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Stereochemistry of Nucleic Acids and their Constituents.
VI. The Crystal Structure and Conformation of Dihydrouracil: a Minor Base of Transfer-Ribonucleic Acid*

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Crystals of dihydrouracil are monoclinic, space group $P2_1/c$, $Z=4$, $a=4\cdot210\pm0\cdot001$, $b=5\cdot816\pm0\cdot001$, $c=19\cdot777\pm0\cdot003$ Å, $\beta=95\cdot15\pm0\cdot01°$, $D_m=1\cdot575$ g.cm^{-3}, $D_x=1\cdot577$ g.cm^{-3}. The structure was solved by direct methods and refined by least squares to an R of $0\cdot073$, with 639 diffractometric intensities. The saturated ring displays a twist half-chair conformation with C(5) and C(6) displaced by $0\cdot14$ and $0\cdot45$ on either side of the dihydrouracil plane. The maximum torsion angle of $45\cdot4°$ is about the saturated C(5)–C(6) bond. The molecule exists in the diketo form, and forms infinite zigzag hydrogen-bonded ribbons such that each base is hydrogen bonded to two adjacent bases related by centers of inversion. O(4) is not involved in hydrogen bonding, whereas O(2) is involved in two hydrogen bonds. The interplanar separation of the bases is $3\cdot34$ Å. The base stacking in dihydrouracil is typical of the ketopyrimidines.

Introduction

Transfer ribonucleic acid (*t*-RNA) is probably the smallest (about eighty nucleotides) of the naturally occurring nucleic acids. In addition to the common nucleotides, guanylic, adenylic, cytidylic and uridylic acids, *t*-RNA is composed of approximately 15–20 per cent of a unique class of minor nucleotides (Holley, Apgar, Everett, Madison, Marquisee, Merrill, Penswick & Zamir, 1965; Madison, Everett & Kung, 1966; Zachau, Dütting & Feldman, 1966; RajBhandary, Chang, Stuart, Faulkner, Hoskinson & Khorana, 1967). The majority of the minor nucleotides differ from the common forms only in the composition of the base, although sometimes 2'-*O*-methylated derivatives are also isolated. It is believed that the minor components influence significantly the secondary and tertiary structures of *t*-RNA. To determine the role of the minor components in *t*-RNA, the structural analyses of several minor constituents are presently being

carried out in our laboratory (Rao & Sundaralingam, 1969). In this article, we present the results of the crystal structure of the minor base dihydrouracil (DiHU), which is one of the more common minor bases and is located in the loops of the cloverleaf model for *t*-RNA proposed by Holley *et al.* (1965). A preliminary report on this work has already appeared (Rohrer & Sundaralingam, 1968). Dihydrouracil differs from the common base uracil in that the C(5)–C(6) bond is saturated.

Experimental

Dihydrouracil, purchased from Sigma Chemical Company, St. Louis, Missouri, was crystallized in dimethyl sulfoxide. The crystals showed preferred elongation in the *a*-axis direction and very pronounced cleavage parallel to the (001) plane, thus making selection of a suitable crystal difficult. More than 20 crystals were examined before one without partial cleavage was found. The crystal data for dihydrouracil are given in Table 1. Three-dimensional diffractometric intensities were collected up to $2\theta=134°$, on a crystal mounted with the long direction parallel to the φ axis of the diffractometer, using the θ–2θ scan mode and a scan speed of 1° per minute. Altogether 823 independent reflections were scanned, and 690 were con-

sidered to be non-zero using a cut-off of $3\sigma(I)$, where the standard deviation in the intensity $\sigma(I)$ is taken to be $\sigma(I)=[C_t+(0\cdot05\ C_n)^2]^{1/2}$, C_t is the total number of scanned plus background counts and C_n is the scanned minus background counts. A standard reflection was used to monitor the crystal alignment and the fluctuations in the electronics. During the intensity measurement a maximum variation in the standard of 7% was observed. The data were corrected for the variation in the standard and the usual Lorentz and polarization factors, but no correction for absorption was made.

Table 1. *Crystal data*

Crystal system: Monoclinic
a = $4\cdot210\pm0\cdot001$ Å, λ(Cu $K\alpha$)=$1\cdot5418$ Å
b = $5\cdot816\pm0\cdot001$
c = $19\cdot777\pm0\cdot003$

β = $95\cdot15$ $\pm0\cdot01°$

Space group: $P2_1/c$; $h0l$, $l=2n$, $0k0$, $k=2n$
D_c = $1\cdot577$ g.cm^{-3}
D_m= $1\cdot575$ g.cm^{-3} (by flotation in a mixture of CCl$_4$–CHCl$_3$)
Z = 4

Crystal dimensions: $0\cdot1\times0\cdot2\times0\cdot5$ mm

Structure determination

The centric space group and the short a ($4\cdot2$ Å) axis made feasible the solution of the structure by direct methods in projection. The intensities were converted to $|E^2|$ by the relation:

$$E^2(hkl)=F^2(hkl)/\langle F^2\rangle,$$

$\langle F^2\rangle$ values being obtained by a graphical method using a curve of F^2 *versus* $\sin\theta/\lambda$ for all the data. The Σ_2 relations and sign probabilities were then determined (Karle & Karle, 1963). The two reflections 0,6,5 and 0,3,13 with the largest E values in the $0kl$ zone were used to define the origin for the projection analysis. Only one additional symbol was required to generate the signs needed, giving two possible E maps. One of the maps clearly showed all eight of the heavy atoms and a few spurious peaks. The y and z atomic coordinates were obtained from this map. For the $h0l$ projection, the origin was again specified by two reflections, but it was necessary to use two symbols to generate the signs, thus giving four E maps. The interpretation of these E maps was difficult because there were very few reflections in this projection. However, one of the maps did show some indication of the tilt and position of the molecule. From this knowledge and packing criterion, approximate coordinates for all the atoms were determined.

