The Crystal Structure of Orotic Acid Monohydrate (Vitamin B_{13})

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The crystal structure of orotic acid monohydrate (Vitamin B_{13}) has been determined by the method of X-ray diffraction. The crystals are triclinic with the space group of $P\bar{1}$ and with cell dimensions of $a=9.561$, $b=7.261$, $c=5.895$ Å, $\alpha=117.6°$, $\beta=107.6°$, and $\gamma=90.4°$. The structure was determined by an inspection of the sharpened Patterson map. The final R value was 5.75% for 1345 observed reflections. The uracil group of orotic acid resembles uracil itself in its molecular dimensions. The molecules are arranged in layers closely parallel to the $(\bar{2}\ 1\ 1)$ plane. The orotic acid molecules are linked through two kinds of N–H···O hydrogen bonds in zig-zag chains extending in the [1 1 1] direction. Each chain is joined, by three kinds of O–H···O hydrogen bonds through the medium of a water molecule, with two neighboring chains, and each forms a sheet parallel to the $(\bar{2}\ 1\ 1)$ plane. The hydrogen bond of the water molecule as an acceptor is of the F type, in which the bisector of lone pairs in the oxygen atom is directed toward a donor group.

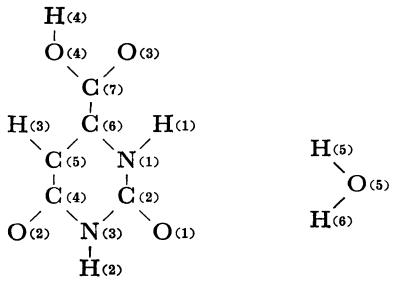
This work is a part of a series of X-ray studies of aromatic carboxylic acids. The series has already covered pyromellitic acid dihydrate,[1] trimellitic acid,[2] hemimellitic acid dihydrate,[3] dipicolinic acid monohydrate,[4] dinicotinic acid,[4] quinolinic acid,[4] and cinchomeronic acid.[4] These investigations have given several interesting results, and it is of interest to elucidate the molecular structure of the carboxylic acid based on the pyrimidine ring and the mode of hydrogen-bond formation. Moreover, the orotic acid is vitamin B_{13} and is a biologically-important substance, as are uracil, thymine, and other compounds with a uracil group. In view of the fact that the crystal structures of many uracil derivatives have been determined by the X-ray method, it is also of interest to compare uracil itself with its derivatives in molecular dimensions and in the hydrogen-bond system of the uracil group.

Experimental

A sample of orotic acid was supplied by the Sigma Chemical Co.; crystallization from water yielded crystals of a suitable size. The unit cell dimensions were measured from zero-layer Weissenberg photographs, which were calibrated with superimposed Al powder lines. The crystal data are given in Table 1. Using a spherically-shaped crystal with an average diameter of 0.3 mm, the intensity data were collected for the 0—6 layers around the c axis and the 0—2 layers around the b axis by the use of the multiple-film equi-inclination integrating Weissenberg technique, with Cu$K\alpha$ radiation. The intensities were estimated visually by comparison with a calibration-intensity standard. Of the 1562 possible reflections within the Cu$K\alpha$ sphere, 1488 independent reflections were measured; 143 were too weak to be observed. No absorption correction was applied. The space group $P\bar{1}$ was assigned on the basis of the statistical average for normalized structure factors.

Table 1. Crystal data for orotic acid monohydrate

Molecular formula	$C_5H_4N_2O_4 \cdot H_2O$
Molecular weight	174.06
Crystal system	Triclinic
Space group	$P\bar{1}$
Cell dimensions;	
a	9.561±0.006Å
b	7.261±0.006
c	5.895±0.006
α	117.6±0.09°
β	107.6±0.08
γ	90.4±0.09
V	340.7±0.4Å^3
Z	2
Density (calculated)	1.697 g/cm^3
Density (by flotation)	1.68
Linear absorption coefficient for Cu$K\alpha$	15.4 cm^{-1}
The atom numbering	



Structure Determination and Refinement

The crystal structure was determined by the inspection of a sharpened Patterson map, which was resolved sufficiently enough to give the orientation and location of the orotic acid molecule in the unit cell. The first postulated structure gave an R value of 63%, which decreased to 35% in three cycles of least-squares refinement with individual isotropic thermal parameters. A difference Fourier map clearly showed the position of water oxygen atom. Since the $\bar{2}\ 1\ 1$ reflection seemed to have a strong extinction effect, it was removed from the later refinements.

Anisotropic thermal parameters were introduced, and

1) F. Takusagawa, K. Hirotsu, and A. Shimada, This Bulletin, **44**, 1274 (1971).

2) F. Takusagawa, K. Hirotsu, and A. Shimada, to be published.

3) F. Takusagawa, K. Hirotsu, and A. Shimada, to be published.

4) F. Takussgawa, K. Hirotsu, and A. Shimada, *Acta Crystallogr.*, **A28**, S15 (1972).

TABLE. 2. THE OBSERVED AND CALCULATED STRUCTURE FACTORS. F_O, F_C, and DF have been multiplied by 10. The unobserved reflections are indicated by an asterisk. The reflections with $|F_O-F_C|/|F_O|$ larger than 0.3 are indicated by a plus sign.

