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The Crystal Structure of Nicotine Dihydroiodide

by

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Nicotine Dihydroiodide의 結晶構造

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要 約

니코틴 二沃化水素酸鹽의 結晶은 直角非等軸結晶系(斜方晶系)에 屬하며 空間群은 $P2_12_12_1$이다. 單位格子의 크기는 $a=7.61$, $b=11.01$ 및 $c=17.27$ Å이며 單位格子안에 들어 있는 化學單位의 數는 4이다.

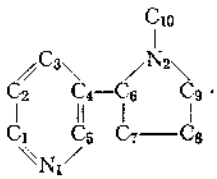
이 結晶의 構造를 X-線廻折法에 依하여 解析하였으며 R値 $\sum||F_o|-|F_c||\div\sum|F_o|$가 F_{okl}와 F_{kol}에 關하여 各各 0.16 및 0.14의 값을 이를 때까지 精密化하였다.

原子間 距離의 精密化를 試圖하지는 않았지만 피리딘 고리 안의 C—C 및 C—N의 平均距離는 各各 1.40 및 1.35 Å이며 피롤리딘 고리에 있어서는 各各 1.56 및 1.48 Å의 값을 가진다

피리딘 고리 內의 各原子는 實驗誤差內에서 同一平面上에 있으며 피롤리딘 고리에서는 C_6, C_7, C_8 및 N_2 原子는 大略 同一平面上에 있으나 C_9는 이 平面으로 부터 約 0.22 Å 멀어져 있다.

피리딘 고리의 平面과 C_6, C_7, C_8 및 N_2가 이루는 平面의 各 法線은 約 94°의 角을 이루고 있다. 니코틴 二沃化水素酸鹽의 한 分子內의 두個의 요오드 原子中 한개는 피리딘 고리의 窒素原子와 3.55 Å의 距離로 連結되여 있으며 다른 한개는 피롤리딘 고리의 窒素原子와 3.58 Å의 距離로 連結되여 있다. 結晶內에서 各 分子는 Van der Waals force로 서로 接觸되여 있다.

Abstract

Crystals of nicotine dihydroiodide, 

· 2HI, are orthorhombic with space group $P2_12_12_1$.

The unit cell, of dimensions $a=7.61$, $b=11.01$, $c=17.27$ Å, contains four formula units. The structure has been determined by X-ray diffraction method and has been refined to give the R-index, $\sum||F_o|-|F_c||\div\sum|F_o|$, of 0.16 and 0.14 for F_{okl} and F_{kol} respectively.

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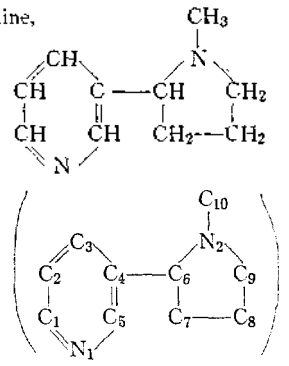
The mean lengths of C—C and C—N bonds in pyridine ring are 1.40 and 1.35 Å and those in pyrrolidine ring 1.56 and 1.48 Å respectively, though accurate measurement of bond length has not been attempted.

The six atoms in the pyridine ring are coplanar and on the other hand C_6, C_7, C_8 and N_2 atoms in pyrrolidine ring form a plane within accuracy of the analysis, and C_9 atom is distant 0.22 Å out of the plane consist of C_6, C_7, C_8 and N_2 atoms. The normals to the two planes form an angle of 94° with each other. Iodine atom is distant 3.55 Å from nitrogen atom in pyridine ring and the other iodine atom 3.58 Å from nitrogen atom in pyrrolidine ring, so that the nitrogen and iodine atoms are firmly linked.

It seems that the only forces binding nicotine dihydroiodide molecules together in the crystal are Van der Waals forces.

Introduction

The nicotine,



is an alkaloid of considerably physiological importance. Structure analysis of this compound was initiated in order to determine the shape of nicotine residue and the N··· I contact in the crystal.

