favoured by the distortion of the NH_2 group, caused by its coordination by Zn. An N–H · · · S hydrogen bond, 3·26 Å long, is described by Penfold (1953) in α-thiopyridone.

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The Crystal Structure of α-Pyrazinamide*

By Yoshito Takaki,† Yoshio Sasada‡ and Tokunosuké Watanabé
Faculty of Science, Osaka University, Nakanoshima, Osaka, Japan

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α-Pyrazinamide, $C_5H_5N_3O$, obtained from alcohol–water solution, is monoclinic, space group $P2_1/a$, with four molecules in a unit cell of dimensions

$$a=23{\cdot}07,\ b=6{\cdot}73,\ c=3{\cdot}73\ \text{Å},\ \beta=101{\cdot}0^\circ.$$

The detailed crystal structure has been determined by two-dimensional difference syntheses and least squares based on ($hk0$) and ($h0l$) reflexions.

The pyrazine ring is completely planar, with mean C–N = 1·348 and C–C = 1·383 Å, and makes an angle about 5° to the amide group ($C–O = 1{\cdot}24_4$ and $C–N = 1{\cdot}31_2$ Å). The molecules are connected by NH–O hydrogen bonds, 2·90 Å, forming dimers, and there are indications of NH–N hydrogen bonds, 3·14 Å, linking the dimers into endless chains extended along [011].

Anisotropic thermal vibration parameters of each atom were obtained, and they were interpreted by dividing into translational and angular oscillation of the rigid molecule. It was observed that the amide group makes probably a torsional motion.

Introduction

Structural investigation of pyrazinamide (pyrazine-2-carboxyamide), a potential antituberculosis drug, is a part of serial studies, attempted by us, on crystal structures of carboxyamides having rings with nitrogen. One of the main objects of these researches is to determine the accurate molecular configuration with special emphasis on the steric effects on the variation of bond lengths and angles.

Recently it has been reported (Tamura & Kuwano, 1959) that pyrazinamide has two modifications: one form is obtained from alcoholic solution and the other from melt. We shall call the former α and the latter β. On the other hand, crystal structures of a number of carboxyamides already reported can be grouped into two types of molecular arrangement. Therefore, it will be interesting to examine whether each of these two modifications has a related crystal structure to each of these types or not.

In the present paper will be reported a detailed crystal structure of the α-modification of pyrazinamide. An analysis of the anisotropic thermal motion of the molecule using Cruickshank's method (1956*a*) will also be given.

Experimental

Crystals were obtained from alcohol–water solution as fine colourless needles elongated along the c axis, sometimes as laths with (010) well developed. Twins were found frequently.

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* A preliminary note on this structure has been published (Takaki, Sasada & Watanabé 1959*a*).

† Present address: Osaka University of Liberal Arts and Education, Tennoji, Osaka, Japan.

‡ Present address: Institute for Protein Research, Osaka University, Nakanoshima, Osaka, Japan.

The crystal and physical data obtained were as follows:

Pyrazinamide, $C_5H_5N_3O$, m.p. 188–193 °C.
Monoclinic,

$$a = 23{\cdot}07_2 \pm 0{\cdot}02,\ b = 6{\cdot}72_7 \pm 0{\cdot}01,\ c = 3{\cdot}72_5 \pm 0{\cdot}01\ \text{Å}\,,\quad \beta = 101{\cdot}0 \pm 0{\cdot}4°,$$

axial lengths being deduced from the indexed powder patterns recorded on the Norelco diffractometer.
Absent spectra, ($h0l$) when h is odd, ($0k0$) when k is odd.
Space group, $P2_1/a$–C_{2h}^5.
Four molecules per unit cell.
Volume of the unit cell, 567·5 Å^3.
Density (by floatation), $1{\cdot}44_0$ g.cm.$^{-3}$.
Density (calculated), $1{\cdot}44_1$ g.cm.$^{-3}$.
Linear absorption coefficient for Cu $K\alpha$ radiation, $\mu = 10{\cdot}88$ cm.$^{-1}$.
Total number of electrons per unit cell, $F(000) = 256$.

Using Cu $K\alpha$ radiation, complete sets of relative intensities for ($hk0$) and ($h0l$) were taken by the use of the integrated Weissenberg procedure. The specimens used had the following maximum and minimum dimensions at right angles to the axis of rotation; 0·01 × 0·02 cm. for the c axis rotation, and 0·02 × 0·03 cm. for the b axis rotation. Intensities were estimated by visual comparison with a calibrated strip prepared using the same crystal. The multiple-film technique was used to correlate strong and weak reflexions, ranging in relative intensities from 2500 to 1 and 7000 to 1 for ($hk0$) and ($h0l$) reflexions respectively. The maximum $\sin\theta$ observed was 0·985. Within this limit, 153 reflexions were measured out of 195 possible ($hk0$) and 91 out of 107 ($h0l$).

Corrections for Lorentz and polarization factors were applied in the usual way and that for absorption was neglected. Observed structure factors were first set onto an absolute scale using Wilson's method (1942), and were further improved during the later stages of the refinement.

Structure determination

(*a*) *Approximate structure on the* (001) *projection*

Since it seemed probable from the information of the crystal structures of the related compounds that the pyrazinamide molecule would occur as approximately planar in the crystal, a molecular model for trial was set up which is planar having conventional bond lengths and angles. The problem was then to determine the arrangement of this hypothetical molecules in the unit cell. The shortness of the c axis suggests that the molecule could not be inclined steeply with respect to the (001) plane. Therefore, it was to be expected that an approximate crystal structure might be revealed from, the electron-density projection on (001). The allowable regions of the molecules were allocated systematically by geometrical considerations of the molecule and crystal, and the orientation of the molecule was determined by means of the trial method using the structure factor maps successively. After these procedures a structure has been obtained for which the agreement between the observed and calculated structure factors is fairly good. The ordinary Fourier synthesis followed.