H	FO	FC	DF	H	FO	FC	DF	H	FO	FC	DF	H	FO	FC	DF	H	FO	FC	DF	H	FO	FC	DF	H	FO	FC	DF
K=L= 0	0		7	79	80	0	7	14	13	0	-5	220	223	-2	3	83	-79	-4	2	18	19	0	-3	408	-391	-16
2	292	-305	13	8	11	-13	1	8*	0	0	0	-4	170	-171	0	4	21	21	0	3*	0	0	0	-2	270	-281	11
3	252	248	4	9*	0	-5	5	9+	3	-1	-1	-3	80	80	0	5	70	-77	7	4	87	-95	8	-1	179	157	21
4	114	-119	4	K=L=	5	0		K=L=	-5	1		-2	190	-193	2	6	33	-30	-3	5	38	-36	-1	0	135	-142	7
5	76	-68	-7	-10*	0	-4	4	-9	6	5	0	-1	118	-117	-1	7	37	41	-3	6	20	21	0	1	157	150	6
6	43	-40	-3	-9*	0	-4	4	-8	18	18	0	0+	25	-33	8	8	24	-24	0	7	9	-10	0	2	35	30	5
7	33	-29	-3	-8	7	-9	1	-7	42	-39	-2	1	66	-64	-2	9+	6	-12	5	8+	5	-7	2	3	176	-161	-15
8	83	-82	-1	-7	51	48	2	-6	55	52	2	2	171	-183	12	K=L=	4	1		K=L=	-6	2		4	49	57	-8
9	11	-11	0	-6	40	38	1	-5	35	-35	0	3	247	-237	-9	-11*	0	-1	1	-8	21	19	1	5	97	95	2
10+	13	8	5	-5	15	-16	0	-4	282	-272	-10	4	80	87	-6	-10	21	-19	-1	-7	27	-27	0	6	130	-128	-1
11	35	-31	-4	-4	31	-31	0	-3	20	21	0	5	14	-14	0	-9*	0	-2	2	-6	34	34	0	7	10	-12	1
K=L=	1	0		-3	97	-89	-7	-2	69	70	-1	6	28	31	-2	-8	9	-7	-1	-5	29	29	0	8	103	95	7
-11*	0	-2	2	-2	67	63	4	-1	72	-68	-3	7	121	113	7	-7	21	-22	0	-4	26	-26	0	9*	0	-1	1
-10	45	-45	0	-1	42	41	1	0	36	38	-1	8	12	12	0	-6	37	-36	-1	-3	25	-28	3	10	7	5	1
-9+	18	12	6	0	68	-63	-4	1	94	87	7	9	13	-15	1	-5*	0	2	-2	-2	50	48	2	K=L=	-1	2	
-8	15	-14	-1	1	27	27	0	2*	0	0	0	10	36	35	0	-4	65	-60	-5	-1*	0	3	-3	-12	9	9	0
-7+	5	-8	2	2	37	34	2	3	30	30	0	11*	0	-5	5	-3	50	-49	0	0	32	-32	0	-11	28	28	0
-6	7	-9	1	3	13	13	0	4	47	49	-2	K=L=	0	1		-2	51	51	0	1	27	29	-2	-10	18	20	-2
-5	177	-173	-3	4	18	-16	-2	5	7	-7	0	-12*	0	3	-3	-1+	13	-5	-7	2	26	-27	1	-9	14	-13	0
-4	74	78	-4	5	5	6	0	6	24	26	-1	-11	67	-60	-6	0*	0	-3	3	3	28	-28	0	-8	56	57	-1
-3	125	126	0	6	8	-7	0	7	20	21	-1	-10	45	-41	-4	1	64	59	4	4	17	19	-1	-7	60	62	-1
-2	326	338	-11	7	19	16	2	8	9	10	-1	-9	19	17	1	2	65	60	4	5	16	16	0	-6	23	-28	5
-1	179	173	6	K=L=	6	0		9	11	-11	0	-8	12	11	0	3	29	-27	-2	6	34	-33	0	-5	26	-26	0
0	169	-167	-1	-9	7	8	0	10	12	-12	0	-7	67	62	4	4	14	15	0	7	17	18	0	-4	95	103	-7
1	93	93	0	-8	8	9	0	K=L=	-4	1		-6	93	-85	-8	5	38	41	-3	8	39	37	2	-3	155	-162	6
2	96	97	0	-7*	0	1	-1	-10+	7	12	-5	-5	85	-79	-5	6	11	14	-2	9+	17	-23	6	-2	241	-252	11
3	104	-105	1	-6	11	11	0	-9	21	22	0	-4	88	81	7	7*	0	6	-6	K=L=	-5	2		0	222	-232	10
4	133	-139	5	-5+	5	2	3	-8	11	-11	0	-3	60	63	-3	K=L=	5	1		-9	23	20	2	1	43	-43	0
5	89	89	0	-4*	0	3	-3	-7*	0	1	-1	-2	155	-149	-5	-10+	3	5	-2	-8	12	-13	1	2	52	-53	1
6+	7	4	3	-3	48	50	-1	-6	19	-23	4	-1	135	132	2	-9	24	-23	0	-7	47	-49	2	3	95	-96	0
7	21	26	-5	-2	19	15	3	-5	12	14	-2	0	316	331	-14	-8*	0	-6	6	-6	46	50	-3	4	54	-54	0
8	65	-67	2	-1	36	-32	-4	-4	25	25	0	1	135	134	1	-7	13	14	0	-5	80	-84	4	5	23	-27	3
9	109	-106	-2	0	53	50	2	-3	45	47	-1	2	102	101	1	-6*	0	-4	4	-4	144	-143	-1	6	258	244	14
10	14	11	3	1	10	9	0	-2	117	-117	0	3	271	-254	-16	-5	9	10	0	-3	45	-48	3	7	69	70	-1
11+	3	-4	1	2	166	-160	-6	-1	50	46	3	4	5	-4	0	-4	41	-42	0	-2	36	-40	3	8	22	-23	1
K=L=	2	0		3	28	-24	-3	0	152	148	3	5+	8	-1	-7	-3	73	-68	-4	-1	115	119	-3	9	45	44	0
-11	11	-11	0	4	39	36	2	1	206	-199	-7	6	29	-27	-2	-2	22	21	0	0*	0	2	-2	10*	0	-4	4
-10*	0	1	-1	5	32	-31	-1	2	57	-54	-3	7	32	35	-2	-1	21	21	0	1	86	85	0	K=L=	0	2	
-9	61	62	0	6	13	12	1	3	46	-49	3	8	80	-75	-4	0	31	29	2	2	48	50	-2	-12+	5	-3	-1
-8	25	25	0	K=L=	7	0		4	100	98	1	9*	0	-2	2	1*	0	-6	6	3	39	-41	2	-11	31	-27	-3
-7*	0	-3	3	-7*	0	-1	1	5	131	127	4	10*	0	3	-3	2	22	20	1	4	87	91	-4	-10+	7	-2	-5
-6	38	40	-2	-6	8	9	0	6	25	-25	0	K=L=	1	1		3	55	49	5	5	26	27	0	-9	25	-24	0
-5	110	-115	4	-5	18	19	-1	7	7	5	1	-11	4	-5	1	4	21	22	0	6	10	-11	0	-8	99	94	5
-4	92	-98	6	-4	8	7	1	8	14	-14	0	-10	39	-36	-2	5	53	52	1	7	8	-8	0	-7	113	101	12
-3	30	-25	-5	-3	12	11	1	9	15	-14	-1	-9	13	-12	0	6	7	-7	0	8	23	-24	1	-6	80	-79	0
-2+	18	-9	-9	-2*	0	-4	4	10*	0	-2	2	-8	18	-17	-1	K=L=	6	1		9	12	-14	2	-5	21	25	-3
-1	94	-100	6	-1	14	-12	-1	K=L=	-3	1		-7	57	-50	-6	-9*	9	14	-5	K=L=	-4	2		-4	98	-96	-2
0	170	-173	3	0	68	-62	-6	-10	10	-11	0	-6	54	-55	0	-8	13	12	0	-10	13	15	-1	-3	52	-58	5
1	87	83	3	1	54	-47	-7	-9	72	72	0	-5	120	125	-4	-7	4	-3	-1	-9	39	-35	-4	-2	24	-20	-4
2	183	-186	3	2	25	24	1	-8	30	22	8	-4	167	-170	3	-6	14	-14	0	-8	50	51	-1	-1	70	-63	-6
3	253	261	-8	3	21	-19	-2	-7	73	72	1	-3	8	9	0	-5	34	-32	-1	-7	36	-37	0	0	171	-154	-16
4	257	254	2	4	12	-12	0	-6	37	41	-4	-1	38	37	0	-4	21	21	0	-6	313	-302	-11	1	239	-217	-21
5	108	-110	1	K=L=	8	0		-5	11	-11	0	0	246	-251	5	-3	31	28	4	-5	18	22	-4	2	83	84	-1
6	30	29	0	-4	5	-4	0	-4	99	96	3	1	222	227	-4	-2	26	-23	-2	-4	71	77	-6	3	17	-18	0
7	73	-77	4	-3	6	-6	0	-3	17	18	0	2	117	-120	2	-1	9	10	-1	-3	93	-94	0	4	32	37	-5
8	31	-27	-3	-2*	0	-1	1	-2	119	118	1	3	68	-65	-2	0	35	30	4	-2	59	60	-1	5	139	141	-2
9	37	41	-4	-1	14	-13	-1	-1	397	-407	9	4	52	-54	1	1	9	7	1	-1	128	126	1	6	22	21	1
10	21	-21	0	0	8	-8	0	0	267	-256	-10	5	38	-37	0	2	12	-10	-1	0*	0	0	0	7	14	-13	0
K=L=	3	0		K=L=	-8	1		1	128	129	0	6	116	-114	-1	3	5	5	0	1	77	74	2	8	52	47	4
-11	30	30	0	-3	10	10	0	2	103	-107	4	7	16	-17	1	4	3	-3	0	2	117	124	-7	9+	5	-3	-1
-10	93	88	4	-2	35	32	3	3	95	93	1	8	21	17	4	K=L=	7	1		3	27	-29	2	K=L=	1	2	
-9*	0	-6	6	-1	8	8	0	4	11	12	-1	9	49	-44	-5	-7*	0	-3	3	4	55	56	-1	-12	18	-18	0
-8	36	-36	0	0	17	17	0	5	118	-112	-6	10+	11	-4	-6	-6*	0	3	-3	5	41	43	-2	-11	7	7	0
-7	20	-24	3	1*	0	2	-2	6	34	36	-1	K=L=	2	1		-5	25	23	1	6	15	16	-1	-10	11	9	1
-6	20	-23	2	2	4	4	0	7	49	48	0	-11*	0	-1	1	-4	3	4	0	7	18	-20	2	-9	30	30	0
-5	30	-28	-2	3*	0	0	0	8	89	-86	-3	-10*	0	-3	3	-3	11	-11	0	8	29	-30	1	-8	37	-36	0
-4	116	-116	0	4	13	11	1	9*	0	-3	3	-9	5	-6	1	-2	32	28	4	9	5	5	0	-7	45	-48	2
-3	30	32	-1	5*	0	-1	1	10	60	59	1	-8*	0	-6	6	-1*	0	3	-3	10	11	-13	1	-6	43	42	1
-2	178	-174	-4	6	45	-43	-2	11*	0	3	-3	-7	55	-56	1	0	67	-70	3	K=L=	-3	2		-5	15	17	-2
-1	139	-135	-4	K=L=	-7	1		K=L=	-2	1		-6	29	30	-1	1	13	-13	0	-11	13	14	-1	-4	84	-79	-5
0	129	130	-1	-6	14	15	0	-11+	10	6	4	-5	58	60	-2	2	14	17	-3	-10	10	-10	0	-3	49	52	-2
1+	11	-16	5	-5	21	-18	-2	-10	12	13	0	-4	179	168	10	K=L=	-9	2		-9+	7	-4	-2	-2	151	143	8
2	16	-19	2	-4	25	24	1	-9	38	42	-4	-3	109	107	1	-1*	0	5	-5	-8	29	-27	-2	-1	62	63	0
3	92	96	-4	-3	25	24	1	-8	29	31	-1	-2	94	-89	-4	0	13	-14	0	-7+	7	1	5	0	57	54	2
4	110	114	-3	-2	20	-17	-2	-7	22	-25	3	-1	53	58	-5	1	19	-18	0	-6	20	24	-4	1	173	-167	-6
5	30	-32	2	-1	21	-21	0	-6	110	112	-1	0	72	71	0	2	3	3	0	-5	44	46	-2	2*	0	1	-1
6	26	29	-2	0	15	14	0	-5	98	99	0	1	87	-87	0	3*	0	2	-2	-4	120	-123	3	3+	15	9	5
7	43	48	-4	1	7	-6	0	-4	27	-35	7	2	115	-120	5	K=L=	-8	2		-3	52	48	3	4	20	-19	0
8	12	14	-2	2	15	-14	0	-3	29	-31	1	3	79	74	4	-5	52	47	5	-2	221	203	17	5	33	38	-5
9	7	9	-1	3	7	8	0	-2	163	176	-13	4*	0	-4	4	-4	12	11	1	-1	261	-272	11	6	87	-82	-4
10	24	25	-1	4	16	-16	0	-1	223	-218	-4	5	17	22	-4	-3+	3	6	-2	0	74	-65	-8	7*	0	0	0
K=L=	4	0		5	14	-12	-1	0	297	-314	16	6	66	-71	4	-2	18	17	1	1	82	-84	2	8*	0	5	-5
-11*	0	0	0	6	14	14	0	1	98	104	-5	7	127	-125	-2	-1	4	-3	0	2	181	177	4	9	4	5	-1
-10	48	-44	-4	7	9	8	1	2	242	-243	1	8	19	17	1	0	6	6	0	3	255	234	20	K=L=	2	2	
-9	16	13	2	8	12	-12	0	3	36	-36	0	9	7	-9	1	1	32	30	1	4	52	-54	1	-12	9	-11	2
-8	15	16	0	K=L=	-6	1		4	41	-45	3	K=L=	3	1		2	11	-10	0	5	29	34	-5	-11*	0	-2	2
-7	58	-57	-1	-7	22	21	1	5	73	-71	-2	-11	26	26	0	3	19	-19	0	6	31	-35	4	-10+	4	-6	2
-6*	0	-3	3	-6	13	-14	1	6	53	-50	-2	-10	19	18	0	4	52	46	6	7	19	-21	2	-9	31	-29	-1
-5	39	37	2	-5	40	-40	0	7	14	-15	1	-9*	0	1	-1	5	10	-11	0	8	8	8	0	-8	12	-14	2
-4	35	-35	0	-4	42	41	1	8	178	173	4	-8	12	11	1	6	50	-47	-3	9	33	-33	0	-7	39	43	-3
-3	45	49	-4	-3	78	-74	-4	9	54	53	0	-7	24	-25	1	K=L=	-7	2		10	24	-22	-1	-6	64	-70	6
-2	122	-122	0	-2	105	-110	4	10	18	-17	0	-6	25	-26	0	-7	12	11	0	K=L=	-2	2		-5	10	9	0
-1	208	-207	0	-1	29	-31	1	11	26	26	0	-5	6	-5	-1	-6	34	-30	-3	-11	38	39	-1	-4	418	398	20
0	65	65	0	0	20	-20	0	K=L=	-1	1		-4*	0	-2	2	-5	20	21	-1	-10	14	15	-1	-3	30	31	-1
1	23	24	0	1	53	51	2	-11	30	31	0	-3	50	-49	0	-4	52	51	0	-9	44	46	-1	-2	113	-111	-1
2	70	69	1	2	9	10	0	-10	17	-15	-2	-2	82	-75	-6	-3	7	8	-1	-8	30	32	-1	-1	106	102	4
3	9	-10	0	3	49	45	3	-9	48	-52	4	-1	31	30	0	-2	43	45	-1	-7*	0	-3	3	0	50	-53	2
4	35	35	0	4	22	23	0	-8	18	13	4	0	105	-97	-7	-1	9	-7	-1	-6	70	71	0	1	49	-43	-6
5	74	73	0	5	12	-11	-1	-7	71	-73	2	1	145	153	-8	0	16	17	0	-5	13	16	-3	2	38	-36	-1
6	19	24	-5	6	36	34	2	-6	207	202	5	2	163	170	-7	1	16	16	0	-4	96	100	-3	3	29	-30	0

