Acta Cryst. (1954). 7, 283

The Crystal Structure of Nicotinamide

By W. B. Wright and G. S. D. King*

The Lyons Laboratories, Hammersmith Road, London W. 14, England

(*Received 5 October* 1953)

The crystal structure of nicotinamide has been determined by two- and three-dimensional X-ray methods. The atomic positions obtained from Fourier projections were refined by three-dimensional differential Fourier syntheses, and by the method of steepest descents using LEO, the Lyons electronic calculator. The bond lengths, determined with a probable error of 0·012 Å are: pyridine ring C–C = 1·40 Å, C–N = 1·36 Å, amide group C_2–C_6 = 1·52 Å, C_6–N_2 = 1·34 Å, C_6–O = 1·22 Å. Each molecule is linked by two weak hydrogen bonds from its amide nitrogen atom to the oxygen atom of one neighbouring molecule and to the ring nitrogen atom of another, in such a way that two-dimensional networks parallel to (010) are formed.

Introduction

Nicotinamide, 3-pyridine carboxamide, was investigated simultaneously with its parent acid, nicotinic acid, in the belief that their crystal structures would prove to be very similar, and so that some comparison of the bond-length determinations in the pyridine ring, for the two substances, could be obtained. It very soon became apparent, however, that the two crystal structures were quite different, and they were, therefore, studied independently and by different methods. The optical properties, unit-cell dimensions and space group of nicotinamide were reported in a preliminary paper (Wright & King, 1950); the present communication describes the determination of the structure by Fourier projections and its subsequent refinement by three-dimensional differential syntheses and by the application of the method of steepest descents.

Experimental

Nicotinamide crystallizes from most common solvents in the monoclinic system with unit-cell dimensions

$$a = 9{\cdot}435\pm0{\cdot}001,\ b = 15{\cdot}65\pm0{\cdot}01,\ c = 3{\cdot}974\pm0{\cdot}001\ \text{Å},\ \beta = 99°8'\pm5'$$

and in the space group $P2_1/a$. Multiple-film equi-inclination Weissenberg photographs were taken about the $a(h = 0 \rightarrow 4)$, $b(k = 0 \rightarrow 6)$, $c(l = 0 \rightarrow 1)$, $[\bar{1}02](h+2l = 0 \rightarrow 5)$ and $[102]$ $(h-2l = 0 \rightarrow 5)$ axes using copper radiation. In this way all but 10 of the 1311 reflexions within the limiting sphere for copper $K\alpha$ radiation could have been recorded, but 362 of the reflexions were too weak to be observed. The intensities were estimated visually by comparison with a set of standard spots. As the crystals were tabular on (010), but less than 0·5 mm in diameter, a correction was made for variations in spot shape (Broomhead, 1948), but no correction was made for absorption. Lorentz and polarization corrections were applied, using the method of Goldschmidt & Pitt (1948). The intensities of some of the strongest reflexions were estimated from powder photographs.

Determination of the structure

The c-axis projection

The small c dimension of the unit cell combined with the space group $P2_1/a$ make overlapping of the nicotinamide molecules in the c direction improbable. It was thought, therefore, that the best preliminary picture of the structure would be obtained from a c-axis Fourier projection. A trial position of the molecule for this projection was obtained from the c-axis Patterson projection (Fig. 1).

For any peak with coordinates (x, y) in the Fourier projection the space group $P2_1/a$ requires an intermolecular peak at the point $(2x, 2y)$ in the Patterson projection, with related peaks of double weight at points $(\frac{1}{2}-2x, \frac{1}{2})$ and $(\frac{1}{2}, \frac{1}{2}-2y)$. Such groups of related peaks are $F\,P\,R$, $L\,I\,P$, $Q\,H\,P$ and $I\,R\,O$, of which F, L, Q and I respectively may be represented by $(2x, 2y)$ and could be due to vectors between the centres of pyridine rings. A, B, C, D, E and G were considered to be due to intramolecular vectors.