In the structure-factor calculations, a spherically symmetric temperature factor $\exp\{-3{\cdot}0\,(\sin\theta/\lambda)^2\}$ was applied. After three successive Fourier refinements, the discrepancy index,

$$R = \Sigma\,||F_o| - |F_c||/\Sigma|F_o|\,,$$

became 0·17.

(*b*) *Approximate structure on the* (010) *projection*

Relative values for z parameters of individual atoms were obtained by assuming the planarity of the molecule with x and y coordinates determined from the (001) projection.

Two sets of the relative parameters were found to be allowable. However, one of these was excluded because it could not interpret the most intense reflexion, ($40\bar{1}$). The solution of the structure was reduced to a one-parameter problem; namely z for the centre of the molecule, which was determined by using the structure factor maps.

Starting from this position, three successive Fourier syntheses and two cycles of refinement by least-squares method were made. By comparing the calculated structure factors with observed ones at this stage, it was found that anisotropic thermal motion exists, the largest components lying in the direction of the c axis. Then a temperature factor of the form

$$\exp\{-3{\cdot}0\,(\sin\theta/\lambda)^2\}\,\exp\{-1{\cdot}7l^2c^{*2}\sin^2\beta^*\}$$

was applied. Agreement between observed and calculated structure factors was improved very much, and R index decreased to 0·20 after one more cycle of the refinement by least squares.

Refinement of the structure

Further refinement of the structure was made by repeated difference syntheses on the (001) and the (010) projections. Three hydrogen atoms were first placed on the molecular plane at a distance of 1·0 Å from the carbon atoms and two hydrogen were at a distance of 1·0 Å from the nitrogen atom on the lines of $N_8 \cdots O_9'$ and $N_8 \cdots N_1''$. At each step of refinement, these hydrogen positions were replaced by new positions estimated from the successive difference maps. The scaling factor was also improved on each step of the refinement by comparing the observed structure factors with those calculated.

The corrections for the atomic positions were first made by the formula deduced by Cochran (1951). When the shifts in the positional parameters became very small with an average value of 0·02 Å, the significant features of anisotropic thermal vibrations of the atoms appeared on the difference map, and the estimation of the maximum electron-density slope and their directions at the assumed atomic positions were very difficult. Therefore, further improvement of the atomic positions was made by using somewhat modified expressions. These are

$$\Delta\xi = (\partial^2 D/\partial\xi^2)(\xi_p-\xi_a)/(\partial^2\varrho/\partial\xi^2)$$
$$\Delta\eta = (\partial^2 D/\partial\eta^2)(\eta_p-\eta_a)/(\partial^2\varrho/\partial\eta^2)$$

where $(\partial^2 D/\partial\xi^2)$ and $(\partial^2 D/\partial\eta^2)$ are the curvatures of the parabola, approximate representation of the $(\varrho_o-\varrho_c)$ curves in the neighbourhood of an atomic centre in the directions of the principal axes, ξ and η, of the ellipsoid of thermal vibration of an atom, and (ξ_a, η_a) is the assumed position of the atomic centre and (ξ_p, η_p) the peak position of the $(\varrho_o-\varrho_c)$.

Thermal parameters were also corrected by using $(\varrho_o-\varrho_c)$ maps. In an early few refinements for (001), the equation for isotropic B (Atoji, 1957) was employed. For the anisotropically vibrating atoms, the scattering factor of the form

$$f=f_0 \exp\left[-\{\alpha\cos^2(\varphi-\psi)+\beta\sin^2(\varphi-\psi)\}(\sin\theta/\lambda)^2\right]$$

Table 1. *Observed and calculated structure factors*

*h*00	F_o	F_c
0		1280
2	106*	101
4	170*	−176
6	80	−70
8	74	−76
10	253*	253
12	95	89
14	75	75
16	15	16
18	9	−9
20	17	−18
22	—	4
24	27	23
26	20	−14
28	—	0
*h*10		
1	86	−86
2	173*	−174
3	254*	284
4	85	−87
5	114	−109
6	110	−107
7	10	10
8	10	12
9	132	−125
10	57	51
11	10	15
12	31	−28
13	88	88
14	68	−65
15	—	1
16	10	12
17	16	16
18	20	−23
19	29	−27
20	80	−86
21	10	−11
22	—	−2
23	—	−9
24	—	−5
25	11	10
26	—	−1
27	14	10
28	—	1
*h*20		
0	13	−19
1	36	−35
2	70	−72
3	117	−114
4	94	−92
5	10	−14
*h*20	F_o	F_c
6	249*	−248
7	35	−30
8	119	−115
9	20	18
10	77	75
11	67	64
12	—	9
13	20	21
14	21	24
15	—	4
16	83	−81
17	88	−93
18	88	−89
19	15	21
20	11	11
21	24	26
22	24	28
23	20	−25
24	20	23
25	—	8
26	—	4
27	15	−14
28	11	−13
*h*30		
1	33	31
2	50	48
3	139	−132
4	28	−30
5	37	−34
6	7	−10
7	66	61
8	119	115
9	27	26
10	23	−20
11	8	−8
12	47	49
13	33	−36
14	—	−4
15	14	−16
16	—	−7
17	17	15
18	54	57
19	12	−14
20	—	−3
21	12	−13
22	31	33
23	10	11
24	10	8
25	14	12
26	—	6
27	6	8
*h*40	F_o	F_c
0	51	50
1	30	−27
2	114	108
3	60	−54
4	10	12
5	63	56
6	49	−45
7	25	24
8	15	−15
9	40	39
10	35	35
11	—	3
12	115	118
13	81	−81
14	9	11
15	22	27
16	38	−39
17	9	14
18	—	−5
19	19	18
20	—	−1
21	16	18
22	17	16
23	—	4
24	18	18
25	7	8
*h*50		
1	30	27
2	25	−26
3	11	11
4	10	13
5	52	50
6	14	−16
7	38	−41
8	10	−12
9	—	4
10	12	−14
11	17	−20
12	9	11
13	—	4
14	21	−22
15	65	70
16	39	−45
17	—	−5
18	12	−11
19	—	−9
20	—	9
21	—	−3
22	16	16
23	12	−11
*h*60	F_o	F_c
0	37	35
1	17	16
2	42	45
3	40	−41
4	76	−77
5	64	−61
6	70	−73
7	17	23
8	—	7
9	27	30
10	9	−9
11	—	11
12	18	23
13	—	−8
14	14	−13
15	27	−30
16	—	−6
17	10	−9
18	—	−1
19	—	3
20	11	−9
*h*70		
1	31	−30
2	47	−45
3	17	−19
4	17	−18
5	50	48
6	—	5
7	20	−20
8	15	17
9	23	−23
10	25	25
11	—	1
12	—	0
13	—	−4
14	13	13
15	—	−5
16	—	5
*h*80		
0	—	3
1	14	−15
2	10	10
3	10	−10
4	9	−7
5	—	−3
6	—	2
7	—	3
8	16	18
9	10	11
10	5	8

