clearly shown that this reaction is catalyzed by acids and bases, and thus one would expect lower activation energies (and higher rates for stress-relaxations) of samples contaminated with trace amounts of catalytically active materials.

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SCHENECTADY, N. Y.

[CONTRIBUTION FROM DEPARTMENT OF ANATOMY, SCHOOL OF MEDICINE, UNIVERSITY OF WASHINGTON]

The Crystal Structure of Isonicotinic Acid Hydrazide[1]

BY L. H. JENSEN

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The crystal structure of isonicotinic acid hydrazide has been solved by two-dimensional projections. Within the pyridine ring, the C–C bonds are all within experimental error of the expected values while the C–N bond lengths are somewhat less than the usually accepted value. The N–N bond length is within experimental error of the covalent radii sum (1.40 Å.) but considerably less than the value for hydrazine (1.46 Å.).

Isonicotinic acid hydrazide is the monosubstituted hydrazide of pyridine-4-carboxylic acid. This investigation was carried out to provide relatively accurate molecular parameters, bond lengths and angles, from the solid state structure of this biologically important compound.

Unit Cell and Space Group.—Crystals of isonicotinic acid hydrazide satisfactory for X-ray diffraction studies were supplied by E. K. Squibb & Co. Crystals of the same phase and habit grow from 95% ethanol as well developed needles elongated in the direction of the *c*-axis with {010} and {120} prominent.

The unit cell and space group were determined from equi-inclination Weissenberg and rotation photographs about the *a*- and *c*-axes using Cu K_α radiation (λ = 1.542 Å.). The dimensions of the orthorhombic unit cell were found to be: a_0 = 11.33 Å.; b_0 = 14.74 Å.; c_0 = 3.84 Å., with an error estimated as ±0.3%.

The density measured by flotation was found to be 1.411 g.cm.$^{-3}$; calculated, 1.420 g.cm.$^{-3}$ assuming 4 molecules in the unit cell. All (h00), (0k0) and (00l) reflections for odd h, k and l, respectively, were absent. Since no other systematic absences were found, the space group was assumed to be $P2_12_12_1$ with four asymmetric molecules lying in general positions.

Intensity Data.—Data were collected using a number of crystals of different size. The smaller crystals were used to minimize extinction effects, the larger to maximize the number of observed reflections. Crystals used for (hk0) were of fairly uniform cross-section, but for the other two axial zones it was necessary to cut the crystals to reduce absorption effects.

Some difficulty was experienced in obtaining consistent intensities for the most intense reflections from different crystals. Presumably the effect was due to extinction since it was dependent on the size and history of the crystal. One crystal was immersed repeatedly in liquid nitrogen; this reduced but did not eliminate the effect.

Several exposures using multiple films were taken for each of the three axial zones. The camera used was an integrating Weissenberg type[2] set to integrate along the film coördinate at right angles to the rotation axis. The optical density was measured on a Moll type microphotometer[3] feeding into a speedomax recorder by scanning along the film coördinate at right angles to the direction of integration by the camera. The integrated intensity was taken as proportional to the area under the curve of optical density *vs.* film coördinate within the linear response limits of the film used. For some of the weakest reflections, data were taken from unintegrated photographs, peak heights of the photometric tracings being assumed proportional to intensities. Of the 322 principal zone reflections accessible, 51 were too weak to observe even on prolonged exposure.

Intensities from the films for each axial zone were brought to an arbitrary scale by multiplying by appropriate scale factors, dividing by the Lorentz and polarization factors, and converted to relative values, $|F_r|$. Finally data for each zone were brought onto an absolute scale by multiplying by $\Sigma|F_c|/\Sigma|F_r|$.

In an earlier communication it was reported that Wilson's method of putting the hk0 intensities on an absolute scale yielded values which were too high.[4] That result was partly due to a pair of errors. A plot of the eye estimated data for $\sin\theta < 0.75$ indicates a negligible temperature factor and a scale factor high by *ca.* 1.7 instead of *ca.* 3 as reported. However, a similar plot using integrated intensities for the *complete* range accessible to Cu K_α radiation results in a temperature factor of expected magnitude and a scale factor within 10% of the final value. Calculation of the root-mean-square unitary structure factors including the temperature factor and consideration of the number of unobserved reflections for the eye estimated data accounts satisfactorily for the difficulties noted in the early data.