The optical properties indicate that the pyridine ring is inclined at 66½° to the c axis. Using this information in conjunction with standard bond lengths and bond angles, and assuming that the molecule is planar, a c-axis projection of the molecule was drawn. The centre of the pyridine ring of this model was placed on a c-axis projection of the unit cell at each of the four positions corresponding to the vector triplets in the Patterson projection. In each of these

---

* Present address: Birkbeck College Research Laboratory, 21 Torrington Square, London W. C. 1, England.

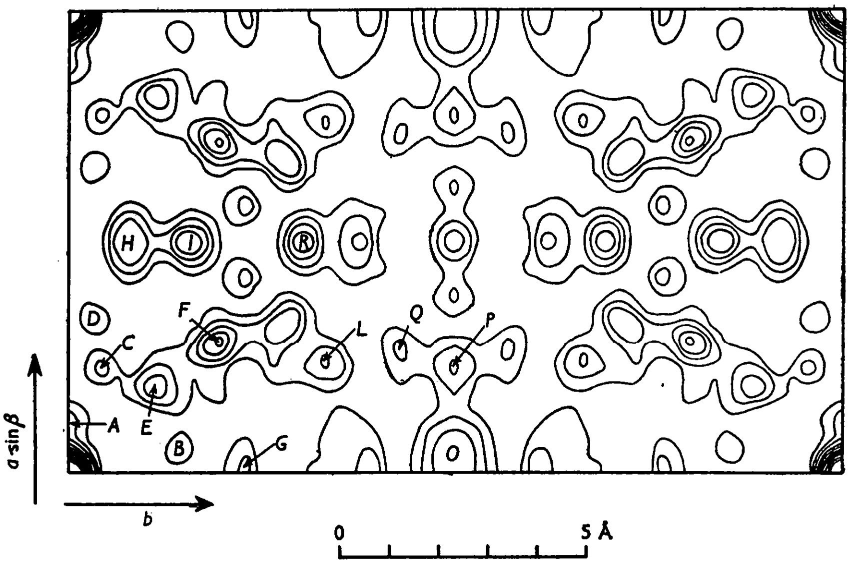

Fig. 1. The c-axis Patterson projection.

