Crystal Structure of Salicylamide

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The polymorphism observed in the crystals of most amides may be expected to correspond to the varied types of molecular arrangement connected by hydrogen bonds with each other.[1] Such variations in molecular linkage are due to the fact that the amide group is a bivalent donor and a bivalent acceptor of hydrogen bonding at the same time.

If a group attached to an amide group is a donor or an acceptor of hydrogen bonding, more different types of molecular association can be presumed, and this compound might show more crystallographic modifications. In fact, one of the authors has observed that pyrazinamide has four modifications and has determined, from the structure determination, that each modification has a characteristic molecular linkage by hydrogen bonds.[1-3]

The determination of the molecular arrangement in amide crystals will be of some interest in determining the relationship between the delicate balance of intermolecular interactions and the molecular geometry. As a part of a series of studies of the amide crystals,[1-4] this account will deal with the crystal structure of salicylamide obtained from X-ray analysis.

Experimental and Crystal Data

Crystals were obtained from an alcohol-water solution as colorless laths elongated along the b-axis. Twins were found frequently, and X-ray photographs showed that this twinning occurs with a common ba plane.

The crystal and physical data found are as follows:

Salicylamide: $C_7H_7NO_2$, m. p. 139°C
Monoclinic: $a=12.92\pm0.04$, $b=4.98\pm0.02$, $c=21.04\pm0.05$ Å, $\beta=91.8\pm0.4°$
Absent spectra: (hkl) when $h+k+l$ is odd, ($h0l$) when h and l are odd, ($0kl$) when $k+l$ is odd, ($hk0$) when $h+k$ is odd, and ($0k0$) when k is odd.
Space group: $I\ 2_1/a-C^6_{2h}$
Eight molecules per unit cell
Volume of the unit cell: 1353.0 Å^3
Density (by floatation): 1.34_9 g. cm^{-3}
Density (calculated): 1.34_5 g. cm^{-3}
Linear absorption coefficient for Cu$K\alpha$ radiation: $\mu=9.73$ cm^{-1}
Total number of electrons per unit cell: $F(000)=576$

Using Cu$K\alpha$ radiation with a nickel filter, complete sets of relative intensities for ($h0l$), ($h1l$) and ($h2l$) were obtained by the Weissenberg procedure. The specimen used was 0.04×0.02 cm. at right angles to the axis of rotation. Precession photographs were also taken using Cu$K\alpha$ radiation for the ($0kl$) and ($hk0$) zones. Intensities were estimated by visual comparison with a calibrated scale prepared using the same crystal. The multiple-film technique was applied to correlate strong and weak reflections, ranging in relative intensity from 5400 to 1. The maximum $2\sin\theta$ observed was 1.95. Within this range, 133 reflections were measured out of the 172 possible ($h0l$).

Corrections for Lorentz and polarization factors were applied in the usual way, while that for absorption was neglected. The observed structure factors were first set onto an absolute scale by Wilson's method,[5] and the scale factor was further improved during the later stage of the refinement.

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1) C. Tamura, H. Kuwano and Y. Sasada, *Acta Cryst.*, **14**, 693 (1961).

2) Y. Takaki, Y. Sasada and T. Watanabe, ibid., 13, 693 (1960).

3) Y. Takaki et al., to be published.

4) S. Orii, T. Nakamura, Y. Takaki, Y. Sasada and M. Kakudo, This Bulletin, **36**, 788 (1963).

5) A. J. C. Wilson, *Nature*, **150**, 152 (1942).

TABLE I. ATOMIC COORDINATES AND TEMPERATURE FACTORS

Atom	x/a	y/b	z/c	B_{11}	B_{33}	B_{13}
C_1	0.0799	0.177	0.3720	0.00440	0.00180	−0.00003
C_2	0.1861	0.230	0.3601	0.00405	0.00153	0.00015
C_3	0.2600	0.067	0.3934	0.00450	0.00188	0.00020
C_4	0.2284	−0.124	0.4360	0.00533	0.00190	0.00000
C_5	0.1254	−0.174	0.4468	0.00568	0.00200	0.00035
C_6	0.0524	−0.020	0.4150	0.00533	0.00213	0.00040
C_7	0.2120	0.452	0.3134	0.00358	0.00138	0.00033
N_8	0.3099	0.480	0.3005	0.00360	0.00150	0.00065
O_9	0.1424	0.580	0.2870	0.00375	0.00175	0.00020
O_{10}	0.0050	0.326	0.3418	0.00405	0.00223	0.00015