Scattering factors as listed by McWeeny[5] were used in calculating structure factors, F_c. An isotropic temperature factor, $e^{-B\sin^2\theta/\lambda^2}$ was assumed for F_{hk0} and an anisotropic factor, $e^{-(B + C\cos^2\phi)\sin^2\theta/\lambda^2}$,[6]

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[1] Presented at the 124th meeting of the American Chemical Society, Sept., 1953.

[2] E. H. Wiebenga and D. N. Smits, *Acta Cryst.*, **3**, 265 (1950).

[3] H. S. Bennett, *et al.*, *Applied Spectroscopy*, **7**, No. 3 (1953).

[4] L. H. Jensen, *Nature*, **171**, 217 (1953).

[5] R. McWeeny, *Acta Cryst.*, **4**, 513 (1951).

[6] L. Helmholz, *J. Chem. Phys.*, **4**, 316 (1936).

for F_{0kl} and F_{h0l} where $B = 2.0$ Å.^{2}, $C = 1.5$ Å.^{2}, ϕ = angle between normal to the plane and c-axis.

Determination of the Structure.—From the dimensions of the unit cell, it was apparent that a projection on (001) would show the atoms well resolved. An unsuccessful attempt was made to solve this projection by the method proposed by Zachariasen.[7] A Patterson projection on (001), Fig. 1, showed at once the orientation of the ring. The approximate position of the molecule was clearly indicated from packing considerations and the magnitude of a few low index F's, *e.g.*, F_{200}, F_{210}, F_{110}, F_{120}. A molecular model with bond lengths of *ca* 1.4 Å. and bond angles of 120° in the approximate position and orientation indicated determined the signs of enough F's to lead to the correct projection on (001). Reasonable x and y coördinates for H_1, H_2, H_3, H_5 and H_6 were assigned assuming the atoms to which they are bonded to be trigonal with C–H and N–H bond lengths of 1.0 Å. This projection was refined by a series of F_0 syntheses.

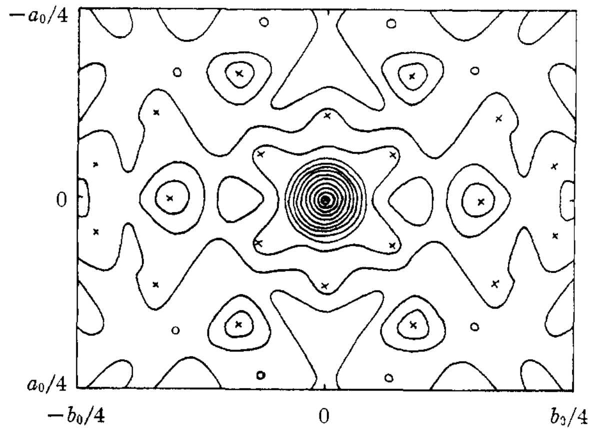

Fig. 1.—Patterson projection on (001); contours at arbitrary intervals, peaks indicated by ×.

The projection on (001) indicated that the long axis of the molecule was inclined at 20–30° to (001). An angle of 25° was assumed and z-coördinates assigned to make the calculated value of F_{021} approximate that observed. With these values of z and y coördinates from the projection on (001), F_{0kl} were calculated and several F_o syntheses on (100) were evaluated. The atoms were, however, unresolved in pairs and no accurate values for the z-coördinates could be determined. Next, F_o syntheses on (010) were computed. In this projection seven of the ten heavier atoms in the molecule were sufficiently well resolved to permit reasonable evaluation of their z-coördinates. Projections of the electron density on (100), (010) and (001) are shown in Fig. 2.