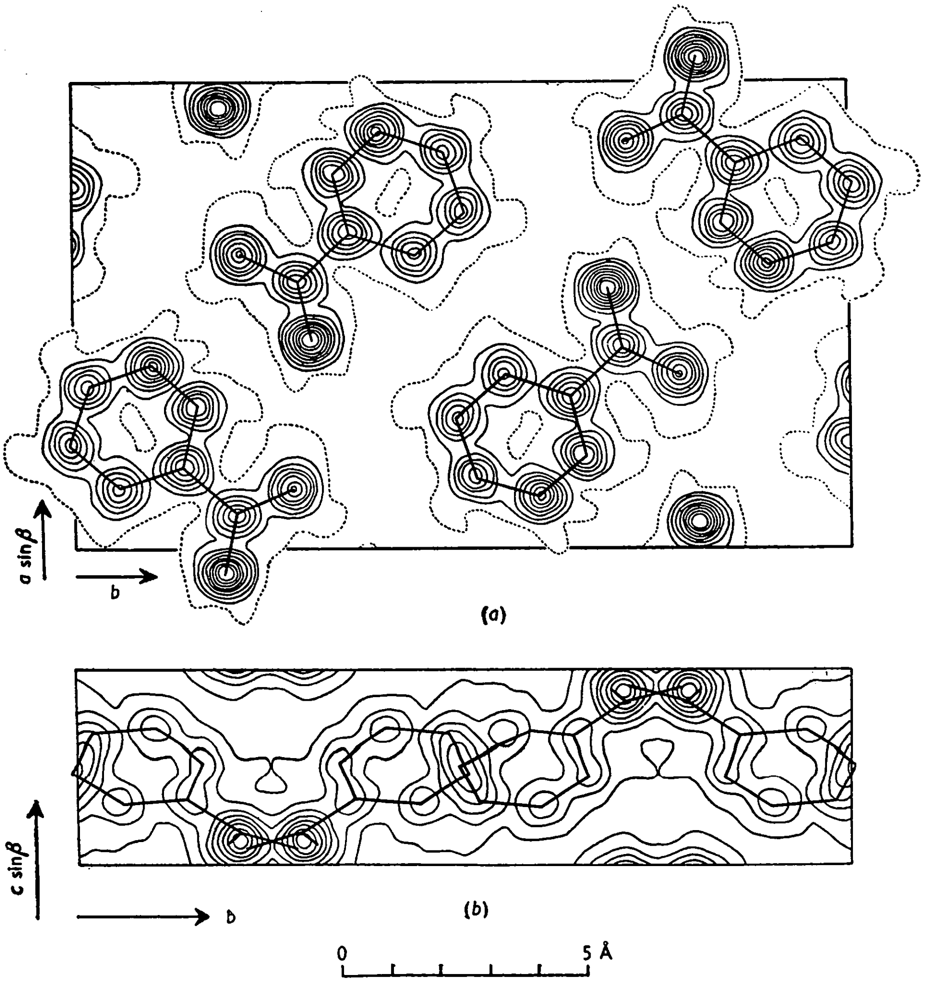

Fig. 2. (a) The c-axis Fourier projection; contours at intervals of 1 e.Å^{-2} starting at 1 e.Å^{-2} (broken line). (b) The a-axis Fourier projection; contours at intervals of 2 e.Å^{-2}.

positions the molecule was oriented so that the Patterson peaks A, B, C, D, E and G corresponded to intramolecular vectors. The $h00$ and $0k0$ structure factors were calculated for each of those orientations that were compatible with the packing of the molecules in the unit cell. The best agreement between the observed and calculated structure factors was obtained in the position corresponding to the triplet $I\,R\,O$. This agreement was improved by making the amide group normal to the plane of the pyridine ring instead of coplanar with it. A Fourier projection was calculated using strong low-order terms only, and from this it was apparent that the amide group was approximately in the plane of the pyridine ring. There are two positions in the ring which can be occupied by the nitrogen atom, and associated with each of these two possibilities are two alternative positions for the nitrogen of the amide group, making four possible orientations in all. In the course of the refinement of this projection by means of nine Fourier syntheses, the identities of the atoms were established beyond doubt. The x and y coordinates of the atoms were corrected for termination-of-series errors by means of an F_c synthesis, and the structure factor disagreement $R = \Sigma||F_o|-|F_c|| \div \Sigma|F_o|$ obtained at this stage was 20·6%. The c-axis Fourier projection based on the final atomic coordinates obtained from the three-dimensional analysis is shown in Fig. 2(a).

The a-axis projection

The inclination of the molecular plane obtained from the optical data was used, together with the x and y coordinates of the atoms calculated from the c-axis projection, to construct a projection of the molecule normal to the a axis. The projected molecule was then moved in the c direction until the calculated $00l$ structure factors were in the best agreement with the observed values. The $0kl$ structure factors were calculated and a Fourier projection normal to the a axis was computed; R was 45%. This projection gave some degree of confirmation to the z coordinates assumed for the atoms in the pyridine ring but no information about the other atoms, owing to the considerable amount of overlap. The a-axis projection computed from the final atomic coordinates obtained from the three-dimensional analysis is shown in Fig. 2(b).

The three-dimensional analysis

To refine a structure by differential Fourier synthesis (Booth, 1946) it is necessary that the initial errors in atomic positions shall be less than

$$\left(-\frac{\varrho_o}{2d^2\varrho/dr_o^2}\right)^{\frac{1}{2}}$$

where ϱ_o and $d^2\varrho/dr_o^2$ are the electron density and its

Table 1. *Refinement of atomic parameters*

(Atomic coordinates expressed as fractions of the cell edges.)

