)	115·4 (2)
C(6)——N(1)—H(1)	119 (1)
C(2)——N(1)—H(1)	115 (1)
C(4)——N(3)—H(3)	117 (2)
C(2)——N(3)—H(3)	117 (2)
H(71)—C(7)—H(72)	107 (2)
H(81)—C(8)—H(82)	109 (2)
H(81)—C(8)—H(83)	110 (2)
H(82)—C(8)—H(83)	113 (2)
H(91)—C(9)—H(92)	100 (2)
H(101)-C(10)-H(102)	106 (2)
H(101)-C(10)-H(103)	121 (2)
H(102)-C(10)-H(103)	103 (2)

(ii) Urea

N(2)-C——O	122·0 (2)°
O——C——N(4)	121·2 (2)
N(4)-C——N(2)	116·9 (2)
C——N(2)-H(21)	110 (2)
C——N(2)-H(22)	123 (2)
H(21)—N(2)—H(22)	126 (3)
C———N(4)—H(41)	116 (2)
C———N(4)—H(42)	121 (2)
H(41)—N(4)—H(42)	122 (3)

The hydrogen bonding

In the crystal structure of the 1:1 barbital/urea complex, the most important intermolecular interactions are the NH···O=C hydrogen bonds, which link the molecules to form a three-dimensional network (Fig. 2). The hydrogen-bonding environments of barbital and urea are shown separately in Figs. 3 and 4. Barbital molecules are hydrogen bonded exclusively to urea molecules and *vice versa*, *i.e.*, there are only $B_d\cdots A_a$ and $A_d\cdots B_a$ hydrogen bonds. The two barbital NH groups both form hydrogen bonds with the urea oxygen atom with N···O distances of 2·78 and 2·80 Å. Only two of the four urea hydrogen atoms form hydrogen bonds, and both of these involve the same barbital oxygen atom, O(2). The N···O distances (2·95 and 3·16 Å) are significantly longer for the $(\mathrm{NH})_{\mathrm{urea}}\cdots\mathrm{O(2)}_{\mathrm{barb}}$ hydrogen bonds than for the $(\mathrm{NH})_{\mathrm{barb}}\cdots\mathrm{O}_{\mathrm{urea}}$ hydrogen bonds, and in the former, the NH···O angles are more severely bent (Table 4). The NH···O=

Table 4. *Hydrogen-bonding distances and angles*

Parameters for atoms not in the crystal chemical unit (as listed in Table 1) may be derived by operations specified by the 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 tabulated values.

N(1)····O	2·803 (3) Å	N(1)···O———C	129·9 (2)°
H(1)····O	1·96 (2)	N(1)——H(1)····O	177 (2)
N(3)····O_i	2·777 (3)	N(3)···O_i———C_i	116·6 (1)
H(3)····O_i	1·92 (2)	N(3)——H(3)····O_i	171 (2)
N(2)····$\mathrm{O(2)}_j$	2·953 (3)	N(2)···$\mathrm{O(2)}_j$——$\mathrm{C(2)}_j$	145·2 (2)
H(22)···$\mathrm{O(2)}_j$	2·10 (3)	N(2)——H(22)···$\mathrm{O(2)}_j$	150 (2)
N(4)····$\mathrm{O(2)}_j$	3·157 (3)	N(4)···$\mathrm{O(2)}_j$——$\mathrm{C(2)}_j$	165·5 (2)
H(42)···$\mathrm{O(2)}_j$	2·39 (3)	N(4)——H(42)···$\mathrm{O(2)}_j$	144 (2)