Structure refinement

The initial x,y,z coordinates and individual atomic temperature factors of $2\cdot0$ Å^2 led to an $R(=\sum||F_o|-|F_c||/\sum|F_o|)$ index of $0\cdot54$. Three cycles of full-matrix least-squares refinement with unit weights, varying the atomic positions and their isotropic temperature factors, reduced R to $0\cdot16$. A difference Fourier synthesis (Fig. 1) showed all six of the hydrogen atoms at reasonable positions. Inclusion of these hydrogen atoms in two further isotropic cycles in which the positional and thermal parameters of all the atoms were varied lowered R to $0\cdot11$. The weighting scheme $1/\sqrt{\omega}=[\sigma(F)+0\cdot05|F|]$, where $\sigma(F)=([C_t+(0\cdot05C_n)^2]/C_n)^{1/2}/2(Lp)^{1/2}$, was used in the above and subsequent
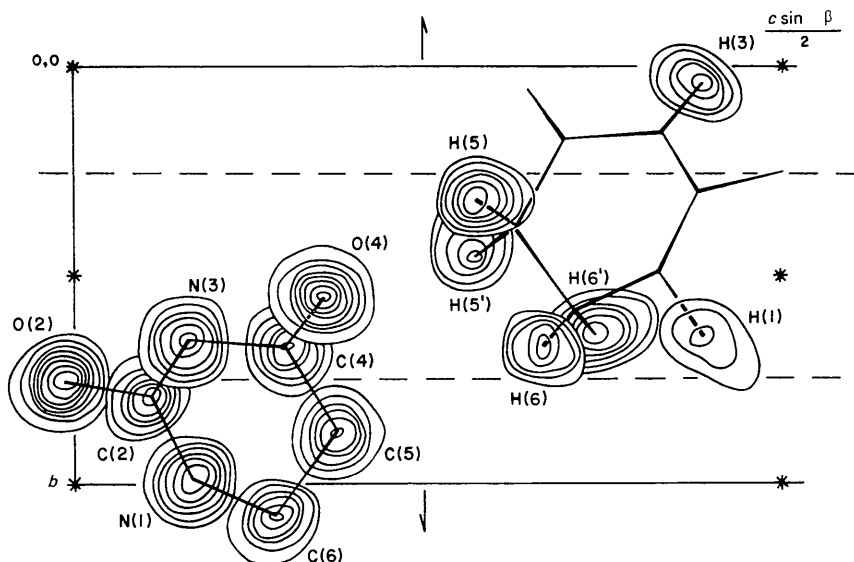

Fig. 1. A final composite Fourier electron density and the initial Fourier difference electron density syntheses viewed down the a^* axis. Electron density contours are at intervals of $1\cdot0$ e.Å^{-3}, beginning at $1\cdot0$ e.Å^{-3}. Difference electron density contours are at intervals of $0\cdot1$ e.Å^{-3}, beginning at $0\cdot1$ e.Å^{-3}.

cycles. Two cycles of refinement in which the positional parameters for all the atoms and the anisotropic thermal parameters of the nonhydrogen atoms were varied gave an R of 8·6%. Two more cycles of anisotropic refinement omitting those reflections with $|(F_o-F_c)|/\sigma(F)>3$ (Table 2) resulted in an R of 0·073 for 639 reflections.

Throughout the refinement, Hoerni & Ibers's (1954) scattering factors were used for carbon, nitrogen and oxygen. Stewart, Davidson & Simpson's (1965) scattering factors were used for hydrogen. The observed and calculated structure factors are listed in Table 2. The final atomic parameters and their estimated standard deviations are given in Table 3.

Results and discussion

We were pleasantly surprised at the lack of disorder in this crystal structure, because the related molecule dihydrothymine (Furberg & Jensen, 1968), not found in *t*-RNA, exhibits disorder in the crystal. The low and essentially uniform atomic thermal parameters, the 'clean' difference density maps, the well-resolved hydrogen electron densities, and the reasonable bond distances in dihydrouracil give assurance that there is no disorder.

Saturation of the C(5)–C(6) bond has puckered the molecule, Fig. 2, to an approximately half-chair conformation, so that C(5) and C(6) atoms show pro-

Table 2. *Observed and calculated structure factors*

Column 1, l index, columns 2 and 3, $10|F_o|$ and $10F_c$ respectively. Reflections suspected of suffering from secondary extinction are indicated by 'less than' signs, those less than $3\sigma(I)$ by asterisks, and those with $|\Delta F|/\sigma(F)>3$ by 'greater than' signs.