		(1)	(2)	(3)	(4)
Atom	Parameter	Coordinates from Fourier projections	z coordinates from line syntheses	Coordinates from 6th differential Fourier iteration	Final coordinates from 4th steepest descents iteration
C_1	x	0·304	—	0·3058	0·3054
	y	0·159	—	0·1602	0·1626
	z	0·521	0·529	0·5349	0·5329
C_2	x	0·177	—	0·1734	0·1735
	y	0·142	—	0·1418	0·1420
	z	0·311	0·338	0·3440	0·3420
C_3	x	0·128	—	0·1296	0·1270
	y	0·057	—	0·0577	0·0572
	z	0·328	0·326	0·3211	0·3185
C_4	x	0·221	—	0·2206	0·2192
	y	0·995	—	0·9958	0·9934
	z	0·460	0·474	0·4792	0·4788
C_5	x	0·347	—	0·3487	0·3507
	y	0·018	—	0·0194	0·0188
	z	0·663	0·662	0·6622	0·6642
C_6	x	0·073	—	0·0699	0·0707
	y	0·207	—	0·2084	0·2093
	z	0·150	0·159	0·1665	0·1660
N_1	x	0·394	—	0·3931	0·3948
	y	0·102	—	0·1013	0·1008
	z	0·674	0·689	0·6909	0·6916
N_2	x	0·127	—	0·1273	0·1287
	y	0·283	—	0·2819	0·2830
	z	0·150	0·122	0·0939	0·0864
O	x	0·945	—	0·9444	0·9436
	y	0·193	—	0·1923	0·1918
	z	0	0·062	0·1023	0·1036

second differential at the centre of the atom respectively. In the case of nicotinamide it was estimated that the maximum permissible error was 0·22 Å, corresponding to an error of 0·055 in the z coordinates. It was therefore considered advisable to obtain the z coordinates for the atoms by line syntheses in the c direction.

The *hkl* structure factors were calculated using the assumed z coordinates, the x and y coordinates from the c-axis refinement and unitary scattering factors which were weighted means of the values for C, N and O given by Viervoll & Ögrim (1949). The signs of these structure factors were used with the observed magnitudes to compute line syntheses parallel to the c axis at the nearest 1/60th intervals in the x and y directions to the centre of each atom. These syntheses were computed using Beevers–Lipson strips. The initial coordinates and the new z coordinates obtained are shown in columns (1) and (2) respectively of Table 1.

The new z coordinates, together with the x and y coordinates, were taken as the starting point of an iterative differential refinement using LEO, the Lyons electronic calculator (Thompson *et al.*, 1954). The limit of the refinement was set at a maximum change in any coordinate corresponding to an atomic shift of 0·001 Å, i.e. 0·0006 in x, 0·0004 in y and 0·0015 in z. This low limit was set to guarantee complete refinement, even if convergence was slow. In fact, convergence was rapid and in view of series-termination errors a limit of 0·005 Å would have sufficed. Six iterations taking 35 min. each were required to reach the set limit and the final coordinates obtained are shown in column (3) of Table 1. These coordinates were used to calculate a new set of *hkl* structure factors, the calculations being done using desk machines, as LEO's high speed output facilities were not, at that time, available. An anisotropic temperature factor of the form $\exp[-4{\cdot}12(\sin\theta/\lambda)^2+0{\cdot}00447\,h^2]$ was calculated by the method of least squares and used to obtain a new set of unitary scattering factors.

These scattering factors were used, together with the final coordinates obtained from the differential Fourier syntheses and the observed structure amplitudes, in a further iterative refinement by the method of steepest descents (Qurashi, 1949), adapted for use with LEO (Thompson *et al.*, 1954). The changes in coordinates produced by the fourth iteration were all less than 0·001 Å. The structure factors calculated for the fourth iteration were recorded on magnetic tape for subsequent printing, a process which increased the time taken for one iteration, which was 40 min., by about 10 sec. These calculated structure factors, together with the observed values, are given in Table 2*. The final coordinates obtained from the refinement by the method of steepest descents are shown in column (4) of Table 1 and for these coordinates

$$R_{hkl} = 19{\cdot}0\%,\ R_{hk0} = 20{\cdot}5\%,\ R_{h0l} = 13{\cdot}6\%,\ R_{0kl} = 14{\cdot}0\%,$$

excluding terms too weak to be observed.