Table 1 (*cont.*)

$h00$	F_o	F_c	$h0\bar{1}$	F_o	F_c	$h0\bar{2}$	F_o	F_c	$h0\bar{3}$	F_o	F_c
2	104*	101	2	51	53	2	52	53	6	17	−20
4	171*	−176	4	463*	467	4	60	−57	8	—	10
6	81	−70	6	16	−10	6	10	−17	10	—	− 8
8	74	−76	8	18	25	8	59	−61	12	34	−34
10	259*	253	10	167	−163	10	17	−19	14	—	1
12	92	89	12	—	− 1	12	24	29	16	—	− 2
14	75	75	14	153	145	14	52	−48	18	—	− 1
16	16	16	16	33	30	16	9	−10	20	15	−16
18	8	− 9	18	—	5	18	11	12	22	7	− 9
20	17	−18	20	33	40	20	21	−23	24	22	−18
22	—	4	22	22	27	22	23	−26	26	9	−12
24	28	23	24	14	−17	24	39	41			
26	17	−14	26	24	22	26	20	19	$h04$		
28	—	0	28	11	− 7	28	—	− 2	0	28	29
									2	16	12
$h01$			$h02$			$h03$			4	13	−13
0	227*	−250	0	56	−66	0	30	−34	6	—	0
2	113	107	2	87	−90	2	42	−44	8	10	−10
4	158	−158	4	85	−91	4	53	57	10	16	17
6	9	− 9	6	56	−60	6	29	32			
8	27	−28	8	55	61	8	7	13	$h0\bar{4}$		
10	26	31	10	10	11	10	21	−28	2	9	− 9
12	22	21	12	40	47	12	58	−61	4	—	− 1
14	30	−33	14	79	−85	14	40	41	6	25	25
16	15	17	16	99	−96	16	19	17	8	12	−13
18	76	−76	18	29	30	18	—	0	10	27	−27
20	39	−36	20	9	10				12	—	6
22	12	−10	22	20	21	$h0\bar{3}$			14	7	4
24	—	− 3				2	6	− 6	16	26	23
26	21	15				4	11	−13	18	—	—
									20	13	−15

* Shows the value corrected for secondary extinction.

was applied, where f_0 is the atomic scattering factor at rest, ψ the angle of the direction of the maximum vibration from a^* and φ the angle of the reciprocal vector from a^*. Corrections of the thermal parameters in this expression were made by the method proposed by us (Takaki, Sasada & Watanabé, 1959*b*).

After five successive difference syntheses for each of the (001) and (010) projections, the discrepancy indices were reduced to 0·068 and 0·070 for (*hk*0) and (*h*0*l*) respectively. Observed and calculated structure factors, *F*(*hk*0) and *F*(*h*0*l*), are listed in Table 1. In the refinement stage mentioned above, all the calculations of the structure factors were made on an automatic digital computer, Bendix G 15 D, using programs written by us. Atomic scattering factors used were calculated by an expansion of Gaussian functions, with constants given by Vand, Eiland & Pepinsky (1957), which fit the values taken from Berghuis, Haanappel, Potters, Loopstra, MacGillavry & Veenendaal (1955) for carbon, nitrogen and oxygen, and from McWeeny (1951) for hydrogen.

Table 2. *Atomic coordinates*

Atom	*x*/*a*	*y*/*b*	*z*/*c*
N_1	0·0901	0·5076	$0{\cdot}544_5$
C_2	0·1105	0·3334	0·443
C_3	0·1702	0·2908	0·501
N_4	0·2112	0·4192	0·656
C_5	0·1912	0·5950	0·760
C_6	0·1319	0·6380	$0{\cdot}703_5$
C_7	0·0657	0·1853	0·262
N_8	0·0099	0·2336	0·225
O_9	0·0829	0·0298	$0{\cdot}136_8$
H_3	0·181	0·167	0·380
H_5	0·221	0·685	0·920
H_6	0·117	0·753	0·783
H'_N	0·001	0·326	0·367
H''_N	−0·018	0·156	0·113

Table 3. *Thermal parameters*

	From (001)			From (010)		
Atom	α	β	ψ	α	β	ψ
N_1	3·78	2·42	0	4·18	3·78	90
C_2	3·53	2·58	5	3·53	3·53	—
C_3	3·72	3·34	6	4·74	3·72	90
N_4	3·76	3·25	80	5·45	3·25	90
C_5	4·30	3·14	135	4·26	3·72	90
C_6	4·25	2·91	0	4·65	4·25	90
C_7	3·50	2·95	0	3·90	3·50	90
N_8	3·85	3·30	95	6·95	3·30	90
O_9	3·94	3·18	5	6·24	3·94	90
H_3	3·5			4·5		
H_5	3·5			4·5		
H_6	3·5			3·5		
H'_N	3·5			3·5		
H''_N	3·5			3·5		

Final atomic coordinates for carbon, nitrogen and oxygen atoms are listed in Table 2. The hydrogen coordinates given in Table 2 were those estimated from the final difference maps which were derived by subtracting all the atoms but the hydrogen from observed ϱ. The temperature factors, α, β and ψ are listed in Table 3. The final Fourier projections of the electron density and $(\varrho_o-\varrho_c)$ maps are shown in Figs. 1 and 2 respectively.