The structure was further refined by a series of $F_o - F_c$ syntheses. Corrections from these difference syntheses were taken as[8]

$$\delta x_i = \delta(\rho_o - \rho_c)/\delta x_i/C(\rho_o)$$

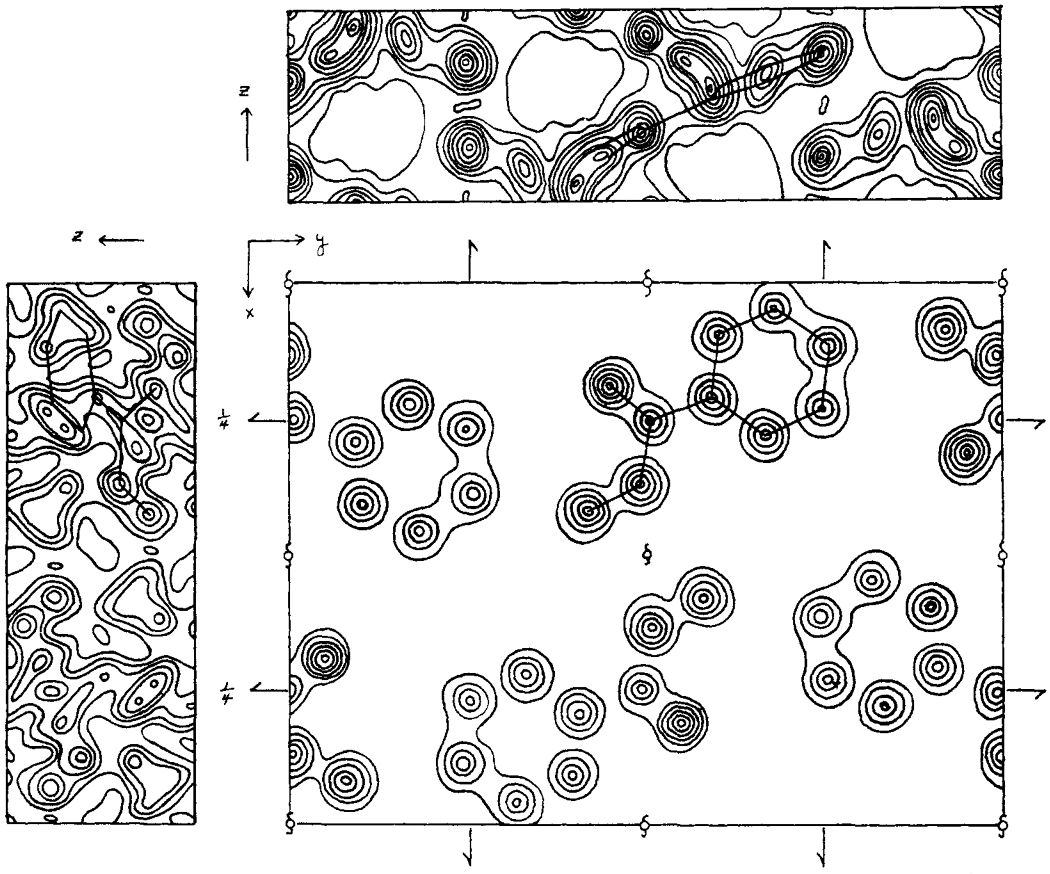

Fig. 2.—Projection of electron density on (100), (010) and (001): contours at even integral values of eÅ.$^{-2}$ with omission of zero contour.

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[7] W. H. Zachariasen, *Acta Cryst.*, **5**, 68 (1952).

[8] W. Cochran, *ibid.*, **4**, 408 (1951).

Final corrections for x- and y-coördinates were taken from the fourth difference synthesis on (001); final corrections for z-coördinates were taken as the average of the corrections from the seventh difference syntheses on (100) and (010). Difference syntheses from which the final corrections to the coördinates were made are shown in Figs. 3, 4 and 5.

Approximate x- and y-coördinates for H_4 and H_7 were determined from the first difference synthesis on (001); subsequent syntheses were used to correct these coördinates and the x- and y-coördinates of H_1. Reasonable z-coördinates for all hydrogens were assigned on the basis of their x- and y-coördinates and an assumed C–H and N–H bond length of 1.0 Å. Table I lists the observed structure factors, F_o, and the final F_c.[9]

TABLE II

ATOMIC PARAMETERS

	x/a_0	y/b_0	z/c_0
C_1	0.2554	0.5045	0.3755
C_2	.2289	.7431	.7469
C_3	.2806	.6660	.6021
C_4	.2112	.5912	.5232
C_5	.0899	.5995	.5885
C_6	.0464	.6798	.7255
O	.1900	.3501	.2268
N_1	.1130	.7518	.8005
N_2	.3716	.4917	.3969
N_3	.4254	.4162	.2352
H_1	.438	.537	.510
H_7	.419	.359	.406
H_5	.039	.539	.526
H_6	.955	.685	.776
H_3	.368	.661	.534
H_2	.279	.803	.807
H_4	.365	.402	.047

TABLE III

BOND LENGTHS, Å.