Experimental and Crystal Data

The nicotine dihydroiodide was prepared by reaction between nicotine in ethyl alcoholic solution and freshly prepared hydroiodic acid. And then crystals were grown by slow evaporation in a desiccator from the solution at room temperature. Its melting point was 195°C. The crystals were thin flakes, rectangular or square in crosssection. The crystallographic axes, a and b, lie in the directions of plate edges. The samples used for the structure determination were reduced by slicing and dissolving to cylinder about 0.1mm. in diameter.

Rotation and Weissenberg photographs were taken around the a and b axes, using Cu—K_α radiation. Multiple films and visual estimation were used to obtain the intensities. The intensities were corrected for Lorentz and polarization effects, not for absorption or extinction.

The unit cell, determined by rotation and Weissenberg photographs was found to be orthorhombic, with $a=7.61$, $b=11.01$, $c=17.27$ Å. A higher degree of accuracy is not claimed because no allowance was made for film shrinkage. On the assumption of four molecules in the unit cell, the density was calculated as 1.919 g. cm^{-3}.

The systematic absences determined from zero and first layer Weissenberg photographs led uniquely to the space group $P2_12_12_1$.

Determination of the Structure

The structure has been determined by making use of the heavy atom method.[1,2] From sharpened Patterson projections on (1 0 0) and (0 1 0) it was possible to locate the iodine atoms, I_1 and I_2, at $x=0.50$, $y=0.60$, $z=0.20$ and $x=0.86$ $y=0.51$, $z=0.43$ respectively. Using the phases derived only from the positions of the iodine atoms, the F_o Fourier projections on (1 0 0) and (0 1 0) were computed. At this stage of our research many difficulties were caused due to the heavy atoms in the molecule. Apart from errors in the observed $|F_o|$'S, owing to absorption, the diffraction effect of the iodine atoms could be enough to distort the shapes and heights of the electrondensity peaks of other atoms.

The presence of a number of peaks in Fourier maps which were not assigned to atom positions, therefore, suggested a cautious approach.

On the resulting Fourier maps projected on (1 0 0) and (0 1 0), the iodine atoms were well resolved, but the positions of the nicotine residue could not be unambiguously fixed. After laborious trials by spatial considerations and structure factor calculations, an approximate structure was obtained with the disagreement factors $R=0.18$ for okl and $R=0.16$ for hol reflexions. However, it was not possible to distinguish between the positions of the nitrogen atoms and that of carbon atoms by the heights of electron contour in

the Fourier maps.

Second Fourier syntheses projected on (1 0 0) and (0 1 0) were calculated. The phases for the syntheses were determined by the structure factors which were calculated by using all the fourteen independent atoms in the molecule. The atomic scattering factor for carbon atom was used for the all atoms in nicotine residue in the structure factor calculation because no distinction between nitrogen and carbon atoms were possible. A careful check of the second Fourier maps revealed that the peak heights of the postulated atoms increased or remained constant while the heights of the doubtful peaks decreased in general.

Yet, the distinction of the positions between nitrogen and carbon atoms were still ambiguous. In the fifth stage of trials by structure factor calculation, the R-factor for the *okl* reflexion was reduced from 0.18 to 0.17 and for the *hol* reflexion from 0.16 to 0.15.

In the stage of the crystal analysis interatomic distances between the atoms in nicotine residue and iodine atoms were calculated. The shortest distances were 3.55 and 4.47 Å for the values between the atoms in pyridine ring and I_1 and 3.58 and 4.04Å for the values between the atoms in pyrrolidine ring and I_2. On the other hand the shortest distance between atoms in pyridine ring and I_2 was 4.03 Å and the shortest distance between atoms in pyrrolidine ring and I_1 was 4.34 Å.

