BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 42 3099—3105 (1969)

The Crystal and Molecular Structure of the Sodium Salt of Xanthine

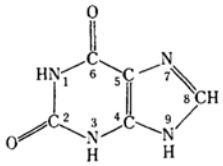
Hiroshi MIZUNO, Takaji FUJIWARA and Ken-ichi TOMITA

Faculty of Pharmaceutical Sciences, Osaka University, Toyonaka, Osaka

(Received May 6, 1969)

The crystals of sodium salt of xanthine, $C_5H_3N_4O_2Na \cdot 4H_2O$, are monoclinic with four molecules in a unit cell of dimensions; $a=7.31$, $b=19.52$, $c=7.17$ Å, $\beta=100.0°$, space group $P2_1/c$. The structure has been determined by application of the sign relationship $S(hkl)S(h'k'l') \sim S(h+h', k+k', l+l')$ from $(hk0)$ intensity data and refined by three-dimensional least-squares methods. The positions of the hydrogen atoms were determined by a three-dimensional difference Fourier analysis, and it was confirmed that deprotonation took place at the position of the imino N(3)H of the xanthine molecule. Each Na^+ cation is surrounded by six water molecules and each xanthine anion participates in ten hydrogen bonds, forming a close-packed system.

Xanthine, 2,6-dioxypurine, is well known as a



metabolic intermediate related to the common bases in nucleic acids. In man, the end product of purine metabolism is uric acid, and xanthine oxydase, an enzyme found in the liver, is capable of oxydizing xanthine to uric acid. Xanthine is a purine base which is not common in ribonucleic acid or deoxyribonucleic acid, but the deamination of guanine results in xanthine base, and this base is still able to pair with cytosine by two hydrogen bonds. Therefore the deamination of guanine by nitrous acid cannot be mutagenic, while adenine or cytosine deaminated by nitrous acid is lethal.

Its sodium salt was crystallized as the tetrahydrate from a ethanol-water solution, and this crystal structure was investigated by X-ray method. It is of particular interest to study the nature of the hydrogen bond between xanthine and water molecules, to determine the predominant resonance forms of the xanthine anion and also to investigate the environment around the sodium ion.

Experimental

The sample of the sodium salt of xanthine was purchased from the Nakarai Chemicals Ltd. (Kyoto), and recrystallized by slow evaporation of a ethanol-water solution at room temperature. The obtained crystals were in the form of colorless needles elongated along the c axis. Weissenberg photographs around the c axis demonstrated that the crystals were twins consisting of two components, in which only the a axis has different directions rotating 20.0° about the b axis, and which are united about a twin plane (100). Crystallographic data obtained from measurements of rotation, Weissenberg and precession photographs around the c axis are listed in Table 1.

Partial three-dimensional intensity data ($l=0$ to 5) with Ni-filtered Cu$K\alpha$ radiation were collected by the multiple film method using the equi-inclination Weissenberg camera. A needle-shaped crystal about 0.15×0.15 mm in cross-section was used. The crystals being twins as mentioned above, the reflection of each component was easily separable from that of the other, and the intensity was estimated by visual comparison with a caribrated scale. 1516 reflections were recorded, 1175 of which had measurable intensities. Lorentz and

TABLE 1. CRYSTAL DATA

$C_5H_3N_4O_2Na \cdot 4H_2O$
Monoclinic
$P2_1/c$
$a=7.31\pm0.02$ Å
$b=19.52\pm0.04$ Å
$c=7.17\pm0.02$ Å
$\beta=100.0\pm0.5°$
$Z=4$
μ (for Cu$K\alpha$) $=18.0$ cm^{-1}
$D_m=1.64$ g/cm^3
$D_c=1.62$ g/cm^3

polarization corrections were applied, but no further corrections were made to the intensities, which were then converted to the absolute scale by means of the usual averaging process.

Structure Determination

For the reflections of appropriately large unitary structure factors (U) in centrosymmetric space groups, the sign relations

$$S(hkl)S(h'k'l') = S(h+h',\ k+k',\ l+l') \quad (1)$$

$$S(hkl) = S\{\sum_{h'k'l'} S(h'k'l')S(h+h',\ k+k',\ l+l')\} \quad (2)$$

are applicable, where $S(hkl)$ is the sign of $U(hkl)$.[1-3] The root-mean-square value (σ) for the unitary structure factors of this crystal was equal to

$$\sigma = \{\sum_j Z_j^2/(\sum_j Z_j)^2\}^{1/2} = 0.116$$

where Z_j is the number of electrons in the jth atom. This value seems to be suitable for the application of a direct method described by Zachariasen.[3]

A sharpened Patterson synthesis was previously calculated with the three-dimensional data. Many peaks on the Patterson sections at $W=0$ and $W=1/4$, and the two strongest reflections, (002) and (004), indicated that the xanthine anions were approximately parallel to the (001) plane. It was, therefore, to be expected that the approximate crystal structure might be revealed by the Fourier projection on (001) with only the signs of large structure factors.

For those reflections which lie within the range of $|U(hk0)|\geq 1.5\sigma=0.174$, Eq. (1) was used to determine the signs. 17 out of 132 reflections fell in this category, where the signs of two structure factors were chosen arbitrarily in order to fix the origin. The signs of remaining structure factors for $|U(hk0)|\geq 0.100$, were determined by Eq. (2). Thus the signs of 44 reflections were finally determined from Eqs. (1) and (2), but of which 7 reflections, all with the low magnitude of U, were later shown to be incorrect.

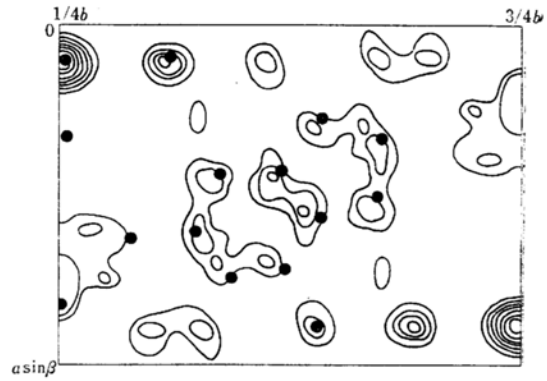


Fig. 1. First Fourier projection on (001) calculated with the signs of 44 reflections which were determined by the direct method. The black circles show the final atomic positions. One of the water oxygen atom is hidden by another one ($x=0.11$, $y=0.37$).