C_1–C_4	1.485
C_2–C_3	1.394
C_3–C_4	1.388
C_4–C_5	1.403
C_5–C_6	1.385
C_1–O	1.234
C_1–N_2	1.332
C_2–N_1	1.335
C_6–N_1	1.334
N_2–N_3	1.413
N_2–H_1	1.10
N_3–H_7	1.07
N_3–H_4	1.02
N_2–H_1---N_3	2.97
N_3–H_7---N_1	3.04

TABLE IV

BOND ANGLES, DEGREES

N_2–C_1–O	122.0	C_1–C_4–C_5	118.3
C_6–N_1–C_2	116.5	C_1–N_2–N_3	120.7
N_1–C_2–C_3	123.6	C_1–N_2–H_1	128
C_2–C_3–C_4	119.8	N_3–N_2–H_1	112
C_3–C_4–C_5	116.5	N_2–N_3–H_7	109
C_4–H_5–C_6	119.4	N_2–N_3–H_4	101
C_5–C_6–N_1	124.1	H_7–N_3–H_4	98
C_3–C_4–C_1	125.2	N_2–H_1---N_3	165
C_4–C_1–O	122.2	N_3–H_7---N_1	173
C_4–C_1–N_2	115.5		

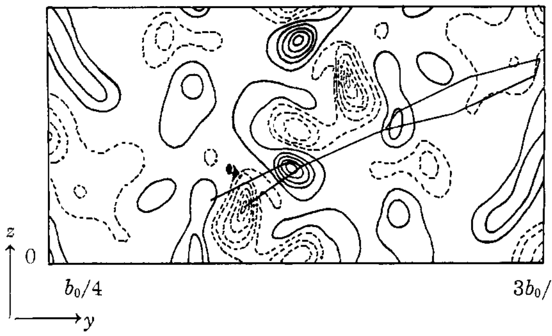

Fig. 3.—F_o–F_c synthesis on (100): contours at intervals of 0.25 eÅ.$^{-2}$, zero contour omitted, negative contours broken.

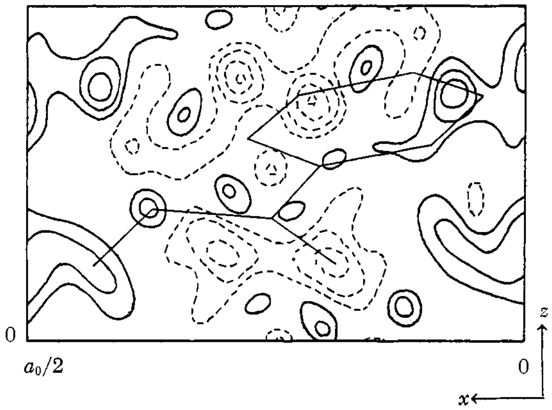

Fig. 4.—F_o–F_c synthesis on (010): contours at intervals of 0.25 eÅ.$^{-2}$, zero contour omitted, negative contours broken.

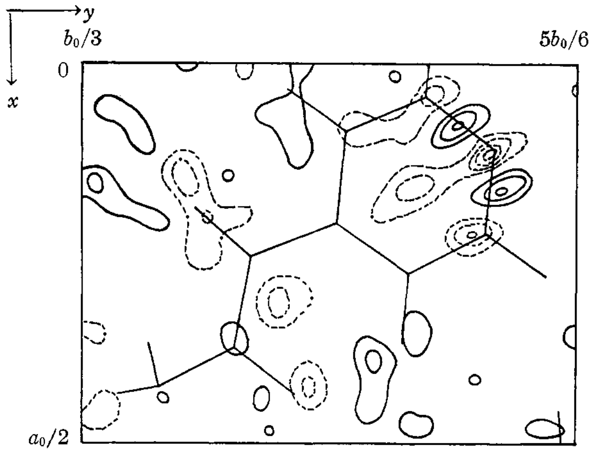

Fig. 5.—F_o–F_c synthesis on (001): contours at intervals of 0.25 eÅ.$^{-2}$, zero contour omitted, negative contours broken.