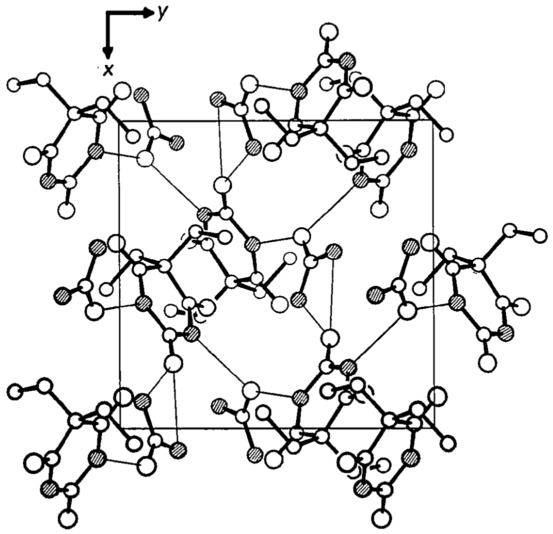

Fig. 2. The crystal structure viewed down **c**. Circles of decreasing size represent oxygen, nitrogen and carbon atoms respectively. Nitrogen atoms are also cross-hatched. Hydrogen bonds are shown as thin lines.

C hydrogen bonds in which urea is donor ($A_d\cdots B_a$) are thus considerably weaker than those in which barbiturate is donor ($B_d\cdots A_a$). This conclusion is supported by a comparison with the structure of the 1:1 barbital/acetamide complex (Hsu & Craven, 1974*a*), which is isomorphous with the 1:1 barbital/urea complex. The CH_3 group of acetamide, which does not hydrogen bond, replaces one of the NH_2 groups of urea, with only minor perturbation of the crystal structure.

The existence of both strong and weak NH···O=C hydrogen bonds in the barbital/urea crystal structure may be the result of the overall packing requirements of more or less rigid molecules. However, the N···O distance* may also depend to some extent, on the electronic structures of the molecules which provide the particular NH donor group and carbonyl oxygen acceptor atom. A similar effect has been noted in the hydrogen bonding of ammonium ions with oxyanions in the crystal structures of inorganic salts. Baur & Khan (1970) find that the N···O distances in such NH···O hydrogen bonds increase with the coordination number of the oxygen acceptor atom.

Table 5 lists the N···O distances determined from crystal structures with NH···O=C hydrogen bonds in which a barbiturate provides either the NH donor, the carbonyl acceptor or both. A remarkable feature is the narrow range (2·82 to 2·92 Å) of the $B_d\cdots B_a$ hydrogen bond N···O distances in the crystal structures of the barbituric acids themselves [Table 5(*a*)]. The barbiturate ring (Fig. 1) has one carbonyl group C(2)–O(2) covalently bonded to two NH groups and two equivalent carbonyl groups C(4)–O(4) and C(6)–O(6) bonded to one NH group. The N···O distances for hydrogen bonds between barbiturate NH donors and these two kinds of barbiturate oxygen atoms have very similar distributions. The average values are 2·88 Å and 2·89 Å for distances involving O(4) and O(2), respectively. It should be noted that in many cases, the oxygen atoms accept a second hydrogen bond. The

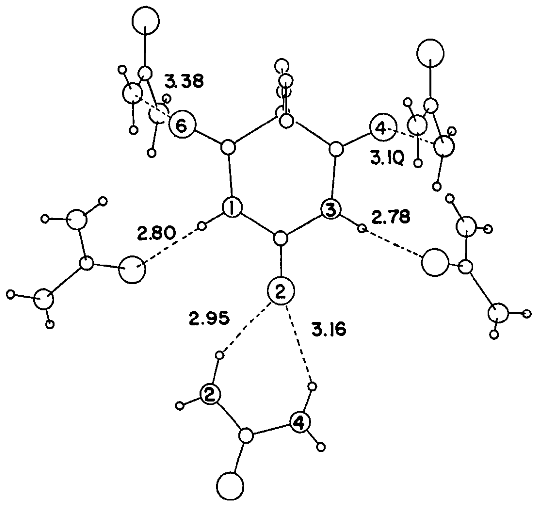

Fig. 3. The environment of the barbital molecule viewed normal to the plane of the pyrimidine ring. Distances N···O are shown in Å.