-4,0,L		
2	57	59
4	126	133
6	103	99
8	29*	-10
10	33	36
12	117	125
14	16*	33
-4,1,L		
1	68	75
2	48>	-23
3	76	-85
4	34>	-8
5	39	-28
6	52	54
7	20*	11
8	76	74
9	36	-36
10	32>	6
11	75	80
12	42	31
13	40	35
14	38	29
15	61	-66
-4,2,L		
1	31*	-5
2	48	-30
3	81	80
4	80	-80
5	77	-82
6	131>	-156
7	68	-70
8	60	-66
9	22*	4
10	28*	-14
11	43	37
12	35	-18
13	52	45
-4,3,L		
1	30	19
2	35>	19
3	41>	5
4	57	56
5	46	40
6	41	-37
7	67	-65
8	47	-52
9	70	-76
10	28	-13
11	26*	28
-4,4,L		
1	56	50
2	44	31
3	54	51
4	41	32
-3,0,L		
2	140	-130
4	90	-89
6	155	-144
8	143	133
10	77	79
12	183	-181
14	35	-31
16	39	-28
18	32	-10
-3,1,L		
1	73	58
2	136	150
3	39>	10
4	88	98
5	61	-61
6	58	60
7	13*	24
8	87	86
9	64	50
10	146	155
11	24*	-5
12	21*	31
13	28*	-20
14	38	36
15	28*	-28
16	36	38
17	27*	14
18	67	-65
19	29	18
-3,2,L		
2	39	-32
3	38	-40
4	63	64
5	90	89
6	54	-50
7	53	51
8	71	69
9	36	-26
10	142>	160
11	61	-64
12	33	-16
13	47	-39
14	38	-33
15	33>	4
16	28*	19
17	45	-43
18	46	-44
-3,3,L		
2	142	-133
3	196	-217
4	119	-136
5	98	-104
6	55	-73
7	135>	156
8	100	-114
9	70	74
10	32	-28
11	44	41
12	26*	-16
13	27*	-6
14	20*	-11
15	73	-78
16	25*	-5
-3,4,L		
1	93	110
2	25*	-15
3	27*	16
4	26*	-13
5	149	-171
6	25*	-11
7	17*	-14
8	49	-52
9	58	64
10	25*	3
11	26*	-4
12	28>	6
13	70	82
14	32	-34
-3,5,L		
1	38	34
2	25*	9
3	26*	1
4	22*	15
5	31*	24
6	96	104
7	21*	0
8	41	37
-2,0,L		
2	386<	-321
4	57>	-33
6	123	-101
8	352	-323
10	63	-64
12	90	-93
14	55	-63
16	115	112
18	78	-89
20	95	-96
22	34	-28
-2,1,L		
1	33	-28
2	33	-19
3	218	-223
4	77	76
5	90	87
6	32	19
7	329	332
8	150	-142
9	110	-98
10	125	-117
11	71	-72
12	31*	19
13	44	43
14	56	-51
15	54	-58
16	73	71
17	32*	21
18	159	169
19	90>	104
20	26*	5
21	29	21
-2,2,L		
1	75	85
2	76	-76
3	29*	16
4	273	299
5	202	-225
6	349	384
7	32>	11
8	94	103
9	48	44
10	43	39
11	14*	-2
12	27*	-16
13	70	63
14	37	-29
15	55	-51
16	0*	26
17	36	-34
18	75	79
19	39	31
20	102	114
21	34	34
-2,3,L		
1	45	37
2	41	-40
3	150	165
4	21*	-4
5	23*	-32
6	113	122
7	30*	15
8	28*	11
9	43	-37
10	25*	8
11	135>	-158
12	83	91
13	27*	-16
14	81	-88
15	29*	2
16	64	-67
17	29	-20
18	32	23
-2,4,L		
1	227	-239
2	184	-211
3	67	76
4	31*	-29
5	83	95
6	40	-35
7	35	-34
8	24*	8
9	50	54
10	55	-47
11	48	47
12	94	-105
13	50	-48
14	40	-45
15	57	-52
16	37	-35
17	30>	9
-2,5,L		
1	71	-65
2	85	-94
3	13*	-20
4	64	-73
5	30*	9
6	28*	-5
7	45	47
8	26*	-23
9	40	43
10	70	69
11	40>	12
12	44	44
13	48	44
-2,6,L		
1	63>	-30
2	97	103
3	53>	23
4	72	74
5	26*	4
6	26*	-17
7	52	-47
-1,0,L		
2	167>	-123
4	717	672
6	208	191
8	123	-112
10	49	39
12	79>	-62
14	217	-214
16	28*	-10
18	60	65
20	116	-127
22	87	-87
-1,1,L		
1	209	230
2	577<	-626
3	658<	722
4	516	-550
5	297	-288
6	210	-207
7	101	-99
8	53	-49
9	7*	17
10	34	-30
11	182	-187
12	25*	-13
13	128	130
14	35	-31
15	81	86
16	132	-144
17	35	-35
18	102	-106
19	36>	-11
20	35>	-12
21	83	-83
22	67	-65
-1,2,L		
1	168	-174
2	79	79
3	282	296
4	111	111
5	123	120
6	140	-140
7	148	-142
8	253	-267
9	175	185
10	0*	8
11	78	-74
12	54	45
13	83	-82
14	94	79
15	191	208
16	182	197
17	54	45
18	35	38
19	51	-48
20	47	-43
21	20*	-11
22	34	31
-1,3,L		
1	67	-56
2	198	212
3	73	73
4	92	88
5	97	97
6	147	150
7	55	-49
8	146	152
9	92	-92
10	46	41
11	40	-34
12	46	-34
13	49	-46
14	40	42
15	39>	24
16	73	72
17	109	104
18	45	47
19	54	47
20	56	57
-1,4,L		
1	12*	-19
2	62	62
3	61	-43
4	56	49
5	47	-44
6	41	44
7	17*	6
8	129	-136
9	36	27
10	27*	-1
11	120	-125
12	30*	15
13	82	-86
14	30*	-14
15	30>	-6
16	69>	40
17	56	-59
18	95	-93
-1,5,L		
1	79	85
2	43	43
3	5*	27
4	94	-93
5	36	28
6	31>	13
7	61	62
8	29*	-16
9	30*	-16
10	132	-131
11	50>	-38
12	58	-59
13	33	21
14	45	-36
15	43	41
-1,6,L		
1	54	-46
2	58	-56
3	30	17
4	43	41
5	31	-19
6	75	72
7	62	60
8	29	-8
9	92	94
10	42	-35
0,0,L		
2	256	255
4	314	-323
6	351	340
8	295	-291
10	64	53
12	375	358
14	168	158
16	50	38
18	65	-68
20	66	70
22	139	150
0,1,L		
1	131	131
2	480	517
3	27	17
4	39	44
5	178	-163
6	199	197
7	128	-128
8	98	-78
9	88	91
10	275	-253
11	109	-111
12	72	-69
13	5*	-4
14	53	-41
15	98	102
16	53	-45
17	83	-93
18	75	-80
19	39	-32
20	83	-96
21	67	69
22	26*	-12
23	30	-26
0,2,L		
0	39	-42
1	197	-194
2	341	-330
3	238	-236
4	356	-348
5	252	253
6	128	-117
7	67	67
8	209	-204
9	93	-87
10	48	-40
11	171	177
12	64	55
13	22*	-25
14	93	-87
15	147	-152
16	66	-64