Structure Determination

Structure Projected on the (010) Plane.—It seemed reasonable to set up a planar molecular model of salicylamide on the basis of the information already obtained on some related crystal structures. The problem in the first step was to determine the arrangement of these hypothetical molecules in the unit cell. From the unit cell dimensions and the disposition of symmetry elements required by the space group, the molecule could not be inclined steeply with respect to the (010) plane but would lie approximately in the region with the dimensions of $a/4\times c/4$. There are four possible arrangements of the symmetry elements, as Fig. 1 shows, and the hydroxyl and amide groups can be arbitrarily taken to point downward in this drawing. It was expected from the normal van der Waals radii and hydrogen bond distances that the atoms would be located only outside the circles centered on the symmetry elements shown in Fig. 1. The initial coordinates of the atoms in the molecule were chosen in the rather limited allowable region so as to give large calculated values for some strong reflections, such as (202). By the systematic use of the structure factor maps for reflections with a larger spacing than 2 Å, the coordinates were adjusted so that a fairly good agreement between observed and calculated structure factors was obtained. Ordinary Fourier syntheses followed. After four cycles of Fourier refinement, the (F_o-F_c) synthesis technique was applied twice in succession. Four hydrogen atoms were first placed on the molecular plane at a distance of 1.0 Å from the carbon atoms, and the hydrogen atoms of the hydroxyl and amino groups were located at positions which could reasonably be expected from the second difference map. At this stage, the discrepancy index, $R=\sum||F_o|-|F_c||/\sum|F_o|$, was 0.16. After that, the anisotropy in the thermal motion of each atom was taken into account in terms of $\exp\{-(h^2B_{11}+hlB_{13}+l^2B_{33})\}$. The anisotropic temperature factors were derived and refined from four successive (F_o-F_c) syntheses by the method of Takaki and Sakata.[6] The effect of secondary extinction was also allowed for. The discrepancy index thereby decreased to 0.087. The final atomic coordinates and the temperature factors of carbon, nitrogen and oxygen atoms are listed in Table I, while the observed and calculated structure factors are shown in Fig. 2. In the refinement stage, all calculations of the structure factors and Fourier syntheses were made on an automatic digital computer, NEAC 2203, using programs devised by Yoriko Ogawa of this laboratory. The final electron density distribution projected on the (010) plane is shown in Fig. 3.

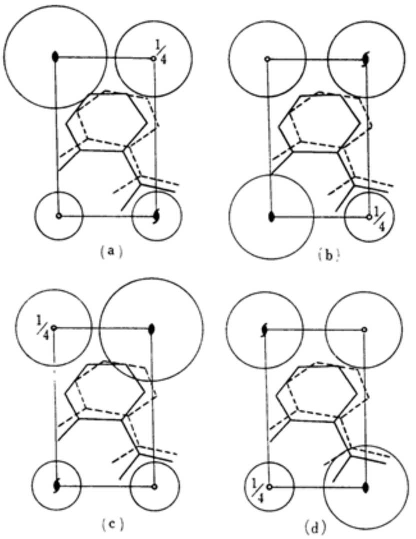

Fig. 1. Arrangement of symmetry elements and trial structure (solid line). Final projected structure is shown by broken lines. Correct arrangement of symmetry elements is (b).

Determination of the y-Parameters.—As no

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[6] Y. Takaki and Y. Sakata, *Memoirs of the Osaka University of Liberal Arts and Education*, **9**, 98 (1960).