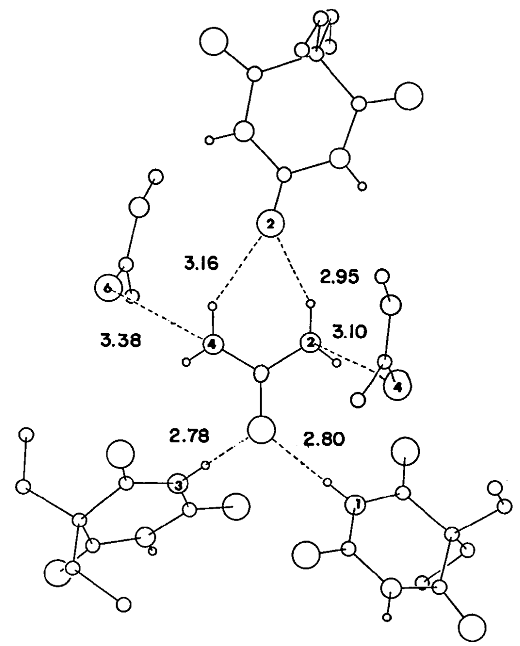

Fig. 4. The environment of the urea molecule viewed normal to the plane of the molecule. Distances N···O are shown in Å.

---

* The N···O distance gives a convenient, although not a definitive measure of hydrogen-bond strength. Nakamoto, Margoshes & Rundle (1955) have correlated NH infrared stretching frequencies with N···O distances in NH···O hydrogen bonds.

angles N–H···O range between 155 and 177°, with an average value of 170°. The N···O=C angles are grouped in the ranges 124–131° and 160–177°. There is no obvious correlation between either of these angles and the N···O distance.

The N···O distances for $B_d\cdots B_a$ hydrogen bonds in crystal structures of 1-methylbarbituric acids [Table 5(*b*)], barbiturate anions [Table 5(*c*)] and barbiturate molecular complexes [Table 5(*d*)] fall within the same range as found in Table 5(*a*) (2·82 to 2·92 Å) except for one slightly shorter distance of 2·78 Å in calcium barbital trihydrate, and three slightly longer distances of 2·93, 2·94 and 2·98 Å in 2:1 barbital/caffeine. Thus changes in barbiturate structure, electronic charge and molecular environment appear to have at most a small effect on the observed N···O distances in NH···O=C hydrogen bonds which involve barbiturates as both donor and acceptor. These hydrogen bonds may be considered to have a distance N···O of 2·9 Å subject to variations of ±0·1 Å.*

---

* Table 5 lists hydrogen-bonding data for barbiturates with non-polar C(5) substituents. Voet & Rich (1970) list data for barbituric acid, its dihydrate and other non drug-active barbiturates with polar C(5) substituents. The N···O distances in these crystal structures range from 2·79 to 3·07 Å. The long N···O distances of 3·00 and 3·07 Å in perdeuterated violuric acid monohydrate have been explained (Craven & Takei, 1964) in terms of an unusual kind of intermolecular packing.

Table 5. *Distances* N···O *in* NH···O=C *hydrogen bonds involving barbiturate derivatives with nonpolar* C(5) *substituents*