Considering the facts that nitrogen and carbon atoms have their own electronegativity trend and that the

Table I Final Parameters of the Atoms.

	x	*y*	*z*		*x*	*y*	*z*
I_1	0.497	0.618	0.213	C_4	0.413	0.567	0.612
I_2	0.870	0.525	0.441	C_5	0.307	0.644	0.653
N_1	0.355	0.707	0.717	C_6	0.358	0.505	0.537
N_2	0.400	0.528	0.454	C_7	0.375	0.367	0.550
C_1	0.523	0.718	0.740	C_8	0.408	0.318	0.467
C_2	0.642	0.647	0.698	C_9	0.395	0.420	0.403
C_3	0.590	0.576	0.635	C_{10}	0.353	0.637	0.439

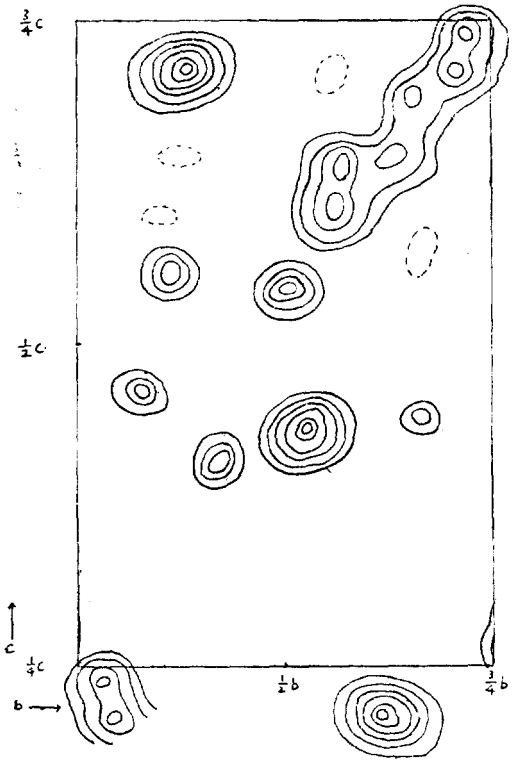


Fig. 1 Electron density of projection on (1 0 0). The Contour line are drawn an arbitrary scale.

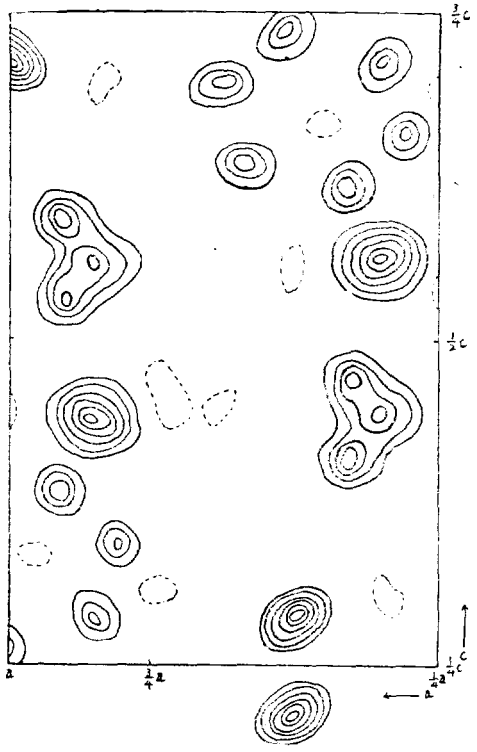


Fig. 2 Electron density projection on (0 1 0). The Contour lines are drawn an arbitrary scale.