TABLE 2. Continued.

H	FO	FC	DF	H	FO	FC	DF	H	FO	FC	DF	H	FO	FC	DF	H	FO	FC	DF	H	FO	FC	DF	H	FO	FC	DF
4	87	-95	8	3	20	-18	-1	-2	48	-44	-3	-8	26	-28	1	-6	53	56	-2	-6	60	-57	-3	5+	12	16	-3
5	14	-17	3	4	103	-95	-7	-1	73	-68	-5	-7	5	5	0	-5	16	-15	0	-5	23	21	2	K,L=	-6	5	
6	16	18	-2	5*	0	-4	4	0	190	169	20	-6	128	124	4	-4	28	33	-4	-4	17	-17	0	-9	47	46	0
7	42	-42	0	6	12	-12	0	1	266	247	19	-5	18	20	-2	-3	47	45	1	-3	59	56	3	-8	24	22	1
8*	0	-1	1	7	6	-7	0	2	66	-63	-3	-4	38	-41	3	-2	24	23	1	-2	17	15	2	-7	8	10	-1
K,L=	3	2		K,L=	-6	2		3	44	49	-5	-3	34	35	-1	-1+	9	4	5	-1	82	-76	-6	-6	33	-34	0
-11*	0	-3	3	-9	16	12	4	4	45	-49	4	-2	7	-8	1	0	223	-206	-17	0	30	31	-1	-5	45	-48	2
-10*	0	-2	2	-8	30	-30	0	5	23	-24	0	-1	24	-25	0	1	79	-81	2	1	61	53	7	-4*	0	4	-4
-9	8	-8	0	-7	25	26	-1	6	18	19	-1	0	14	-14	0	2	25	27	-1	2	97	-93	-3	-3	13	-10	-2
-8	9	7	1	-6	62	58	3	7	50	-50	0	1	16	-15	0	3	27	-28	1	3	18	-19	0	-2	23	22	0
-7	17	21	-3	-5*	0	5	-5	8	36	-35	0	2	49	-51	1	4	11	-14	2	4	83	78	5	-1	7	6	1
-6	68	74	-5	-4	68	68	0	9	10	-9	0	3	9	-12	2	5	20	24	-3	5	12	-11	-1	0*	0	-1	1
-5	55	51	3	-3	21	-20	-1	K,L=	-1	3		4	9	11	-2	6	16	19	-2	6*	0	2	-2	1	26	27	0
-4	41	-44	3	-2	30	32	-2	-12	8	7	0	5	23	-27	3	7	15	15	0	K,L=	1	4		2	25	24	0
-3+	10	14	-3	-1	47	41	6	-11	17	20	-2	K,L=	4	3		K,L=	-4	4		-11	10	10	0	3	11	-13	1
-2	36	36	0	0	22	23	0	-10	17	19	-1	-10*	0	1	-1	-11	9	-11	2	-10	3	-2	0	4	4	4	0
-1	52	-54	2	1*	0	1	-1	-9+	5	3	2	-9	5	6	0	-10	16	18	-2	-9*	0	-6	6	5	14	15	0
0	66	-62	-4	2	168	-167	-1	-8	30	31	0	-8	26	30	-4	-9	23	23	0	-8*	0	4	-4	K,L=	-5	5	
1	34	36	-2	3	66	-64	-1	-7	14	16	-1	-7	23	22	0	-8	12	-14	1	-7	19	-21	1	-10	14	14	0
2*	0	-6	6	4	26	28	-1	-6	40	43	-2	-6	21	-20	0	-7	11	-11	0	-6	26	-27	0	-9	3	4	0
3	9	9	0	5	19	-20	1	-5	179	-187	8	-5*	0	0	0	-6	48	50	-1	-5+	12	16	-4	-8	15	13	2
4	50	-47	-3	6	11	-12	0	-4	151	-154	3	-4	16	14	1	-5	12	14	-1	-4	25	-23	-2	-7	11	-13	1
5	100	-95	-5	7	19	22	-2	-3	78	84	-6	-3	28	-27	0	-4	35	-37	1	-3	29	-30	0	-6*	0	2	-2
6	12	12	0	8	10	12	-2	-2	73	-77	4	-2	28	-26	-1	-3	45	44	1	-2	19	-20	1	-5	37	40	-2
7*	0	-5	5	K,L=	-5	3		-1	125	115	10	-1	11	13	-1	-2	45	-46	1	-1	14	-14	0	-4	17	-18	0
K,L=	4	2		-10	19	16	2	0	35	31	4	0*	0	-3	3	-1	61	-61	0	0	38	-35	-3	-3	68	-64	-3
-10*	0	2	-2	-9	23	-23	0	1	154	-136	-17	1*	0	1	-1	0+	17	11	6	1	23	-22	0	-2	112	115	-3
-9*	0	0	0	-8	31	31	0	2	49	54	-5	2	18	-20	2	1	25	24	1	2	144	133	10	-1	17	-15	-1
-8*	0	-1	1	-7	31	29	1	3	101	97	4	3	41	-48	6	2	78	-82	4	3	49	49	0	0	150	-143	-6
-7*	0	0	0	-6	23	-24	1	4	191	-131	0	4*	0	3	-3	3	17	22	-4	4	17	-19	2	1	7	9	-2
-6	5	-5	0	-5	22	-23	1	5	17	-21	4	K,L=	5	3		4	104	99	4	5	30	37	-6	2	28	-27	0
-5	22	-24	1	-4	72	68	3	6	114	106	7	-7*	0	-10	10	5	78	-75	-3	6*	0	-2	2	3	3	-5	1
-4	23	-24	1	-3	14	16	-2	7	9	-9	0	-6	10	-7	-2	6	22	-23	1	K,L=	2	4		4	22	23	0
-3*	0	0	0	-2	48	-47	-1	8+	7	5	2	-5+	7	-3	-3	7	8	9	-1	-10	7	-8	0	5*	0	4	-4
-2	35	-34	0	-1	55	52	2	K,L=	0	3		-4+	4	-11	7	K,L=	-3	4		-8	8	-6	-1	6	2	-2	0
-1	58	53	5	0	37	-41	3	-12	11	10	1	-3	10	12	-1	-11	10	-11	1	-7	8	-7	-1	K,L=	-4	5	
0	73	69	3	1	50	-49	-1	-11	7	-6	-1	-2+	12	21	-9	-10	27	26	0	-6+	4	-7	3	-10	23	23	0
1	27	-27	0	2	15	16	-1	-10	20	18	2	-1	2	-3	0	-9	38	-37	-1	-5	18	-17	0	-9*	0	3	-3
2*	0	3	-3	3	23	23	0	-9	31	28	3	0*	0	-2	2	-8	74	-76	1	-4	23	-22	-1	-8	26	25	1
3	54	-53	0	4	63	-66	2	-8	13	-12	-1	1	26	-27	1	-7	23	-28	4	-3	23	-22	-1	-7*	0	0	0
4	20	-20	0	5	22	22	0	-7	14	-14	0	K,L=	-9	4		-6	17	-19	1	-2	7	7	0	-6	21	20	0
5	26	31	-4	6	73	72	0	-6	28	30	-1	-3	6	7	-1	-5	73	76	-3	-1	4	-3	0	-5	24	23	1
6	16	-17	0	7	56	-51	-4	-5	68	-66	-1	-2	31	-26	-4	-4	6	-6	0	0	31	30	1	-4	24	21	2
K,L=	5	2		8	17	-19	2	-4	102	-100	-2	-1	18	-17	-1	-3	64	63	1	1	70	67	2	-3	6	6	0
-9	11	-11	0	9*	0	3	-3	-3	45	44	0	0	3	3	0	-2	55	53	2	2	10	9	0	-2	177	-168	-8
-8	8	-10	2	K,L=	-4	3		-2	102	-97	-4	1	11	10	1	-1	62	-59	-2	3	5	-6	0	-1	75	-73	-2
-7*	0	-1	1	-11	16	16	0	-1	44	-37	-7	2	10	9	0	0	151	138	12	4	24	26	-1	0	19	22	-3
-6	18	-17	0	-10	12	-12	0	0	42	-38	-4	3+	9	13	-4	1	35	33	1	K,L=	3	4		1	26	-28	2
-5	14	-14	0	-9	32	-32	0	1	57	-57	0	K,L=	-8	4		2	28	-29	0	-9*	0	-1	1	2	12	-13	1