Crystal structure	$(\mathrm{NH})_{\mathrm{barb}}\cdots\mathrm{O}(4)=\mathrm{C}_{\mathrm{barb}}$	$(\mathrm{NH})_{\mathrm{barb}}\cdots\mathrm{O}(2)=\mathrm{C}_{\mathrm{barb}}$
(*a*) Barbituric acids		
5,5-Diethylbarbituric acid (barbital), form I (Craven, Vizzini & Rodrigues, 1969)	2·87 Å	2·89 Å
Barbital, form II (Craven, Vizzini & Rodrigues, 1969)	2·87	–
Barbital, form IV (Craven & Vizzini, 1971)	2·90, 2·87, 2·91, 2·91, 2·92, 2·91, 2·92, 2·85	–
5-Ethyl-5-isoamylbarbituric acid (amobarbital), form I (Craven & Vizzini, 1969)	2·89	2·92
Amobarbital, form II (Craven & Vizzini, 1969)	2·91, 2·86	2·92, 2·88
5-Ethyl-5-(3,3-dimethylbutyl)barbituric acid (Gartland & Craven, 1971)	2·82	2·88
5-Ethyl-5-(1-methylbutenyl)barbituric acid (Craven & Cusatis, 1969)	2·87, 2·92	–
5-Ethyl-5-butylbarbituric acid (Bideau, 1971)	2·86	2·87
5-Ethyl-5-(1-cyclohexen-1-yl)barbituric acid (Bideau & Artaud, 1970)	2·87	2·90
5-Ethyl-5-(1-cyclohepten-1-yl)barbituric acid (Bideau, Leroy & Housty, 1969)	2·89, 2·87	–
5-Ethyl-5-phenylbarbituric acid, form III (Williams, 1974)	2·89, 2·91	–
5-Methyl-5-phenylbarbituric acid (Bravic, Housty & Bideau, 1968)	2·90	2·89
5-Ethylbarbituric acid (Gatehouse & Craven, 1971)	2·85	2·89
(*b*) 1-Methylbarbituric acids		
1-Methyl-5,5-diethylbarbituric acid (Wunderlich, 1973)	2·84	–
1-Methyl-5-ethyl-5-(1-cyclohexen-1-yl)barbituric acid (Bideau, Leroy & Housty, 1970)	2·88	–
1-Methyl-5-ethyl-5-phenylbarbituric acid (Bideau, Marly & Housty, 1969)	2·89	–
(*c*) Barbiturate anions		
Sodium barbital (Berking & Craven, 1971)	2·84	–
Calcium barbital trihydrate (Berking, 1972)	–	2·82, 2·78, 2·86, 2·85
Guanidinium barbital dihydrate (McClure & Craven, 1973)	–	2·85

(*d*) Barbiturate molecular complexes

Crystal structure	$(\mathrm{NH})_{\mathrm{barb}}\cdots(\mathrm{O{=}C})_{\mathrm{barb}}$	$(\mathrm{NH})_{\mathrm{barb}}\cdots(\mathrm{O{=}C})_{\mathrm{other}}$	$(\mathrm{NH})_{\mathrm{other}}\cdots(\mathrm{O{=}C})_{\mathrm{barb}}$
5-Ethyl-5-phenylbarbituric acid/8-bromo-9-ethyl-adenine (1:2) (Kim & Rich, 1968)	–	–	2·97, 3·19 Å
5-Isopropyl-5-bromoallylbarbituric acid/9-ethyl-adenine (1:1) (Voet & Rich, 1972)	–	–	3·34, 3·12
5,5-Diethylbarbituric acid/9-ethyladenine (1:1) (Voet, 1972)	–	–	3·22, 3·39
5,5-Diethylbarbituric acid/caffeine (2:1) (Craven & Gartland, 1970)	2·98, 2·94, 2·93	–	–
5,5-Diethylbarbituric acid/aminopyrine (1:1) (Kiryu, 1971)	2·82	2·75	–
5,5-Diethylbarbituric acid/urea (1:1) (This paper)	–	2·78, 2·80	2·95, 3·16
5,5-Diethylbarbituric acid/acetamide) (1:1) (Hsu & Craven, 1974*a*)	–	2·82, 2·82	2·95, 3·08
5-Ethyl-5-isoamylbarbituric acid/salicylamide (1:1) (Hsu & Craven, 1974*b*)	2·92	–	3·00
5,5-Diethylbarbituric acid/imidazole (1:1) (Hsu & Craven, 1974*c*)	2·91	–	3·21