Estimation of accuracy

The standard deviations of the electron density and atomic coordinates were estimated by the method of Cruickshank (1949; Ahmed & Cruickshank, 1953). The values obtained were:

$\sigma(\varrho) = 0{\cdot}103$ e.Å^{-2} for the (001) projection,
$\sigma(\varrho) = 0{\cdot}126$ e.Å^{-2} for the (010) projection.

From the (001) projection:

$\sigma(x) = 0{\cdot}0045$ Å $\quad \sigma(y) = 0{\cdot}0037$ Å for oxygen,
$\sigma(x) = 0{\cdot}0048 \quad \sigma(y) = 0{\cdot}0043$ for nitrogen,
$\sigma(x) = 0{\cdot}0061 \quad \sigma(y) = 0{\cdot}0048$ for carbon

From the (010) projection:

$\sigma(x) = 0{\cdot}0044$ Å $\quad \sigma(z) = 0{\cdot}0068$ Å for oxygen,
$\sigma(x) = 0{\cdot}0048 \quad \sigma(z) = 0{\cdot}0072$ for nitrogen,
$\sigma(x) = 0{\cdot}0060 \quad \sigma(z) = 0{\cdot}0070$ for carbon.

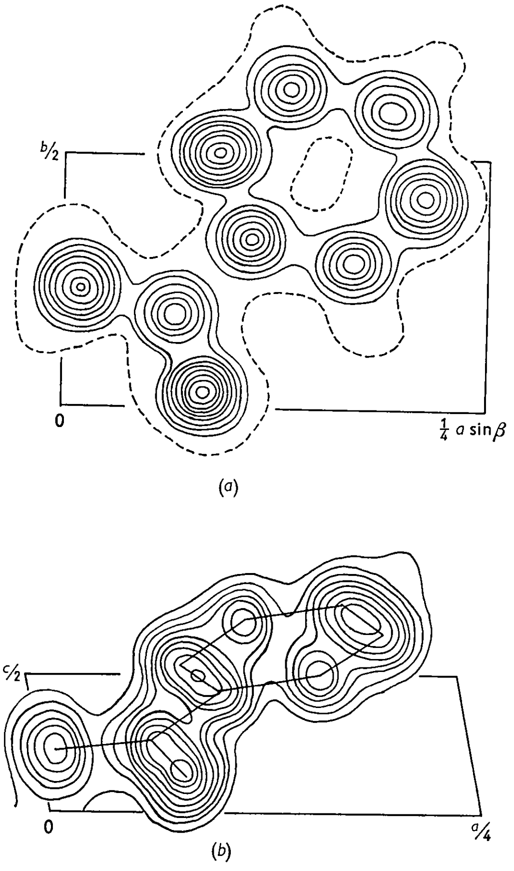

Fig. 1. The final electron-density projections (a) along the c axis, (b) along the b axis. Contours at an interval of 1 e.Å^{-2}. Contour at 1 e.Å^{-2} is broken.