-4	13	13	0	-8	44	42	2	2	50	-46	-3	-6	3	3	0	3	25	-25	0	-8	17	-19	1	3	19	22	-3
-3*	0	-2	2	-7	66	-66	0	3	29	-30	0	-5	6	-7	0	4	51	-51	0	-7+	3	5	-1	4	18	21	-2
-2*	0	0	0	-6	120	-125	4	4	243	223	20	-4	7	-7	0	5	28	-27	0	-6	22	21	0	5	19	19	0
-1	29	27	1	-5	42	-46	3	5	72	68	3	-3	14	13	1	6	8	-6	-1	-5	5	6	0	6	17	16	1
0	16	18	-2	-4	38	-39	1	6	26	-24	-1	-2	41	-42	0	8+	6	8	-2	-4*	0	3	-3	K,L=	-3	5	
1	20	-18	-1	-3	133	137	-4	7	58	50	7	-1*	0	-4	4	K,L=	-2	4		-3*	0	-5	5	-11	13	13	0
2*	0	2	-2	-2*	0	-7	7	8+	3	-6	2	0	12	-12	0	-11	13	-15	1	-2	7	6	0	-10	4	-4	0
3	24	27	-3	-1	100	101	0	K,L=	1	3		1	6	-6	0	-10	110	-105	-5	-1	11	10	0	-9	3	-2	0
4	10	11	-1	0	65	71	-6	-12	4	-5	0	2	33	35	-1	-9	6	-6	0	0	6	7	0	-8	21	21	0
K,L=	6	2		1	67	-74	6	-11*	0	-3	3	3	9	10	-1	-8	42	42	0	1*	0	0	0	-7*	0	3	-3
-7*	0	1	-1	2	150	151	0	-10	30	32	-1	4	7	8	0	-7	34	-35	1	2	24	-27	3	-6	17	-16	-1
-6	12	-12	0	3	36	37	-1	-9	31	30	1	5+	4	6	-2	-6	20	18	1	3*	0	0	0	-5	18	18	0
-5	19	-18	0	4	27	-27	0	-8	26	-26	0	K,L=	-7	4		-5	68	67	1	K,L=	4	4		-4	39	-37	-2
-4	5	6	0	5	19	-20	1	-7*	0	-1	1	-8	25	-25	0	-4	18	16	1	-8+	27	36	-8	-3	46	-51	5
-3	11	12	0	6	39	-42	3	-6	30	-29	0	-7	67	65	1	-3	54	52	2	-7	8	9	-1	-2	7	8	-1
-2	8	8	0	7	24	-23	0	-5	20	-21	1	-6	29	27	1	-2	84	100	-15	-6	11	-13	2	-1	19	18	1
-1*	0	-3	3	8*	0	-1	1	-4	11	-10	0	-5+	10	14	-4	-1	21	-20	0	-5	11	11	0	0	60	-61	1
0	8	9	-1	9	18	17	1	-3	37	-36	0	-4	38	-38	0	0	50	50	0	-4*	0	2	-2	1	16	19	-3
1	23	24	0	K,L=	-3	3		-2	67	-68	0	-3	51	-52	1	1	45	46	0	-3	10	-11	1	2	85	88	-2
2	13	14	-1	-11	23	-21	-2	-1	97	-93	-4	-2*	0	5	-5	2	11	8	3	-2*	0	-4	4	3	70	-67	-3
K,L=	-9	3		-10	32	33	0	0	34	36	-2	-1	11	-9	-2	3	27	-30	3	-1	7	-6	0	4	18	-19	0
-2+	4	-1	-2	-9	27	-28	0	1	8	-8	0	0	20	19	0	4	57	-54	-2	0	20	-21	1	5	9	11	-2
-1	6	5	1	-8	219	-213	-6	2	37	39	-2	1	8	9	0	5	13	12	1	1*	0	-5	5	6	4	-4	0
0	24	-24	0	-7*	0	5	-5	3	117	116	0	2+	4	1	3	6	24	-23	0	K,L=	-9	5		K,L=	-2	5	
1	3	-3	0	-6	61	66	-4	4	19	18	1	3	17	18	0	7	7	-6	0	-2	15	18	-3	-11	17	-16	-1
2	7	-8	0	-5	70	-73	2	5	7	-9	1	4	14	14	0	K,L=	-1	4		-1	19	-19	0	-10	38	-35	-2
3*	0	-2	2	-4	46	48	-2	6	40	42	-2	5	10	-12	1	-11	9	-8	-1	0	27	-31	3	-9	10	-12	1
K,L=	-8	3		-3	119	114	5	7*	0	-2	2	6*	0	1	-1	-10	25	22	3	K,L=	-8	5		-8	4	-5	1
-5	61	62	-1	-2+	8	11	-2	K,L=	2	3		K,L=	-6	4		-9	11	12	0	-6	10	-9	0	-7	22	20	1
-4	28	24	4	-1	88	87	1	-11	11	11	0	-9	58	54	3	-8	29	-28	0	-5	7	8	-1	-6*	0	-3	3
-3	14	11	2	0	167	160	6	-10	13	-14	0	-8	18	17	0	-7	38	35	2	-4	34	-35	0	-5	24	22	2
-2	29	-28	-1	1	42	-40	-1	-9	22	-24	1	-7+	5	7	-1	-6	65	61	3	-3	22	-20	-2	-4	24	22	1
-1	36	-38	2	2	73	74	0	-8	17	16	1	-6	24	24	0	-5	78	-74	-4	-2	6	6	0	-3	21	-19	-2
0	4	4	0	3	60	59	1	-7*	0	0	0	-5+	10	-14	3	-4	24	-22	-2	-1	17	16	0	-1	24	21	2
1*	0	-1	1	4	14	15	-1	-6	39	-42	3	-4*	0	6	-6	-3	27	-27	0	0	14	14	0	0	14	-14	0
2	11	9	1	5	26	-29	2	-5	15	18	-2	-3	43	50	-7	-2	84	87	-2	1	23	23	0	1	18	-16	-1
3	11	11	0	6	50	-51	0	-4	53	54	0	-2	20	-20	0	-1	131	143	-11	2*	0	-1	1	2	41	-40	0
4*	0	5	-5	7	10	9	0	-3	18	20	-2	-1	74	-76	2	0	42	-37	-5	3	6	-6	0	3	24	-22	-1
5	7	7	0	8	21	-22	0	-2	14	16	-1	0	132	125	6	1	26	26	0	K,L=	-7	5		4	5	-6	1
6	4	3	0	9	8	-7	-1	-1	49	-50	1	1	23	-21	-1	2	36	-36	0	-7	8	-8	0	5	25	24	0
K,L=	-7	3		K,L=	-2	3		0	5	5	0	2	148	-142	-5	3	16	-18	1	-6	9	-8	0	K,L=	-1	5	
-7	61	62	-1	-12	5	-5	0	1	14	13	0	3*	0	4	-4	4	14	15	0	-5	14	13	0	-11	5	-6	1
-6	17	16	1	-11	7	-6	0	2*	0	0	0	4	24	-24	0	5	52	-49	-2	-4	44	-46	1	-10	20	21	0
-5+	6	9	-2	-10	20	-24	4	3	16	16	0	5	5	-6	1	6	35	-36	1	-3*	0	-4	4	-9	13	-12	0
-4	29	25	4	-9	9	-7	-1	4	56	-56	0	6	16	18	-1	7	14	-14	0	-2	11	-12	0	-8+	5	2	3
-3	9	-9	0	-8	28	28	0	5*	0	0	0	7+	12	5	7	K,L=	0	4		-1	6	-8	1	-7	31	33	-1
-2	9	8	1	-7	24	27	-2	6*	0	2	-2	K,L=	-5	4		-11	5	4	1	0	47	47	0	-6	14	13	0
-1	42	46	-3	-6	69	-73	4	K,L=	3	3		-10	17	-18	0	-10	12	10	1	1	11	12	0	-5	20	18	2
0	18	-17	-1	-5	49	46	2	-11+	10	-13	3	-9	17	19	-1	-9	12	11	0	2	12	13	0	-4	43	37	5
1	50	-50	0	-4	143	139	3	-10*	0	-2	2	-8	47	45	2	-8	15	14	1	3+	3	5	-1	-3+	4	0	-3
2	99	90	9	-3	177	-186	9	-9	12	13	-1	-7*	0	4	-4	-7	62	-59	-2	4	20	21	0	-2	23	20	3