The first electron density projection on (001) calculated with the signs of 44 reflections is shown in Fig. 1, and there appeared significant peaks to be the purine ring atoms across a center of symmetry. Using the phases based on these peak positions, a second electron density map was calculated with all the observed ($hk0$) data, which showed the peaks of two carbonyl oxygen atoms and water oxygen atoms.

Succesive Fourier approximations by superimposing two water oxygen atoms O(5) and O(6) at $x=0.11, y=0.37$ along the c axis indicated a reasonable agreement between the observed and calculated amplitudes. At this stage the discrepancy factors, $R=\Sigma||F_o|-|F_c||/\Sigma|F_o|$, was 0.30 for ($hk0$) reflections. Because of the overlap, however, no further refinement of the structure on the projection was attempted.

An initial set of z coordinates was derived by considering the packing of the xanthine anions. Thus a three-dimensional Fourier synthesis was carried out with signs based on the phases of the xanthine ring atoms, and five peaks were newly and immediately identified; one peak was supposed to be the sodium ion in view of the peak height, and the others to be the water oxygen atoms. The second three-dimensional Fourier map calculated with the phases of all the non-hydrogen atoms showed the whole structure more clearly, and R-factor was now dropped to 0.26.

The positional parameters thus obtained, together with isotropic temperature factors, initially set to $B=3.0$ Å^2, were used as starting parameters for five cycles of block-diagonal least-squares refinement, and at the end of these cycles, the R-factor was

1) W. Cochran, *Acta Cryst.*, **5**, 65 (1952).
2) D. Sayre, *ibid.*, **5**, 60 (1952).
3) W. H. Zachariasen, *ibid.*, **5**, 69 (1952).

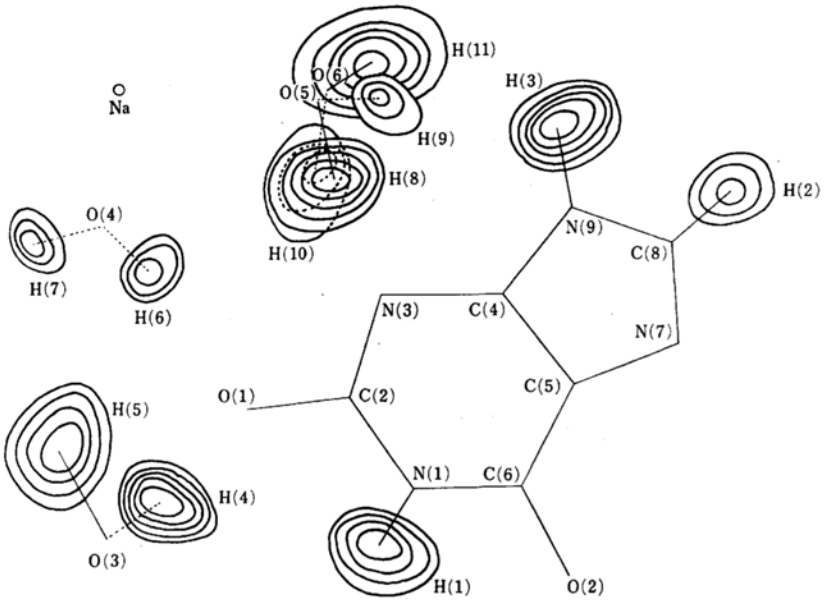


Fig. 2. A projection along the c axis of sections of a difference Fourier map for the location of hydrogen atoms. Contours are at interval of 0.1 e.Å^{-3}, starting with the 0.2 e.Å^{-3} contour.

reduced to 0.13. Anisotropic temperature factors in the form of

$$\exp[-(B_{11}h^2+B_{22}k^2+B_{33}l^2+B_{12}hk+B_{13}hl+B_{23}kl)]$$

were now used for all the non-hydrogen atoms. In the last few cycles, the contribution of the hydrogen atoms except H(7) were introduced to the calculation, and the coordinate of each hydrogen atom was located assuming the C–H, N–H and O–H distances to be 1.08, 1.03 and 1.00 Å, respectively, and also each hydrogen atom was given a temperature factor equal to the final isotropic value of the covalently bonded carbon, nitrogen or oxygen atom, but none of these parameters was refined. The R-factor at the end of the refinement was 0.11 for all observed reflections.

A three-dimensional difference Fourier synthesis was then calculated, where only H(7) was excluded for structure factor calculation. As illustrated in Fig. 2, locations of all the hydrogen atoms are clearly shown.

The final atomic coordinates and thermal parameters are listed in Tables 2 and 3. The observed and calculated structure factors are listed in Table 4. Some discrepancies between F_0 and F_c of low-order reflections may be due to absorption and

Table 2. The atomic coordinates and their standard deviations

	x/a	$\sigma(x)$	y/b	$\sigma(y)$	z/c	$\sigma(z)$
Na	0.1019	0.003	0.2452	0.003	0.4859	0.004
C(2)	0.6024	0.008	0.3876	0.008	0.3112	0.009
C(4)	0.4310	0.007	0.4843	0.008	0.2565	0.008
C(5)	0.5771	0.007	0.5260	0.008	0.2381	0.008
C(6)	0.7563	0.007	0.4970	0.008	0.2632	0.008
C(8)	0.3424	0.008	0.5898	0.008	0.1961	0.010
N(1)	0.7567	0.006	0.4270	0.006	0.2976	0.007
N(3)	0.4350	0.006	0.4161	0.006	0.2933	0.007
N(7)	0.5199	0.006	0.5941	0.007	0.2009	0.007
N(9)	0.2792	0.006	0.5255	0.007	0.2290	0.007
O(1)	0.6306	0.006	0.3249	0.006	0.3454	0.007
O(2)	0.9068	0.005	0.5274	0.005	0.2575	0.006
O(3)	0.8507	0.006	0.2402	0.006	0.1634	0.007
O(4)	0.3252	0.006	0.2357	0.006	0.2797	0.007
O(5)	0.1148	0.005	0.3669	0.005	0.4605	0.007
O(6)	0.1022	0.006	0.3720	0.006	0.0264	0.007