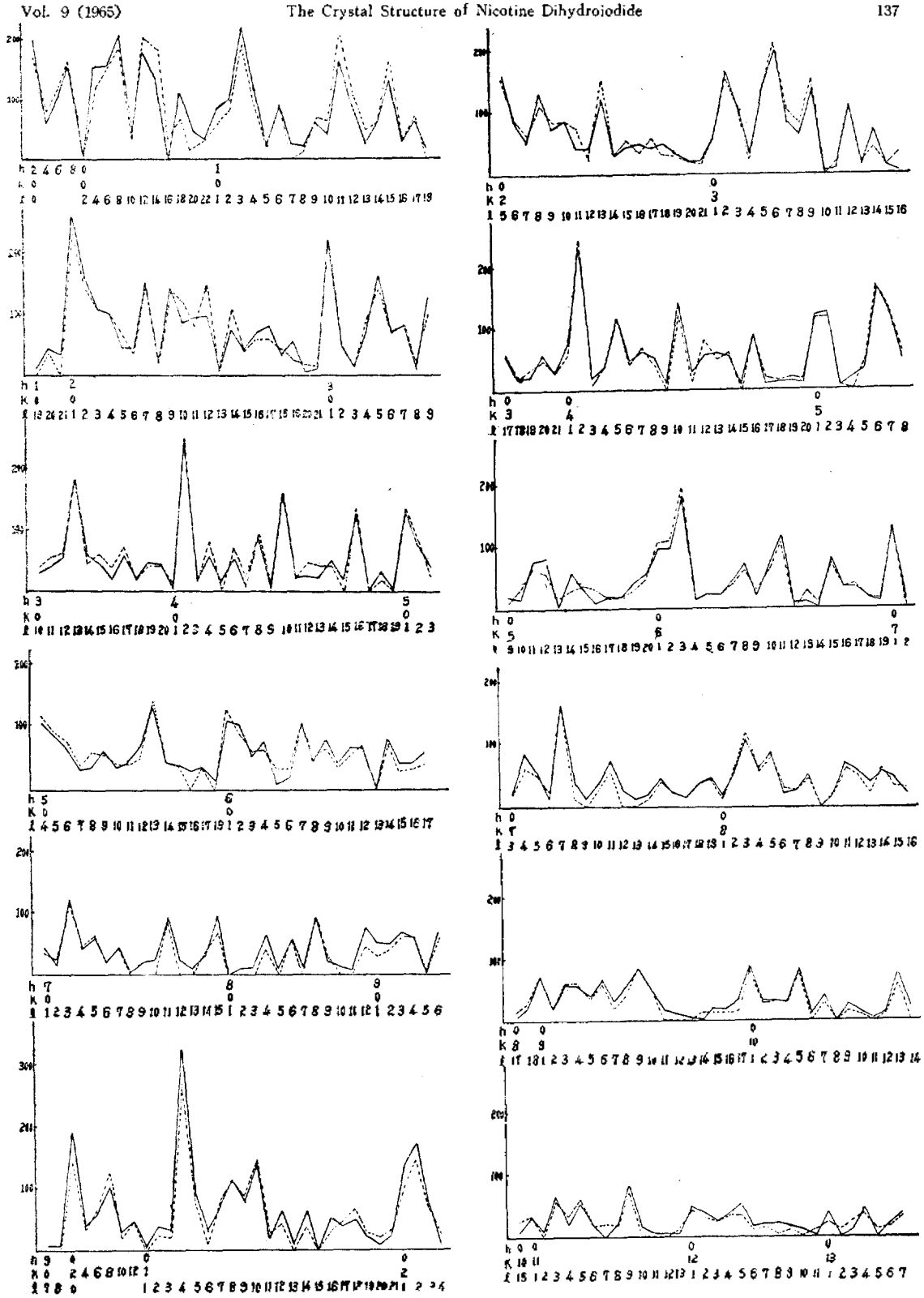


Fig. 3 Comparison of observed (dotted line) and calculated (full line) structure factors for nicotine dihydroiodide.

nicotine is an organic base and HI a strongest acid of the hydrogen halides, it seems that each of the two hydrogen atoms of 2HI in nicotine dihydroiodide were attached respectively to the nitrogen atom in pyridine

Table Ⅱ Interatomic Distances and Bond Angles.

(Ⅰ) Interatomic Distances.

Bond	Length(Å)	Bond	Length(Å)
N_1—C_1	1.35	C_9—N_2	1.48
C_1—C_2	1.39	C_6—N_2	1.48
C_2—C_3	1.40	N_2—$C_{10}(CH_3)$	1.48
C_3—C_4	1.41	N_1···I_1	3.55, 4.47
C_4—C_5	1.38	N_2···I_2	3.58, 4.04
C_5—N_1	1.35	N_1···I_2	4.03
C_4—C_6	1.52	N_2···I_1	4.34
C_6—C_7	1.55	I···I	4.96, 5.05
C_7—C_8	1.56	C···C	3.79, 4.05
C_8—C_9	1.57	C···I	3.84, 3.85
		C···N	5.50

(Ⅱ) Bond Angles(°).