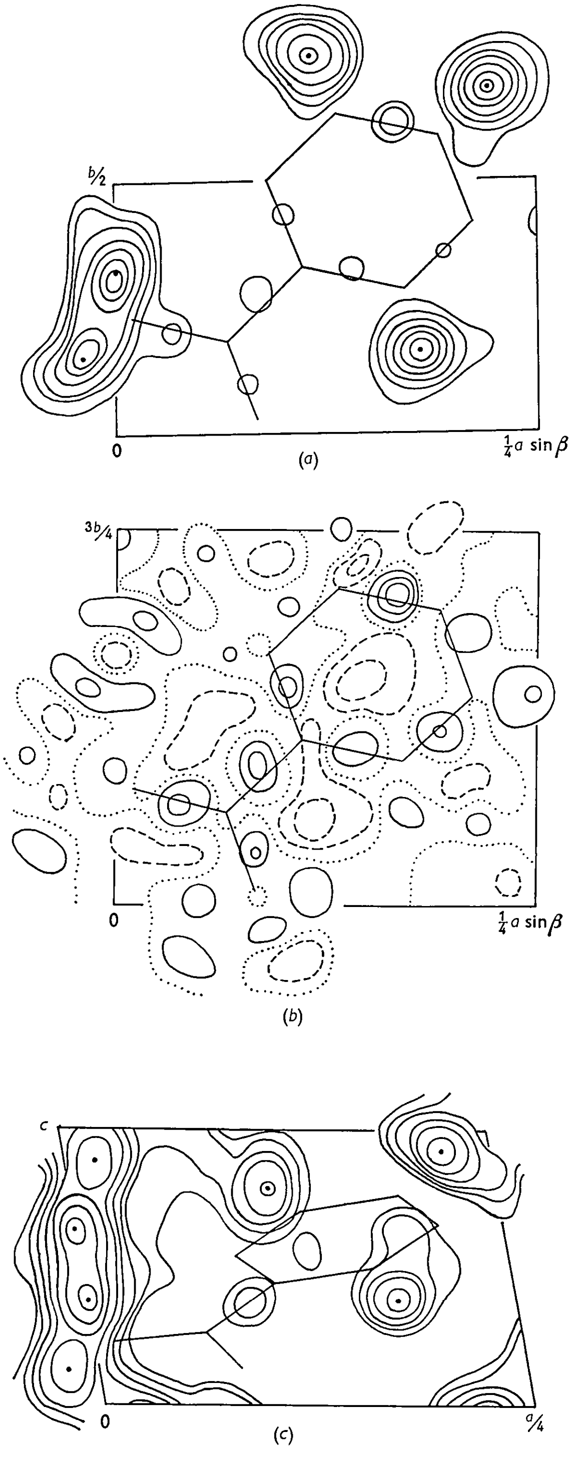

Fig. 2. The final $(\varrho_o-\varrho_c)$ projections (a), (b) along the c axis. (c) along the b axis. Contours at an interval of 0·1 e.Å^{-2}. In (a) and (c), all atoms except hydrogen are subtracted, and lower contours than 0·2 e.Å^{-2} omitted. In (b), zero and negative contours are dotted and broken respectively.

From these results, the standard deviations of C–C and C–O bonds come out to be about 0·0084 Å and 0·0074 Å, respectively. The standard deviations of C–N bonds in the pyrazine ring and the amide group are 0·0073 Å and 0·0078 Å, respectively. The standard deviation of bond angles was found to be 0·6°.

In these calculations, a half of the highest value which could remain unobserved has been given when F_o is zero, and the contribution from (310) reflexion was omitted owing to the uncertainty of the observed value.

Description of the structure and discussion

(*a*) *Molecular structure*

Bond lengths and bond angles found in the pyrazinamide molecule are shown in Fig. 3 and in Table 4. These values were corrected for the angular oscillations (Cruickshank, 1956*b*); the mean correction for the bond lengths was 0·004 Å. The corrected bond lengths and bond angles are also listed in Table 4.

Small fluctuations among the C–N and C–C bond lengths observed in the pyrazine ring are probably significant and may be caused by the effect of conjugation with the amide group. However, detailed discussion on this point is reserved until theoretical treatment will be made. The average bond lengths found in pyrazinamide (C–N = 1·348, C–C = 1·383 Å) are in good agreement with those reported for pyrazine determined by X-ray (Wheatley, 1957) and by electron diffraction investigation (Schomaker & Pauling, 1939). In some closely related compounds, bond lengths obtained from X-ray crystal analyses are found to be 1·34 Å for C–N. $1{\cdot}38_5$ Å for C–C in nicotic acid (Wright & King, 1953) and 1·36 Å for C–N, 1·40 Å for C–C in nicotinamide (Wright & King, 1954). Theoretical values estimated from the bond orders in pyrazine (Chalvet & Sandorfy, 1949; Orgel, Cottrell, Dick & Sutton, 1951) using curves given by Coulson (1951) for C–C bonds and by Cox & Jeffrey (1951) for C–N bonds are also compatible with these experimental values.

Table 4. *Bond lengths and bond angles*

Bond	Without rotational correction	With rotational correction
N_1–C_2	$1{\cdot}34_4$ Å	$1{\cdot}35_0$ Å
C_2–C_3	$1{\cdot}38_3$	$1{\cdot}38_9$
C_3–N_4	$1{\cdot}32_9$	$1{\cdot}33_1$
N_4–C_5	$1{\cdot}35_3$	$1{\cdot}35_5$
C_5–C_6	$1{\cdot}37_5$	$1{\cdot}37_7$
C_6–N_1	$1{\cdot}35_4$	$1{\cdot}35_6$
C_2–C_7	$1{\cdot}50_0$	$1{\cdot}50_3$
C_7–N_8	$1{\cdot}30_9$	$1{\cdot}31_2$
C_7–O_9	$1{\cdot}24_1$	$1{\cdot}24_4$
C_3–H_3	$1{\cdot}0_0$	
C_5–H_5	$1{\cdot}0_2$	
C_6–H_6	$0{\cdot}9_2$	
N_8–H_N'	$0{\cdot}8_7$	
N_8–H_N''	$0{\cdot}8_7$	

Angle	Without rotational correction	With rotational correction
$C_6N_1C_2$	115·4°	115·3°
$N_1C_2C_3$	121·9	121·9
$C_2C_3N_4$	122·6	122·5
$C_3N_4C_5$	116·0	116·0
$N_4C_5C_6$	121·4	121·6
$C_5C_6N_1$	122·4	122·4
$N_1C_2C_7$	117·2	117·2
$C_3C_2C_7$	120·9	120·9
$C_2C_7N_8$	117·5	117·5
$C_2C_7O_9$	119·1	119·1
$N_8C_7O_9$	123·2	123·1

The average angle for C–N–C is found to be 115·7°, which is also in good agreement with that found in pyrazine (Wheatley, 1957) and in other planar heterocyclic molecules containing nitrogen (Wright & King, 1953, 1954; Liquori & Vaciago, 1956*a*, *b*; Wheatley, 1955; Lancaster & Stoicheff, 1956; Bertinotti, Giacomello & Liquori, 1956). That this value is less than 120° is probably caused by the effect of the lone pair

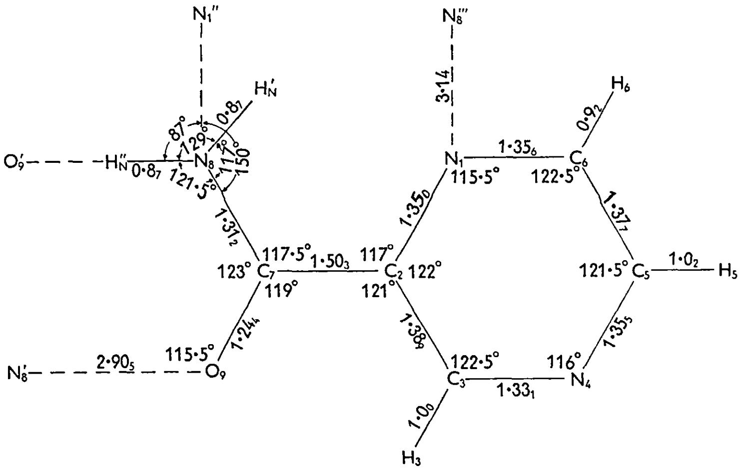

Fig. 3. Bond lengths (Å) and bond angles (°).

electrons of nitrogen to the hybridization (Hameka & Liquori, 1956).