The observed range of N···O distances in all NH···O=C hydrogen bonds is considerably greater. The shortest reported distances which we could find were 2·55 Å in cysteylglycine sodium iodide (Dyer, 1951) and 2·62 Å in guanine hydrochloride monohydrate (Broomhead, 1951). Since these structure determinations were based only on zonal X-ray intensity data, a more reliable lower limit for N···O distances might be 2·67 Å which occurs in the urea/parabanic acid complex (Colman & Medlin, 1970; Table 6). At the other extreme, there are N···O distances in NH···O=C interactions which are doubtfully described as hydrogen bonds. In the 1:1 complex of barbital with 9-ethyladenine (Voet, 1972), there is an NH···O=C interaction in which the NH···O atoms are collinear, with an N···O distance of 3·39 Å [Table 3(*d*)]. However, the H···O distance (2·47 Å) is too long for hydrogen bonding according to Hamilton & Ibers (1968), who state that the H···O distance should be shorter than the van der Waals distance (2·6 Å) by at least 0·2 Å.

It is possible that additional N···O distances in $B_d\cdots B_a$ barbiturate hydrogen bonds will be found which will make their range conform more closely to the range of all N···O distances in NH···O=C hydrogen bonds. This would imply that there is little value in characterizing an N···O distance on the basis of the particular donor and acceptor groups which are involved. However, the available evidence is to the contrary. The five N···O distances in Table 5(*d*) for $B_d\cdots A_a$ hydrogen bonds are all between 2·75 and 2·82 Å which is at the short limit of the range for $B_d\cdots B_a$ hydrogen bonds. The 12 distances for $A_d\cdots B_a$ hydrogen bonds are between 2·95 and 3·39 Å which is at and beyond the long limit of the range for $B_d\cdots B_a$ hydrogen bonds. These data are consistent with the drug-active barbiturates being more effective as donors than as acceptors in NH···O=C hydrogen bonds.

The N···O distances for hydrogen bonds in which urea is both donor and acceptor have an average value of 2·98 Å and range between 2·84 and 3·13 Å (Table 6). In urea complexes, 21 hydrogen bonds have N···O distances for which urea is donor and other molecules are acceptor, but only eight of these involve a carbonyl oxygen acceptor atom. The latter have an average value of 3·07 Å and range from 2·91 to 3·24 Å. There are four NH···O=C hydrogen bonds in which urea is acceptor and all are short, ranging from 2·67 to 2·80 Å. The available data for the NH···O=C hydrogen bonding of urea are fewer than for the barbiturates, but they are suggestive of a trend which is complementary to that of the barbiturates, namely for urea to be more effective as an acceptor than as a donor.

Thus, while barbital and urea both have hydrogen-bonding donor and acceptor capability, their association in the 1:1 crystal complex may be considered to be essentially that of a hydrogen-bonding acid (barbital) with a hydrogen-bonding base (urea). The association of barbiturates with adenine derivatives in the complexes listed in Table 5(*d*) would appear to be of a similar nature, with barbital as the hydrogen-bonding acid and adenine as the hydrogen-bonding base. The strong hydrogen bonds in these complexes are of the type NH···N involving barbiturate as donor. The N···N distances in these and other NH···N barbiturate hydrogen bonds are discussed in our report of the crystal structure determinations of the 1:1 complexes of barbital with imidazole and with 2-aminopyridine (Hsu & Craven, 1974*c,d*).

This work was supported by the U. S. Public Health Service, National Institutes of Health, Grant No. NS-

Table 6. *Distances* N···O *in* NH···O *hydrogen bonds involving urea and the uronium ion*