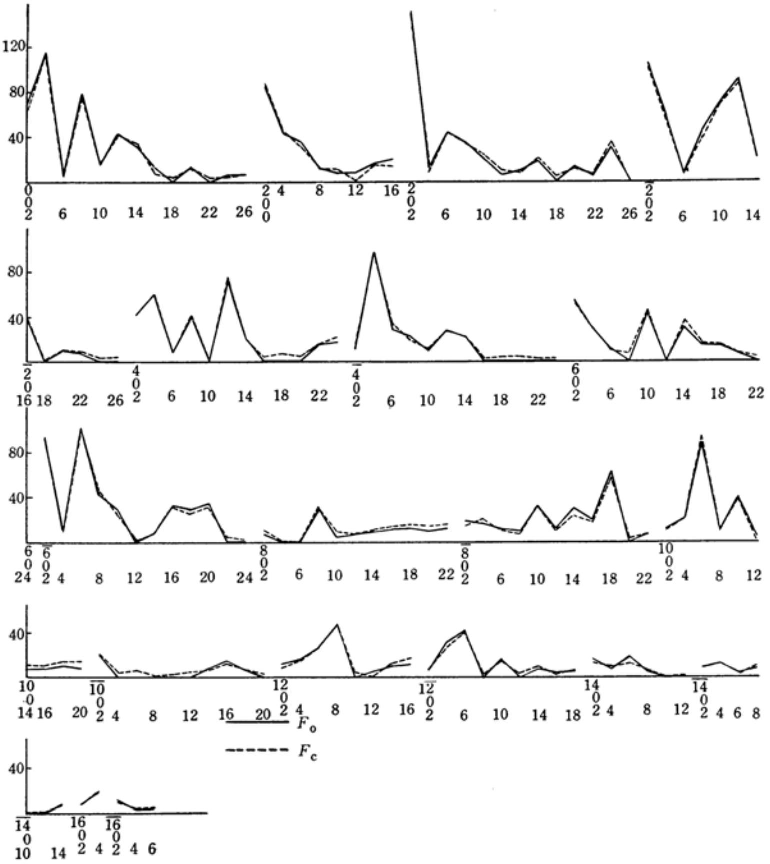

Fig. 2. Observed and calculated structure factors, $F(h0l)$.

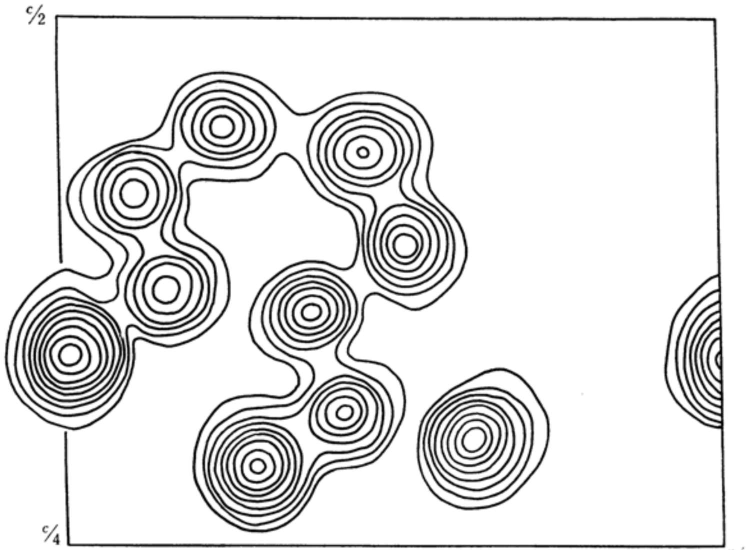

Fig. 3. The final electron density projection on (010). Contours at intervals of 1 e. Å^{-2}, with the lowest solid contour of 2 e. Å^{-2}.

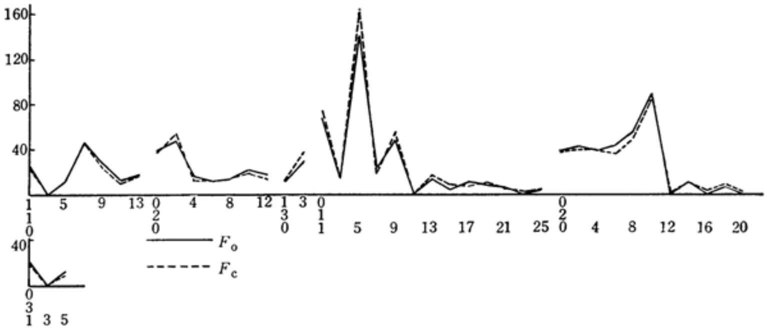

Fig. 4. Observed and calculated structure factors, $F(hk0)$ and $F(0kl)$.