Bond	Angles	Bond	Angles
C_1—N_1—C_5	123	C_6—C_7—C_8	102.1
N_1—C_1—C_2	114.3	C_7—C_8—C_9	113.1
C_1—C_2—C_3	122.6	C_8—C_9—N_2	99.1
C_2—C_3—C_4	122.1	C_9—N_2—C_6	115.4
C_3—C_4—C_5	111.7	C_6—N_2—C_{10}	106.5
C_4—C_5—N_1	125.7	C_9—N_2—C_{10}	131
C_3—C_4—C_6	122.7	C_1—N_1···I_1(hydrogen bonded)	125.6
C_5—C_4—C_6	124	C_5—N_1···I_1(hydrogen bonded)	110.2
C_4—C_6—C_7	106.7	C_{10}—N_2···I_2(hydrogen bonded)	105.7
C_4—C_6—N_2	133.1	C_9—N_2···I_2(hydrogen bonded)	91.3
N_2—C_6—C_7	107.4	C_6—N_2···I_2(hydrogen bonded)	107.9

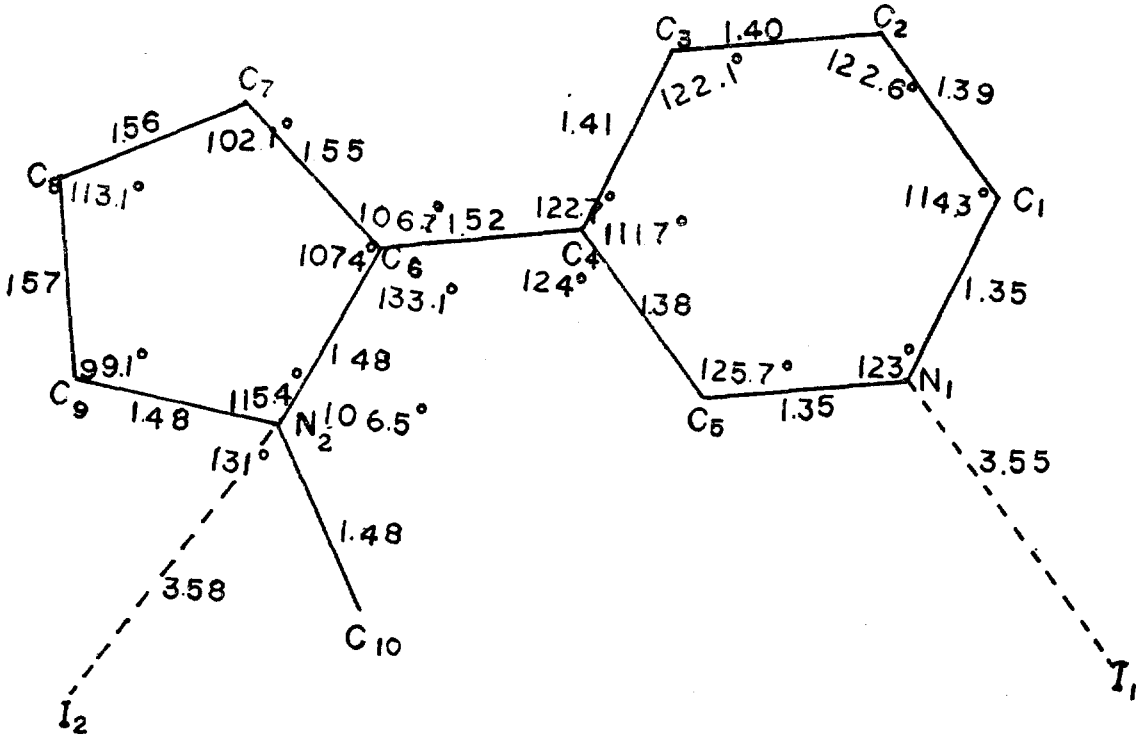


Fig. 4 Molecular dimensions of the nicotine dihydroiodide.