17	31	14
18	91	-92
19	34	29
20	119	-120
21	32	24
22	20*	-11
0,3,L		
1	176	176
2	59	62
3	83	81
4	89	-93
5	300	-294
6	112	109
7	17*	14
8	90	-77
9	118	115
10	117	-118
11	58	54
12	196	198
13	254	268
14	97	91
15	34	33
16	27*	17
17	170	-181
18	105	113
19	38	-26
20	25*	9
0,4,L		
0	106	107
1	55	-47
2	166	163
3	63	61
4	106	104
5	36	32
6	56	48
7	173	-165
8	56	46
9	73	-79
10	18*	16
11	28*	-24
12	80	77
13	52	37
14	30*	28
15	125	127
16	28	16
17	30	19
18	88	88
0,5,L		
1	29*	-10
2	62	-60
3	94	93
4	23*	3
5	90	-91
6	48	44
7	132	-133
8	27*	-23
9	34	-24
10	56	-49
11	34	-32
12	33	30
13	48	-43
14	37	-29
15	39	-28
16	118	-118
0,6,L		
0	53>	54
1	66	-64
2	29*	-14
3	97	96
4	84	-84
5	149	149
6	90	-88
7	72	-68
8	81	-77
9	26*	-12
10	26	-4
11	20*	4
1,0,L		
0	678<	-508
2	64	60
4	212	-195
6	162>	118
8	265	237
10	80	62
12	169	170
14	15*	-14
16	58	63
18	193	213
20	29	-23
22	25*	-2
1,1,L		
0	72	70
1	408	-454
2	202	216
3	29	21
4	257	253
5	230	-233
6	117	-113
7	210	-199
8	220	216
9	240	230
10	216	196
11	141	136
12	36	-34
13	0*	-8
14	35	31
15	86	-91
16	72	71
17	61	-63
18	105	117
19	44	44
21	23*	7
22	26*	24
1,2,L		
0	175	189
1	123	141
2	157	-161
3	145	137
4	181	-184
5	128	-131
6	127	126
7	267	-250
8	101	-95
9	34	-27
10	28*	-24
11	73	-80
12	44	51
13	23*	23
14	221	-234
15	128	129
16	174	-190
17	38	-39
18	27*	21
19	44	-41
20	35>	-17
21	21*	-9
1,3,L		
0	256	-275
1	106	-99
2	17*	4
3	101	105
4	185	-181
5	103	104
6	212	-223
7	6*	4
8	89	87
9	157	165
10	25*	-12
11	62	-65
12	86	-91
13	182	-187
14	26*	0
15	70	65
16	86	-86
17	18*	14
18	77	-79
19	28>	0
1,4,L		
0	143	154
1	65	-62
2	124	-140
3	24*	28
4	121	-125
5	73	73
6	41	43
7	36	-30
8	40	24
9	136	148
10	133	140
11	171	173
12	103	110
13	103	-103
14	11*	-3
15	34	-22
16	19*	1
17	50	50
1,5,L		
0	117	125
1	97	-88
2	246	260
3	150	-150
4	50	-43
5	47	-43
6	35	-28
7	33	-25
8	44	38
9	38	29
10	38	-29
11	55	56
12	76	72
13	26*	5
14	94	103
1,6,L		
0	49	-39
1	61	58
2	34>	14
3	72	-69
4	48	-42
5	58	-55
6	21*	-5
7	72	-74
8	73	71
9	61	-63
2,0,L		
0	236	-199
2	301<	-250
4	297	-264
6	72	65
8	74	70
10	19*	-8
12	103	-94
14	141	-142
16	89	-101
18	52	-50
20	30>	0
2,1,L		
0	132	145
1	142	-144
2	0*	-17
3	63	53
4	74	-66
5	226	217
6	134	124
7	53	47
8	23*	-2
9	82	86
10	55	57
11	133	-130
12	249	257
13	154	-153
14	118	127
15	145	157
16	15*	17
17	13*	8
18	30>	4
19	37	-36
20	29>	9
2,2,L		
0	108	122
1	81	-86
2	184	192
3	246	-258
4	38	-63
5	46	47
6	163	182
7	128	128
8	170	169
9	16*	-8
10	135	-136
11	70	71
12	26*	-1
13	80	-83
14	109	110
15	54	-55
16	61	74
17	36	47
18	93	96
19	48	-42
2,3,L		
0	29*	16
1	150	-180
2	20*	1
3	33	-37
4	66	-75
5	46	-48
6	46	-32
7	71	-73
8	35	-24
9	36	31
10	107	-109
11	36	23
12	62	-59
13	62	-65
14	42	-37
15	45	-40
16	89	-84
17	57	56
2,4,L		
0	188	-185
1	95	80
2	38>	4
3	92	-95
4	42	-48
5	105	111
6	58	65
7	42	28
8	38	38
9	98	-110
10	154	-161
11	44	44
12	51	-50
13	61	62
14	33	-27
15	59	-54
2,5,L		
0	95	-91
1	46>	-8
2	41	-32
3	51	54
4	26*	-6
5	77	85
6	22*	-10
7	93	109
8	156	165
9	29*	24
10	42	43
11	34	-31
12	46	-41
2,6,L		
0	38>	-16
1	64	-66
2	42	-28
3	78	-86
4	65	70
5	22*	-27
3,0,L		
0	23*	-21
2	196	173
4	42>	-5
6	33>	8
8	181	-178
10	373	-371
12	41	27
14	46	41
16	78	-75
3,1,L		
0	175	-205
1	60	-44
2	0*	-32
3	45	43
4	29*	21
5	97	96
6	32	-17
7	81	-73
8	100	96
9	64	-63
10	74	-71
11	72	66
12	163	-171
13	20*	-17
14	42	-33
15	0*	-15
16	53	-47
3,2,L		
0	81	-83
1	36>	-6
2	94	103
3	81	92
4	67	70
5	35	24
6	39	37
7	60	-57
8	84	84
9	22*	15
10	51	44
11	58	51
12	80	85
13	31	17
14	81	83
15	64	-63
16	10*	17
3,3,L		
0	90	-85
1	67	-59
2	42	38
3	25*	10
4	95	108
5	133	150
6	49	-50
7	70	-77
8	66	65
9	99	-106
10	70	65
11	23*	0
12	36	-27
13	32	28
14	40	37
3,4,L		
0	53>	2
1	31	-20
2	30*	5
3	65	-66
4	24*	0
5	34	-25
6	74	-74
7	40>	33
8	46	-47
9	30	-13
10	34	-29
11	24*	-24
3,5,L		
0	71	-76
1	64	56
2	32	-17
3	66	75
4	20*	33
5	33	22
6	57	-59
4,0,L		
0	33	13
2	64	60
4	80	-64
6	128	-128
8	150	149
10	104	108
12	46	-38
4,1,L		
0	50	30
1	43	39
2	12*	-18
3	21*	-7
4	58	-56
5	21*	0
6	119	-122
7	104	-108
8	107	-113
9	27*	-11
10	27*	-2
11	72	68
4,2,L		
0	31*	-4
1	66	71
2	73	73
3	62	-58
4	22*	-9
5	68	67
6	79	-86
7	71	73
8	36	-27
9	86	-86
10	34	-30
4,3,L		
0	47	49
1	86	94
2	36>	9
3	36>	-26
4	41	42
5	48	-45
6	60	67
7	48	43
4,4,L		
0	41	31
1	31	19

