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X-RAY STRUCTURE DETERMINATION OF TRYPTAMINE HYDROCHLORIDE

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In the preceding paper[1], we have described the crystal and molecular structure of 5-hydroxy-DL-tryptophan which has an excellent radiation protective ability[2]. On the other hand, tryptamine, $C_{10}H_{12}N_2$ was found to have the protective action against a lethal dose of ionizing radiation[3]. With this communication we report briefly the X-ray structure analysis of tryptamine hydrochloride and compare its structure with those of the other related compounds in order to provide the additional information concerning the correlation between the three dimensional structure and its pharmacodynamic action.

Tryptamine hydrochloride, m.p.=256-257°C[4], was crystallized from aqueous solution as transparent yellow prism-shaped crystals. The cell dimensions, which were refined by the manual four circles diffractometer, were found to be: a = 8.545, b = 10.025, c = 24.252 Å. From systematic absence, the space group was determined to be Pbca. The density measured by flotation method in a benzene-carbon tetrachloride mixture was 1.261 g/cc. while the calculated one was 1.258 g/cc. as containing eight molecules per unit cell.

Intensity data of 875 independent reflections were collected by the multiple-film, equi-inclination Weissenberg photographs of the layers h 0 l to h 7 l.

Intensities were estimated by visual comparison with a standard scale, and were applied to the Lorentz-polarization and spot-shape corrections. With Wilson's method an overall temperature factor (B = 3.35 Å) and the scaling factor were determined.

The structure was solved by the symbolic addition procedure for centrosymmetric crystals proposed by Karle and Karle[5]. Normalized structure factor, E, and Σ_2 lists ($|E| > 1.3$, probability greater than 95%) were calculated with

program 'SIGMA' written by Dr. T. Ashida. The application of Σ_1 formula[6] to the reflection (4 4 6) whose |E| = 1.71 indicated that it has a positive sign with a probability of 0.88.

Five reflections, as listed in Table 1, were selected to initiate the symbolic addition procedure and the phases of one hundred and fifty-seven reflections were calculated by hand in terms of the initial signs and letters.

Table 1.

starting set for application of Σ_2

h	k	l	sign	|E|
2	2	3	+	3.11
5	4	16	+	2.77
2	5	14	+	2.69
5	2	3	A	2.81
6	4	8	B	3.10

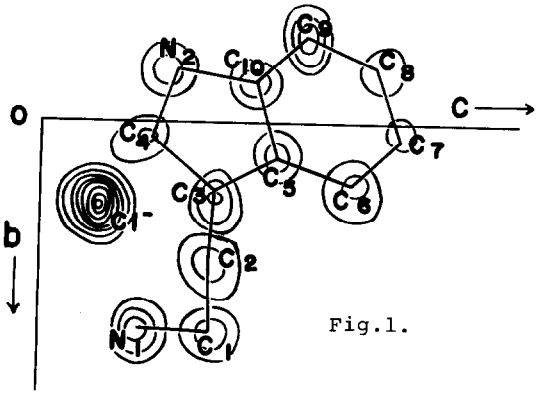

Fig.1.

The sign relation in Σ_2 lists strongly suggested A = B = +. A three dimensional E-map computed with the phases assuming the signs of A and B as both positive, revealed the high peaks corresponding to the atomic positions of tryptamine hydrochloride molecule except hydrogen atoms. Fig.1 shows the superimposed E-map of the molecule viewed along a-axis. It was shown later that only two signs out of 157 determined phases had been allotted as incorrect signs.

The coordinates of the thirteen atoms as selected from the E-map were subjected to three dimensional Fourier synthesis. At this stage a structure factor calculation for 875 reflections gave discrepancy factor, R, of 0.25.

Refinement of the structural parameters was carried out by the block-diagonal least-squares program 'HBLS IV' written by Dr. T. Ashida.

After five cycles refinement with isotropic temperature factors for each atoms, the layer ratio of b-axis data was adjusted to that of calculated value.

Following five cycles refinement with individual anisotropic thermal motions of heavy atoms except hydrogen atoms, decreased R value to 0.15.

Then a three-dimensional difference Fourier synthesis was calculated in order

to get positional parameters for the hydrogen atoms. The orientations of hydrogen atom in the NH_3^+ groups were determined by considering the hydrogen-bond network, and confirmed by the plausible peaks in the difference electron density map.

The average of six C-C bond lengths in the six-membered ring is 1.399 Å, while those of C-N and C-C bond lengths in the five-membered ring are 1.406 Å and 1.413 Å, respectively. The mean deviation of the individual atoms from the least-squares plane through the atoms in the indole ring is about 0.01 Å, and they are in a plane within the standard deviation.

The hydrogen bonding system and the packing of the molecules projected down the b-axis are illustrated in Fig.2.

All feasible hydrogen atoms available for hydrogen bonding have been utilized. Three hydrogen atoms of the NH_3^+ group are involved in the normal hydrogen bonds with neighboring chloride ions with average distance of 3.18 Å and approximate tetrahedral angle. Every chloride ion performs as an acceptor for four hydrogen bondings. The weakly basic nitrogen atom N(2) of the indole ring takes part in the hydrogen bond with neighboring chloride ion as in the serotonin-creatinine sulphate complex[7].

N(1)-H---Cl hydrogen bonds form infinite columns around the screw axes along a-axis. Tryptamine hydrochloride are arranged in double layers parallel to (0 0 1), and the separation into layers of polar groups and layers of non-polar groups can be recognized as in the case of 5-hydroxy-DL-tryptophan and L-tryptophan hydrochloride[8].

It is in agreement with the absence of any marked cleavage that indole rings are packed as the pleated sheet and the hydrogen bonding system is essentially a three-dimensional network. No unusually short contacts between non-bonded atoms are found in the structure.

Full detailed data of the structure will be published elsewhere in the near future and this work was partly supported by a grant from the Ministry of Education, Japan.

We wish to express our thanks to the staffs of computation centers of this university and the University of Tokyo for numerical computation.

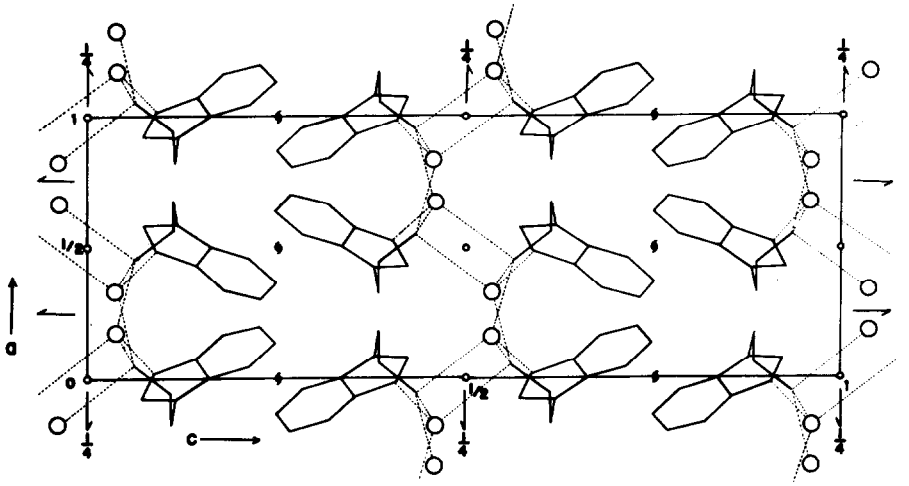

Fig.2.

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