Crystal structure	$(NH)_{urea}\cdots(O{=}C)_{urea}$	$(NH)_{urea}\cdots O_{other}$	$(NH)_{other}\cdots(O{=}C)_{urea}$
Urea (Pryor & Sanger, 1970)	2·98, 3·04 Å	–	–
Barbital/urea (1:1) (This paper)	–	2·95*, 3·16* Å	2·78, 2·80 Å
Parabanic acid/urea (1:1) (Colman & Medlin, 1970)	3·01	3·07*, 3·20*, 3·24*	2·67
5-Nitro-2-furaldehyde-oxime/urea (1:1) (Mathew & Palenik, 1972)	2·84	2·94, 3·07	–
L-Cysteine ethyl ester hydrochloride/urea (1:1) (Haas, 1965)	2·88	3·06*	2·70
Hydrogen peroxide/urea (1:1) (Lu, Hughes & Giguère, 1941)	2·94	–	–
2,6-Lutidine/urea (1:1) (Lee & Wallwork, 1965)	3·05	–	–
Estradiol/urea (1:1) (Duax, 1972)	2·85	3·03, 3·15, 3·04	–
Oxalic acid/urea (1:1) (Harkema, Bats, Weyenberg & Feil, 1972)	2·94	3·00*, 3·12, 2·91*, 2·94	–
Phosphoric acid/urea (1:1)† (Mootz & Albrand, 1972; Kostansek & Busing, 1972)	3·10, 3·13	2·98, 3·16	–
Uronium nitrate (Worsham & Busing, 1969)	–	2·98, 2·97, 2·90, 2·92	–
Range	2·84–3·13	2·90–3·24	2·67–2·80

* This hydrogen bond involves a carbonyl oxygen atom as acceptor.

† This crystalline compound is intermediate in character between an adduct and a salt, because of the very strong more or less centered O–H···O hydrogen bond between the two components.

02763. We thank Dr R. Shiono for the computer programs which we used.

References

BAUR, W. H. & KHAN, A. A. (1970). *Acta Cryst.* **B26**, 1584–1596.

BERKING, B. (1972). *Acta Cryst.* **B28**, 98–113.

BERKING, B. & CRAVEN, B. M. (1971). *Acta Cryst.* **B27**, 1107–1115.

BIDEAU, J. P. (1971). *C. R. Acad. Sci. Paris*, **272**, 757–760.

BIDEAU, J. P. & ARTAUD, M. (1970). *C. R. Acad. Sci. Paris*, **271**, 806–809.

BIDEAU, J. P., LEROY, F. & HOUSTY, J. (1969). *C. R. Acad. Sci. Paris*, **268**, 1590–1592.

BIDEAU, J. P., LEROY, F. & HOUSTY, J. (1970). *C. R. Acad. Sci. Paris*, **271**, 500–502.

BIDEAU, J. P., MARLY, L. & HOUSTY, J. (1969). *C. R. Acad. Sci. Paris*, **269**, 549–551.

BRAVIC, G., HOUSTY, J. & BIDEAU, J. P. (1968). *C. R. Acad. Sci. Paris*, **266**, 969–971.

BROOMHEAD, J. M. (1951). *Acta Cryst.* **4**, 92–100.

CARON, A. & DONOHUE, J. (1964). *Acta Cryst.* **17**, 544–546.

COLMAN, P. M. & MEDLIN, E. H. (1970). *Acta Cryst.* **B26**, 1547–1553.

CRAVEN, B. M. & CUSATIS, C. (1969). *Acta Cryst.* **B25**, 2291–2298.

CRAVEN, B. M., CUSATIS, C., GARTLAND, G. L. & VIZZINI, E. A. (1973). *J. Mol. Struct.* **16**, 331–342.

CRAVEN, B. M. & GARTLAND, G. L. (1970). *J. Pharm. Sci.* **59**, 1666–1670.

CRAVEN, B. M. & TAKEI, W. J. (1964). *Acta Cryst.* **17**, 415–420.

CRAVEN, B. M. & VIZZINI, E. A. (1969). *Acta Cryst.* **B25**, 1993–2009.

CRAVEN, B. M. & VIZZINI, E. A. (1971). *Acta Cryst.* **B27**, 1917–1924.

CRAVEN, B. M., VIZZINI, E. A. & RODRIGUES, M. M. (1969). *Acta Cryst.* **B25**, 1978–1993.