Table 3. *Final positional and thermal parameters of dihydrouracil**

(Estimated standard deviations)

	x/a	y/b	z/c	β_{11} ($\times 10^4$)	β_{22} ($\times 10^4$)	β_{33} ($\times 10^4$)	β_{12} ($\times 10^4$)	β_{13} ($\times 10^4$)	β_{23} ($\times 10^4$)
N(1)	0·2480 (8)	0·9772 (6)	0·0833 (1)	278 (21)	111 (10)	13 (1)	39 (11)	−3 (3)	−1 (2)
C(2)	0·3360 (9)	0·7911 (6)	0·0501 (2)	265 (24)	118 (11)	9 (1)	5 (12)	2 (3)	1 (2)
N(3)	0·5757 (8)	0·6571 (6)	0·0837 (1)	283 (21)	131 (10)	11 (1)	22 (12)	−5 (3)	−4 (2)
C(4)	0·6929 (10)	0·6750 (7)	0·1501 (2)	303 (23)	116 (11)	11 (1)	−28 (13)	−4 (3)	5 (2)
C(5)	0·5544 (11)	0·8694 (7)	0·1891 (2)	371 (27)	180 (13)	11 (1)	0 (14)	−12 (4)	−3 (3)
C(6)	0·4349 (11)	1·0653 (7)	0·1438 (2)	389 (25)	134 (12)	12 (1)	0 (15)	−2 (4)	−7 (3)
O(2)	0·2211 (6)	0·7339 (5)	−0·0062 (1)	299 (18)	168 (9)	11 (1)	40 (9)	−3 (2)	−4 (2)
O(4)	0·8918 (7)	0·5414 (5)	0·1737 (1)	418 (21)	176 (10)	17 (1)	16 (11)	−20 (3)	5 (2)

				B					
H(1)	0·122 (13)	1·067 (10)	0·060 (3)	3·5 (2·0) Å²					
H(3)	0·648 (13)	0·546 (10)	0·060 (3)	3·2 (2·1)					
H(5)	0·372 (16)	0·806 (11)	0·212 (3)	4·6 (1·9)					
H(5′)	0·741 (14)	0·911 (9)	0·218 (3)	3·6 (2·0)					
H(6)	0·330 (11)	1·179 (8)	0·171 (2)	2·4 (1·7)					
H(6′)	0·628 (13)	1·155 (9)	0·128 (2)	3·7 (1·9)					

* The temperature factor is of the form, $T_i = \exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{23}hl + 2\beta_{23}kl)]$ for nonhydrogen atoms, and of the form $T_H = \exp[-B(\sin\theta/\lambda)^2]$ for hydrogen atoms.
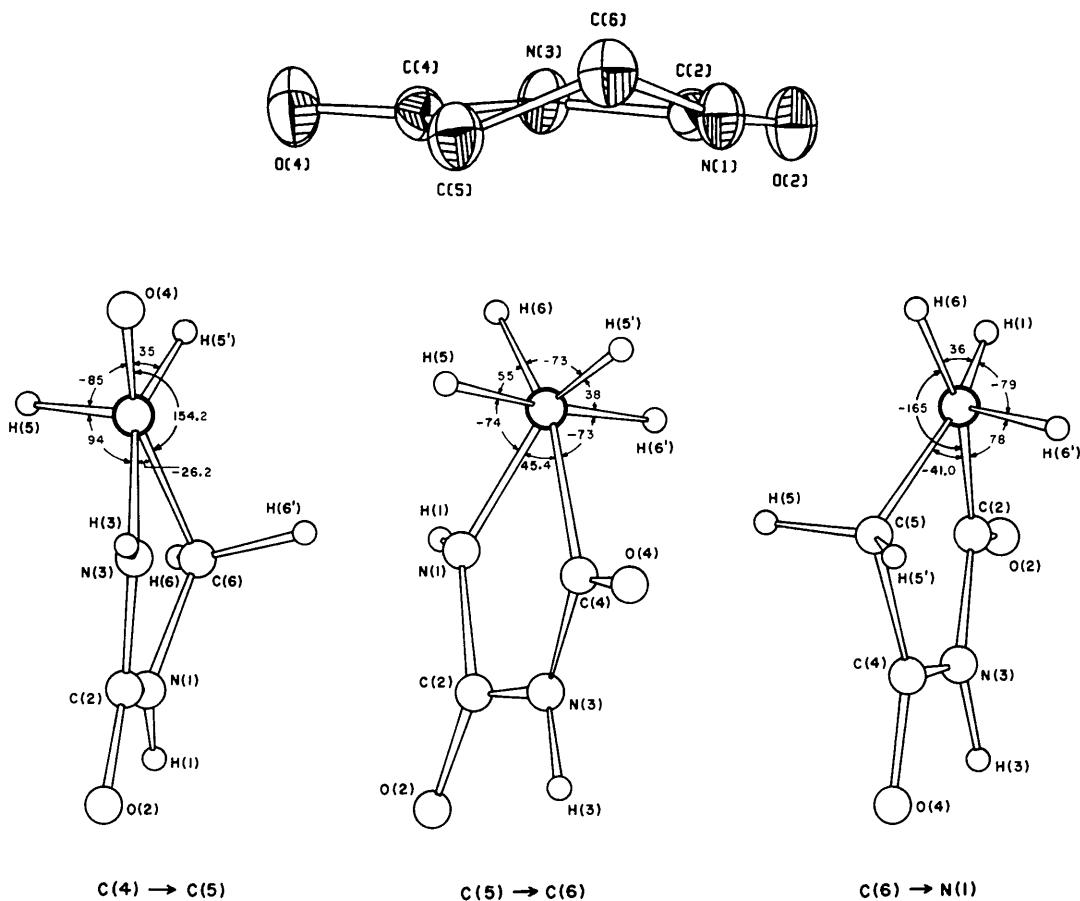

Fig. 2. (*a*) A view of the thermal ellipsoids showing the marked displacements of the atoms C(5) and C(6) from the molecular plane (plane 1, Table 4). (*b*), (*c*) and (*d*) represent views of the molecule down the C(4)–C(5), C(5)–C(6) and C(6)–N(1) bonds respectively.

nounced displacements of 0·14 and 0·45 Å respectively, on opposite sides of the plane defined by the remaining ring atoms (plane 2, Table 4). C(6) is displaced almost three times as much as C(5). The torsional angles given in Table 5 present a more accurate picture of the puckering of the ring. The saturated C(5)–C(6) bond has the largest torsion angle (45·4°). The two bonds attached to the saturated carbon atoms, C(4)–C(5) and C(6)–N(1), also have reasonably large torsional angles of 26·2 and 41·0° respectively. Views down these three bonds are shown in Fig. 2(b)–(d). It is seen that the substituent atoms have assumed a nearly staggered arrangement. The conjugated portion of the molecule

$$O(2) \qquad N(3) \qquad O(4)$$
$$\diagdown\!\!\!\diagdown \quad /\cdot\cdot\diagdown \quad /\!\!\!/$$
$$C(2) \qquad\quad C(4)$$
$$|$$
$$N(1){:}$$
$$\diagdown$$
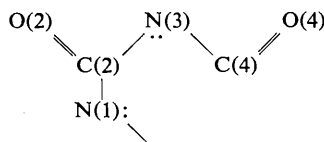
also shows significant nonplanarity (Table 4). The smallest torsional angle of 3·0° involves the N(3)–C(4) bond. There are considerable differences between the torsional angles in dihydrouracil and those in the disordered forms of dihydrothymine (see Table 5).