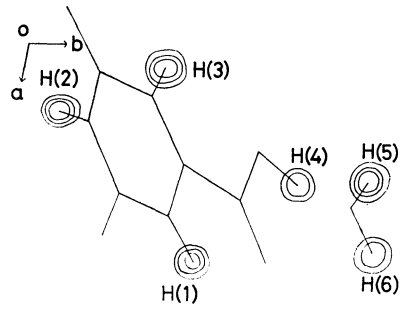


Fig. 1. A composite drawing of the electron density associated with the hydrogen atoms. The contours are at intervals of 0.2 e Å^{-3}, beginning with the 0.2 e Å^{-3} contour.

the block-diagonal least-squares refinement was continued, reducing the R value to 8.1%. At this stage, a difference Fourier map was computed, from which the positions of six hydrogen atoms were then found (Fig. 1). There was no unexplainable peak on this map except those due to hydrogen atoms. With anisotropic thermal parameters for non-hydrogen atoms and isotropic thermal parameters for hydrogen atoms, the final R value was found to be 5.75%, excluding unobserved reflections. The $\sum w(F_o-F_c)^2$ function was minimized, where;

$$w = 0.5 \text{ for } |F_o| \leqq 0.5,$$
$$w = 1.0 \text{ for } 0.5 < |F_o| < 5.0 \text{ and}$$
$$w = 5.0/|F_o| \text{ for } 5.0 \leqq |F_o|.$$

The atomic scattering factors used were those listed in the International Table for X-ray Crystallography for C, N, and O atoms and the spherical scattering factors proposed by Stewart, Davidson, and Simpson[5] for the H atom. The observed and calculated structure factors are listed in Table 2, while the fractional coordinates and thermal parameters are listed in Table 3.

Results and Discussion

Molecular Structure of Orotic Acid. The bond lengths and angles are listed, along their estimated standard deviations, in Table 4 and are shown in Fig.

TABLE 3. THE FINAL PARAMETERS AND THEIR ESTIMATED STANDARD DEVIATIONS (IN PARENTHESES)
The coordinates of the non-hydrogen atoms have been multiplied by 10^4; those of the hydrogen atoms, by 10^3. The anisotropic thermal parameters of non-hydrogen atoms are of the form $\exp[-(B_{11}h^2+B_{22}k^2+B_{33}l^2+B_{12}hk+B_{13}hl+B_{23}kl)]$, and have been multiplied by 10^5. For the hydrogen atoms the values listed are isotropic thermal parameters B(Å^2).

Atom	x	y	z	B (Å^2)
N (1)	3299(2)	4692(3)	1900(4)	—
C (2)	2931(2)	3262(3)	2603(4)	—
N (3)	1531(2)	2073(3)	1065(4)	—
C (4)	547(2)	2116(3)	−1141(4)	—
C (5)	1028(2)	3630(3)	−1787(4)	—
C (6)	2373(2)	4868(3)	−237(4)	—
C (7)	2984(2)	6557(3)	−638(4)	—
O (1)	3750(2)	3045(3)	4484(4)	—
O (2)	−671(2)	917(3)	−2384(3)	—
O (3)	4204(2)	7570(3)	792(4)	—
O (4)	2079(2)	6773(3)	−2625(4)	—
O (5)	3148(2)	9579(3)	−3310(4)	—
H (1)	424(3)	557(4)	297(6)	4.4(0.5)
H (2)	123(3)	116(4)	151(6)	3.2(0.6)
H (3)	28(3)	376(4)	−336(6)	4.1(0.6)
H (4)	267(3)	788(4)	−274(6)	6.4(0.8)
H (5)	250(3)	962(4)	−464(6)	7.4(0.9)
H (6)	400(3)	1021(4)	−267(6)	9.6(1.1)

Atom	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
N (1)	892(19)	2273(43)	4086(74)	−444(45)	129(60)	3100(96)
C (2)	870(21)	2264(48)	3939(82)	−208(51)	265(66)	2950(106)
N (3)	852(19)	2305(42)	4213(76)	−426(44)	194(60)	3426(96)
C (4)	860(21)	2114(46)	3934(82)	−253(49)	357(66)	2664(103)
C (5)	916(21)	2280(48)	4093(85)	−78(51)	456(68)	3286(108)
C (6)	927(21)	2079(45)	3968(82)	155(50)	952(68)	2844(103)
C (7)	1067(24)	2191(49)	4224(89)	−77(54)	877(74)	2974(111)
O (1)	1022(18)	3151(47)	5151(76)	−611(46)	−452(59)	5033(103)
O (2)	931(17)	2899(44)	5033(76)	−1030(43)	−429(57)	4536(98)
O (3)	1326(23)	3602(56)	6438(98)	−1703(58)	−559(75)	5983(127)
O (4)	1134(19)	2934(45)	5619(80)	−357(46)	541(62)	5096(104)
O (5)	1244(22)	3636(55)	6317(94)	−747(54)	−48(72)	6550(127)

5) R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, **42**, 3175 (1965).