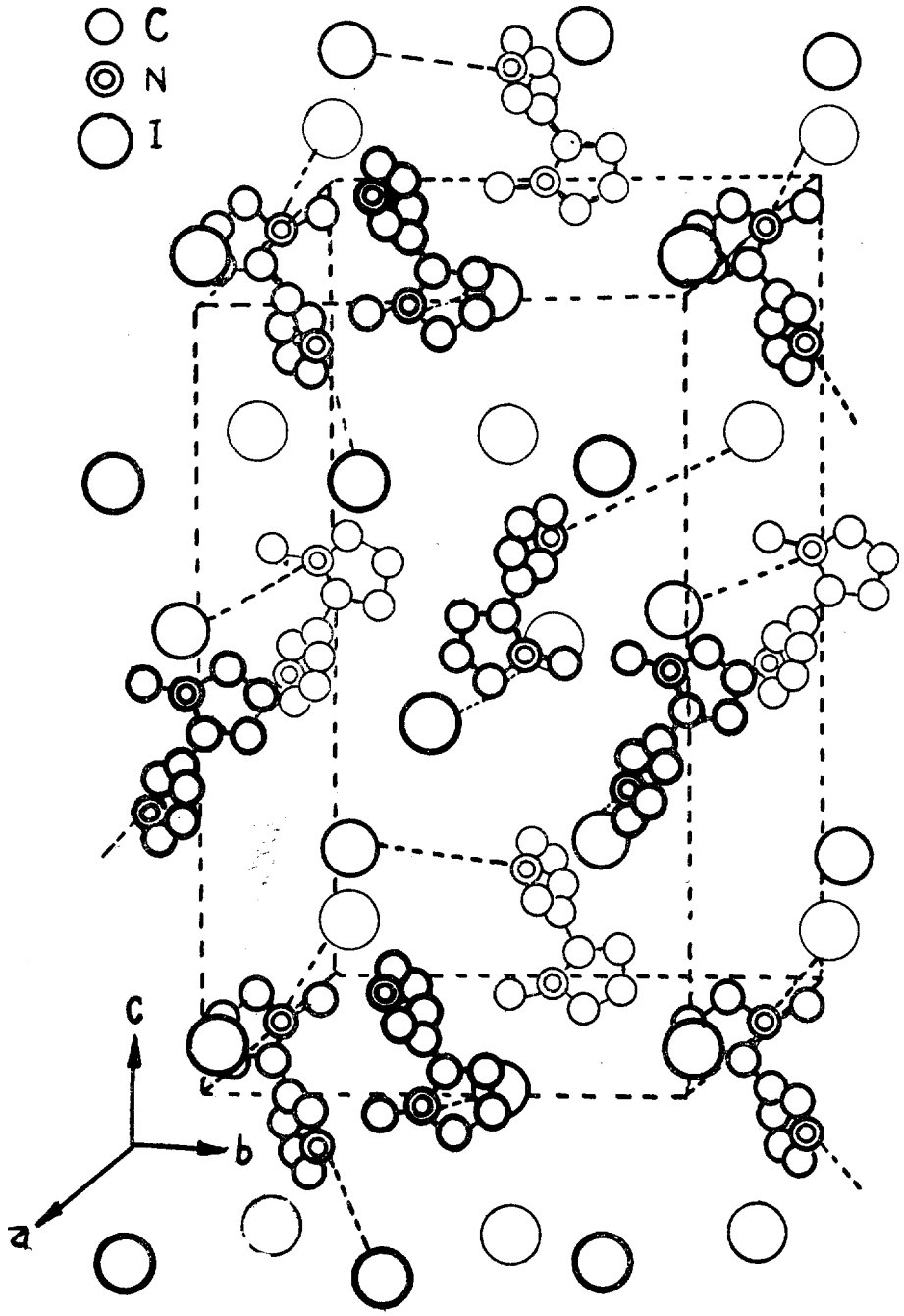


Fig. 5 Arrangement of the molecules in the unit cell.