Description of the structure

Bond lengths and interatomic distances calculated from the final atomic coordinates are shown in Table 3 and bond angles in Table 4. A diagram of the molecule is shown in Fig. 3 and a clinographic projection of half the unit cell in Fig. 4. Molecule M is related to M' by the screw axis at $(\frac{1}{4}, y, 0)$, to M'' by the symmetry centre $(\frac{1}{2}, \frac{1}{2}, \frac{1}{2})$, to M''' by the glide plane $(x, \frac{1}{4}, z)$ and to ${}_xM$ and ${}_zM$ by unit translations in the x and z directions respectively. Molecules M' and M'' are omitted from Fig. 4 for clarity. The pyridine ring is planar and its equation, determined by the method of least squares, is

$$-9{\cdot}6759x+2{\cdot}9792y+6{\cdot}5332z = 1\ .$$

Table 3. *Interatomic distances*

Intramolecular bond lengths

Bond	Length	Standard deviation of bond length
N_1–C_1	1·370 Å	0·017 Å
C_1–C_2	1·388	0·017
C_2–C_3	1·397	0·018
C_3–C_4	1·409	0·020
C_4–C_5	1·396	0·020
C_5–N_1	1·349	0·018
C_2–C_6	1·524	0·017
C_6–N_2	1·336	0·019
C_6–O	1·217	0·014

Intermolecular distances

N_2–O'''	2·987 Å
N_2–N_1'''	3·088
N_1–${}_zC_6'''$	3·761
C_6–O'''	3·887
C_1–O'''	3·242
C_3–${}_{\bar{x}\bar{y}\bar{z}}C_3$	3·665
${}_zC_3'$–C_3'''	3·482
C_5–${}_{\bar{y}z}C_5''$	3·340

Table 4. *Bond angles*

C_5–N_1–C_1	118·4°	C_2–C_6–O	118·2°
N_1–C_1–C_2	121·4°	N_2–C_6–O	125·0°
C_1–C_2–C_3	120·1°	C_6–N_2–O'''	123·5°
C_2–C_3–C_4	118·6°	C_6–N_2–${}_{\bar{x}\bar{z}}N_1'''$	110·0°
C_3–C_4–C_5	118·0°		
C_4–C_5–N_1	123·4°	${}_{\bar{x}\bar{z}}N_1'''$–$N_2$–$O'''$	124·2°
C_3–C_2–C_6	117·1°		
C_1–C_2–C_6	122·7°	N_2–O'''–C_6'''	156·9°
C_2–C_6–N_2	116·8°		
		C_1–N_1–${}_zN_2'''$	99·0°
		C_5–N_1–${}_zN_2'''$	142·0°

---

* *Editorial note.*—Table 2 has been withdrawn and has been deposited with the Institute of Physics, 47 Belgrave Square, London S.W. 1, England. Application to inspect this table should be made to the Secretary of the Institute.

This plane makes angles of 34°, 6° and 64° with the *a*, *b* and *c* axes respectively. The displacements of the atoms from this plane are shown in Table 5.

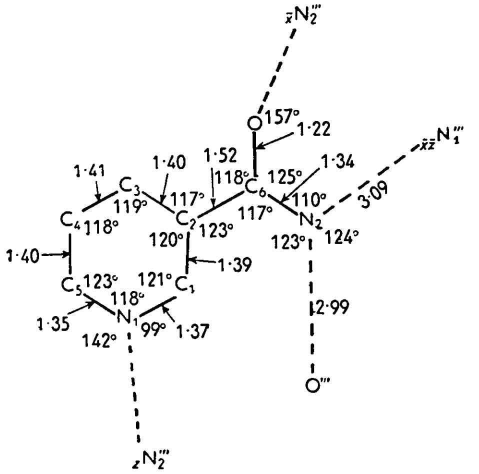

Fig. 3. Bond lengths and bond angles in nicotinamide.

