Structural Studies of Tryptophan Metabolites by X-ray Diffraction Method. II. The Crystal and Molecular Structure of Tryptamine Hydrochloride

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The crystal structure of tryptamine hydrochloride has been solved by the application of the symbolic addition method, and refined by successive Fourier syntheses and least-squares procedures. The crystals are orthorhombic, space group Pbca, with lattice parameters $a=8.545$, $b=10.025$ and $c=24.252$ Å. All the positions of hydrogen atoms were found in the difference Fourier map and included in the refinement. The ethylamine side chain bound to the indole ring is in a folded configuration as found in the crystal structure of serotonin picrate monohydrate. A weakly basic nitrogen atom of the indole ring takes part in the hydrogen bonding with the adjacent ion. Every chloride ion behaves as an acceptor for four hydrogen bonds. This is in line with the absence of any marked cleavage where indole rings are packed together to form a pleated sheet and a three-dimensional network structure is essentially stabilized by the hydrogen bond formation.

Tryptamine, a tryptophan metabolite, was first isolated from shoots and flowers of *Acacia* species.[1] A significant biological implication of this compound lies in its role as starting material for the biosynthesis of alkaloids containing an indole ring. It has been also reported to have anti-radiation ability[2-4] as well as serotonin and 5-hydroxytryptophan. In order to study the correlation between the molecular structure and its pharmacodynamic action, it is necessary to elucidate the stereoconfiguration of the molecule. In the course of studies on tryptamine hydrochloride, we found that the aminoethyl side chain of this molecule is in folded configuration.[5] Extended conformation was reported in the case of a serotonin-creatinine sulphate complex.[6] The same folded configuration was found in the crystal structure of serotonin picrate monohydrate.[7] The present paper gives a more detailed account of the methods and the results of analysis. The structure is compared with that of other tryptophan metabolites, some structural features of radiation protective agents being described.

Experimental

Crystals were prepared by slow evaporation from an aqueous solution, and obtained as transparent yellow prismatic crystals. Preliminary rotation and Weissenberg photographs showed them to be orthorhombic, the space group being uniquely determined as Pbca from the absent spectra. The unit-cell dimensions were finally determined with a Rigaku Denki manual four-circle diffractometer at room temperature. Melting point of this crystal measured with a DSC (differential scanning calorimeter) is in agreement with the reference value.[8] The density was measured by the flotation method in a benzene-carbon tetrachloride mixture. It was confirmed that no solvent of crystallization is contained in the crystal, the result coinciding with DSC results. The physical and crystal data obtained are given in Table 1.

TABLE 1. CRYSTAL DATA OF TRYPTAMINE HYDROCHLORIDE

$C_{10}H_{12}N_2 \cdot HCl$, M.W. 196.68, mp 256—257°C	
Yellowish prism-shaped crystals. Orthorhombic	
$a=8.545(9)$, $b=10.025(8)$, $c=24.252(16)$ Å	
$V=2077.5$ Å^3, $Z=8$, $F(000)=832$	
Absorption coefficient for X-rays ($\lambda=1.5418$ Å):	
$\mu=29.2$ cm^{-1}, $D_m=1.261$ g·cm^{-3}, $D_x=1.258$ g·cm^{-3}	
Absent spectra	$(0kl)$: $k=2n+1$
	$(h0l)$: $l=2n+1$
	$(hk0)$: $h=2n+1$
Space group; Pbca	

Intensities of 875 independent non-zero reflections were measured visually on equi-inclination Weissenberg photographs of 0 to 7th layers around the b-axis, with the use of Ni-filtered Cu$K\alpha$ radiation. Corrections were made for the Lorentz-polarization factors and spot-shape. No absorption effect was taken into account, since the crystal used was sufficiently small. The data were then adjusted to the absolute scale by means of Wilson's method. The overall temperature factor obtained at this stage was 3.35 Å^2. The SIGMA program was utilized to list the E-values and Σ_2 relationships with their probabilities.

Determination and Refinement of Structure

The structure of tryptamine hydrochloride was successfully solved by using the direct method. Reflections with $|E|>1.3$ were selected, five of them being given a sign or a letter symbol as follows.

h	k	l	phase	$\|E\|$
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

Application of Σ_1 formula to reflection (446) indicated that it has a positive sign of 88% probability. It is also included in the initial starting set. The sign

1) E. P. White, *New Zealand J. Sci. Tech.*, **25B**, 137 (1944).
2) H. Langendorff and R. Koch, *Strahlentherapie*, **98**, 245 (1955).
3) P. Alexander and Z. M. Bacq, *Radiat. Res.*, **2**, 292 (1955).
4) I. I. Sapezhinskii and N. M. Emanuel, *Dokl. Akad. Nauk. SSSR*, **132**, 1441 (1960).
5) A. Wakahara, T. Fujiwara, and K. Tomita, *Tetrahedron Lett.*, **1970**, 4999.
6) I. L. Karle, K. S. Dragonette, and S. A. Brenner, *Acta Crystallogr.*, **19**, 713 (1965).
7) U. Thewalt and C. E. Bugg, *ibid.*, **B28**, 82 (1972).
8) A. H. Jackson and A. E. Smith, *J. Chem. Soc.*, **1965**, 3498.