Table 4. Least-squares planes* for dihydrouracil

	Plane 1 Displacement	Plane 2 Displacement
N(1)	−0·073† Å	0·021† Å
C(2)	−0·012†	−0·043†
N(3)	0·119†	0·045†
C(4)	−0·019†	−0·023†
C(5)	−0·277†	−0·141
C(6)	0·269†	0·449
O(2)	−0·062†	−0·170
O(4)	0·055†	0·003
H(1)	−0·04	0·08
H(3)	0·25	0·09
H(5)	−1·27	−1·12
H(5′)	0·21	0·38
H(6)	0·00	0·27
H(6′)	1·30	1·48
Δ_{rms}	0·148	0·035
$\sigma(\Delta_{rms})$	0·004	0·004
A	0·7929	0·7690
B	0·4825	0·5551
C	−0·3722	−0·3170
D	2·9147	3·3032
Interplanar separation	3·338	3·237

* The equations of the planes are of the form $lX + mY + nZ = d$, where l, m, n are the direction cosines of the normal to the plane, and d(Å) is the distance of the plane from the origin. X, Y, Z are coordinates in Å units (axes $a, b, c*$).
† Atoms included in calculations of least-squares planes.

The bond distances, uncorrected for thermal motion, are shown in Table 6 and Fig. 3. Bond distances involving C, N and O have estimated standard deviations of 0·005–0·006 Å, and those involving hydrogen atoms have e.s.d.'s about ten times larger. The C(5)–
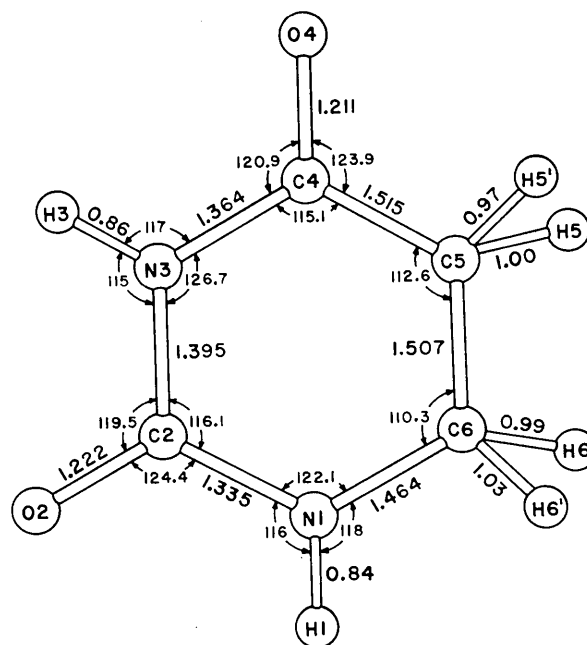
Fig. 3. Bond lengths (Å) and bond angles (°) in dihydrouracil. Bond angles involving hydrogen atoms that are not shown in the Figure are: C(4)–C(5)–H(5), 107 (2)°; C(4)–C(5)–H(5′), 100 (3)°; H(5)–C(5)–C(6), 109 (2)°; H(5′)–C(5)–C(6), 111 (2)°; H(5)–C(5)–H(5′), 115 (3)°; C(5)–C(6)–H(6), 108 (2)°; C(5)–C(6)–H(6′), 109 (2); H(6)–C(6)–N(1), 117 (2); H(6′)–C(6)–N(1), 108 (2); H(6)–C(6)–H(6′), 103 (2). Estimated standard deviations are in parentheses.

C(6) bond distance of $1·507 \pm 0·006$ Å is significantly shorter than the normal $Csp^3\!-\!Csp^3$ single bond value of 1·533 Å (Bartell, 1959). A part of this difference may be attributed to thermal motion of the molecule. Interestingly, the $C(4)sp^2\!-\!C(5)sp^3$ bond distance of $1·515 \pm 0·006$ Å is as long as the saturated C(5)–C(6) bond distance.

As expected, dihydrouracil and uracil (Stewart & Jensen, 1967) show the greatest difference (0·167 Å) in the C(5)–C(6) bond length. Other large differences involve the C(4)–C(5) and C(6)–N(1) bonds. It is seen that the bond distances in the saturated pyrimidine ring are generally larger than those in uracil, except the N(1)–C(2) bond distance which is significantly shorter (0·036 Å). This shortening in dihydrouracil is attributable to the strong conjugation of the lone pair of electrons on N(1) with the carbonyl group, C(2)=O(2). In uracil, in addition to the conjugation of the nonbonded electron pair with the carbonyl group C(2)=O(2), there is also conjugation with the C(5)–C(6) double bond. Further evidence of the interaction between the lone pair electrons on N(1) and the adjacent carbonyl group is borne out by the slight lengthening (0·01 Å) of the C(2)–O(2) bond over the C(4)–O(4) bond. However, it might be argued that the above lengthening may also be due to the hydrogen bonding to O(2). The reverse trend is observed in uracil. These observations indicate that electronic delocalization of the form

$$-\overset{\parallel \frown}{N}(1)-C(6){=}\overset{\frown}{C(5)}-\overset{\frown}{C(4)}{=}\overset{\frown}{O(4)} \leftrightarrow$$

$$-\overset{+}{N}(1){=}C(6)-C(5){=}C(4)-\overset{-}{O}(4)$$

I
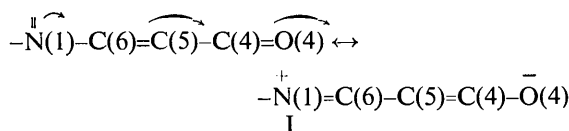
is more important in uracil than in dihydrouracil, while

$$-\overset{\parallel \frown}{N}(1)-\overset{\frown}{C(2)}{=}\overset{\frown}{O(2)} \leftrightarrow -\overset{+}{N}(1){=}C(2)-\overset{-}{O}(2)$$

II
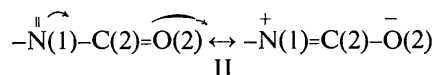
is more important in dihydrouracil than in uracil. The bond distances in dihydrouracil are generally in good agreement with those of dihydrothymine.