Table 3. The thermal parameters and their standard deviations ($\times 10^4$)

	B_{11}	σ	B_{22}	σ	B_{33}	σ	B_{12}	σ	B_{13}	σ	B_{23}	σ
Na	147	6	16	1	150	11	5	4	90	12	3	5
C(2)	118	16	15	2	99	24	−15	9	26	28	−18	11
C(4)	82	13	21	2	15	21	1	9	32	23	−2	10
C(5)	129	15	19	2	−14	21	0	9	28	24	2	10
C(6)	112	15	18	2	46	22	11	9	50	25	7	10
C(8)	113	15	17	2	153	27	20	10	57	29	18	12
N(1)	107	12	16	2	56	19	8	7	51	21	3	8
N(3)	101	13	14	2	102	20	−16	7	22	23	−9	9
N(7)	119	13	16	2	102	20	3	8	52	23	1	9
N(9)	88	12	22	2	88	20	8	8	71	22	4	9
O(1)	133	12	13	2	237	20	−2	7	33	23	5	9
O(2)	90	10	16	2	171	18	3	7	59	19	17	8
O(3)	144	12	21	2	166	20	−3	8	49	23	−20	9
O(4)	109	11	23	2	196	20	−15	7	79	22	−13	9
O(5)	129	11	15	2	164	18	−7	7	60	21	2	8
O(6)	173	11	17	2	142	19	−19	8	22	23	9	8