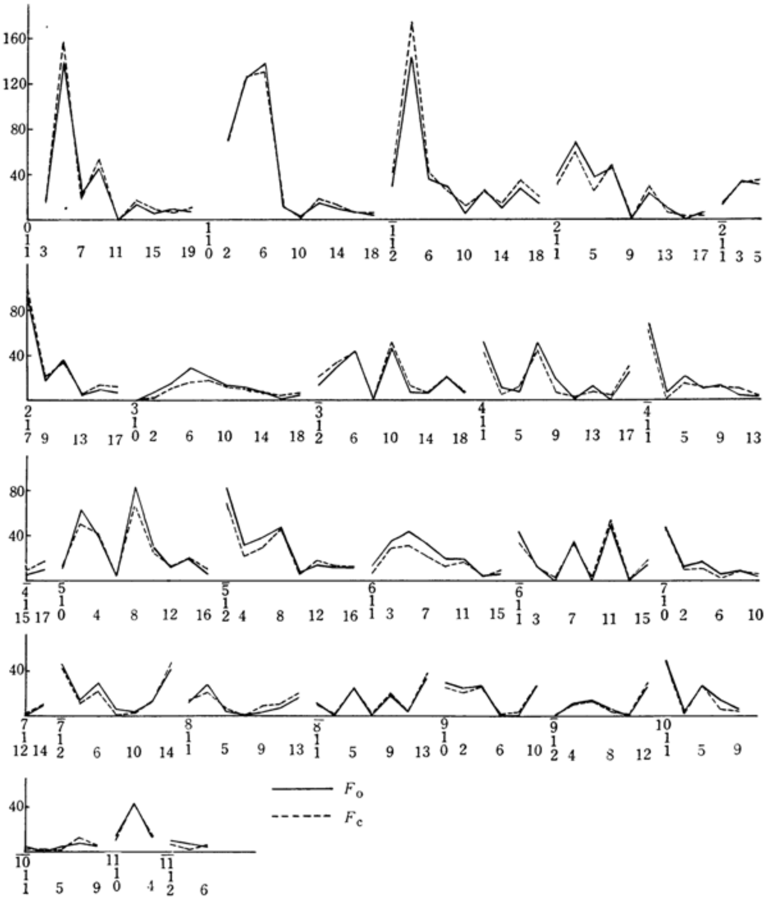

Fig. 5. Observed and calculated structure factors, $F(h1l)$.

complete intensity set for $(0kl)$, $(hk0)$ or (hkl) was taken and a serious overlapping of atoms was expected in the projections along the a and c axes, we attempted to refine the y-coordinates by the full-matrix least-squares technique for $(hk0)$ and $(0kl)$ intensity data, with fixed x and z coordinates obtained from the (010) projection. The structure projected on the (010) plane suggested that the relative arrangement of the symmetry elements in Fig. 1(c) is impossible because of too close van der Waals contacts around C_4. Arrangements (a) and (d) also seemed to be less probable. As the inclination of the molecular plane with respect to the (010) plane could be estimated, it was not difficult to choose approximate y-coordinates for the atoms referred to the arrangement (b) of the symmetry elements, thus explaining some characteristic structure factors using the structure factor maps. The program of the full-matrix least-squares refinement was written in MALT language⁷⁾ and executed on an electronic computer NEAC 2206. After a few cycles of refinement, the discrepancy index decreased from 0.47 to 0.22. As the molecule suffered considerable deformation, however, the y-coordinates so obtained were adjusted to recover a reasonable molecular shape and were then again refined by the least-squares program. When this process was repeated several times, the discrepancy index reached 0.120. The overall isotropic temperature factor was 3.27.

The unsatisfactory convergence at the earlier stages of refinement may be due to the shortage of the intensity data and to the less accuracy of some of the structure factors. We had the feeling that in such a case a technique similar to that used in the analysis of 2-amino azulene⁸⁾ would be adequate, although we did not actually apply one.

Observed and calculated structure factors for (*hk*0) and (0*kl*) are shown in Fig. 4. To confirm the above-mentioned results further, we have calculated the structure factors for (*h*1*l*). The agreement between observed and calculated structure factors for (*h*1*l*) was fairly good, as Fig. 5 shows; the discrepancy index was 0.184.

Description of the Structure and Discussion

Molecular Structure.—Bond lengths and bond angles in salicylamide are shown in Fig. 6.

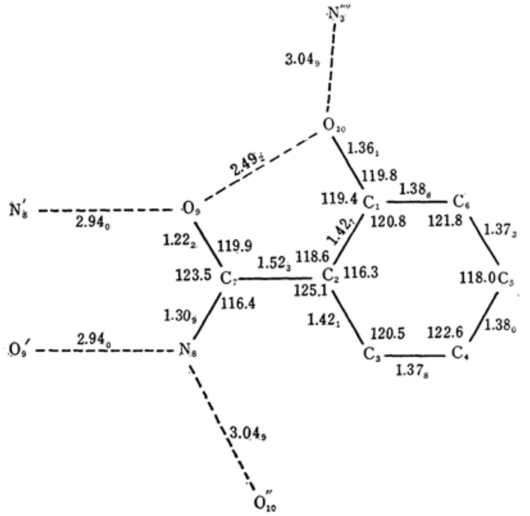

Fig. 6. Bond lengths (Å) and bond angles (°).