Table 5. *Displacement of atoms from the plane of the pyridine ring*

Atom	Displacement (Å)
C_1	− 0·006
C_2	0·012
C_3	− 0·012
C_4	0·007
C_5	− 0·001
N_1	0·001
C_6	− 0·013
N_2	0·459
O	− 0·435

Accuracy of the determination

The standard deviations $\sigma(x)$ etc. of atomic coordinates were calculated from the differences ΔF between the observed and calculated values of the structure factors by the method of Cruickshank (1949). The values of $d^2\varrho/dx^2$ etc. were those printed at the end of the sixth iteration of the differential Fourier refinement. The standard deviations in bond lengths were calculated by compounding the values for $\sigma(x)$, $\sigma(y)$ and $\sigma(z)$ in the bond directions, and are shown in Table 3. The bond lengths in the pyridine ring are not significantly different from 1·39 Å for C–C and 1·37 Å ± 0·03 Å for C–N, as found for pyridine by Schomaker & Pauling (1939).

Discussion of the structure

A comparison of the bond lengths and bond angles in the amide group for L-glutamine (Cochran & Penfold, 1952), acetamide (Senti & Harker, 1940) and nicotinamide is shown in Table 6.

Table 6. *Comparison of the amide groups in* L-*glutamine, acetamide and nicotinamide*

	L-Glutamine	Acetamide	Nicotinamide
C–O	1·27 Å	1·28 Å	1·22 Å
C–N	1·28	1·38	1·34
C–C–O	118°	129°	118°
C–C–N	118°	109°	117°
O–C–N	123°	122°	125°

The value of 1·34 Å found for the C_6–N_2 bond in nicotinamide is not significantly different from the

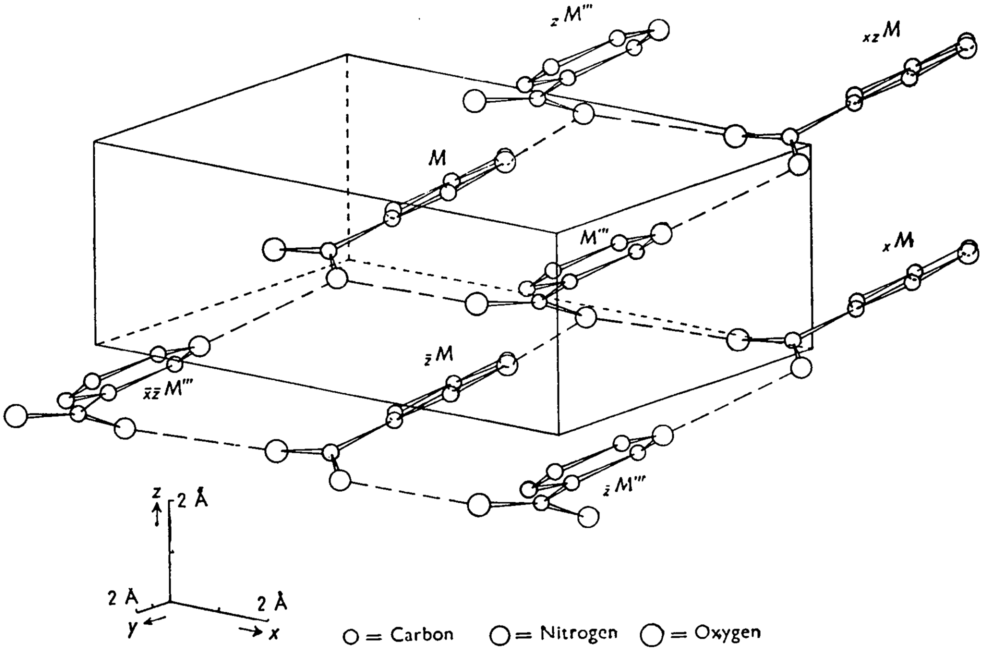

Fig. 4. The structure showing one half of the contents of a unit cell and associated molecules.

values of 1·28 Å and 1·38 Å found for the C–N bonds in the amide groups of glutamine and acetamide respectively, taking into account the errors in these values. The amide group bond angles in nicotinamide, however, are very close to those found for the amide group in glutamine but differ from those found for acetamide. It may therefore be concluded that, as in the case of glutamine, the C–N bond of the amide group in nicotinamide has a greater degree of double-bond character than the corresponding bond in acetamide.