TABLE 4. OBSERVED AND CALCULATED STRUCTURE FACTORS

K	FO	FC
H,L=	0	0
2	33	49
4	43	47
6	55	-70
8	84	107
10	8	-8
12	44	46
14	33	-31
16	10	10
18	32	-32
20	15	-15
24	5	6
H,L=	1	0
0	41	-25
1	12	-8
2	51	-61
3	26	24
4	25	25
5	2	1
7	33	34
8	58	57
9	54	-53
10	58	-59
11	6	-6
12	27	-24
13	10	9
15	5	5
16	29	28
17	10	-10
18	10	-12
19	10	10
20	5	3
22	6	-6
24	6	4
H,L=	2	0
0	5	-7
1	50	-55
2	7	8
3	51	-49
4	37	-37
5	59	58
6	6	-7
7	3	3
8	4	5
9	27	-30
10	9	9
11	10	-11
12	7	-6
14	13	-14
15	22	24
16	11	-10
17	8	-10
18	8	-8
21	5	5
23	6	6
H,L=	3	0
0	22	-24
1	53	-54
2	5	-4
3	51	-49
4	5	2
5	55	-58
6	22	21
8	28	-28
9	46	-50
10	7	6
11	10	-8
13	16	-14
14	8	-5
15	19	-19
16	8	-6
17	32	-32
18	10	10
19	5	6
20	7	-6
21	4	5
23	8	7
H,L=	4	0
0	54	-63
1	27	-29
2	50	50
3	43	46
5	8	-8
6	8	8
7	31	29
8	36	-36
9	33	-31
10	25	28
11	13	14
12	5	2
13	10	9
14	25	24
15	23	24
16	11	-12
18	9	9
20	6	5
21	6	-4
H,L=	5	0
0	36	-42
1	11	-11
2	15	14
3	7	-8
4	15	-14
6	19	20
8	30	-31
9	8	9
10	20	21
13	23	-22
14	8	7
17	5	3
18	18	17
19	4	4
H,L=	6	0
0	36	-35
1	29	28
2	31	-30
3	11	11
4	10	-9
6	11	-12
7	11	-12
8	11	-13
12	5	3
13	7	7
16	6	-6
17	6	6
18	8	7
H,L=	7	0
0	5	4
2	8	8
3	5	-5
4	10	10
8	7	7
9	19	18
H,L=	8	0
0	10	8
1	15	15
4	8	-8
5	8	8
7	10	-9
9	18	17
H,L=	0	1
1	12	11
2	21	24
3	16	-17
4	21	-25
5	7	7
6	48	-54
7	5	4
8	8	-9
9	14	-17
10	55	-57
11	8	9
12	9	-7
14	26	-30
15	7	6
16	7	7
18	9	11
20	18	17
21	4	-4
22	6	-6
23	3	4
24	7	5
H,L=	1	1
1	26	-26
2	4	3
3	12	13
4	9	-8
5	25	-26
6	7	-8
7	6	5
8	24	-28
9	5	3
11	8	-8
12	13	-14
13	4	-4
16	9	-11
17	23	-25
20	7	-5
21	4	6
22	4	4
23	3	2
H,L=	2	1
1	25	-27
2	10	-13
3	51	-55
5	15	12
6	9	9
7	5	7
8	17	-18
9	5	4
10	27	27
11	16	-16
12	8	-11
13	7	-4
14	11	13
15	7	-6
16	5	-5
17	19	21
18	7	7
20	8	-8
22	7	5
24	6	-5
H,L=	3	1
1	8	-8
2	9	9
3	5	-5
4	21	-23
5	14	-13
6	7	-5
7	15	-14
10	19	1
12	8	10
13	28	28
15	19	23
16	19	-21
17	12	10
19	4	4
21	8	6
23	7	7
H,L=	4	1
1	4	-5
2	8	-9
3	7	9
4	7	9
5	16	-16
6	18	19
8	7	-8
10	7	7
12	15	-16
13	9	-7
14	7	8
15	5	5
17	5	-3
18	8	7
19	7	6
20	5	-4
H,L=	5	1
2	25	24
3	12	-13
4	20	20
5	7	8
6	5	6
8	5	-4
10	7	5
12	9	10
13	5	-2
14	11	11
15	11	-9
17	9	8
19	7	-5
H,L=	6	1
1	15	-15
2	11	-11
4	9	-8
6	5	5
8	29	32
10	7	5
11	7	-7
12	11	10
14	12	-10
18	5	-3
H,L=	7	1
1	16	16
3	7	5
4	9	8
6	7	-6
8	8	-7
9	4	4
12	5	2
14	3	3
H,L=	8	1
1	12	9
3	6	4
5	11	10
8	3	2
H,L=	-1	1
1	20	18
2	22	-23
3	9	12
4	17	20
5	17	18
6	29	-32
7	6	-6
8	7	-6
9	6	-4
11	6	6
12	4	-3
13	8	7
14	10	-11
15	5	3
16	13	14
17	5	4
18	19	-21
20	5	-4
24	6	7
H,L=	-2	1
1	23	18
3	67	68
4	29	-30
5	9	-8
6	3	-2
7	3	1
8	21	22
9	8	-10
10	9	8
11	17	19
12	8	7
15	7	7
17	27	-30
24	5	5
H,L=	-3	1
1	8	6
2	5	-5
3	3	-3
5	21	19
6	5	-4
7	20	21
8	7	8
9	11	-13
10	18	-20
12	5	6
13	39	-41
14	7	-7
15	27	-29
16	5	4
17	5	-4
18	7	-7
21	12	-10
22	3	-2
23	6	-6
H,L=	-4	1
1	5	-6
2	15	-13
3	13	11
4	21	19
5	16	15
6	19	21
7	16	-17
9	8	9
11	9	-10
12	9	-9
13	18	18
14	7	8
16	7	8
17	7	5
19	8	-8
H,L=	-5	1
1	18	16
2	27	22
3	4	3
4	6	7
5	10	-11
6	19	20
7	9	-10
9	10	11
10	5	6
12	11	12
13	7	8
14	17	19
16	7	-7
17	4	4
18	6	6
21	3	4
H,L=	-6	1
1	7	8
2	24	-25
4	5	-5
6	10	13
6	9	10v
7	7	8
8	20	23
10	10	12
12	5	6
14	4	-5
17	9	9
18	6	-5
19	6	-6
H,L=	-7	1
1	14	-12
2	7	8
3	9	-9
4	9	9
5	7	-6
6	5	-4
7	5	-3
8	14	-13
9	5	6
10	4	-4
11	10	-11
14	5	6
15	3	-2
16	2	2
H,L=	-8	1
1	4	-6
3	14	-11
5	10	-10
12	2	-4
H,L=	0	2
0	158	-145
1	47	50
2	104	-121
3	59	61
4	79	-70
5	9	-6
8	26	22
9	28	-24
10	47	-48
12	32	-29
13	18	17
14	6	5
16	32	35
20	13	12
21	6	-6
24	8	8
H,L=	1	2
0	68	111
1	52	-88
2	40	-41
3	42	-45
4	7	9
6	55	-60
7	33	37
8	67	67
10	16	-16
11	10	9
12	15	15
13	18	-18
14	9	-8
15	10	10
16	10	9
17	12	-11
18	15	-18
20	6	5
24	4	4
H,L=	2	2
0	61	61
1	57	-59
2	44	-43
3	23	25
4	22	22
5	24	-24
6	5	-3
7	37	40
8	23	22
9	40	-43
10	23	-23
11	24	24
12	18	17
14	7	-6
15	7	6
16	21	24
17	24	-26
H,L=	3	2
0	10	-9
1	7	-8
2	30	30
3	27	25
4	10	11
5	39	42
6	12	-13
7	48	55
8	10	-11
9	6	-7
10	9	8
11	15	15
12	12	11
13	22	25
14	12	13
15	24	28
16	7	-7
18	6	-6
19	8	8
H,L=	4	2
0	38	-41
1	18	-17
2	8	-5
3	21	-21
4	6	5
5	11	12
6	11	14
8	13	-16
10	7	4
11	7	-7
12	12	-12
13	12	-13
14	10	-9
16	6	-10
17	6	-7
18	10	12
H,L=	5	2
0	19	-19
1	9	8
2	18	18
3	15	15
5	7	-7
6	10	11
8	24	-27
10	12	16
11	7	7
13	9	9
14	6	-4
16	21	-22
H,L=	6	2
0	12	-12
2	38	42
3	10	-9
4	12	12
5	7	-6
6	21	25
8	9	-9
9	9	11
10	9	10
12	10	-8
13	5	-6
14	9	9
16	8	-7
H,L=	7	2
1	11	12
2	6	-4
3	6	4
4	11	-11
7	16	-14
8	8	-5
9	7	7
10	5	3
H,L=	8	2
0	7	7
1	7	4
4	4	5
5	6	-6
8	5	3
H,L=	-1	2
0	79	151
1	1	5
2	30	31
3	13	12
4	63	-58
5	22	-18
6	16	-18
7	17	-16
8	18	19
9	23	23
10	21	18
11	17	-11
12	19	18
13	11	-19
15	12	-10
16	9	7
17	16	18
18	10	-8
20	6	-6
23	6	-3
24	4	6
H,L=	-2	2
0	11	-12
1	82	80
2	12	14
3	33	-33
4	31	31
5	25	26
6	8	-6
7	74	-74
8	7	9
9	41	43
10	8	-9
11	20	-22
13	9	6
14	20	21
15	7	-9
16	10	10
17	19	21
19	9	-10
H,L=	-3	2
0	46	-46
1	54	64
2	14	16
3	71	-74
4	13	-14
5	32	-33
6	22	23
7	67	-65
8	21	-21
9	22	23
10	23	22
11	31	-33
12	6	-6
13	9	-6
14	7	-5
15	41	-45
16	10	-7
18	13	13
H,L =	-4	2
0	16	-20
1	4	6
2	8	8
3	28	28
4	5	4
5	28	25
6	8	7
7	10	-11
8	30	-27
9	6	4
10	13	13
13	10	10
14	12	-11
15	14	14
16	22	-21
17	11	13
19	10	-7
20	7	-6
H,L=	-5	2
0	19	-22
1	11	-11
2	12	11
3	9	-7
4	27	27
5	6	-4
7	11	10
8	12	-9
9	7	-4
12	7	-6
13	7	-10