Although small fluctuations among the C–C bond lengths in the benzene ring are observed and the slight elongation of C_1–C_2 is probably of some significance, no detailed discussion will be given because of low degree of accuracy of the y-coordinates. The average C–C bond length in the benzene ring is 1.39_5 Å, and the average bond angle C–C–C is 120.0°, in good agreement with the standard value. The bond length, C_1–O_{10}, is 1.36_1 Å, which is nearly the same as the values observed in salicylic acid,⁹⁾ 1.36_1 Å, and in *p*-amino salicylic acid,¹⁰⁾ 1.37 Å. The dimensions of amide group found in the present compound are close to those found in the related compounds: for example, C–N$=1.31_2$ Å and C–O$=1.24_6$ Å in α-pyrazinamide.²⁾

The final (F_o-F_c) synthesis projected on the (010) plane is shown in Fig. 7; this was obtained using the structure factors calculated without the contributions from hydrogen. Electron density peaks corresponding to hydrogen atoms are easily recognized, although their heights and coordinates are not so accurate. The hydrogen atom attached to O_{10} lies near the line joining O_9 and O_{10}. The position of this hydrogen atom and the interatomic distance between O_9 and O_{10}, 2.49 Å, clearly show that an intramolecular hydrogen bond is formed between these atoms, as has been observed in salicylic acid⁹⁾ and *p*-amino salicylic acid¹⁰⁾ also.

The plane of the benzene ring (including C_7 and O_{10}) can be represented by the equation:

$$y=-0.0526\,x'-1.1098\,z'+9.6211$$

where x', y and z' are referred to the orthogonal axes a, b and c*, so that $x'=x+z\cos\beta^*$ and $z'=z\sin\beta^*$; the values of the coefficients were determined by means of the least-squares method. The perpendicular displacements of atoms from the mean plane, shown in Table

TABLE II. PERPENDICULAR DISPLACEMENTS OF ATOMS FROM THE MEAM PLANE OF THE BENZENE RING

Atom	Displacement Å
C_1	0.010
C_2	0.003
C_3	0.013
C_4	−0.012
C_5	0.001
C_6	−0.003
C_7	−0.009
N_8	0.085
O_9	−0.012
O_{10}	−0.002

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7) Y. Yasui, to be published.

8) Y. Takaki, Y. Sasada and I. Nitta, *J. Phys. Soc. Japan*, **14**, 771 (1959).

9) W. Cochran, *Acta Cryst.*, **6**, 260 (1953).

10) F. Bertinotti, G. Giacomello and A. M. Liquori, ibid., **7**, 808 (1954).

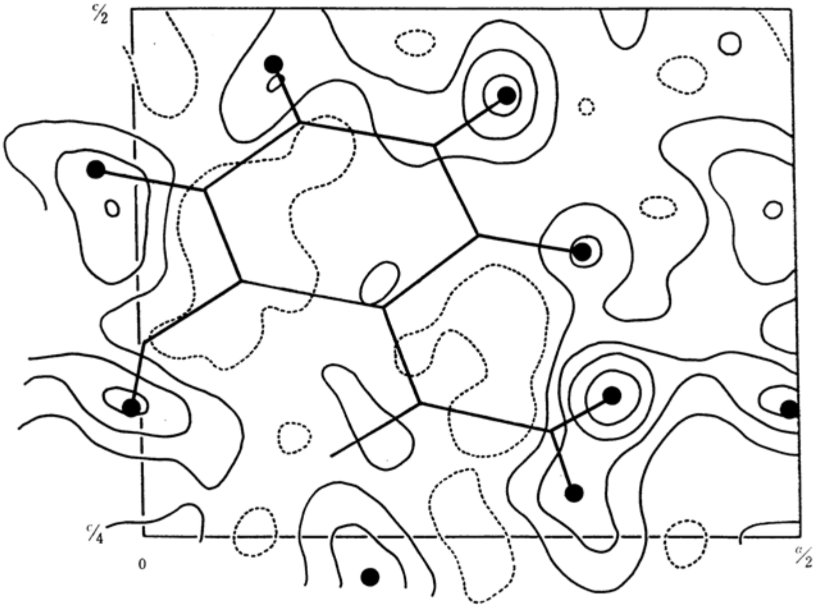

Fig. 7. The final (F_o-F_c) projection on (010).
Contours at intervals of 0.2 e. Å^{-2}, zero contour being broken.