The bond angles involving the two sp^3 carbon atoms, C(5) and C(6), are 112·6 and 110·3° respectively (Table 7). The smaller angle at C(6) is due to the larger puckering of C(6). The bond angles in the conjugated portion show as much as 6° deviation from the expected 120° angle, which is in agreement with the values found in dihydrothymine. The exocyclic bond angles

N(3)–C(4)–O(4) and C(5)–C(4)–O(4) differ by about 3°, while the angles N(3)–C(2)–O(2) and N(1)–C(2)–O(2) differ by about 5°. Similar differences are exhibited by dihydrothymine and uracil. Bond angles involving the hydrogen atoms in dihydrouracil are given in Fig. 3.

The anisotropic temperature factors for the non-hydrogen atoms, shown in Table 3, produce only a small correction, about 0·003 Å, on the bond lengths. The direction cosines of the principal axes (Table 8) of the thermal ellipsoids indicate that the largest vibrational amplitudes are approximately perpendicular to the best plane of the molecule, Fig. 2(a).

In the crystal lattice, the molecules related by the symmetry centers are joined by two N–H···O hydrogen bonds, N(1)–H···O(2), 2·916 Å, and N(3)–H···O(2), 2·913 Å, Fig. 4. The carbonyl oxygen atom O(4) is not involved in any hydrogen bonding, in contrast to uracil where O(4) is involved in hydrogen bonding while O(2) is not. Infinite zigzag ribbons of hydrogen-bonded molecules run diagonally in the ab plane, separated by a distance of $c/2$ in the c-axis direction. In this direction, the only forces holding

Table 5. *Torsional angles* for dihydrouracil, dihydrothymine and uracil*

	Dihydrouracil† (This work)	Dihydrothymine‡ (Furberg & Jensen, 1968)		Uracil (Stewart & Jensen, 1967)
		1(60%)	2(40%)	
C(6)–N(1)–C(2)–N(3)	13·0 (5)°	−14·0°	15·3°	0·0°
N(1)–C(2)–N(3)–C(4)	11·1 (6)	−1·8		−0·5
C(2)–N(3)–C(4)–C(5)	−3·0 (6)	−14·9	20·2	0·8
N(3)–C(4)–C(5)–C(6)	−26·2 (5)	43·2	−46·9	−0·5
C(4)–C(5)–C(6)–N(1)	45·4 (5)	−55·4	57·8	0·0
C(5)–C(6)–N(1)–C(2)	−41·0 (5)	+43·8	−46·2	+0·2
C(6)–N(1)–C(2)–O(2)	−166·9 (4)	+166·1	−164·6	179·7
O(2)–C(2)–N(3)–C(4)	168·9 (4)	178·1		179·7
C(2)–N(3)–C(4)–O(4)	176·4 (4)	178·3		−179·0
O(4)–C(4)–C(5)–C(6)	154·3 (4)	−150·5	154·9	179·3

* The torsion angle A–B–C–D is the projected angle between AB and CD. When viewed down the B–C bond, the clockwise rotation of bond C–D with reference to bond A–B is considered positive.
† Standard deviations in torsion angles calculated by formula of Huber-Buser & Dunitz (1961).
‡ Number 2 represents the values for the lower weighted form while 1 represents the higher weighted form.

Table 6. *Bond lengths and standard deviations of dihydrouracil compared with those of dihydrothymine and uracil* (Å)

	Dihydrouracil	Dihydrothymine* 1(60%)	2(40%)	Uracil
N(1)–C(2)	1·335 (5)	1·326 (2)		1·371 (2)
C(2)–N(3)	1·395 (5)	1·383 (2)		1·376 (2)
N(3)–C(4)	1·364 (5)	1·358 (3)		1·371 (3)
C(4)–C(5)	1·515 (6)	1·531 (6)	1·555 (8)	1·430 (2)
C(5)–C(6)	1·507 (6)	1·516 (38)	1·521 (33)	1·340 (4)
C(6)–N(1)	1·464 (5)	1·450 (20)	1·472 (56)	1·358 (2)
C(2)–O(2)	1·222 (4)	1·235 (2)		1·215 (2)
C(4)–O(4)	1·211 (5)	1·212 (2)		1·245 (3)
N(1)–H(1)	0·84 (5)	0·92 (2)		0·84 (2)
N(3)–H(3)	0·86 (6)	0·89 (2)		0·88 (2)
C(5)–H(5)	1·00 (7)	1·07 (4)	0·79 (7)	0·93 (2)
C(5)–H(5′)	0·97 (6)	—		—
C(6)–H(6)	0·99 (5)	0·93 (7)	0·96 (11)	0·96 (2)
C(6)–H(6′)	1·03 (6)	0·94 (5)	0·88 (8)	—

* Number 1 represents values for the higher weighted form, while number 2 represents values for the lower weighted form.

these ribbons together are van der Waals in nature, thus explaining the strong (001) cleavage property of the crystal. The perpendicular separation between hydrogen-bonded ribbons is 3·34 Å.

Apart from the hydrogen bonds, no unusually short intermolecular contacts were found. The shortest contact involving O(4) is 2·59 Å with H(5) of a screw-related molecule. Along the cleavage plane, the shorter hydrogen–hydrogen contacts are about 2·6 Å. The base stacking pattern in dihydrouracil is typical of the keto pyrimidines as shown in Fig.5 (Sundaralingam, Rao, Bugg & Thomas, 1969). The closest contacts between overlapping bases are shown in Fig.5.

Changes in the electronic distribution (as indicated by the bond distances) in dihydrouracil compared with that in uracil would be expected to destroy Watson–Crick base pairing specificity between dihydrouracil and adenine. Alternative (Donohue, 1956; Donohue &

Trueblood, 1960) base-pairing schemes between dihydrouracil and the other nucleic acid bases of the dihydrouracil loop of *t*-RNA cannot be ruled out, however. A likely proposition is that dihydrouracil (the C=O, N–H and O(2′)–H bonds) might also serve as one of the hydrogen-bonding sites for the enzyme aminoacyl synthetase to *t*-RNA. The enzyme recognition of a *t*-RNA will be dependent not only on the presence of dihydrouracil in the loops of *t*-RNA, but also on the number and distribution of dihydrouracil.

It may be worthwhile to mention that the C(2)–N(1) bond distance and the bond angles about C(2) are very similar to the *cis* peptide geometry (Degeilh & Marsh, 1959).