relations between a number of reflections strongly suggested A=B=+. At the end of the process the phases of 157 independent reflections were determined, and a Fourier synthesis was calculated with normalized structure factors as the coefficients (*E*-map). The three dimensional *E*-map showed the sites of all 13 atoms of this molecule. Another 20 spurious peaks of the same height as that of light atoms appeared. The indole ring plane enables us to distinguish true peaks from false ones. The structure was refined by the block-diagonal-matrix least-squares method, first with isotropic thermal parameters and then with anisotropic temperature factors. The estimated parameters of hydrogen atoms were computed in such a way as to give bond angles as close to trigonal or tetrahedral as possible. The distances were assumed to be 1.08 Å for C–H, 1.01 Å for N–H, and 0.97 Å for O–H. The amino nitrogen atom had to be the protonated form, and three hydrogen atoms were placed on it. This nitrogen atom has three chloride neighbors at reasonable hydrogen-bonding distances and angles. Thus, three hydrogen atoms were placed at proper positions on the N···Cl⁻ line. In order to check the expected positions of hydrogen atoms, a difference Fourier synthesis was prepared and all the hydrogen peaks were obtained near the calculated positions as shown in Fig. 1. This may indicate the correctness of the assumed positions of hydrogen atoms and the assignment of hydrogen bonding system. More refinement cycles were performed, which included refinement of the positional and overall isotropic thermal parameters of the hydrogen atoms. Refinement was stopped when parameter shifts were less than one fourth of their standard deviations, giving an *R* value of 0.094. The N–H and C–H bond lengths are in the ranges 0.99—1.11 Å and 1.03—1.17 Å, respectively. The final electron density map is shown in Fig. 2. The final observed and calculated structure factor amplitudes are given in Table 2 and final atomic positional and thermal parameters in Table 3. The scattering factors used throughout the refinement were taken from *International Tables for X-ray Crystallography* (1962). All calculations were done on an NEAC 2200—500 of this University, using programs written by T. Ashida and the authors.

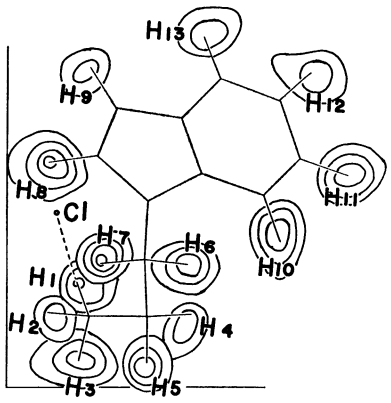

Fig. 1. The location of hydrogen atoms from a three-dimensional difference Fourier map. Contours from 0.2 e.Å^{-3} at intervals of 0.2 e.Å^{-3}.

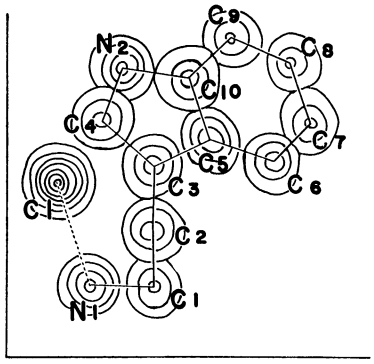

Fig. 2. A composite drawing of the final electron density map, viewed along a-axis. Contour intervals of 2.0 e.Å^{-3} for light atoms and 4.0 e.Å^{-3} for the chloride ion, the first contour begins at 2.0 e.Å^{-3}.

Description and Discussion of the Structure

Molecular Dimensions. The bond lengths and angles are shown in Fig. 3 and Table 4 together with those of the other tryptophan metabolites. The numbering of other metabolites corresponds to that of tryptamine in Fig. 3. We see some interesting structural features of radiation protective agents containing indole ring (indicated with asterisk in Table 4). The C(3)–C(4) bond, 1.342—1.387 Å, is apparently shorter than a normal aromatic C–C bond (1.395 Å). The corresponding bond of four radiation protectors is longer than that of other indole derivatives, and is compatible to 1.381 Å of yohimbane hydrobromide[9] and 1.395 Å of reserpine.[10] On the other hand, the C(2)–C(3) distance of the protector is slightly shorter than that of the other related compounds. The corresponding length of yohimbane and reserpine is 1.489 Å and 1.444 Å, respectively. It is of biological in-

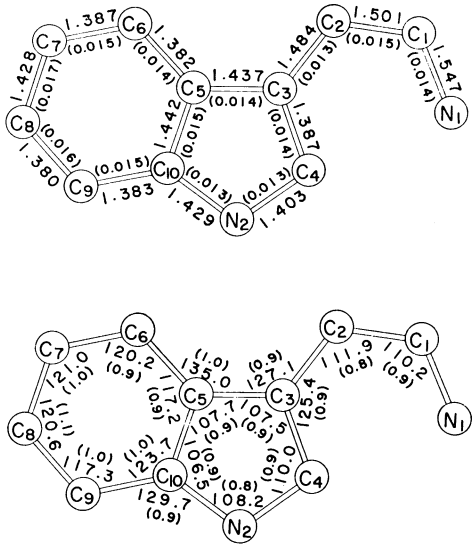

Fig. 3. Bond lengths (Å) and valency angles (°). The standard deviations are given in parentheses.