The length of C_2–C_7 (1·50 Å) is somewhat less than the normal single C–C bond and it may indicate that there is some double bond character caused by the resonance between the amide group and the pyrazine ring.

Dimensions of the amide group found in the present investigation are close to those found in related compounds; for example, 1·31 Å for C–N, 1·24 Å for C–O in benzamide (Penfold & White, 1959) and 1·34 Å for C–N, 1·22 Å for C–O in nicotinamide (Wright & King, 1954).

It is pointed out that the positions of hydrogen atoms were determined directly from the difference maps projected on the two planes, and bond distances C–H are very reasonable, although their standard deviations are rather large (about 0·1 Å).

The plane of the pyrazine ring can be represented by the equation

$$z' = 0{\cdot}0490x' + 0{\cdot}4155y + 0{\cdot}1116\ ,$$

where x', y and z' are referred to the orthogonal axes a^*, b and c, so that $x' = x \sin\beta$ and $z' = z + x\cos\beta$, and the values of the coefficients were determined by means of the least squares. The perpendicular displacements of individual atoms from the mean plane, shown in Table 5, vary from 0·003 to 0·001 Å, and the mean value of these is 0·002 Å. As the standard deviations of the atomic coordinates is 0·007 Å as described above, these displacements are not significant, that is, the pyrazine ring is concluded to be planar.

Table 5. *The displacements of atoms from the mean plane*

Atom	Δ	Atom	Δ
N_1	0·001 Å	N_8	0·018 Å
C_2	−0·002	O_9	−0·131
C_3	0·003	H_3	−0·15
N_4	−0·003	H_5	0·16
C_5	0·002	H_6	0·05
C_6	−0·001	H_N	0·32
C_7	−0·014	H'_N	−0·03

On the other hand, the atoms in the amide group deviate significantly from the plane of the pyrazine ring, and the angle between the planes of the ring and the amide group is about 5°.

It was reported that in nicotinamide (Wright & King, 1954) and benzamide (Penfold & White, 1959) the ring plane makes an angle about 25° to the amide group. Penfold & White have explained that these facts are mainly caused by the interaction between hydrogen atoms attached to the amide group and to the atom in ortho position. This idea may interpret well the planarity of molecules in the crystals of nicotic acid (Wright & King, 1953) and benzoic acid (Sim, Robertson & Goodwin, 1955) whose molecules are very similar in shape to their amides.

In the present substance, there are no repulsive forces exerting as in nicotinamide and benzamide, because there are no hydrogen atoms attached to N_1 atom and the amino group is oriented on the same side of ring nitrogen N_1 with respect to the bond C_2–C_7. Therefore, it is reasonable that the molecule as a whole tends to be planar, stabilized by the conjugation between the pyrazine ring and the amide group.

The slight tilt of the amide group from the ring plane (about 5° above mentioned) seems to be due to the effects of the hydrogen bonding and other crystalline field.

In conclusion, it is pointed out that there are some characteristic features in the final difference map, as shown in Fig. 2(*b*). They are the negative regions with minimum of approximately $-0{\cdot}25$ e.Å^{-2} enclosed by the six-membered rings, the negative regions hold between two bonds in the amide group and the slightly positive regions ranging 0·1 to 0·3 e.Å^{-2} around the lines joining adjacent atoms. These features have been found by Cochran (1953) and Cruickshank (1956*c*, 1957*b*) in their detailed analyses on salicylic acid, naphthalene and anthracene, although full explanation has not yet been given.

(*b*) *Crystal structure*

The projections of the structure along the c and b axes are shown in Fig. 4.

The molecules are connected by NH–O hydrogen bonds, 2·90 Å, forming dimers across the centre of symmetry. There are, probably, NH–N hydrogen bonds, 3·14 Å, linking the dimers into endless chains extended along [011].

While one of the hydrogen bond angles C–N–O′ is of a reasonable value (122°), the other angle C–N–N″ (150°) is somewhat larger than the normal value. As seen from the final $(\varrho_o - \varrho_c)$ maps which are shown in Fig. 2, H'_N could be located considerably far from the line $N \cdots N''$, while H''_N lies on $N \cdots O'$. This NH–N hydrogen bond, therefore, is considered to be rather weak.

As mentioned above, this crystal consists of the endless chains linked by weak NH–N hydrogen bond and intermolecular contacts between these chains are slightly larger than the sum of the van der Waals radii. This structure well explains the presence of the cleavage on the (100) plane.

