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Crystal and Molecular Structure of ω-Amino Acids, ω-Amino Sulfonic Acids and Their Derivatives. IV. The Crystal and Molecular Structure of γ-Aminobutyric Acid (GABA), a Nervous Inhibitory Transmitter

Ken-ichi TOMITA, Hideko HIGASHI, and Takaji FUJIWARA

Faculty of Pharmaceutical Sciences, Osaka University, Toneyama, Toyonaka, Osaka 560

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The structure of γ-aminobutyric acid (GABA), $C_4H_9NO_2$, was determined by single-crystal X-ray diffraction analysis using the data collected on a four-circle diffractometer. The compound was crystallized from an aqueous ethanol solution as needles of the monoclinic space group $P2_1/c$ with four molecules in the following unit cell; $a=7.193$, $b=10.120$, $c=8.260$ Å and $\beta=111.05°$. The structure was solved directly by a symbolic addition method and refined by a least-squares procedure. The final R is 9.3%. The molecular geometry is not a planar *trans*-zigzag configuration as found in γ-guanidinobutyric acid hydrochloride or homotaurine, but a *gauche* configuration with respect to $C_\alpha-C_\beta$ bond. The expected zwitterionic structure is evident from the locations of the hydrogen atoms in a difference Fourier map, each molecule being connected with three N–H···O hydrogen bonds to form a three-dimensional network.

Unusual amino acids, in particular ω-amino acids, are of interest with respect to their characteristic biological actions. γ-Aminobutyric acid (GABA) occurs especially in the mammalian brain[1] where it is enzymatically produced.[2] By virtue of its potent synaptic effect and other extensive evidence, GABA may play the physiological role of "inhibitory transmitter" in the mammalian central nervous system.[3-7]

It seems important to determine the molecular structure of such biologically active compounds and to compare it with that of other related derivatives in order to elucidate the close relation between molecular conformation and its specific physiological action.

The crystal data and some structural features of GABA and its derivatives were reported briefly.[8] As a part of this project, the details of structure analysis of homotaurine and γ-guanidinobutyric acid hydrochloride and hydrobromide were recently given.[9-10] This paper deals with precise analyses of crystal and molecular structure of γ-aminobutyric acid.

Experimental

Commercial γ-aminobutyric acid (GABA) was used, colorless needle-like crystals elongated along *a* axis being obtained by slow evaporation of an aqueous ethanol solution. They were somewhat hygroscopic and were used for X-ray investigation on being sealed in a quartz capillary together with a few piece of ssilica gel. Oscillation and Weissenberg photographs showed the crystals to be monoclinic. Systematic extinctions, $0k0$ absent with k odd and $h0l$ absent with l odd, indicated the space group to be $P2_1/c$. Unit-cell dimensions, $a=7.193(4)$, $b=10.120(5)$, $c=8.260(5)$ Å and $\beta=$

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2) E. Roberts and S. Frankel, *ibid.*, **187**, 55 (1950).
3) D. P. Purpura, M. Girado, and H. Grundfest., *Science*, **125**, 1200 (1957).
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8) K. Tomita, *Tetrahedron Lett.*, **1971**, 2587.
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111.05(7)° were determined on a diffractometer. The calculated density corresponding to four molecules in the unit cell is 1.226 g·cm^{-3} and in good agreement with the observed density of 1.225 g·cm^{-3}, determined by flotation in a mixture of benzene and carbon tetrachloride. Using a cuboid crystal with an edge of 0.3 mm, all the intensities of 1243 independent reflections within $2\theta<55°$ were measured on a Rigaku-Denki computer-controlled four-circle diffractometer with Zr-filtered MoK_α radiation. The ω-2θ scanning was employed at a rate of 2° per min, and backgrounds were measured for 10 sec at each start and end point of the scan interval. Lorentz and polarization corrections were applied, but neither extinction nor absorption corrections were considered. The observed structure factors were adjusted to their absolute values by Wilson's method and then normalized structure factors $|E|$ were obtained.