15	9	-8
16	12	-13
19	13	12
H,L=	-6	2
0	14	24
1	12	-10
2	36	38
3	12	12
4	7	4
5	7	-5
6	22	21
7	10	8
8	10	-9
9	24	-23
10	14	14
11	6	6
12	6	4
13	9	7
15	10	7
16	7	-5
17	12	-11
H,L=	-7	2
0	18	-19
1	29	-32
2	7	-6
3	7	7
4	10	-11
7	23	24
8	6	-6
9	6	-5
11	16	13
13	7	-6
14	4	5
15	10	9
H,L=	-8	2
0	8	7
3	6	6
7	9	9
8	11	10
10	4	-4
11	9	8
12	8	-4
H,L=	-9	2
0	4	3
1	6	5
2	5	-5
3	5	3
4	5	-4
5	13	10
H,L=	0	3
1	11	-19
2	36	29
3	21	20
5	6	-5
8	30	28
10	41	39
12	11	12
H,L=	1	3
1	16	17
3	12	-12
4	23	18
5	3	2
6	14	-13
7	17	16
9	3	-3
10	19	18
H,L=	2	3
1	32	33
2	15	14
3	6	6
4	12	-13
5	6	-7
6	3	-4
7	10	12
8	6	8
9	8	-7
11	10	10
12	6	5
14	9	-9
15	11	11
16	12	-12
17	6	-7
18	4	5
20	6	5
21	3	-3
22	4	-2
H,L=	3	3
1	7	7
3	8	8
4	11	12
6	19	18
8	12	-14
9	7	8
10	4	-5
11	27	-30
12	13	-14
13	13	-12
14	12	12
15	12	-13
16	4	4
17	10	-10
18	8	7
19	12	-12
20	5	-6
21	4	-2
H,L=	4	3
1	8	9
3	12	-13
4	4	4
5	6	7
6	4	-3
8	7	-7
9	9	9
12	7	7
15	11	-10
16	6	-8
17	10	10
18	4	-4
19	6	-6
H,L=	5	3
1	6	-6
2	11	-13
3	6	7
4	18	-20
5	4	4
10	4	-5
12	4	-6
14	3	-2
15	3	2
16	9	-10
18	3	2
H,L=	6	3
1	14	15
3	6	6
5	6	-7
6	4	-3
7	7	-8
8	18	-18
9	6	7
10	6	-6
11	8	8
12	8	-7
13	6	6
14	6	6
15	4	0
H,L=	7	3
3	3	-4
5	6	7
8	5	5
9	5	-7
11	4	-4
H,L=	-1	3
2	38	29
3	6	-5
4	6	-5
7	6	5
9	35	-32
11	24	24
H,L=	-2	3
1	30	-35
2	5	-6
3	1	0
4	32	27
6	4	-4
7	29	-26
8	10	-9
9	5	-5
10	13	-14
H,L=	-3	3
1	9	-10
3	8	10
4	15	-17
5	3	2
6	11	10
7	36	-35
8	7	8
9	15	13
11	9	10
15	6	6
16	9	-10
H,L=	-4	3
1	4	3
2	20	-22
3	13	-14
4	5	-6
8	7	-6
9	4	2
10	13	-14
13	12	-12
15	17	-18
17	7	6
18	6	-7
19	6	1
H,L=	-5	3
1	18	-20
2	19	-23
4	3	4
5	11	10
6	6	-6
8	7	-9
10	20	-23
11	19	-20
14	7	-7
18	11	-10
19	6	-5
20	5	5
H,L=	-6	3
1	10	13
2	9	11
3	10	-13
5	20	-19
7	7	-8
8	13	-16
9	6	6
10	14	-14
13	4	4
14	6	7
16	3	-3
18	9	7
H,L=	-7	3
1	10	14
2	8	-11
3	6	5
4	6	-6
5	7	7
6	6	6
7	17	16
8	4	5
9	4	-4
10	12	11
12	6	-6
13	8	-6
15	10	9
H,L=	-8	3
1	9	9
2	3	5
3	7	8
6	7	-6
7	5	5
9	5	4
10	5	4
12	1	2
H,L=	-9	3
1	2	-3
2	7	6
3	6	-5
H,L=	0	4
0	110	101
1	26	-24
2	40	38
3	61	-57
4	48	44
5	6	-6
6	6	-4
7	4	4
8	48	46
9	34	32
10	6	-4
11	8	-8
12	5	5
13	16	-15
14	5	-3
15	10	-12
18	17	-19
19	4	-5
21	5	5
22	5	-5
H,L=	1	4
0	28	31
1	3	3
2	3	-2
3	37	33
4	25	-22
5	7	6
6	8	7
7	6	-5
8	4	2
9*	24	-24
10	10	-10
11	5	5
12	5	-1
13	9	9
14	5	-3
15	11	11
16	12	15
17	5	-6
H,L=	2	4
0	8	7
1	17	-17
4	6	5
6	9	-9
7	35	32
8	7	5
9	20	-19
10	11	-10
15	9	10
16	5	-5
18	16	-14
19	14	12
H,L=	3	4
0	17	-18
1	53	-48
2	26	-23
4	7	5
5	29	-28
8	10	9
9	43	-41
10	9	-8
11	5	-4
12	9	-8
13	21	-22
14	10	-11
17	19	-18
18	6	6
19	3	-3
20	5	5
H,L=	4	4
0	7	7
1	14	-13
2	13	14
3	10	12
5	12	-10
7	14	15
8	13	-15
9	10	-8
10	11	12
11	13	16
12	14	16
13	4	6
14	4	3
15	4	5
16	8	-7
17	8	-5
H,L=	5	4
0	21	-21
2	7	6
3	9	-9
4	10	10
6	5	5
8	7	-7
11	7	-6
14	11	10
16	2	2
H,L=	6	4
0	12	-14
1	6	8
2	11	-12
3	4	6
4	15	-18
5	4	6
6	12	-12
7	7	-7
8	11	-11
9	6	6
10	6	5
12	4	2
13	2	0
H,L=	7	4
0	8	-8
1	8	7
2	7	8
5	3	-3
6	11	12
7	3	-3
8	5	-4
H,L=	-1	4
1	47	81
2	55	-49
3	7	-7
4	10	9
5	33	29
6	5	-5
7	43	-36
8	19	19
9	25	26
10	23	-24
11	13	-12
12	5	-7
13	29	30
14	7	-8
15	9	-7
16	9	10
17	9	9
19	9	-8
21	6	-5
H,L=	-2	4
0	6	6
1	23	23
2	8	-7
3	18	-16
4	20	-20
5	22	21
7	17	-15
9	38	36
10	6	5
11	12	-13
12	5	-3
13	7	-7
14	15	-17
15	9	-11
17	13	15
19	6	-5
22	3	-3
H,L=	-3	4
1	17	19
2	17	18
3	30	31
4	18	16
5	20	22
6	20	-18
7	10	10
8	9	-9
9	20	23
10	5	4
11	10	14
12	5	6
13	15	18
14	10	12
15	9	10
16	7	-7
17	15	16
18	4	-4
H,L=	-4	4
0	30	-29
1	4	3
3	15	-18
5	17	-19
6	20	20
7	7	-8
8	12	-16
10	10	12
14	5	8
15	16	-18
16	4	5
17	6	-8
18	19	21
H,L=	-5	4
0	31	-30
1	20	-18
2	21	21
3	10	11
4	25	-27
6	10	12
7	5	4
8	19	-22
9	9	-8
10	22	25
11	9	11
14	8	8
15	11	11
16	3	-12
18	3	5
H,L=	-6	4
0	46	-46
1	14	-14
2	15	-14
3	10	10
4	15	-14
5	7	-7
7	16	18
8	9	-11
9	10	-10
10	5	-5
11	4	4
12	11	-12
13	4	-5
14	7	6
H,L=	-7	4
0	28	28
2	8	9
5	5	-2
7	4	-5
9	13	-13
11	5	-4
14	2	-2
H,L=	-8	4
1	7	-6
6	5	-4
11	3	-2
H,L=	0	5
1	5	3
3	5	3
4	1	-3
5	7	-6
6	29	-26
8	11	-12
9	10	-9
11	8	7
12	12	-14
14	10	-10
15	10	12
16	10	9
H,L=	1	5
1	4	4
2	21	21
3	10	-8
5	5	-6
6	11	-10
7	5	5
8	8	-8
9	10	-8
10	6	7
12	12	-14
13	8	-10
14	8	-8
16	9	-11
17	5	-8
18	9	12
H,L=	2	5
1	9	-9
2	7	6
3	9	-8
4	5	3
5	10	-10
7	6	8
8	6	-5
11	12	-13
14	5	5
H,L=	3	5
2	8	-9
3	16	-15
5	8	-10
6	6	-5
7	12	15
9	6	5
10	6	10
11	6	8
12	5	7
15	12	15
17	8	10
18	5	-5
H,L=	4	5
4	6	-5
6	8	8
15	3	6
H,L=	5	5
1	5	7
4	8	10
5	8	-7
6	5	7
7	5	-9
9	7	9
H,L=	6	5
1	11	-14
3	4	-3
4	4	5
5	4	10
6	4	6
H,L=	-1	5
3	24	22
4	9	-7
5	13	13
6	12	-13
7	13	-12
8	10	11
9	7	6
12	7	6
13	11	11
14	5	-7
15	10	-10
17	5	-4
18	6	-5
20	3	-4
21	7	8
H,L=	-2	5
1	1	0
2	2	-2
3	7	11
4	3	-5
5	23	25
7	3	-1
8	8	8
10	6	7
11	7	7
12	7	6
14	7	-6
15	17	-17
20	6	6
21	4	-2
H,L=	-3	5
1	9	-9
2	12	-12
3	12	14
4	19	17
5	3	3
6	5	4
7	8	-7
8	6	-6
9	8	-9
10	26	-26
11	7	-4
13	12	-13
15	14	-15
16	15	14
17	12	-11
18	11	-7
H,L=	-4	5
3	7	6
4	7	6
5	4	4
6	9	10
7	8	-9
8	8	7
10	9	-6
12	17	17
13	15	16
14	5	5
15	4	5
16	6	-4
17	6	4
18	7	-5
H,L=	-5	5
1	16	18
2	11	-13
3	8	-7
5	8	-6
6	19	20
8	5	5
9	7	6
10	10	11
11	7	6
14	14	12
17	6	4
H,L=	-6	5
1	7	-7
3	5	4
5	7	10
6	5	6
7	19	18
10	4	4
11	14	-13
13	8	-7
14	6	5
15	8	6
16	5	-5
H,L=	-7	5
2	8	8
3	17	-18
5	16	-16
7	6	-7
9	4	4
10	4	-4
13	2	2
H,L=	-8	5
3	5	-7