There seems to be at least two types of arrangements of molecules having an amide group in crystals. In the first type, molecules are connected to form chains extended along a certain direction, to which belongs benzamide (Penfold & White, 1959). α-pyrazinamide is confirmed to be of the same type. In the second type, there are two-dimensional sheets of molecules united by hydrogen bonds. Nicotinamide (Wright & King, 1954), formamide (Ladell & Post, 1954), tetradecanamide (Turner & Lingafelter, 1955), acrylamide and methacrylamide (Chatani, 1959) belong to this class. It is suggested that β-modification

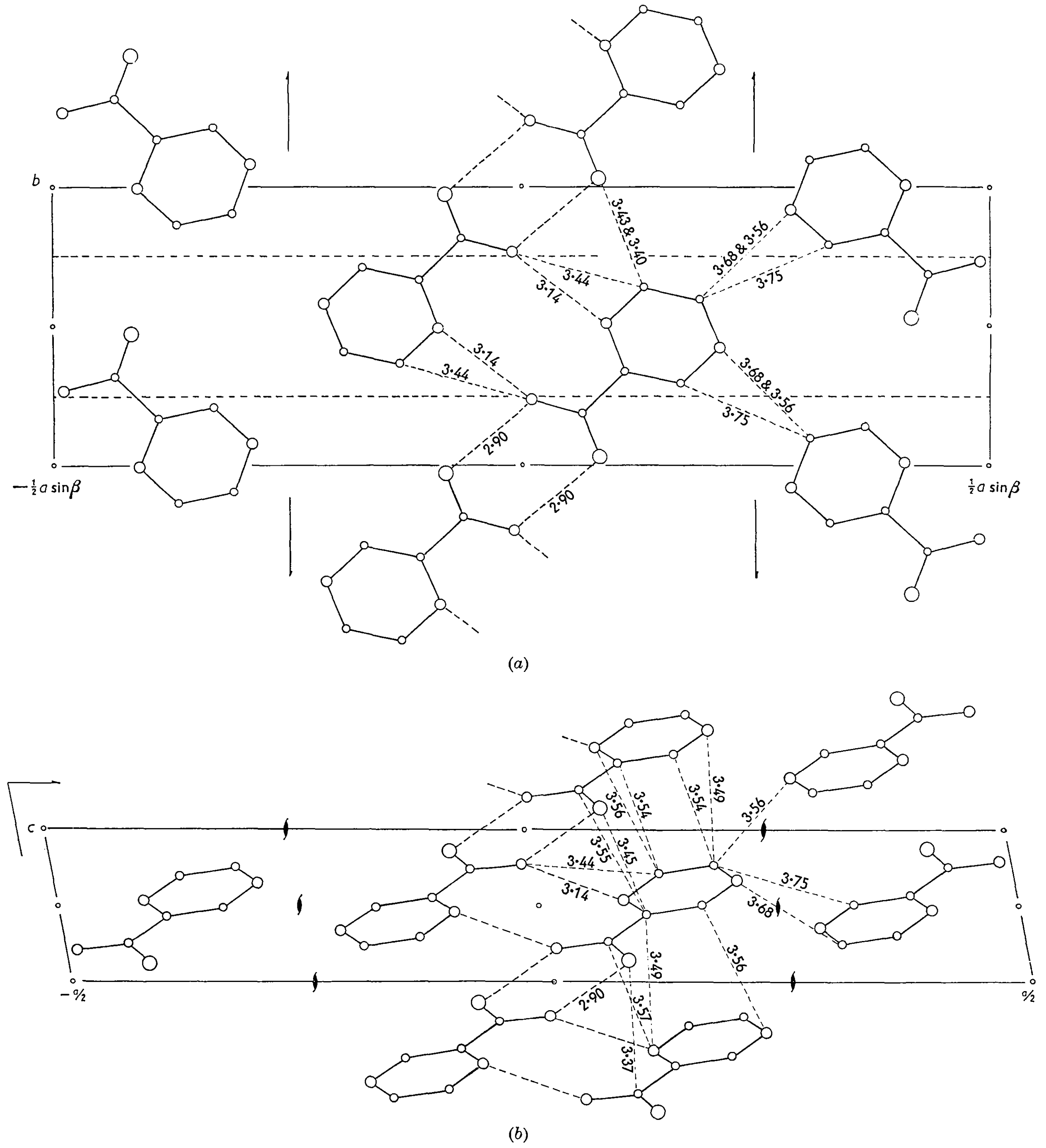

Fig. 4. Arrangement of molecules in the projections (*a*) along the *c* axis, (*b*) along the *b* axis, together with intermolecular distances (Å).

of pyrazinamide may have a two-dimensional sheet structure, belonging to the latter type.

(*c*) *Anisotropic thermal motion*

One out of six parameters which determine the ellipsoid of thermal motion of an atom can not be obtained from two projections. We have attempted to estimate these remained thermal parameters, one for each atom, from (0*kl*) reflexions*. However, the number of reflexions is too small to determine these

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* Intensity data of (0*kl*) planes were estimated from equi-inclination Weissenberg photographs of the *c*-axis rotation.

parameters separately. We have assumed that the direction of maximum vibration of each atom is normal to the molecular plane, as can be expected from the results of analyses on planar molecules by Cruickshank (1956*c*; 1957*a*, *b*).

From the analyses of the *b*- and *c*-axis projections, it was suggested that the direction of the maximum vibration of each atom lies in the (100) plane and is near the *c* axis, which is compatible with the assumption given above. Using this model, we have calculated structure factors $F(0kl)$ and found that the agreement with the observed values is fairly good. We have also calculated the structure factors with a model in which the maximum vibration occurs in the direction of [001]. Considerable change was not found, but the calculated structure factors based on the first model showed definitely better agreement.

Now we have obtained all the necessary data to apply Cruickshank's method (1956*a*) to derive molecular motions in the crystal. The sets of thermal parameters in Table 3 were transformed to U_{ij} referring to the orthogonal molecular axes l_1, l_2 and l_3, where l_1 passes through C_2 and C_5, transverse axis l_2 through C_2 in the molecular plane.