TABLE 4. BOND LENGTHS AND BOND ANGLES

Bond	Length(Å)	e.s.d.(Å)	Bond	Angle(°)	e.s.d.(°)
N(1)–C(2)	1.363	0.003	C(2)–N(1)–C(6)	122.7	0.2
C(2)–N(3)	1.373	0.003	N(1)–C(2)–N(3)	114.7	0.2
N(3)–C(4)	1.369	0.003	C(2)–N(3)–C(4)	126.4	0.2
C(4)–C(5)	1.433	0.004	N(3)–C(4)–C(5)	115.5	0.2
C(5)–C(6)	1.346	0.004	C(4)–C(5)–C(6)	119.0	0.2
C(6)–N(1)	1.365	0.003	C(5)–C(6)–N(1)	121.7	0.2
C(2)–O(1)	1.227	0.003	N(1)–C(2)–O(1)	124.1	0.2
C(4)–O(2)	1.237	0.003	N(3)–C(2)–O(1)	121.2	0.2
C(6)–C(7)	1.498	0.004	N(3)–C(4)–O(2)	119.5	0.2
C(7)–O(3)	1.197	0.004	C(5)–C(4)–O(2)	125.0	0.2
C(7)–O(4)	1.306	0.003	C(5)–C(6)–C(7)	124.3	0.2
N(1)–H(1)	0.94	0.04	N(1)–C(6)–C(7)	114.1	0.2
N(3)–H(2)	0.89	0.04	C(6)–C(7)–O(3)	120.5	0.2
C(5)–H(3)	1.03	0.03	C(6)–C(7)–O(4)	114.1	0.2
O(4)–H(4)	1.02	0.04	O(3)–C(7)–O(4)	125.4	0.2
O(5)–H(5)	0.85	0.03	C(2)–N(1)–H(1)	117	2
O(5)–H(6)	0.82	0.03	C(6)–N(1)–H(1)	121	2
			C(2)–N(3)–H(2)	117	2
			C(4)–N(3)–H(2)	116	2
			C(4)–C(5)–H(3)	117	2
			C(6)–C(5)–H(3)	124	2
			C(7)–O(4)–H(4)	105	2
			H(5)–O(5)–H(6)	121	3

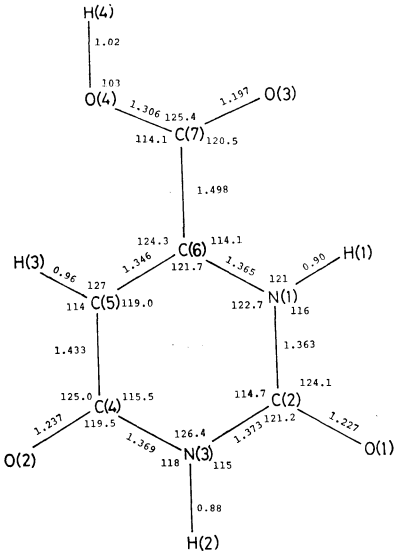


Fig. 2. Dimensions of the orotic acid molecule.

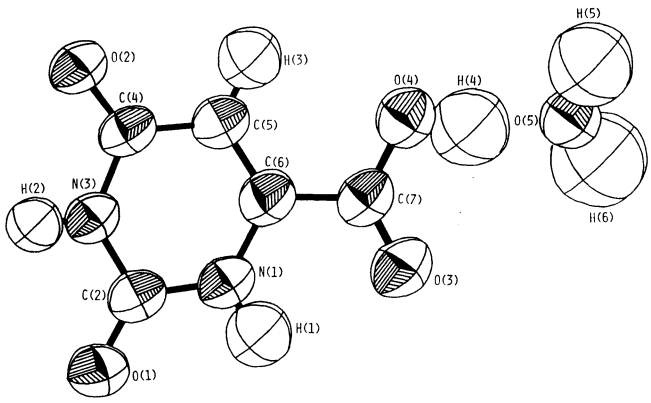
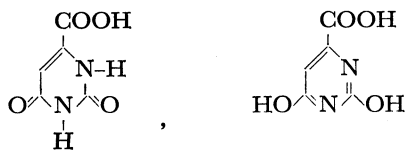


Fig. 3. The anisotropic thermal ellipsoids of non-hydrogen atoms and the isotropic thermal ellipsoids of hydrogen atoms. Ellipsoids are scaled to include the 74% probability.

2. Figure 3 shows the anisotropic thermal ellipsoids of non-hydrogen atoms and the isotropic thermal ellipsoids of hydrogen atoms. Ellipsoids are scaled to include the 74% probability.

The orotic acid molecule may be a mixture of tautomers, such as;



However, according to the present study, the molecule clearly takes the keto form in the crystal. This is quite evident from the assignment of hydrogen atoms in the difference Fourier map. It is also confirmed by the C(2)–O(1) and C(4)–O(2) bond lengths, 1.227(3) and 1.237(3) Å, and the C(2)–N(3)–C(4) and C(2)–N(1)–C(6) bond angles, 122.7(2)° and 126.4(2)° respectively

TABLE 5. THE DISTANCES FROM THE LEAST-SQUARES PLANE DEFINED BY THE SIX NON-HYDROGEN ATOMS OF PYRIMIDINE RING

Atom	Deviation (Å)	Atom	Deviation (Å)
N(1)	0.005	O(3)	0.039
C(2)	−0.018	O(4)	0.100
N(3)	0.019	O(5)	0.134
C(4)	−0.005	H(1)	0.04
C(5)	−0.009	H(2)	0.02
C(6)	0.009	H(3)	0.04
C(7)	0.053	H(4)	0.05
O(1)	−0.043	H(5)	0.16
O(2)	0.002	H(6)	−0.01

TABLE 6. THE COMPARISONS BETWEEN THE CORRESPONDING BOND LENGTHS AND BOND ANGLES OF OROTIC ACID AND URACIL, THYMINE, METHYLTHYMINE, THYMIDINE, METHYLURIDINE, AND DEOXYURIDINE

Bond length	(a)	(b)	(c)	(d)	(e)	(f)	(g)	(g′)
N(1)–C(2)	1.363	1.371	1.355	1.379	1.385	1.377	1.39	1.43
C(2)–N(3)	1.373	1.376	1.361	1.379	1.381	1.376	1.36	1.36
N(3)–C(4)	1.369	1.371	1.391	1.375	1.378	1.384	1.37	1.37
C(4)–C(5)	1.433	1.430	1.447	1.432	1.453	1.437	1.44	1.36
C(5)–C(6)	1.349	1.340	1.349	1.346	1.343	1.345	1.31	1.36
C(6)–N(1)	1.365	1.358	1.382	1.383	1.374	1.361	1.37	1.34
C(2)–O(1)	1.227	1.215	1.234	1.214	1.206	1.196	1.23	1.23
C(4)–O(2)	1.237	1.245	1.231	1.237	1.230	1.223	1.20	1.19
Bond angle								
C(2)–N(1)–C(6)	122.7	122.7	122.8	120.6	121.8	121.6	121.8	118.2
N(1)–C(2)–N(3)	114.7	114.0	115.2	115.4	113.7	114.1	112.4	115.1
C(2)–N(3)–C(4)	126.4	126.7	126.3	126.3	127.5	127.2	128.5	126.8
N(3)–C(4)–C(5)	115.5	115.5	115.6	116.1	115.8	115.4	114.4	114.7
C(4)–C(5)–C(6)	119.0	118.9	118.2	118.3	117.2	117.6	121.2	121.9
C(5)–C(6)–N(1)	121.7	122.3	121.8	123.3	124.1	124.2	121.6	123.0
N(1)–C(2)–O(1)	124.1	123.7	122.7	123.3	124.3	123.0	126.7	124.1
N(3)–C(2)–O(1)	121.2	122.3	122.1	121.3	122.0	122.9	120.9	120.5
N(3)–C(4)–O(2)	119.5	119.2	118.3	120.0	119.7	119.2	123.8	121.5
C(5)–C(4)–O(2)	125.0	125.3	126.1	123.9	124.5	125.4	121.8	123.8

(a) Orotic acid (This Paper). (b) Uracil.[6] (c) Thymine.[7] (d) 1-Methylthymine.[8] (e) Thymidine.[9] (f) 5-Methyluridine.[10] (g) and (g′) Deoxyuridine.[11]

TABLE 7. HYDROGEN BOND DISTANCES (Å) AND ANGLES (degree)

X—H……O	Symmetry	X…O	e.s.d.	X–H	e.s.d.	H…O	e.s.d.	Angle	e.s.d.
N(1)–H(1)…O(1)	(1, 1, 5)	2.874	0.003	0.94	0.04	1.95	0.04	167	3
N(3)–H(2)…O(2)	(1, 1, 2)	2.816	0.003	0.89	0.04	1.92	0.04	177	3
O(4)–H(4)…O(5)	(1, 1, 1)	2.520	0.003	1.02	0.04	1.52	0.03	165	3
O(5)–H(5)…O(2)	(1, 1, 3)	2.772	0.003	0.85	0.03	1.95	0.03	162	3
O(5)–H(6)…O(3)	(1, 1, 4)	2.777	0.003	0.82	0.03	1.98	0.03	164	3
X—O……H	Symmetry	Angle	e.s.d.						
C(2)–O(1)…H(1)	(1, 1, 5)	132	1	Symmetry codes		1=(x, y, z)			
C(4)–O(2)…H(2)	(1, 1, 2)	123	1			2=(−x, −y, −z)			
C(4)–O(2)…H(5)	(1, 1, 3)	131	1			3=(−x, 1−y, −1−z)			
C(7)–O(3)…H(6)	(1, 1, 4)	163	1			4=(1−x, 2−y, −z)			
H(5)–O(5)…H(4)	(1, 1, 1)	113	2			5=(1−x, 1−y, 1−z)			
H(6)–O(5)…H(4)	(1, 1, 1)	124	3						
H(2)…O(2)…H(5)	(2, 1, 3)	105	1						