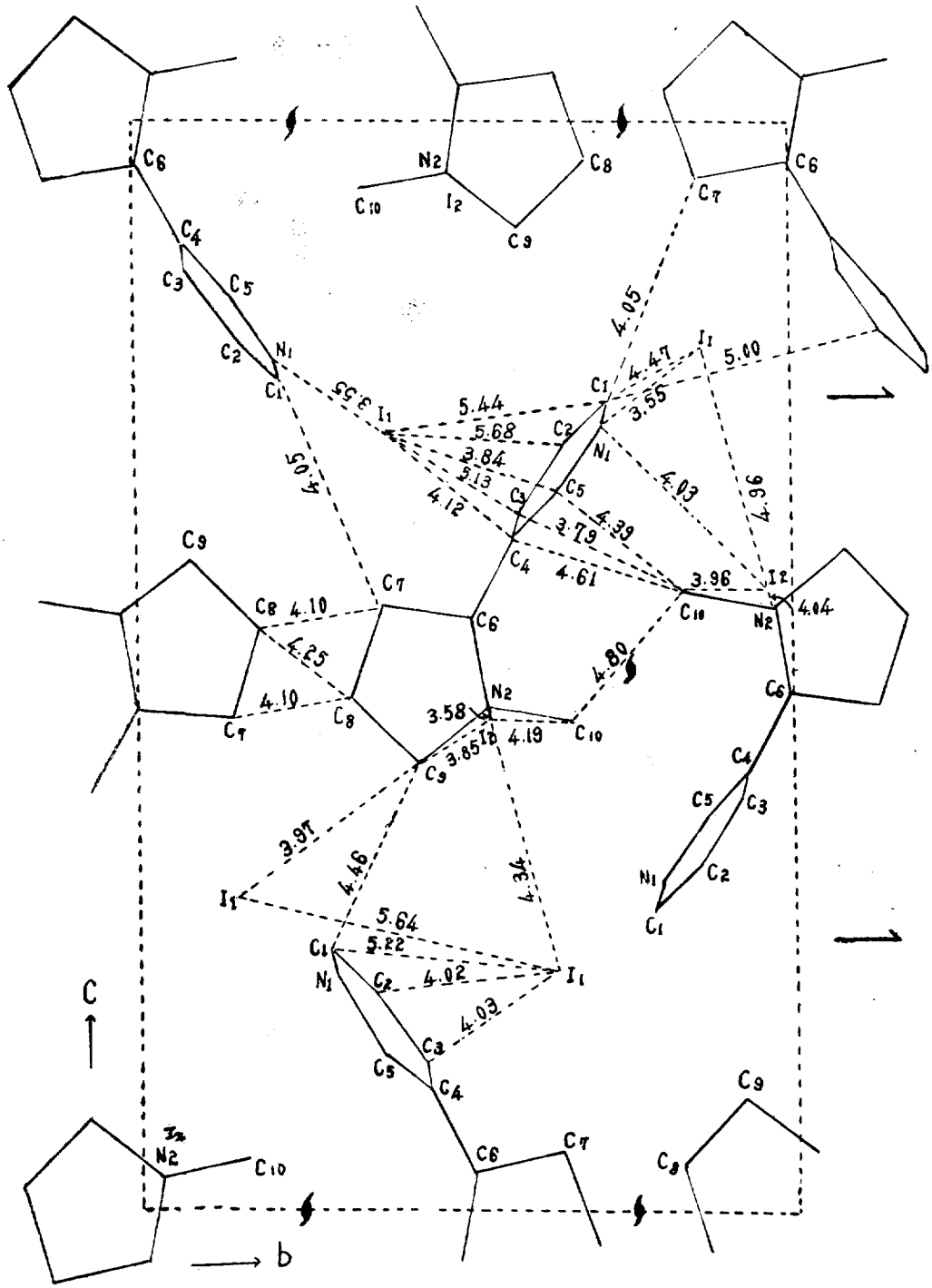


Fig. 6 The view of the structure projected along the *a*-axis.

ring and pyrrolidine ring with the N···I distances of 3.55 and 3.58 Å. The position of the nitrogen atom in each ring was thus determined by this consideration on N···I distances.