Table 6. *Values of* T_{ij} (*in* 10^{-2} Å^2) *and* ω_{ij} (*in* deg.^{2})

$$\mathbf{T} = \begin{pmatrix} 3\cdot93 & -0\cdot50 & 0\cdot06 \\ & 3\cdot64 & -0\cdot01 \\ & & 4\cdot70 \end{pmatrix} \qquad \omega = \begin{pmatrix} 32\cdot8 & 3\cdot8 & 0\cdot1 \\ & 4\cdot7 & 0\cdot6 \\ & & 6\cdot7 \end{pmatrix}$$

Assuming that the molecule is a rigid body, we have obtained from these U_{ij} the translational and rotational vibration tensors **T** and ω respectively. Since U_{33} for N_8 and O_9 calculated using these tensors were found, however, to differ significantly from the observed values, it was suggested that the assumption of the rigid body of the whole molecule might not quite fit to the actual circumstance. Therefore, **T** and ω were redetermined by excluding N_8 and O_9 from the least squares. The results are given in Table 6. The r.m.s. amplitudes of translational oscillation in the directions of the molecular axes, obtained from the square roots of the diagonal elements of **T**, are 0·20, 0·19 and 0·22 Å respectively. The corresponding r.m.s. amplitudes of angular oscillation obtained from ω are 5·7, 2·2 and 2·6°. Comparison between observed and calculated values for U_{ij} of each atom is shown in Fig. 5.

Within experimental errors the principal axes of ω coincide with the molecular axes. The greatest angular oscillation is about the long axis l_1 and the smallest one is about the short axis l_2. This feature of the angular oscillation is similar to those of naphthalene (Cruickshank, 1957*b*) and anthracene (Cruickshank, 1956*c*, 1957*a*). The centre of the angular oscillation coincides approximately with the mass centre of the molecule, suggesting that the effect of the hydrogen bonding NH–O is rather small. We can guess from the characteristics of anisotropic thermal motion that similar situation occurs in the case of benzamide (Penfold & White, 1959). If the linkage between two molecules forming a dimer is very strong, the centre of angular oscillation would be at the centre of the dimer. This is the case, for example, of salicylic acid (Cochran, 1953), where two molecules are linked by strong OH–O hydrogen bonds.

The thermal motions of nitrogen and oxygen in the amide group normal to the molecular plane are greater than those expected from the rigid body motion, as seen in Fig. 5. These large thermal motions would be explained probably by a torsional motion of the amide group about C_2–C_7, since the observed value of U_{33} for C_7 does not deviate from the calculated one.

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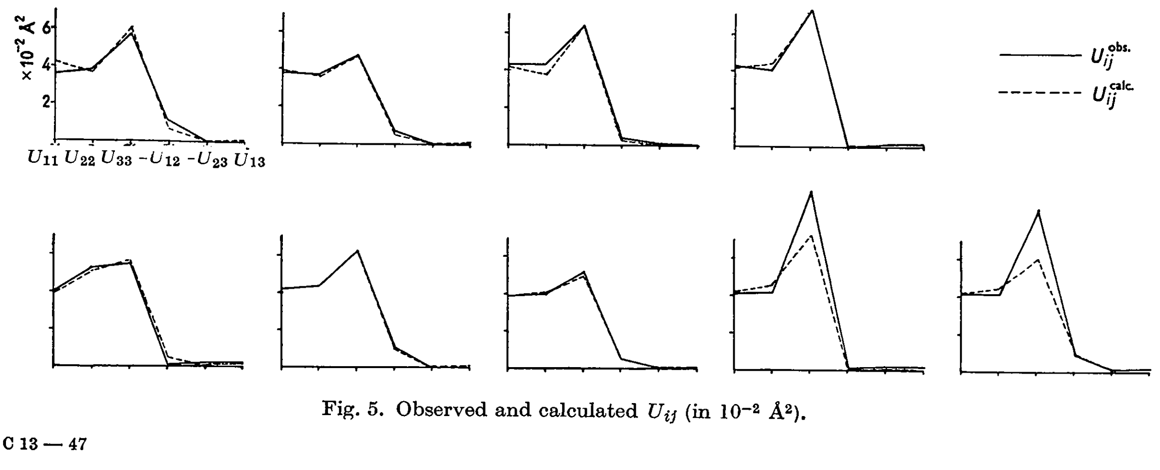

Fig. 5. Observed and calculated U_{ij} (in 10^{-2} Å^2).

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The Crystal and Molecular Structures of Overcrowded Halogenated Compounds. I. Introductory Survey

By G. Gafner and F. H. Herbstein

National Physical Research Laboratory, Council for Scientific and Industrial Research, Pretoria, South Africa

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Crystallographic data are reported for the α (stable below −85 °C.) and β phases of 1:2-4:5-tetrachlorobenzene, and for the β and γ (stable above 46 °C.) phases of 1:2-4:5-tetrabromobenzene; the relationship between X-ray diffraction and nuclear-quadrupole resonance measurements for these compounds is discussed. Crystallographic data are also given for chloranil, hexabromobenzene, 1:4-5:8-tetrachloronaphthalene and octachloronaphthalene.

1. Introduction

Although overcrowded aromatic hydrocarbons show large deviations from regular forms (Harnik, Herbstein, Schmidt & Hirshfeld, 1954), the details of the distortion in the overcrowded region are difficult to study because the positions of hydrogen atoms must be determined. When the overcrowded atoms are halogens this difficulty does not arise; in addition some molecules become overcrowded only when bulky halogens are substituted for hydrogen atoms. We have therefore begun a systematic study of molecules in which the overcrowded atoms are halogens in order to obtain information about the molecular shapes and the interactions among the various halogen atoms. In the present paper crystallographic data are given for various compounds of interest. Determinations of the crystal structures of some of these compounds will be reported in later papers of this series. The compounds investigated fall into two categories of the classification introduced by Harnik *et al.* (1954) viz. Group I, where the overcrowding is due to bulky substituents ortho to one another in a benzene ring; and Group IV, where the overcrowding is due to