The C–O bond in nicotinamide appears to be shorter than the corresponding bonds in glutamine and acetamide. As the difference in length is of possible significance it may be inferred that the C–O bond in nicotinamide has greater double-bond character than the C–O bonds in the other two substances. Both in glutamine and acetamide, however, the evidence is in favour of the keto form for the amide group, and in view of this it seems even more probable that the amide group has the keto configuration in nicotinamide. This is confirmed in some measure by the hydrogen bonding arrangement, in which both hydrogen atoms available for bond formation are attached to atom N_2. Some indication of the positions of the hydrogen atoms is also given by the *c*-axis Fourier projection in which, if normal carbon to hydrogen and nitrogen to hydrogen bonds are used, the positions of the hydrogen atoms lie in regions of electron density of $1 \rightarrow 2$ e.Å^{-2}. It can be seen that there are two such regions around atom N_2.

Nicotinamide forms two hydrogen bonds, one of length 2·99 Å from atom N_2 to the oxygen atom of molecule M''', and the other of length 3·09 Å from atom N_2 to the ring nitrogen atom of molecule ${}_{\bar{x}\bar{z}}M'''$ (Fig. 4). The values are in agreement with those found for bonds of the type N–H · · · N, which range from 2·94 Å to 3·30 Å, and for N–H · · · O, which have values ranging from 2·69 Å to 3·17 Å (Donohue, 1952). No other intermolecular distances are shorter than 3·2 Å. This arrangement of hydrogen bonds links each molecule to four other molecules in two-dimensional networks parallel to (010). The networks are held together by van der Waals forces only.

The authors thank Dr L. H. Lampitt for his continued interest in this investigation and for the arrangements made for the use of the electronic calculator. They also thank Miss A. V. Bell for the preparation of the figures, and the Directors of J. Lyons and Co. Ltd for permission to publish.

References

Booth, A. D. (1946). *Trans. Faraday Soc.* **42**, 444.
Broomhead, J. M. (1948). *Acta Cryst.* **1**, 324.
Cochran, W. & Penfold, B. R. (1952). *Acta Cryst.* **5**, 644.
Cruickshank, D. W. J. (1949). *Acta Cryst.* **2**, 65.
Donohue, J. (1952). *J. Phys. Chem.* **56**, 502.
Goldschmidt, G. H. & Pitt, G. J. (1948). *J. Sci. Instrum.* **25**, 397.
Qurashi, M. M. (1949). *Acta Cryst.* **2**, 404.
Schomaker, V. & Pauling, L. (1939). *J. Amer. Chem. Soc.* **61**, 1769.
Senti, F. & Harker, D. (1940). *J. Amer. Chem. Soc.* **62**, 2008.
Thompson, T. R., Caminer, D. T., Fantl, L., Wright, W. B. & King, G. S. D. (1954). *Acta Cryst.* **7**, 260.
Viervoll, H. & Ögrim, O. (1949). *Acta Cryst.* **2**, 277,
Wright, W. B. & King, G. S. D. (1950). *Acta Cryst.* **3**. 31.

Acta Cryst. (1954). **7**, 288

The Structure of Tropine-Hydrobromide

By J. W. Visser, J. Manassen and J. L. de Vries

Laboratory of General and Inorganic Chemistry, University of Amsterdam, Holland

(*Received* 23 *September* 1953)

Tropine-hydrobromide is monoclinic with $a = 6{\cdot}32$, $b = 20{\cdot}2$, $c = 7{\cdot}44$ Å, $\beta = 95°$; $Z = 4$; space group $P2_1/n$. The molecule has the *trans* chair configuration.

Introduction

The structure of tropinone and its derivatives was determined by a number of chemists in the period of 1880–1900 (see Willstätter & Bommer, 1921). The only remaining ambiguity was the structure of tropine and pseudotropine, both of which were obtained on reduction of tropinone. For these alcohols there are four possible structures (Fig. 1). We can expect that I and II will easily be converted into each other; the same is true for III and IV. The tropinoles were not studied until 1951–2 when three independent groups published their work on these structures.

The first publication was that of Sixma, Siegmann & Beyerman (1951) who, by means of reaction rates, concluded that tropine has configuration IV and pseudotropine the configuration II (see also Siegmann,