Structure factors were recalculated only for nitrogen atoms. The improvement of R-factors obtained by recalculation of structure factors seemed to be significant for *okl* and *hol* reflexions.

Finally, correction for the series termination errors was made through computation of (F_o-F_c)-syntheses for (1 0 0) and (0 1 0). As a result iodine atoms were shifted by small amounts to minimize the slopes at the atomic centers. The final coordinates of the atoms are listed in Table I, expressed as fraction of the unit cell edges. Structure factors were recalculated only for iodine atoms, and the values of R were 0.16 and 0.14 for *okl* and *hol* reflexions respectively.

The final F_o projections on (1 0 0) and (0 1 0) are shown in Fig. 1 and Fig. 2 respectively, and comparison of observed and calculated structure factors are shown in Fig. 3.

Discussion of the Structure

The aim of this investigation is to establish the stereochemistry of nicotine molecule and N···I contact in the crystal. The accuracy of the atomic positions is limited by the quality of the X-ray data, the poor resolution in the electron density projections, and the distortion of electron density peaks of the light atoms. It follows, therefore, that of all the interatomic distances, the most reliable are those between the iodine atoms.

The interatomic distances and bond angles calculated from the parameters given in Table I are tabulated in Table II, and in Fig. 4 the molecular dimensions of nicotine dihydroiodide are shown.

The mean lengths of the C—C and C—N bonds in pyridine ring (1.40 and 1.35 Å respectively) agree comparably well with the lengths of similar bonds in nicotinic acid[3] and nicotinic acid hydrochloride[4] etc. The mean legnths of the C—C and C—N bonds in the pyrrolidine ring (1.56 and 1.48 Å respectively) agree comparably well with the lengths of similar bonds in Tosyl-L-prolyl-L-hydroxy proline monohydrate.[5]

The six atoms in the pyridine ring are coplanar and on the other hand C_6, C_7, C_8, and N_2 atoms in pyrrolidine ring form a plane within the limits of accuracy of the structure determination and C_9 atom is distant 0.22 Å out of the plane consist of C_6, C_7, C_8 and N_2 atoms. The normals to the two planes form an angle of about 94° with each other. The carbon atom within methyl group is distant 0.32 Å out of the plane consist of C_6, C_7, C_8 and N_2 atoms, and the length of C_{10}—N_2 bond 1.48 Å agrees reasonably well with the length of similar bonds in theopylline[6] and caffeine[7].

N_1 atom is linked to I_1 atom only by a bond of length 3.55 Å, and N_2 is linked to I_2 only by a bond of length 3.58 Å. And the distances of next shortest contact of the nitrogen atoms to iodine atoms (4.03, 4.04 Å) are longer than the sum, 3.65 Å, of the nitrogen and iodine Van der Waals radii.

The shortest intermolecular distance of C—C and C—N are 3.79 and 5.50 Å respectively and the shortest intermolecular distance of C—I is 3.84 Å, which is slightly longer than 3.81 Å found in the crystal structure of (+)-Des-(oxymethylene)-Lycoctonine Hydroiodide Monohydrate[8]. Forces amongnicotine dihydroiodide molecules in crystal are presumed to be Van der Waals attraction. Arrangement of the molecules in the unit cell and the view of the structure projectedalong the *a*-axis are shown in Fig. 5 and Fig. 6.

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References

1) J. M. Robertson and I. Woodward, *J. Chem. Soc.* 36 (1940).
2) E. G. Cox, *Rep. Proger. Chem.* **35**, 174 (1938).
3) W. B. Wright and G. S. D. King, *Acta Cryst.* **6**, 305 (1953).
4) C. H. Koo and H. S. Kim, *This Journal*, **7**, 257 (1963).
5) J. Fridrichsons and A. McL. Mathieson. *Acta Cryst.* **15**, 569 (1962).
6) D. J. Sutor, *ibid.* **11**, 83 (1958).
7) D. J. Sutor, *ibid.* **11**, 453 (1958).
8) Maria Przybylska, *ibid.* **14**, 424 (1961).