From the final parameters listed in Table II, the bond lengths and angles of Tables III and IV were computed. The structural formula for isonicotinic acid hydrazide with bond lengths and angles indicated is shown in Fig. 6.

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[9] For the sake of brevity, Table I has been omitted. A copy may be obtained by application to the author.

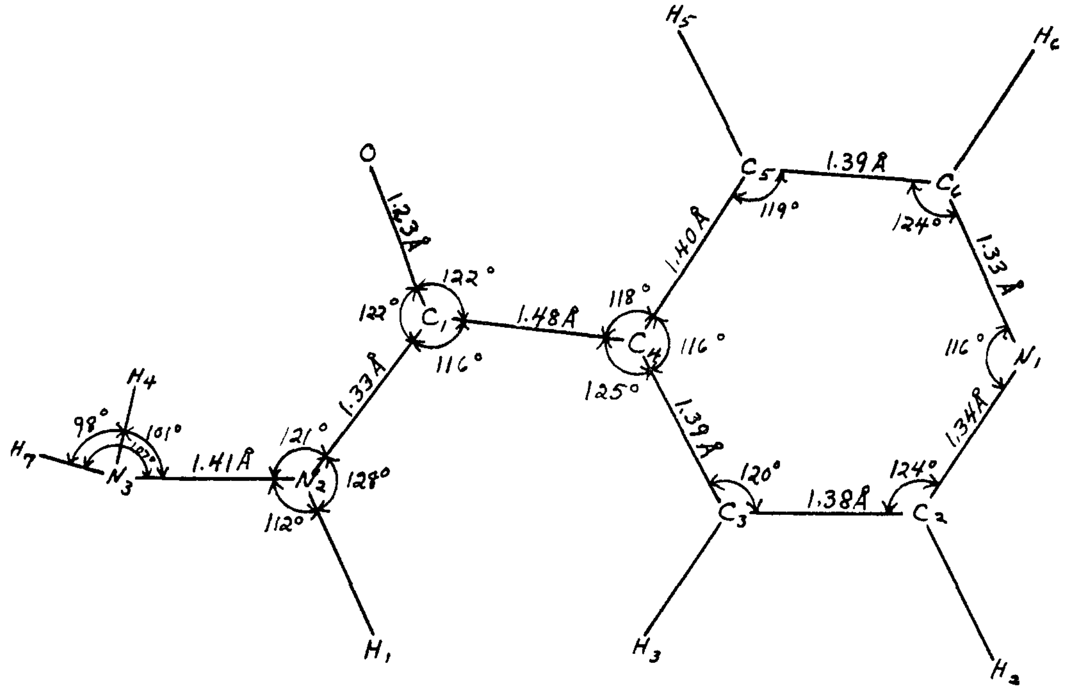


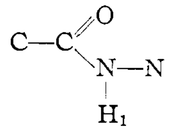
Fig. 6.—Structural formula of isonicotinic acid hydrazide.

The value of the reliability index, $R = \Sigma||F_o| - F_c||/\Sigma|F_o|$ is 9.6, 11.7 and 11.6%, respectively, for (0*kl*), (*h*0*l*) and (*hk*0) including the unobserved *F*'s at half their maximum possible value. Neglecting the unobserved reflections, the corresponding values of *R* are 8.7, 10.5 and 10.8%.