9) J. P. Fennessey and W. Nowacki, *Z. Kristallogr.*, **131**, 342 (1970).

10) I. L. Karle and J. Karle, *Acta Crystallogr.*, **B24**, 81 (1968).

TABLE 2. THE OBSERVED AND THE FINAL CALCULATED STRUCTURE FACTORS

L	FO	FC	L	FO	FC	L	FO	FC	L	FO	FC	L	FO	FC	L	FO	FC	L	FO	FC	L	FO	FC	L	FO	FC
H,K=	0	0	1	117	111	12	16	-15	11	66	-61	24	22	25	13	22	-22	12	27	-34	9	30	28	8	45	-40
4	123	-121	2	124	-120	14	37	-38	13	20	-22	25	27	-25	15	29	-35	14	20	-25	11	35	-30	11	38	-36
6	233	-241	3	233	-268	H,K=	9	1	17	20	-22	27	13	-13	16	40	-40	H,K=	9	4	16	36	33	13	41	-38
8	19	-19	5	19	-20	1	27	29	18	30	33	28	8	-9	17	20	-16	6	12	-15	20	9	-12	14	17	16
10	173	-174	6	114	96	3	21	23	21	29	29	H,K=	4	3	18	30	-31	8	12	-16	H,K=	8	5	15	21	-17
12	79	-80	8	93	97	6	30	-32	H,K=	6	2	0	8	10	20	35	-39	H,K=	10	4	0	30	-32	H,K=	8	6
14	124	-116	9	42	39	8	58	-51	0	48	-42	1	21	17	22	25	-25	5	15	16	4	24	-25	0	24	-24
16	33	-30	10	40	-35	15	17	-21	2	49	-41	2	19	20	25	21	20	H,K=	1	5	6	17	-15	1	10	-14
18	40	39	11	73	71	H,K=	10	1	3	47	-40	3	64	70	H,K=	2	4	1	39	-39	8	26	33	2	35	-36
20	20	-17	12	20	20	0	54	-54	4	16	16	4	142	-163	0	68	-71	2	16	6	10	34	34	8	29	30
24	51	50	13	122	119	3	22	-24	5	65	-58	5	118	118	1	40	-39	3	68	78	11	34	35	9	36	-35
26	66	58	14	50	46	5	36	-37	7	95	-92	7	27	33	2	28	23	6	67	-77	14	22	21	10	10	6
28	27	25	15	17	-19	H,K=	0	2	9	84	-81	8	76	82	3	6	-2	8	69	-79	16	10	13	H,K=	9	6
H,K=	1	0	17	45	-36	2	143	-144	12	42	36	9	74	62	4	127	118	9	49	-56	H,K=	9	5	9	25	25
2	74	-64	18	65	-56	3	44	38	13	20	23	10	44	41	5	53	-48	10	12	11	4	24	25	H,K=	1	7
4	20	-24	20	99	-89	4	34	38	17	46	48	11	57	58	6	63	64	12	29	-27	6	23	28	1	91	-99
6	370	-371	24	28	30	5	146	-148	19	44	43	12	16	16	7	63	-61	15	15	16	10	14	17	2	9	9
8	196	-196	H,K=	2	1	6	62	-65	23	13	15	13	10	9	8	49	-46	16	37	39	12	24	24	4	28	-37
10	25	-22	0	384	331	7	176	-179	H,K=	7	2	15	19	-20	9	26	-29	18	21	28	H,K=	0	6	5	29	27
12	50	51	1	136	-146	8	23	16	1	57	-48	16	27	27	10	72	-68	19	12	-8	2	106	104	9	26	27
14	25	-25	2	87	98	9	149	-160	2	10	-11	17	43	-40	14	33	-29	20	16	19	3	25	28	10	58	63
16	62	55	3	289	279	10	41	-45	3	37	-38	19	45	-47	15	19	18	22	30	24	4	84	96	11	34	31
18	65	66	4	108	-96	11	96	-113	5	23	-24	21	34	-30	16	33	-34	26	9	-13	5	26	27	14	38	-36
20	82	82	5	143	130	12	101	120	6	35	26	22	30	-30	17	24	25	H,K=	2	5	7	51	52	15	27	27
22	13	13	6	46	38	13	21	20	8	23	23	23	41	-34	18	33	-39	0	91	-89	8	76	-83	H,K=	2	7
30	12	-12	7	141	132	14	44	50	11	51	60	H,K=	5	3	19	27	-28	1	36	33	9	65	69	0	32	-26
H,K=	2	0	8	54	50	15	35	37	13	54	61	1	45	40	22	33	36	2	36	-32	10	68	-78	1	18	16
0	196	212	9	18	-20	16	13	-14	15	37	31	2	47	43	23	33	35	3	7	-5	11	71	70	2	21	19
2	8	6	10	15	-20	17	75	86	17	22	23	3	40	42	26	13	12	4	82	-86	12	26	-31	3	74	64
4	219	-256	11	28	32	18	29	-33	23	16	-17	4	78	74	H,K=	3	4	6	33	-29	13	41	-40	4	28	28
6	87	-80	12	122	-106	19	52	53	H,K=	8	2	5	19	17	1	34	33	8	29	24	14	36	-41	5	92	77
8	36	-33	13	55	-49	21	31	33	0	19	20	6	15	15	3	39	-29	9	37	-41	16	20	19	6	29	26
10	65	61	14	140	-120	23	70	65	1	13	-16	7	36	31	4	32	28	10	42	42	17	36	-40	7	62	54