CROMER, D. T. & WABER, J. T. (1965). *Acta Cryst.* **18**, 104–109.

DUAX, W. L. (1972). *Acta Cryst.* **B28**, 1864–1871.

DYER, H. B. (1951). *Acta Cryst.* **4**, 42–50.

GARTLAND, G. L. (1971). Ph. D. Dissertation, Univ. of Pittsburgh, Pittsburgh, Pa.

GARTLAND, G. L. & CRAVEN, B. M. (1971). *Acta Cryst.* **B27**, 1909–1916.

GATEHOUSE, B. M. & CRAVEN, B. M. (1971). *Acta Cryst.* **B27**, 1337–1344.

HAAS, D. J. (1965). *Acta Cryst.* **19**, 860–861.

HAMILTON, W. C. & IBERS, J. A. (1968). *Hydrogen Bonding in Solids*. New York: Benjamin.

HARKEMA, S., BATS, J. W., WEYENBERG, A. M. & FEIL, D. (1972). *Acta Cryst.* **B28**, 1646–1648.

HSU, I-N. & CRAVEN, B. M. (1974*a*). *Acta Cryst.* **B30**, 974–979.

HSU, I-N. & CRAVEN, B. M. (1974*b*). *Acta Cryst.* **B30**, 843–846.

HSU, I-N. & CRAVEN, B. M. (1974*c*). *Acta Cryst.* **B30**, 988–993.

HSU, I-N. & CRAVEN, B. M. (1974*d*) *Acta Cryst.* **B30**, 994–997.

KIM, S. H. & RICH, A. (1968). *Proc. Natl. Acad. Sci. U.S.* **60**, 402–408.

KIRYU, S. (1971). *J. Pharm. Sci.* **60**, 699–703.

KOSTANSEK, E. C. & BUSING, W. R. (1972). *Acta Cryst.* **B28**, 2454–2459.

LEE, J. D. & WALLWORK, S. C. (1965). *Acta Cryst.* **19**, 311–315.

LU, C. S., HUGHES, W. & GIGUÈRE, P. A. (1941). *J. Amer. Chem. Soc.* **63**, 1507–1513.

MCCLURE, R. J. & CRAVEN, B. M. (1973). *Acta Cryst.* **B29**, 1860–1864.

MATHEW, M. & PALENIK, G. J. (1972). *J. Chem. Soc. Perkin II*, pp. 1033–1036.

MOOTZ, D. & ALBRAND, K.-R. (1972). *Acta Cryst.* **B28**, 2459–2463.

NAKAMOTO, K., MARGOSHES, M. & RUNDLE, R. E. (1955). *J. Amer. Chem. Soc.* **77**, 6480–6486.

PRYOR, A. W. & SANGER, P. L. (1970). *Acta Cryst.* **A26**, 543–558.

SEKIGUCHI, K., HIMURO, I., HORIKOSHI, I., TSUKADA, T., OKAMOTO, T. & YOTSUYANAGI, T. (1969). *Chem. Pharm. Bull. (Japan)*, **17**, 191–199.

SNYDER, R. L. & ROSENSTEIN, R. D. (1971). *Acta Cryst.* **B27**, 1969–1975.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

VOET, D. (1972). *J. Amer. Chem. Soc.* **94**, 8213–8222.

VOET, D. & RICH, A. (1970). In *Progress in Nucleic Acid Research and Molecular Biology*, Vol. 10, pp. 183–264. Edited by J. N. DAVIDSON and W. E. COHN. New York and London: Academic Press.

VOET, D. & RICH, A. (1972). *J. Amer. Chem. Soc.* **94**, 5888–5891.

WILLIAMS, P. P. (1974). *Acta Cryst.* **B30**, 12–17.

WORSHAM, J. E. & BUSING, W. R. (1969). *Acta Cryst.* **B25**, 572–578.

WUNDERLICH, H. (1973). *Acta Cryst.* **B29**, 168–173.