TABLE 8. π-BOND ORDERS AND NET CHARGES CALCULATED BY CNDO METHOD

Bond	Bond order	Calcd[a] (Å)	Obsd (Å)	Calcd−Obsd (Å)	Atom	Net charge
N(1)–C(2)	0.389	1.366	1.363	0.003	N(1)	−0.252
C(2)–N(3)	0.394	1.365	1.373	−0.008	C(2)	+0.522
N(3)–C(4)	0.376	1.368	1.369	−0.001	N(3)	−0.326
C(4)–C(5)	0.346	1.450	1.433	0.017	C(4)	+0.437
C(5)–C(6)	0.848	1.359	1.346	0.013	C(5)	−0.212
C(6)–N(1)	0.369	1.370	1.365	0.005	C(6)	+0.163
C(2)–O(1)	0.793	1.227	1.227	0.000	C(7)	+0.409
C(4)–O(2)	0.821	1.222	1.237	−0.015	O(1)	−0.406
C(6)–C(7)	0.243	1.468	1.498	−0.030	O(2)	−0.375
C(7)–O(3)	0.875	1.212	1.197	0.015	O(3)	−0.315
C(7)–O(4)	0.361	1.305	1.306	−0.001	O(4)	−0.267
					H(1)	+0.173
					H(2)	+0.181
					H(3)	+0.082
					H(4)	+0.186

a) The bond lengths are calculated by the following equations,
$D_{C-C}=1.512-0.180P$
$D_{C-N}=1.436-0.180P$
$D_{C-O}=1.370-0.180P$
K. Nishimoto and L. S. Forster, *Theor. Chim. Acta* (Berl.), **4**,155 (1966).

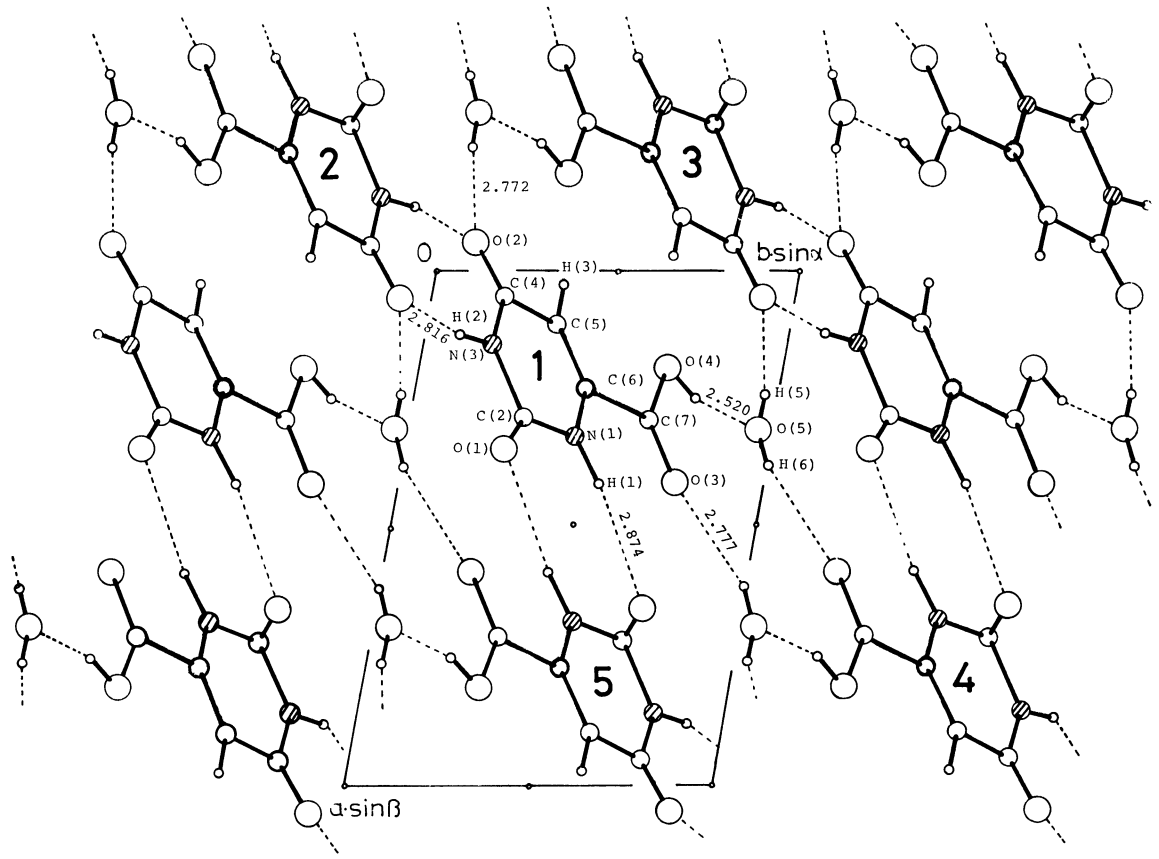


Fig. 4. A view of the crystal structure down the *c* axis. The hydrogen bonds are shown by broken lines.

(the values in parentheses denote the e.s.d.'s in the last digits, here and throughout this paper).

The pyrimidine ring is planar. The equation of the least-squares plane through six atoms of the pyrimidine ring is:

$$-0.6557X + 0.4402Y + 0.6134Z = 0.0078$$

where X, Y, and Z are coordinates in Å referred to an orthogonal set of axes, where X and Z are parallel to the a and c^* axes, and where Y lies in the ab plane; this coordinate system is used throughout this paper. The maximum deviation of a ring atom from this plane is 0.019 Å. The displacements of all the atoms from the plane are listed in Table 5.

The comparisons between the corresponding bond lengths and bond angles of orotic acid, and uracil,[6] thymine,[7] methylthymine,[8] thymidine,[9] methylthymidine,[10] and deoxyuridine[11] are given in Table 6. Those of uracil are in good agreement with those found in orotic acid, except for the C(2)–O(1) bond length and the N(3)–C(2)–O(1) bond angle. This means that the substitution of the carboxyl group does not appreciably change the bond lengths and angles of the uracil group. The C(2)–N(3)–C(4) bond angle is 3.7(2)° larger than the C(2)–N(1)–C(6) bond angle. Many other compounds which have the uracil group show a similar tendency. The net charges on each atom have been calculated by the CNDO method;[12] they are listed, along the π-bond orders, in Table 8. The C(2) atom has the most positive charge (0.522), and the C(4) atom has the second (0.437) in the uracil group. Therefore, the C(2)–N(3)–C(4) bond angle might be larger than the C(2)–N(1)–C(6) bond angle, since the repulsion between the C(2) and C(4) atoms is clearly stronger than that between the C(2) and C(6) atoms. There is a significant difference between the two bond angles, N(1)–C(6)–C(7) (114.1(2)°) and C(5)–C(6)–C(7) (124.3(2)°). A similar difference between the two angles is also observed in uracil. There is a difference of 0.010(3) Å between the C(2)–O(1) and C(4)–O(2) bond lengths. Although this difference

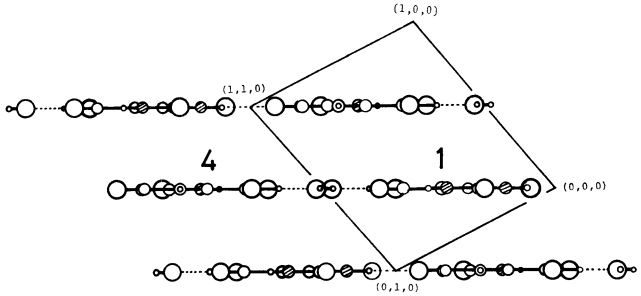


Fig. 5. A view of the crystal structure parallel to the ($\bar{2}$ 1 1) plane. The hydrogen bonds are shown by broken lines.

6) R. F. Stewart, *ibid.*, **23**, 1102 (1967).
7) R. Gerdil, *ibid.*, **14**, 333 (1961).
8) K. Hoogsteen, *ibid.*, **16**, 28 (1963).
9) D. W. Young, P. Tollin, and H. R. Wilson, *ibid.*, **B25**, 1423 (1971).
10) J. Hunt and E. Subramanian, *ibid.*, **B25**, 2144 (1969).
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12) J. A. Pople and D. L. Beverige, "Approximate Molecular orbital Theory," McGraw-Hill Book Co., New York (1970).