12	91	81	15	22	-22	29	18	-14	3	24	24	8	59	-59	5	58	-49	12	59	60	18	21	-23	8	57	-50
14	112	109	16	21	-17	H,K=	1	2	5	43	37	9	26	-22	6	84	75	14	87	104	19	46	-45	9	54	53
18	41	36	17	24	-25	1	102	-87	7	20	19	10	46	37	7	40	42	15	36	45	21	32	-33	13	32	-31
22	52	-50	21	28	-27	2	31	-26	11	45	45	11	44	-37	8	22	-21	16	16	20	H,K=	1	6	14	33	28
26	13	-9	23	24	-21	3	185	-219	14	26	-31	12	25	27	10	75	-77	22	21	-24	1	66	63	16	26	-25
H,K=	3	0	26	33	42	4	64	62	17	14	-14	13	51	-48	12	46	-51	23	11	13	2	64	-57	17	20	-22
2	10	9	H,K=	3	1	5	35	-32	19	23	-23	15	39	-39	16	41	40	24	41	-40	3	74	67	19	34	-38
4	51	49	1	168	147	6	110	114	H,K=	9	2	16	20	-19	17	6	-4	H,K=	3	5	4	71	-61	H,K=	3	7
6	74	-69	2	87	-87	7	14	-15	3	28	28	17	20	-21	H,K=	4	4	1	42	-34	6	43	-39	1	23	25
8	42	-42	3	28	29	8	57	56	H,K=	10	2	20	21	-23	0	32	-27	2	122	129	8	59	-60	2	30	-30
10	80	71	6	189	-226	9	60	56	4	12	-10	25	19	20	1	8	10	4	113	113	9	29	-30	3	89	93
12	95	85	8	120	-127	10	47	-47	6	5	4	H,K=	6	3	2	32	31	5	16	14	10	26	-22	4	34	-38
14	16	-17	9	50	-52	11	93	92	H,K=	1	3	0	30	23	3	6	-3	6	76	85	11	51	-52	5	31	24
16	53	-43	10	37	-31	13	103	109	1	170	201	3	10	-31	5	28	30	8	49	47	12	32	-37	6	29	31
18	44	44	11	30	-28	15	57	56	2	7	-6	6	18	-17	6	72	61	10	58	58	13	24	-30	8	12	-10
22	36	-37	12	27	24	17	61	59	3	95	92	7	48	-50	7	69	-69	11	17	-19	14	29	30	11	66	-77
24	43	-45	13	19	-19	23	33	-34	4	61	60	8	41	40	8	27	-25	12	37	35	15	25	-27	12	22	-22
28	20	24	15	63	-54	25	33	-34	5	80	-67	14	25	-23	9	25	-25	14	49	-48	16	36	36	13	55	-61
H,K=	4	0	16	60	56	29	12	-11	6	26	-27	H,K=	7	3	10	20	-24	16	45	-45	17	30	-30	15	28	-29
0	29	-35	17	73	-73	H,K=	2	2	7	33	-28	2	20	19	12	32	-32	17	32	31	18	16	19	17	22	-23
2	36	-31	18	25	31	0	229	204	9	124	-108	4	45	47	13	20	22	18	28	-27	H,K=	2	6	21	19	20
4	58	-50	19	25	25	1	48	-43	11	50	-52	8	35	-40	14	24	-24	19	12	-12	0	67	-68	24	10	7
6	13	14	20	29	27	2	43	44	12	18	17	11	26	-28	17	32	30	20	39	-38	2	12	-12	H,K=	4	7
8	36	-33	22	29	31	3	290	307	14	35	35	12	24	24	H,K=	5	4	22	29	-26	3	97	-83	0	23	30
10	58	53	23	35	38	4	130	-121	18	28	-28	13	20	-18	1	10	-10	23	15	-18	5	46	-42	1	18	16
12	70	69	H,K=	4	1	5	118	115	20	83	-81	14	30	-29	2	49	-43	H,K=	4	5	6	28	-29	2	37	-34
14	77	70	0	182	-167	6	32	29	22	28	23	15	21	-21	3	57	-52	0	107	112	7	46	-43	4	14	17
16	57	-60	2	60	-55	7	39	40	24	21	23	H,K=	8	3	5	39	-34	1	12	16	8	15	18	5	64	-61
26	11	-14	3	41	-31	8	23	-24	25	26	27	0	20	-22	7	40	40	2	80	72	9	20	-22	6	12	-13
28	19	-20	4	106	-106	9	32	33	27	18	18	2	21	21	8	78	-71	3	20	17	11	22	22	7	31	-34
H,K=	5	0	5	28	24	11	13	15	29	8	6	3	30	-32	9	23	19	4	67	73	14	29	30	9	53	-59
4	57	58	7	66	-68	12	22	17	H,K=	2	3	5	44	-55	10	56	-58	5	21	20	16	50	52	11	44	-45
6	51	58	8	90	90	15	24	-24	0	108	107	7	20	-24	11	29	30	6	24	19	H,K=	3	6	14	26	26
8	69	75	9	70	-82	16	36	-40	1	34	-31	8	20	-20	12	55	-58	7	8	7	2	30	31	15	28	27
10	17	18	10	60	64	19	67	-58	2	74	63	9	20	-22	13	16	8	92	-101	3	23	-18	17	40	39
12	55	53	11	62	-70	H,K=	3	2	3	76	-63	19	13	17	14	35	39	9	19	-18	H,K=	4	6	19	22	27