Discussion

The C–C bond lengths in the pyridine ring are within experimental error of the value to be expected, and the average value of 1.392 Å. agrees well with the average value of 1.385 Å. for the corresponding bonds in nicotinic acid.[10] The C–N bond lengths in the ring are close to 1.34 Å. found in nicotinic acid, but somewhat below 1.37 Å. calculated from the electron diffraction value for the average bond length in the pyridine ring[11] and 1.36 Å. based on bond order of Longuet-Higgins and C–N bond lengths of Cox and Jeffrey.[12,13] The C_1–C_4 bond length of 1.48 Å. is significantly less than the C—C bond length in diamond. Other recent values for similar bonds are 1.48 Å. in nicotinic acid and 1.46 Å. in salicylic acid.[14] The N–N bond length is within experimental error of the radii sum (1.40 Å.,[15]), of 1.40–1.42 Å. in $N_2H_6^{++}$ [16–19] and 1.42 Å. (preliminary value),[20] in *n*-heptanoic acid hydrazide, but significantly less than 1.45 Å. in $N_2H_5^{+}$ [21] or 1.46–1.47 Å. in hydrazine.[22,23] It is to be expected that the N–N bond length in isonicotinic acid hydrazide would be less than in hydrazine because of appreciable s character of the bond. In addition, the formal charge effect and the decrease of repulsion between the unshared pairs of electrons on the N's would tend to shorten further the N–N bond. The C_1–N_2 bond length is almost identical with the C–N bond lengths within the ring. Thus this bond would have *ca.* 50% double bond character. The C_1–O bond length is within experimental error of its expected value.

Bond angles within the pyridine ring agree well with the corresponding angles in nicotinic acid, the average difference being 1.3°. The difference of $\angle C_3C_4C_1$ and $\angle C_4C_1N_2$ from 120° may be attributable to steric effects. While $\angle C_1N_2N_3$ is 121°, $\angle H_1N_2C_1$ is 128° and is accounted for by the stronger hydrogen bond that results. N_3 is pyramidal with the substituents making angles of 109, 101 and 98° with each other.

The  $\mathrm{C{-}C({=}O){-}N(H_1){-}N}$ group is nearly planar, C_4, N_3 and H_1 lying, respectively, 0.09, 0.06 and 0.05 Å. from the plane determined by O, C_1 and N_2. Thus the bonds to C_1 and N_2 are nearly coplanar. The ring atoms of molecule I, Fig. 7, lie close to the plane $-0.1383x + 0.3744y - 0.9620z - 1 = 0$ Their average deviation from this plane is 0.008 Å., C_3 and N_1 are, respectively, 0.011 and 0.014 Å. from it and below, C_2 is 0.016 Å. from it and above. N_1

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[10] W. B. Wright and G. S. D. King, *Acta Cryst.*, **6**, 305 (1953).

[11] V. Schomaker and L. Pauling, THIS JOURNAL, **61**, 1769 (1939).

[12] E. G. Cox and G. A. Jeffrey, *Proc. Roy. Soc.* (*London*), **A207**, 110 (1951).

[13] H. C. Longuet-Higgins and C. A. Coulson, *Trans. Faraday Soc.*, **43**, 87 (1947).

[14] W. Cochran, *Acta Cryst.*, **6**, 260 (1953).

[15] L. Pauling, "Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1940, p. 164.

[16] I. Nitta, K. Sakurai and Y. Tomiie, *Acta Cryst.*, **4**, 289 (1951).

[17] M. L. Kronberg and D. Harker, *J. Chem. Phys.*, **10**, 309 (1942).

[18] R. W. G. Wyckoff, *Am. J. Sci.*, **5**, 15 (1923).

[19] J. Donohue and W. N. Lipscomb, *J. Chem. Phys.*, **15**, 115 (1947).

[20] L. H. Jensen and E. C. Lingafelter, *Acta Cryst.*, **6**, 300 (1953).

[21] K. Sakurai and Y. Tomiie, *ibid.*, **5**, 289 (1952).

[22] R. L. Collin and W. N. Lipscomb, *ibid.*, **4**, 10 (1951).

[23] P. A. Giguere and V. Schomaker, THIS JOURNAL, **65**, 2025 (1943).