Structure Determination and Refinement

The crystal structure of GABA was determined by direct phase determination using the symbolic addition procedure.[11] From a $\sum_2$ list for 169 reflections with $|E|\geqq1.5$ and with probability greater than 97%, the signs of three reflections were chosen for specifying the origin and four symbols for initiating the sign determinations (Table 1). The signs were determined as follows by many different combinations in $\sum_2$ interactions; A=B=C=− and D=+. An E map calculated with the signs of 161 reflections revealed the locations of all atoms except hydrogen atoms in the unit cell. Refinement of the structure was carried out using a block-diagonal least-squares program (BLLS) with unit weight for non-zero reflections. Atomic scattering factors were taken from "International Tables for X-ray Crystallography" (1962). Application of isotropic temperature factor to non-hydrogen atoms decreased the R index ($R=\sum||F_o|-|F_c||/\sum|F_o|$) to 0.21 after five cycles. The following five cycles of anisotropic refinement lowered R to 0.13. A difference Fourier synthesis at this stage was calculated and all hydrogen atoms were shown in this map. The final cycles of refinement including the hydrogen atoms with isotropic temperature factors reduced the R index to 0.093 (0.127 including $|F_o|=0$). The final positional and thermal parameters are given in Table 2, and the observed and calculated structure factors in Table 3.

All the numerical computations were carried out on NEAC 2200-500, NEAC 2200-700 computers in the computing center of this University, and FACOM 230-60 in the data processing center of Kyoto University, using the programs written by Dr. Tamaichi Ashida and by the authors.

Table 1. STARTING SET FOR THE SYMBOLIC ADDITION PROCEDURE

h	k	l	sign	|E|
2	2	−7	+	3.593
4	3	3	+	3.475
3	1	5	−	2.671
0	2	1	A	3.745
1	1	8	B	3.072
6	1	−4	C	2.934
8	3	−7	D	3.963

Results and Discussion

The bond lengths and angles of GABA are shown in Figs. 1(a) and 1(b), respectively. The C4–N bond length of 1.469 Å is very close to the sum of each covalent bond radius for the carbon and nitrogen atom (1.47 Å), being a little less than the average value of 1.487 Å found in α-amino acids.[12] The

Table 2. FINAL POSITIONAL AND THERMAL PARAMETERS

All values × 10^4 for O, N, and C atoms; for H, position parameters × 10^3. E.s.d.'s in parentheses are in units of least significant digit. Isotropic B's for H atoms in Å^2; for other atoms, the expression is: $\exp[-(B_{11}h^2+B_{22}k^2+B_{33}l^2+B_{12}hk+B_{13}hl+B_{23}kl)]$.

Atom	x	y	z	B_{11} or B	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
O1	−196(4)	1513(3)	1757(3)	180(6)	170(4)	179(5)	79(9)	154(9)	82(8)
O2	2268(4)	500(4)	3730(4)	251(8)	217(6)	243(7)	70(11)	185(12)	244(11)
N	8163(4)	1591(3)	4316(4)	176(7)	112(4)	136(5)	−27(8)	123(10)	1(7)
C1	1544(5)	1052(4)	2320(5)	148(7)	102(4)	139(6)	1(9)	72(11)	31(9)
C2	2790(5)	1211(4)	1185(5)	149(8)	150(6)	139(7)	−8(11)	97(11)	−8(10)
C3	4989(5)	907(4)	2091(5)	166(8)	107(5)	168(7)	6(10)	134(12)	−39(9)
C4	6082(5)	1962(4)	3353(5)	164(8)	105(4)	156(7)	−2(9)	131(12)	−33(9)
H1	238(7)	230(5)	85(6)	4.4(12)					
H2	219(6)	71(5)	3(6)	4.0(12)					
H3	557(6)	81(4)	127(5)	3.1(10)					
H4	498(6)	7(4)	254(6)	3.0(10)					
H5	558(6)	210(4)	412(5)	3.5(11)					
H6	607(5)	280(4)	273(5)	2.0(8)					
H7	835(6)	70(5)	520(6)	4.2(12)					
H8	874(6)	245(4)	516(6)	3.4(10)					
H9	905(6)	170(4)	347(6)	4.0(11)					

11) H. Hauptman and J. Karle, "Solution of the Phase Problem," A. C. A. Monograph No. 3. Polycrystal Book Service, Pittsburgh (1953), Chapter I.