14	20	-24	12	48	50	1	136	116	4	39	-37	H,K=	9	3	16	63	68	10	78	-88	0	87	-73	21	20	21
16	61	-64	14	32	37	2	19	17	5	141	-148	1	41	-46	18	13	12	12	26	-20	3	63	-53	24	4	-8
20	39	-40	17	62	62	3	18	19	6	28	26	2	20	-21	23	9	-11	15	39	36	7	17	-19	H,K=	5	7
22	24	-30	19	46	56	4	96	78	7	59	-57	3	31	-38	H,K=	6	4	16	35	-39	8	26	27	1	66	-55
24	20	-22	H,K=	5	1	5	85	-80	9	132	-139	8	33	-37	0	56	-52	18	47	-34	9	19	-19	3	26	-26
26	13	17	1	47	-41	6	37	34	10	33	-32	11	26	34	2	51	-50	19	21	-20	16	20	22	7	13	14
H,K=	6	0	2	50	41	7	17	15	12	25	-24	13	19	19	3	56	58	22	35	31	17	28	30	9	16	13
0	101	107	3	64	-59	8	51	-45	13	15	16	H,K=	10	3	4	57	-59	H,K=	5	5	H,K=	5	6	11	9	10
2	23	22	4	65	62	9	80	-71	14	19	-21	0	29	-32	5	81	81	2	57	-58	1	35	-34	13	11	12
4	68	68	5	23	20	10	42	-44	15	62	50	10	18	20	8	86	85	5	16	-14	2	82	63	15	44	37
6	36	34	6	54	54	15	25	22	16	17	-16	H,K=	0	4	10	35	41	6	10	-10	3	71	-57	H,K=	6	7
8	45	-43	7	17	-20	18	29	28	17	36	33	3	78	74	11	35	39	7	44	43	6	18	23	1	15	14
10	48	-43	9	17	14	H,K=	4	2	19	69	62	4	48	-53	14	12	17	8	62	-68	7	12	8	2	18	-17
12	24	-18	10	31	35	0	17	18	22	20	18	5	56	48	15	18	-22	10	44	-43	8	12	13	3	11	10
14	108	-96	11	45	44	1	19	19	23	20	18	8	79	76	16	40	42	11	21	-21	9	39	34	4	27	27
16	52	-56	13	48	50	2	30	29	26	26	25	9	72	70	18	29	30	12	17	-19	10	33	34	5	21	21
20	13	17	20	28	-27	3	118	105	H,K=	3	3	10	22	24	21	19	-17	13	39	-41	11	26	25	7	14	15
22	33	34	H,K=	6	1	4	64	-63	1	61	-62	11	58	57	22	39	-38	16	40	38	18	26	-25	12	9	-9
24	34	37	0	14	15	5	122	110	2	97	-106	12	137	136	H,K=	7	4	18	24	21	23	7	-8	H,K=	7	7
H,K=	7	0	1	21	-21	6	45	41	3	154	-156	14	74	67	1	12	14	22	19	20	H,K=	6	6	3	17	-15
2	66	-73	5	45	38	7	52	-45	4	43	42	16	42	41	2	71	64	24	16	20	0	8	5	10	9	-7
4	39	-45	8	40	38	8	20	-21	5	44	-43	17	33	-31	3	26	29	H,K=	6	5	1	27	-25	H,K=	8	7
6	95	-104	11	30	-31	9	21	22	6	87	-77	18	37	-37	4	35	37	0	23	26	2	16	15	3	24	21
8	35	-36	13	20	-20	10	23	25	7	24	25	19	86	-80	6	58	57	1	55	47	3	37	31	5	28	32
10	21	-19	14	34	-32	11	14	16	8	48	-46	21	41	-41	10	31	34	2	16	-19	4	41	47	8	4	-4
16	21	24	15	17	-19	12	10	-15	9	21	20	22	36	-30	11	22	-21	3	11	-12	5	87	72	13	11	-10
18	19	23	17	28	29	15	34	-30	10	69	-64	23	36	36	13	19	-20	5	12	16	6	29	38	H,K=	9	7
20	23	26	23	14	-14	16	28	-29	11	103	103	26	26	-25	15	23	-22	6	24	-27	7	37	34	1	25	26
22	19	22	H,K=	7	1	18	25	27	12	12	12	H,K=	1	4	16	28	-28	7	43	-36	10	48	-45	2	20	-18
H,K=	8	0	2	30	29	19	27	-26	13	86	80	1	87	87	17	15	-16	8	12	-8	12	40	-37	3	27	24
0	82	-87	4	40	39	H,K=	5	2	14	26	26	2	161	143	21	19	19	10	25	-20	13	12	-17			
2	42	-48	11	42	40	1	113	112	15	63	52	3	53	44	H,K=	8	4	12	22	22	14	24	-21			
12	57	62	H,K=	8	1	3	97	98	16	59	67	4	79	85	0	53	52	14	27	22	20	15	13			
20	18	19	0	24	24	4	28	31	17	55	47	5	14	14	1	18	-17	16	21	23	22	17	22			
H,K=	9	0	1	26	-28	5	56	-53	20	24	-26	6	125	148	4	22	30	H,K=	7	5	H,K=	7	6			
2	27	-29	2	26	28	6	28	-26	21	28	-33	8	50	54	7	26	-26	2	60	-52	1	34	28			
8	36	36	7	37	34	8	51	-49	22	20	19	10	28	36	9	48	-48	7	12	14	4	33	-32			
H,K=	1	1	9	23	24	9	86	-80	23	33	-33	11	65	-72	10	21	-24	8	35	-38	6	17	-16			