II, vary from 0.001 to 0.013 Å, the mean value being 0.007 Å. On the other hand, oxygen and nitrogen atoms in the amide group considerably deviate from the mean plane, and the angle between planes of amide and benzene ring is about 3°. In many related amide crystals,[3,4,11,12] it is observed that the amide group twists around the connecting C–C bond and that the planes of amide and ring make an angle of about 25°. This twist has been interpreted as the effect of steric hindrance between hydrogen atom in the amino group and that in the ortho position of the ring. In the present compound, however, it may be suggested that this kind of steric hindrance is balanced with the effects of the intramolecular hydrogen bond on another side of the amide group, together with other intermolecular forces, and that the whole molecule remains approximately planar. In this connection, it is of some interest that the C_2–C_7 distance in this molecule is longer than those in similar amide compounds.[3,4,11,12]

Crystal Structure.—The crystal structure of salicylamide is shown in Fig. 8, in which the hydrogen bond is represented by bold broken lines. The molecules are connected by two NH–O hydrogen bonds, the first set, 2.94 Å in length, forming a dimer across the center of symmetry, and the second set, 3.05 Å in length, joining such dimers into an endless chain extended along the a axis. As the latter set is located across the two-fold axis, the

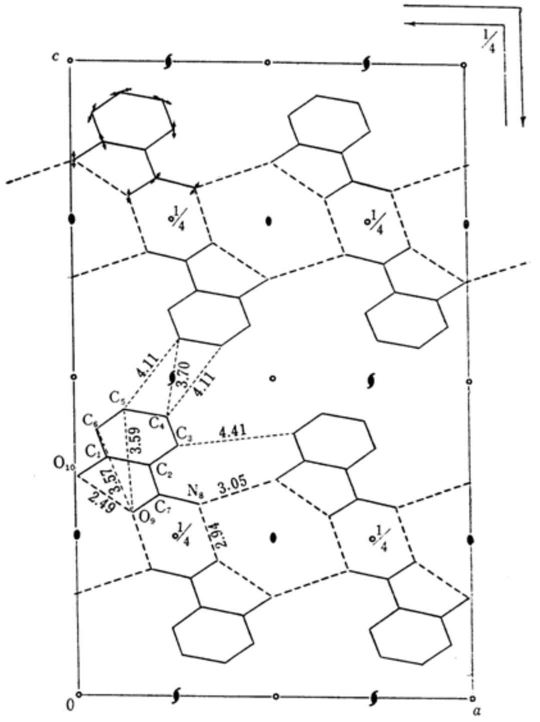

Fig. 8. Arrangement of molecules in the (010) projection with intermolecular distances (Å). Arrows show the direction of the maximum thermal oscillation of atoms.

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[11] W. B. Wright and G. S. D. King, *Acta Cryst.*, **7**, 283 (1954).

[12] B. R. Penfold and J. C. B. White, ibid., **12**, 130 (1959).

inclination of component dimers in a chain changes alternately. In α-pyrazinamide,[2] the atom in the ortho position is a donor of the hydrogen bond which connects the pyrazinamide dimers with each other. It might be said that in this sense the molecular linkage in α-pyrazinamide is similar to that found in the present crystal, although there are some differences between them.

McCrone and Hinch[13] have reported another modification obtained from melt. It is supposed that the molecular association in this modification might be of a type similar to that in β- or δ-pyrazinamide.[3]

The directions of the maximum thermal motions of atoms are illustrated by arrows in Fig. 8 ; they ase derived from the anisotropic temperature factors in Table I. The length of the arrow is proportional to the mean-square displacement of the atom by the thermal motion in this direction. By inspection it seems probable that the molecule is making an angular oscillation around the mass center of a single molecule, suggesting that the NH-O hydrogen bonds forming the dimer are not very strong, a similar situation having also been observed in the crystal of α-pyrazinamide.[2]

This molecular arrangements can reasonably explain the existence of the cleavage parallel to the ba plane and also the twinned crystals frequently obtained, in which the twinning plane is the ba.

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[13] W. C. McCrone and R. J. Hinch, *Analyt. Chem.*, **25**, 1277 (1953).