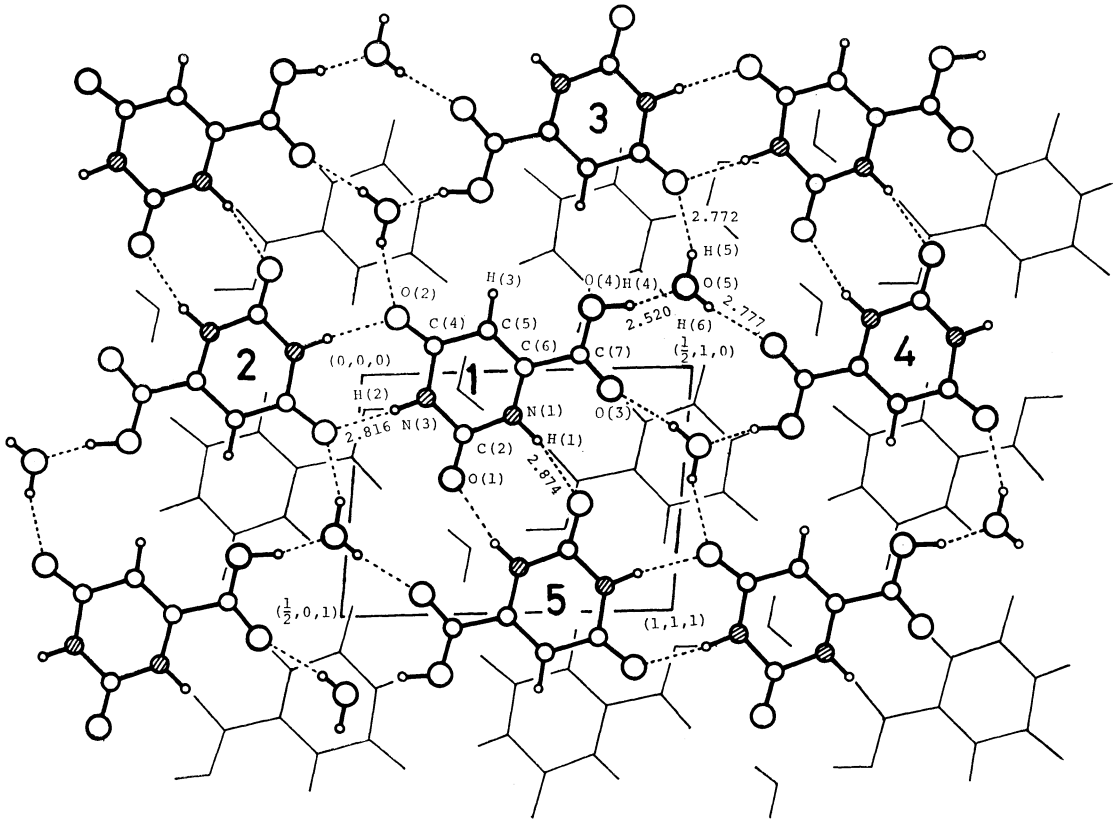

Fig. 6. A view of the crystal structure perpendicular to the ($\bar{2}$ 1 1) plane, showing the relative orientation of the molecules in two adjacent layers parallel to the ($\bar{2}$ 1 1) plane.

may be on the borderline of experimental error, similar differences between the two C=O bond lengths are also observed in thymidine,[9] methyluridine,[10] deoxyuridine,[11] methylthymine,[8] and uracil.[6] The π-bond orders of the C(2)–O(1) and C(4)–O(2) bonds are 0.793 and 0.821 respectively. These values are contrary to the observed lengths, as is shown in Table 8. The difference between the N(3)–C(2)–O(1) and N(3)–C(4)–O(2) bond angles is 1.7(2)°. Similar differences are also observed in uracil, thymine, methylthymine, thymidine, and methyluridine. In a carboxyl group, the C(7)–O(3) bond length is 0.109(3) Å shorter than the C(7)–O(4) bond length. Hence, the carboxyl group clearly consists of carbonyl and hydroxyl groups. The carboxyl group is twisted by 2.2° out of the plane of the pyrimidine ring.

Molecular Arrangement and Hydrogen-bond System.

The crystal structure is shown in Figs. 4, 5, and 6, while the distances and angles of hydrogen bonds are listed in Table 7. The molecules are arranged in layers closely parallel to the ($\bar{2}$ 1 1) plane. This plane has a spacing of 3.102 Å. The best plane, calculated by a least-squares analysis, through the carbon, nitrogen and oxygen atoms of two molecules, 1 and 2, is:

$$-0.6514X + 0.4183Y + 0.6289Z = 0.0000 \quad \text{(i)}$$

The best planes through the molecules, 1 and 3, and the molecules, 1 and 4, are found by the same procedure to be:

$$-0.6573X + 0.4183Y + 0.6289Z = -0.0630 \quad \text{(ii)}$$

$$-0.6580X + 0.4216Y + 0.6239Z = -0.0558 \quad \text{(iii)}$$

respectively. The dihedral angles which these best planes make with the ($\bar{2}$ 1 1) plane are 0.4° (i), 0.6° (ii), and 0.7° (iii). Figures 5 and 6 show the views parallel and perpendicular to the ($\bar{2}$ 1 1) plane respectively, illustrating the relative orientation of the molecules in two neighboring layers. The upper layer in Fig. 6, containing the molecules drawn with heavy lines, passes through the point of origin (0, 0, 0). In Figs. 4, 5, and 6, the same numerals designate the same molecules. The symmetry codes corresponding to these numbers are shown in Table 7.

In crystals of uracil and thymine, one of the oxygen atoms is hydrogen-bonded to the nitrogen atoms, N(1) and N(3), of two different molecules, while the other is not hydrogen-bonded to any nitrogen atom. However, in the case of the orotic acid monohydrate, each oxygen atom of the uracil group is hydrogen-bonded to one nitrogen atom of each of two different molecules. In uracil and thymine, the distances of the two N–H···O hydrogen bonds are equal within the limits of experimental error. There is, however, a significant difference between the two N–H···O hydrogen bond distances, 2.874(3) and 2.816(3) Å, in this crystal. The O(2) atom participates in two kinds of hydrogen bonds (O···H–N; 2.816(3) Å, O···H–O; 2.772(3) Å), while the O(1) atom participates in only one hydrogen bond (O···H–N; 2.874(3) Å).

Each molecule is joined, through two kinds of N–H···O hydrogen bonds around the center of symmetry, with two neighboring molecules and forms a zig-zag chain along the [1 1 1] direction. Each chain

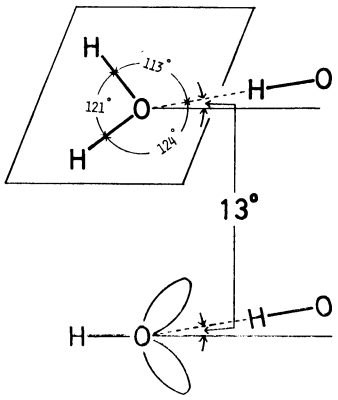

Fig. 7. Diagrammatic view of the water molecule in orotic acid. The value 13° indicates the angle between the O···H vector and the plane of the water molecule.

is joined, by three kinds of O–H···O hydrogen bonds through the medium of the water molecule, with two neighboring chains and forms a sheet parallel to the ($\bar{2}$ 1 1) plane. These three hydrogen-bond distances are 2.772(3) and 2.777(3) Å for O···HOH, which are equal within the limits of experimental error, and 2.520(3) Å for H_2O···HO, which seems to be a nearly symmetrical hydrogen bond.

Each water molecule is hydrogen-bonded to three oxygen atoms. The coordination of a water molecule is approximately trigonal planar. The hydrogen-bonding angles are H(4)–O(5)–H(5)=113(2)°, H(4)–O(5)–H(6)=124(3)°, and H(5)–O(5)–H(6)=121(3)°. The angle which the O(5)···H(4) vector of the hydrogen bond makes with the plane of the water molecule is 13° (Fig. 7). Therefore, the water molecule in this crystal is of the F type, according to the classification of Chidambaram, Sequeira, and Sikka;[13] that is, the bisector of lone pairs of the water oxygen atom is directed toward a hydrogen-bond donor group. In the hydrogen bond O(5)–H(6)···O(3), the C(7)–O(3)··· H(6) hydrogen-bonding angle is 163(1)°. This value also indicates that the bisector of lone pairs in the carbonyl oxygen atom O(3) is directed toward a hydrogen-bond donor group.

Computer Programs. All the calculations were performed on a FACOM 270-30 computer at the Computer Center of Osaka City University, using these modified programs: RSLC-3 (cell constant),[14] RSSFR-3 (Fourier synthesis),[15] HBLS-IV (block-diagonal least-squares refinement),[16] DAPH (bond length, bond angle, least-squares plane),[17] SCALE (film factor, Lp, and layer scaling),[18] TE-I (thermal ellipsoid),[19] and CNINDO (CNDO and INDO calculations).[12]

The authors wish to express their thanks to Dr. K. Nishimoto of this faculty for his useful advice on the CNDO calculations.

13) R. Chidambaram, A. Sequeira, and S. K. Sikka, *J. Chem. Phys.*, **41**, 3616 (1964).
14) T. Sakurai, "The Universal Crystallographic Computing System (I)," ed. by T. Sakurai, Japanese Crystallographic Association, 1967 p. 18.
15) T. Sakurai, Ref. 14, p. 45.
16) T. Ashida, Ref. 14, p. 65.
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18) H. Yoshioka, K. Hirotsu, and F. Takusagawa, unpublished work.
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