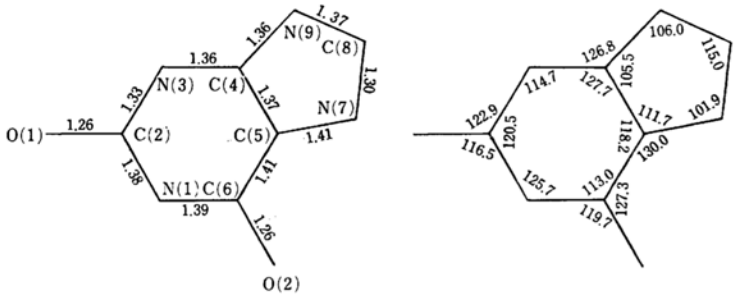


Fig. 3. Bond lengths and angles of xanthine anion.

extinction effects.

All the numerical computations were carried out on the NEAC 2203, NEAC 2206 and the NEAC 2200-model 500 Computors in the Computation Center of Osaka University. The used programs are SFFR for the three-dimensional Fourier synthesis, HBLS IV for the least-squares and DAPH for the bond lengths and angles written by Tamaichi Ashida, and the others by the authors.

Description of the Structure and Discussion

The intramolecular bond lengths and angles are listed in Table 5 and also shown in Fig. 3. The angle C(2)–N(3)–C(4)=114.7°, suggests that a hydrogen atom is not attached to N(3) in the six-membered ring, since Singh's survey[4] has shown that when an extra-annular hydrogen is attached to a nitrogen atom in a six-membered ring, the internal ring angle is 125.3°, whereas it is 116.3° when there is no hydrogen atom attached to the nitrogen atom. It may, of course, be expected that a lone pair electron of nitrogen atom gives rise to a stronger repulsion than a bonding pair. The fact that the difference Fourier map (Fig. 2) reveals no hydrogen peak at the N(3) position supports the compatibility of this empirical rule.