terest that N(1), C(1) and C(2) atoms of the side chain of tryptamine, and C(3)–C(4) bond of an indole ring take part in the formation of a nonplanar six-membered ring of the alkaloids, yohimbane and reserpine. In the comparison of C(3)–C(4) and C(2)–C(3) bond lengths, we included three more indole derivatives, skatole[11] (1.34 and 1.50 Å), glycyl-L-tryptophan[12] (1.338 and 1.534 Å) and 5-methoxy-dimethyltryptamine[13] (1.365 and 1.509 Å) which had been determined by X-ray analysis. The molecular mechanism of the radiation protective action of these compounds containing an indole ring is still obscure, but the facts mentioned above indicate that the mechanism may be to some

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Table 3. Final positional coordinates and thermal parameters with their standard deviations ($\times 10^4$)
Anisotropic thermal parameters are in the form of $\exp[-(B_{11}h^2+B_{22}k^2+B_{33}l^2+B_{12}hk+B_{13}hl+B_{23}kl)]$.

Atom	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
Cl	0.1715 (3)	0.6462 (3)	0.0394 (1)	0.0118 (3)	0.0081 (3)	0.0019 (0)	−0.0002 (6)	−0.0025 (2)	−0.0003 (2)
N(1)	0.4492 (8)	0.8548 (9)	0.0646 (3)	0.0091 (11)	0.0126 (13)	0.0019 (2)	0.0026 (20)	0.0006 (7)	−0.0054 (8)
N(2)	0.4851 (9)	0.4124 (7)	0.0908 (3)	0.0152 (13)	0.0039 (11)	0.0019 (2)	0.0090 (18)	−0.0029 (8)	−0.0009 (6)
C(1)	0.5584 (11)	0.8604 (11)	0.1155 (3)	0.0197 (18)	0.0152 (17)	0.0006 (1)	−0.0251 (30)	0.0004 (8)	0.0002 (8)
C(2)	0.6687 (10)	0.7437 (9)	0.1152 (4)	0.0104 (12)	0.0035 (12)	0.0022 (2)	0.0002 (21)	−0.0007 (9)	0.0014 (7)
C(3)	0.5841 (9)	0.6147 (9)	0.1172 (3)	0.0066 (11)	0.0097 (14)	0.0011 (1)	0.0027 (18)	0.0002 (7)	0.0017 (7)
C(4)	0.5750 (9)	0.5229 (10)	0.0745 (4)	0.0074 (12)	0.0106 (15)	0.0020 (2)	0.0028 (20)	−0.0022 (8)	−0.0020 (9)
C(5)	0.4960 (9)	0.5616 (10)	0.1629 (3)	0.0076 (11)	0.0120 (15)	0.0010 (1)	0.0050 (21)	−0.0003 (7)	0.0017 (7)
C(6)	0.4573 (9)	0.6068 (9)	0.2150 (4)	0.0099 (13)	0.0035 (13)	0.0022 (2)	0.0036 (19)	−0.0014 (8)	0.0010 (7)
C(7)	0.3646 (10)	0.5292 (12)	0.2493 (4)	0.0099 (14)	0.0168 (18)	0.0020 (2)	0.0044 (24)	0.0006 (9)	0.0031 (11)
C(8)	0.3033 (12)	0.4042 (12)	0.2310 (4)	0.0145 (18)	0.0166 (20)	0.0025 (2)	0.0002 (29)	0.0017 (10)	0.0063 (11)
C(9)	0.3381 (10)	0.3564 (10)	0.1790 (4)	0.0096 (12)	0.0071 (14)	0.0026 (2)	−0.0017 (22)	−0.0002 (9)	0.0037 (9)
C(10)	0.4302 (9)	0.4359 (11)	0.1456 (4)	0.0086 (12)	0.0109 (15)	0.0018 (2)	0.0045 (22)	−0.0014 (8)	0.0016 (9)
H(1)	0.363	0.793	0.056						
H(2)	0.522	0.863	0.031						
H(3)	0.401	0.956	0.054						
H(4)	0.499	0.866	0.152						
H(5)	0.635	0.950	0.117						
H(6)	0.737	0.763	0.149						
H(7)	0.734	0.753	0.079	Final thermal parameter for hydrogen atoms: Overall isotropic; 3.3 Å^2					
H(8)	0.616	0.540	0.033						
H(9)	0.461	0.340	0.065						
H(10)	0.504	0.703	0.232						
H(11)	0.339	0.555	0.291						
H(12)	0.239	0.348	0.260						
H(13)	0.294	0.249	0.165						