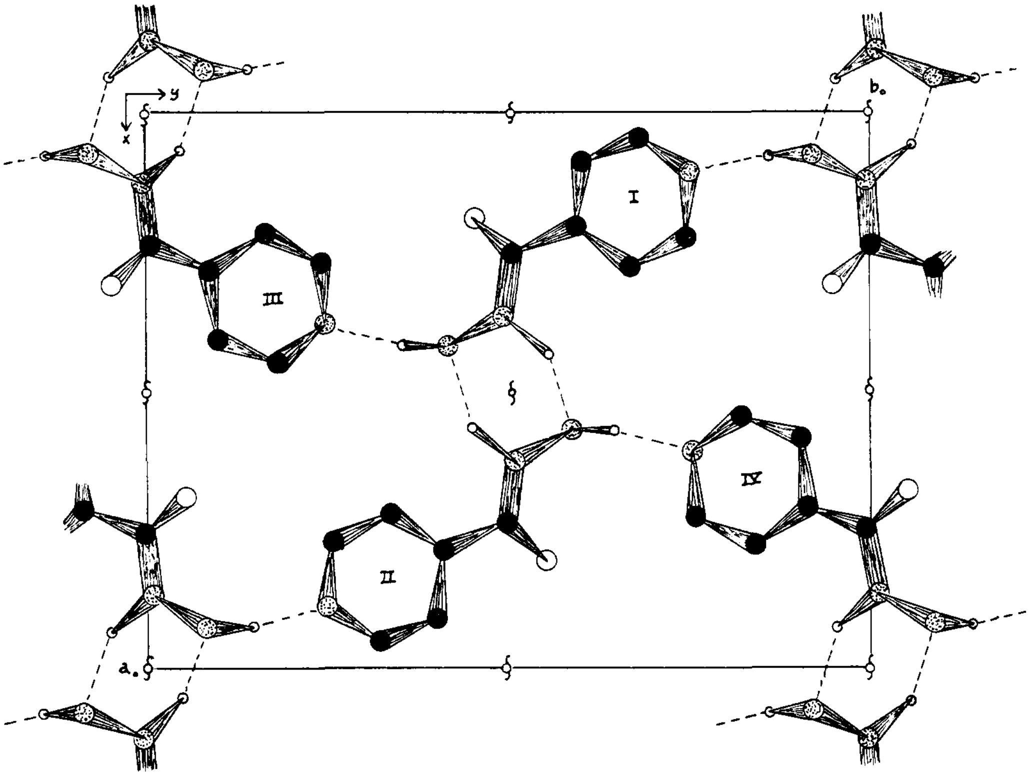

Fig. 7.—Projection of structure on (001) showing system of hydrogen bonds.

and C_3 might be expected to deviate somewhat from the best plane through the ring atoms due to the distorting forces of the hydrogen bond in which N_1 is involved and steric forces between H_3 and H_1.

The two types of intermolecular -N-H---N- bonds present in the structure are shown in Fig. 7. One type links N_2 of molecule I with N_3 of molecule II; N_2 of molecule II with N_3 of molecule I′ above molecule I. Hence, about lines ($x = 0, y = 0$) and ($x = {}^1/_2, y = {}^1/_2$) infinite spirals of molecules result. The other and weaker type is between N_3 of molecule I and N_1 of molecule III.

Difference syntheses show in the limit the difference between the observed electron density

$$\rho_o = \frac{1}{A} \sum_h \sum_k F_{hk0} \cos 2\pi(hx + ky - \alpha_{hk0})$$

for projections on (001), and the assumed electron density used in calculating the structure factors, F_c. Thus approximately for finite series positive regions indicate electron density greater than that assumed, negative regions, electron density less than assumed.

Inspection of the difference syntheses show quite large values of $\rho_o - \rho_c$. Figure 5 shows some notable differences. The scattering factor for oxygen for this projection, as for the other two, is clearly anisotropic. This probably arises from vibration and would indicate the direction of maximum vibration in projection on (001) essentially at right angles to the C_1–O bond. This projection also shows an excess of about ${}^1/_4$ electron in each C–N bond of the pyridine ring with a considerable deficiency at C_2 and C_6 and a somewhat larger deficiency at N_1. This could be explained as resulting from anisotropic thermal vibration of these three atoms with the maximum in the direction of a line through C_2 and C_6. It is possible, however, that the excess of electrons in the C–N bonds is not due to vibration but is a feature of the electronic distribution about N_1 that results in the abnormally weak basic character of pyridine. The nature of the electronic distribution about N_1, C_2 and C_6 is being studied further.

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SEATTLE, WASHINGTON