It is also probable that the reasonable position of the imidazole hydrogen atom is at the N(9) rather than at the N(7) in consideration of the hydrogen H(3) peak position on the difference Fourier map (see Fig. 2).

The C(2)–N(3) bond of 1.33 Å is in good agreement with the C(2)–N(3) bond distances of 1.322 Å found in 9-methyladenine[5] and 1.33 Å in 9-methylguanine hydrobromide;[6] however it is shorter than that of 1.382 Å found in uric acid,[7] indicating that this bond has double bond character as shown in 9-methyladenine(a) or in 9-methylguanine hydrobromide(b) rather than single bond character in uric acid(c), though the essential difference in structure between xanthine(d) and uric acid is the only atom attached to C(8), a hydrogen atom in the former and a carbonyl oxygen atom in the latter (see Fig. 4).

The C(2)–O(1) and C(6)–O(2) bond distances are both equal to 1.26 Å and are significantly longer than the standard double bond distance of 1.20 Å. These results suggest the resonance forms (I), (II) and (III) in Fig. 5 as predominant. These three resonance forms have a common feature, that is, the negatively charged O(1), O(2) or N(3) forms two or three hydrogen bonds (as seen in Fig. 6a) to the surrounding water molecules which have the induced dipolar character, suggesting that resonance forms (I), (II) and (III) contribute extra electrostatic energy to these hydrogen bonds in this crystal structure. It is of considerable interest that the nitrogen N(3) acting as hydrogen acceptor participates in two hydrogen bonds with water molecules as clearly seen in Figs. 6a and 6b.

The best plane through the xanthine ring atoms, as calculated by the least-squares method, is defined by the equation

$$0.04230x-0.18440y-0.98194z-3.39443=0.$$

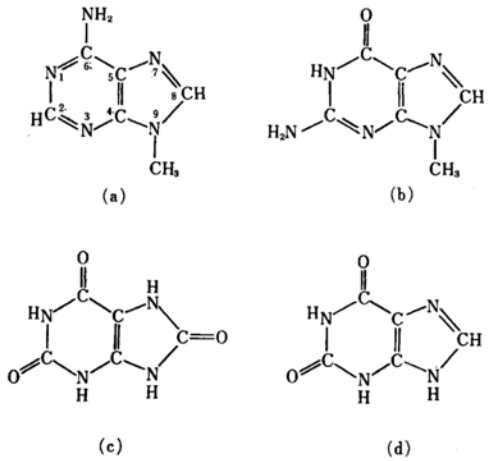


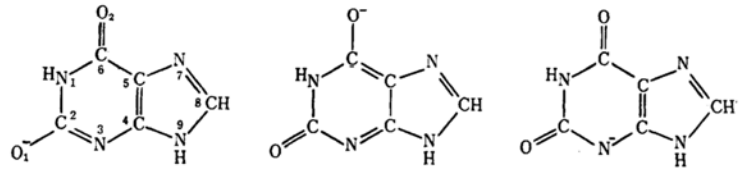
Fig. 4. Purine derivatives.

4) C. Singh, *Acta Cryst.*, **19**, 861 (1965).

5) R. F. Stewart and L. H. Jensen, *J. Chem. Phys.*, **40**, 2071 (1964).

6) H. M. Sobell and K. Tomita, *Acta Cryst.*, **17**, 126 (1964).

7) H. Ringertz, *ibid.*, **20**, 397 (1966).



(I) (II) (III)

Fig. 5. Resonance forms.

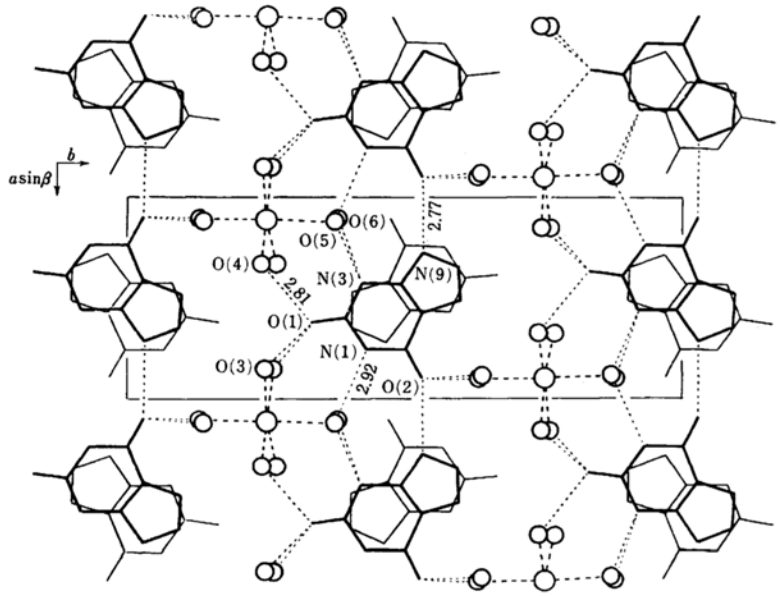


Fig. 6a. The crystal structure viewed down the *c* axis.

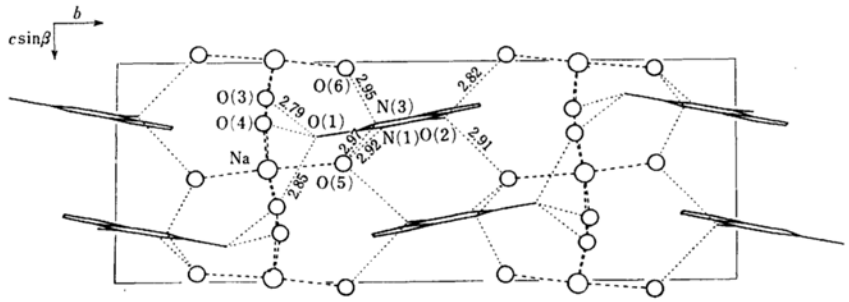


Fig. 6b. The crystal structure viewed down the *a* axis.