TABLE 4. THE MOLECULAR DIMENSIONS OF TRYPTOPHAN METABOLITES

	a*	b*	c*	d*	e	f	g
(A) Bond lengths (in Å)							
N(1)–C(1)	1.547	1.491	1.486	1.51	1.505	1.492	
C(1)–C(2)	1.501	1.502	1.513	1.53	1.539	1.532	
C(2)–C(3)	1.484	1.462	1.494	1.48	1.530	1.500	1.514
C(3)–C(4)	1.387	1.374	1.369	1.38	1.344	1.350	1.342
C(3)–C(5)	1.437	1.442	1.439	1.47	1.451	1.435	1.470
C(4)–N(2)	1.403	1.386	1.362	1.39	1.377	1.371	1.401
C(10)–N(2)	1.429	1.381	1.370	1.39	1.391	1.370	1.385
C(5)–C(10)	1.442	1.414	1.407	1.40	1.382	1.412	1.407
C(5)–C(6)	1.382	1.371	1.403	1.41	1.412	1.393	1.434
C(6)–C(7)	1.387	1.375	1.370	1.42	1.397	1.379	1.409
C(7)–C(8)	1.428	1.400	1.401	1.38	1.386	1.400	1.396
C(8)–C(9)	1.380	1.352	1.375	1.40	1.399	1.368	1.409
C(9)–C(10)	1.383	1.378	1.392	1.43	1.400	1.390	1.422
(B) Valency angles (in degree)							
N(1)–C(1)–C(2)	110.2	109.7	110.9	108	109.7	111.4	
C(1)–C(2)–C(3)	111.9	114.9	114.7	108	114.2	112.5	114.7
C(2)–C(3)–C(4)	125.4	128.4	127.8	131	128.0	125.8	127.2
C(2)–C(3)–C(5)	127.1	125.0	126.4	125	126.5	127.5	125.2
C(4)–C(3)–C(5)	107.5	106.6	105.7	104	105.5	106.6	107.1
C(3)–C(4)–N(2)	110.0	110.4	110.7	113	111.5	110.5	110.3
C(4)–N(2)–C(10)	108.2	108.0	108.8	106	107.4	108.7	108.2
N(2)–C(10)–C(5)	106.5	108.5	107.8	110	107.8	107.5	108.2
N(2)–C(10)–C(9)	129.7	130.3	130.8	128	129.0	130.8	128.2
C(5)–C(10)–C(9)	123.7	121.2	121.4	122	123.2	122.0	123.5
C(3)–C(5)–C(10)	107.7	106.6	106.9	107	107.7	106.8	106.1
C(6)–C(5)–C(10)	117.2	120.3	119.3	121	121.1	119.2	119.8
C(3)–C(5)–C(6)	135.0	133.0	133.7	132	131.2	134.2	134.1
C(5)–C(6)–C(7)	120.2	118.5	118.6	117	114.6	118.7	116.7
C(6)–C(7)–C(8)	121.0	119.7	121.7	122	124.8	121.2	122.2
C(7)–C(8)–C(9)	120.6	123.1	120.5	122	119.7	121.8	122.5
C(8)–C(9)–C(10)	117.3	117.0	118.4	116	116.4	117.7	115.2

a) Tryptamine hydrochloride, this work, b) 5-Hydroxy-DL-trypophan[14], c) Serotonin picrate monohydrate[7], d) Serotonin-creatinine sulfate complex[6], e) L-Tryptophan hydrochloride[15], f) DL-Tryptophan formate[16], g) 3-Indolylacetic acid[17]. * Radiation protective agents.

extent due to the difference in the localization of electron density distribution or the difference in the resonance structure of a five-membered ring of radiation protective agents compared with other indole derivatives.[18–20] The mean C–C distance in the benzene ring of tryptamine hydrochloride is 1.400 Å, while that of a pyrrole ring 1.422 Å. In all indole compounds, the C(3)–C(5) bond is evidently longer than the standard aromatic C–C bond.