Table 7. *Bond angles and standard deviations of dihydrouracil compared with those of dihydrothymine and uracil (in degrees)*

	Dihydrouracil	Dihydrothymine* 1	2	Uracil
C(6)–N(1)–C(2)	122·1 (2)	122·1 (5)	120·8 (8)	122·7 (1)
N(1)–C(2)–N(3)	116·1 (2)	116·6 (2)		114·0 (1)
C(2)–N(3)–C(4)	126·7 (2)	126·3 (2)		126·7 (1)
N(3)–C(4)–C(5)	115·1 (3)	113·4 (3)	113·9 (4)	115·5 (1)
C(4)–C(5)–C(6)	112·6 (3)	108·1 (1·5)	104·5 (1·5)	118·9 (1)
C(5)–C(6)–N(1)	110·3 (3)	108·5	109·5	122·3 (1)
N(1)–C(2)–O(2)	124·4 (2)	123·9 (2)		123·7 (1)
O(2)–C(2)–N(3)	119·5 (2)	119·5 (2)		122·3 (1)
N(3)–C(4)–O(4)	120·9 (2)	121·1 (2)		119·2 (1)
O(4)–C(4)–C(5)	123·9 (3)	124·1 (3)	121·1 (4)	125·3 (1)

* Number 1 represents values for the higher weighted form, and number 2 represents values for the lower weighted form.
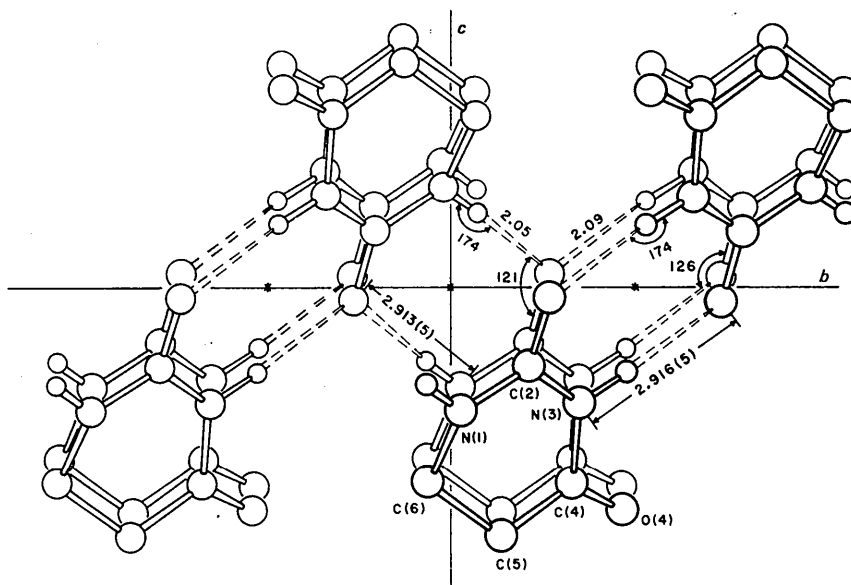

Fig.4. View of the hydrogen-bonding scheme down the *a** axis. Dotted lines indicate hydrogen bonds. Hydrogen atoms on C(5) and C(6) are not shown.

Table 8. *Magnitude and direction cosines of the principal axes of thermal vibrational ellipsoids of dihydrouracil*

|	Axis	B_t	C_{ta}	C_{tb}	C_{tc}
N(1)	1	2·313 Å	0·726	0·202	−0·658
	2	1·816	0·595	0·296	0·747
	3	1·461	0·345	−0·934	0·095
C(2)	1	1·926	0·962	0·028	−0·272
	2	1·634	0·106	0·877	0·468
	3	1·516	0·252	−0·479	0·841
N(3)	1	2·250	−0·825	−0·330	0·460
	2	1·745	−0·406	0·911	−0·074
	3	1·595	−0·394	−0·247	−0·885
C(4)	1	2·400	−0·845	0·228	0·483
	2	1·753	−0·519	−0·132	−0·844
	3	1·508	−0·129	−0·964	0·231
C(5)	1	2·866	−0·938	−0·083	0·335
	2	2·471	−0·104	0·993	−0·046
	3	1·626	−0·329	−0·078	−0·941
C(6)	1	2·858	−0·973	−0·056	0·223
	2	2·005	−0·200	0·681	−0·704
	3	1·682	−0·112	−0·730	−0·674
O(2)	1	2·534	−0·620	−0·730	0·287
	2	2·037	−0·690	0·681	0·243
	3	1·674	−0·374	−0·047	−0·926
O(4)	1	3·545	0·806	−0·008	−0·591
	2	2·471	0·347	0·816	0·463
	3	2·203	0·479	−0·579	0·660
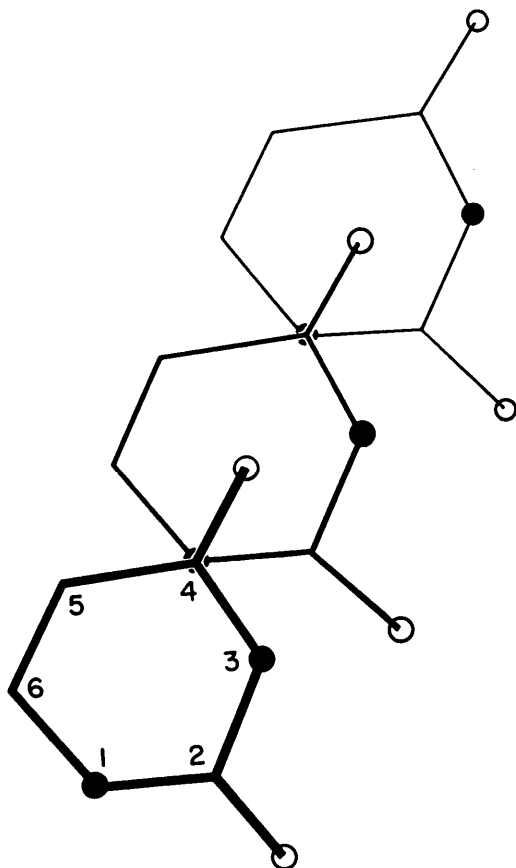
Fig. 5. Base stacking in dihydrouracil. Interbase contacts less than 3·5 Å involving the nonhydrogen atoms are: N(1)···N(3), 3·387 Å; N(1)···C(4), 3·294 Å; and C(2)···N(3), 3·417 Å.

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