The average deviation of the eleven atoms from the plane is 0.01 Å which is within the errors in atomic positions. The molecular plane is inclined at an angle of 11° to the (001) plane. The van der Waals distances between adjacent molecular planes related by the center of symmetry are all nearly 3.5 Å.

A sodium ion is coordinated to six water oxygen atoms: O(3′), O(3″), O(4), O(4′), O(5) and O(6′). The O–Na–O angles range from 84.5 to 97.0°, and the Na–O distances range from 2.31 to 2.69 Å with a mean value of 2.45 Å, forming an approximately regular octahedron (see Table 6). These data are in good agreement with those of an earlier report for six-coordinate sodium compounds.[8]

The sodium-oxygen coordination polyhedrons are joined together by the shared edges O(3′)–O(3″) and O(4)–O(4′), forming a polymer-like chain parallel to the *c* axis by the continuous octahedron repeat. On the other hand, xanthine anions are stacked parallel to the *c* axis, and surrounded by these polymer-like chains.

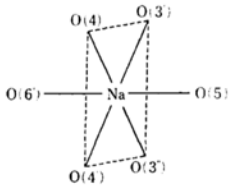
8) "International Table for X-Ray Crystallography," Vol. III, p. 258 (1962).

TABLE 5. BOND DISTANCES AND ANGLES AND THEIR STANDARD DEVIATIONS

N(1)–C(2)	1.38 (0.012) Å	C(6)–N(1)–C(2)	125.7 (0.7) °
C(2)–N(3)	1.33 (0.012)	N(1)–C(2)–N(3)	120.5 (0.8)
N(3)–C(4)	1.36 (0.011)	N(1)–C(2)–O(1)	116.5 (0.8)
C(4)–C(5)	1.37 (0.011)	N(3)–C(2)–O(1)	122.9 (0.9)
C(5)–C(6)	1.41 (0.011)	C(2)–N(3)–C(4)	114.7 (0.7)
C(6)–N(1)	1.39 (0.011)	N(3)–C(4)–C(5)	127.7 (0.7)
C(4)–N(9)	1.36 (0.011)	C(5)–C(4)–N(9)	105.5 (0.7)
N(9)–C(8)	1.37 (0.012)	N(3)–C(4)–N(9)	126.8 (0.7)
C(8)–N(7)	1.30 (0.013)	C(4)–C(5)–C(6)	118.2 (0.7)
C(5)–N(7)	1.41 (0.011)	C(4)–C(5)–N(7)	111.7 (0.7)
C(2)–O(1)	1.26 (0.012)	C(6)–C(5)–N(7)	130.0 (0.7)
C(6)–O(2)	1.26 (0.011)	C(5)–C(6)–N(1)	113.0 (0.7)
		N(1)–C(6)–O(2)	119.7 (0.8)
		C(5)–C(6)–O(2)	127.3 (0.8)
		C(5)–N(7)–C(8)	101.9 (0.7)
		N(7)–C(8)–N(9)	115.0 (0.9)
		C(4)–N(9)–C(8)	106.0 (0.7)

The standard deviations are shown in parentheses.

TABLE 6. BOND LENGTHS AND ANGLES IN THE ENVIRONMENT OF SODIUM ION



O(3')–Na–O(3'')	89.4°	Na–O(3')	2.69Å
O(3')–Na–O(4)	84.5	Na–O(3'')	2.43
O(3'')–Na–O(4')	89.0	Na–O(4)	2.39
O(4)–Na–O(4')	96.8	Na–O(4')	2.46
O(5)–Na–O(3')	90.1	Na–O(5)	2.39
O(5)–Na–O(3'')	88.1	Na–O(6')	2.31
O(5)–Na–O(4)	89.4		
O(5)–Na–O(4')	83.4		
O(6')–Na–O(3')	93.3		
O(6')–Na–O(3'')	92.0		
O(6')–Na–O(4)	90.8		
O(6')–Na–O(4')	93.3		
O(3')–Na–O(4')	173.3		
O(4)–Na–O(3'')	173.4		
O(5)–Na–O(6')	176.7		

TABLE 7. HYDROGEN BONDS

N(1)---O(5)	2.92 Å
N(3)---O(5)	2.97
N(3)---O(6)	2.95
N(9)---O(2')	2.77
O(1)---O(3)	2.79
O(1)---O(3')	2.85
O(1)---O(4)	2.81
O(2)---O(5')	2.91
O(2)---O(6')	2.82

The possible twinning operation of this compound is now presumable from its molecular arrangement in crystal as shown in Fig. 6a. The contact distances between molecules at the twinning boundary are reasonable, provided the additional *b*-glide plane perpendicular to a^*-axis is considered to be the symmetry operation of the space group $P2_1/c$.

All the water molecules may stabilize the crystal lattice in two ways, that is, by coordinating to the sodium ion as above mentioned, and by linking xanthine anion through hydrogen bonds. The lengths and arrangement of hydrogen bonds can be seen in Fig. 6 and Table 7. Seven out of the eight water hydrogen atoms form hydrogen bonds, but only the remaining hydrogen H(7) does not participate in any hydrogen bonds as occasionally seen in crystalline hydrates, for example in $MgSO_4 \cdot 4H_2O$.[9]

All the water molecules lie in the electrostatic fields of the surrounding ions; the positively charged Na^+, and the negatively charged O(1), O(2) and N(3) of xanthine anion. Therefore it seems that the orientation of each water molecule depends mainly upon the electrostatic interactions between the induced dipole of water molecule and the surrounding ions, and in this case, the hydrogen bonds are essentially electrostatic.

We wish to express our thanks to the staff of the Computation Center of Osaka University. Thanks are also due to Dr. Tamaichi Ashida for permission to use the computor programs. Finally, the authors are grateful to emeritus Prof. Tokunosuké Watanabé and Prof. Shuzo Seki for their valuable advice and discussion throughout the course of this work.

9) W. H. Baur, *Acta Cryst.*, **17**, 863 (1964).