Configuration. Aminoethyl side chain is in a folded configuration. The orientation of the C(2)–C(3) bond is *gauche* with respect to C(1)–NH_3^+ bond, and the torsion angles as defined by Klyne and Prelog[21] are −60.6° (*syn-clinal*) and +110.9° (*anti-clinal*) for the atoms N(1)–C(1)–C(2)–C(3) and C(1)–C(2)–C(3)–C(4), respectively. From conformational studies on tryptamine derivatives applying normal stereochemical rules, Chothia and Pauling proposed two possible values, 180° (*anti-periplanar*) and ±60° (*syn-clinal*), for the former torsion angle, and 0° (*syn-periplanar*) and ±90° (center of *clinal* region) for the latter one.[22] The configurations of 5-hydroxytryptophan and serotonin picrate resemble that of tryptamine. On the other hand, *anti-periplanar* conformation about C(1)–C(2) bond was observed in a serotonin-creatinine sulfate complex (+172.5°) and 5-methoxy-*N*,*N*-dimethyltryptamine hydrochloride (+179.2°). The best plane was computed for the atoms in the indole

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TABLE 5. DISTANCES OF ATOMS FROM THE LEAST-SQUARES PLANE THROUGH THE INDOLE RING (in Å)

Atom	Distance	Atom	Distance
C(3)	0.003	C(4)	0.013
C(5)	−0.022	C(6)	0.006
C(7)	−0.002	C(8)	0.009
C(9)	−0.004	C(10)	0.008
N(2)	−0.009	C(2)[a)]	0.024
C(1)[a)]	1.324	N(1)[a)]	2.498

a) Excluded from calculation of the plane.

ring and expressed by the equation, $0.8146X-0.4580Y+0.3559Z=2.2578$ in rectangular coordinates in Ångstrom. The indole part of tryptamine molecule is planar, the mean deviation of the atoms from this plane being 0.008 Å and the maximum deviations are +0.0125 and −0.0217 Å for the atoms C(4) and C(5), respectively. The individual deviations of the atoms from this least-squares plane are given in Table 5. The plane formed by N(1), C(1) and C(2) atoms makes a dihedral angle of 83.9° with that of the indole plane. The corresponding angle in serotonin-creatinine sulfate is 12.6°.

The Molecular Environment. The crystal structure viewed along a-axis is given in Fig. 4 and intermolecular distances less than 3.75 Å including hydrogen bonds in Table 6. The side chains of tryptamine are in a folded configuration, and the packing is dominated by a three-dimensional network of hydrogen bonds. The three hydrogen atoms attached to an amino nitrogen atom form three hydrogen bondings with adjacent chloride ions. These three chloride atoms are approximately at three vertices of a regular tetrahedron centered at the N(1) atom, with the C(1) atom directed toward the fourth vertex, the average N–H···Cl

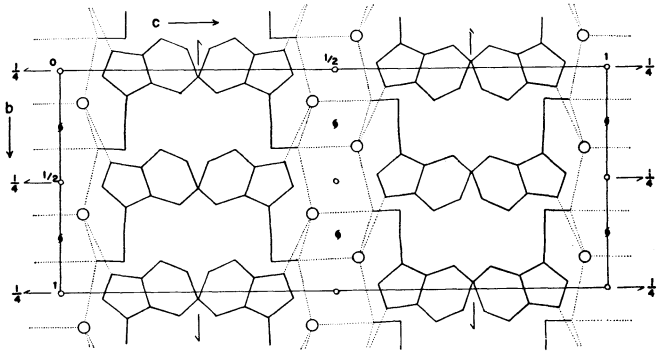

Fig. 4. The crystal structure of tryptamine hydrochloride projected along a-axis.

TABLE 6. INTERMOLECULAR SHORT CONTACTS LESS THAN 3.75 Å

Symmetrycode			
Original molecule	x	y	z
(A)	$-1/2+x$	$3/2-y$	$-z$
(B)	$1/2-x$	$-1/2+y$	z
(C)	$1/2-x$	$1/2+y$	z
(D)	$1/2+x$	y	$1/2-z$
(E)	$1-x$	$-1/2+y$	$1/2-z$
(F)	$3/2-x$	$-1/2+y$	z

(a) Hydrogen bonds

Donor	Acceptor (Original molecule)	Distance	Angle of C-Donor-Acceptor
Original N(1)–H(1)	Cl	3.221 Å	128.2°
(A) N(1)–H(2)	Cl	3.157	105.9
(B) N(1)–H(3)	Cl	3.158	108.5
(C) N(2)–H(9)	Cl	3.235	111.0

(b) Other short contacts

Atom (i)	Atom (j)	Distance (d_{ij})
C(9)	N(1) (B)	3.705 Å
C(9)	C(1) (B)	3.722
C(9)	C(6) (B)	3.659
C(8)	C(6) (B)	3.742
C(6)	C(7) (D)	3.671
C(7)	C(1) (E)	3.748
N(2)	C(2) (F)	3.459
C(4)	C(2) (F)	3.688
C(4)	C(1) (F)	3.668

distance being 3.179 Å. Another hydrogen bond is found between the N(2) atom of indole ring and chloride ion, whose distance is 3.235 Å. As a whole, each chloride atom links with the four neighboring tryptamine cations. N(1)–H···Cl hydrogen bonds form infinite columns around the center of symmetry or along the screw axes, and molecules are arranged in a double layered system parallel to *ab*-plane. In the polar part of the molecules, the hydrogen bond formation is substantial to stabilize the molecular packing. The indole rings are packed by van der Waals forces into the non-polar layer. Unusual short contacts are not observed (Table 6).

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