12) R. E. Marsh and J. Donohue, *Advan Protein Chem.*, **22**, 235 (1967).

TABLE 3. OBSERVED AND CALCULATED STRUCTURE FACTORS (×10)
Reflections with asterisk were omitted from the least-squares refinement.

H FO FC	H FO FC	H FO FC	H FO FC	H FO FC	H FO FC	H FO FC	H FO FC
K,L= 6 -1	1 89-101	7 52 53	9* 0 -11	8 61 50	7 9 16	6 17 -19	6* 0 -9
1* 0 -8	2 49 76	8* 0 -3	K,L= 2 -4	9 21 20	8 16 15	7 21 24	7* 0 16
2* 0 6	3 115 114	9* 0 3	1 48 -53	K,L= 2 -5	9 23 12	8 73 -65	8 5 -6
3 74 -74	4 66 63	K,L= 4 -3	2* 0 14	1 10 20	K,L= 1 -6	K,L= 2 -7	K,L= 3 -8
4 33 -34	5 9 -11	1 44 -62	3 37 41	2 69 -61	1 36 40	1 53 53	1 36 -36
5 53 51	6 91 92	2 45 47	4 26 -44	3 207-214	2 34 41	2 191 189	2 28 -30
6 72 -67	7 18 23	3 116 124	5 14 -18	4 2 -12	3 39 47	3 44 45	3 83 83
7 28 -29	8* 0 17	4 97 96	6 45 44	5 7 18	4 60 59	4 52 -57	4* 0 -8
8* 0 3	K,L= 5 -2	5* 0 1	7 28 -35	6 65 67	5 25 21	5 27 20	5 30 29
K,L= 7 -1	1 131-124	6 100 -95	8* 0 8	7 22 19	6 39 48	6 54 46	6 28 -23
1 12 -12	2 28 -21	7 57 61	9 35 -25	8* 0 -3	7 42 -46	7 30 29	7* 0 -3
2 53 -50	3 79 -75	8 17 15	K,L= 3 -4	9 21 -14	8 81 71	8 12 11	K,L= 4 -8
3 71 73	4 60 -55	K,L= 5 -3	1 110 110	K,L= 3 -5	9 37 33	K,L= 3 -7	1 31 27
4 16 18	5 24 23	1 122-119	2 129-145	1 104-112	K,L= 2 -6	1 5 19	2 54 45
5 9 -10	6 31 24	2 66 73	3 59 -55	2 45 -44	1 49 51	2 50 58	3* 0 1
6 44 -37	7 20 -25	3 22 27	4* 0 1	3 37 -44	2 39 -47	3 52 62	4 21 21
7 3 -16	8 25 -20	4 22 -30	5 68 69	4 45 -46	3 63 -70	4 27 -30	5 17 15
K,L= 8 -1	K,L= 6 -2	5 50 -55	6 30 -30	5 80 -78	4* 0 16	5 12 -14	6 28 24
1 59 63	1 25 19	6 13 -11	7 24 -24	6 113-113	5 12 13	6* 0 4	7* 0 -11
2 34 -40	2 12 -13	7 7 7	8 45 -38	7 32 27	6 3 15	7 15 12	K,L= 5 -8
3 71 66	3 140-140	8 33 32	9 20 17	8* 0 -7	7 30 -25	8 77 66	1 1 9
4 50 45	4 79 -72	K,L= 6 -3	K,L= 4 -4	K,L= 4 -5	8 35 -33	K,L= 4 -7	2* 0 5
5 61 58	5 47 -46	1 41 -36	1) 0 -23	1 108-110	K,L= 3 -6	1* 0 -4	3 7 12
6 14 -14	6 70 64	2 41 -33	2* 0 -16	2 29 37	1* 0 2	2 3 -17	4 19 -21
7 3 -7	7 21 -23	3 43 55	3 77 72	3 109 110	2 64 70	3* 0 3	5 21 -18
K,L= 9 -1	8* 0 -11	4 5 -6	4 39 40	4* 0 -4	3 109-103	4* 0 -1	6 30 -18
1 43 42	K,L= 7 -2	5* 0 9	5 33 -34	5 17 -20	4 36 36	5 50 -45	7 40 34
2* 0 -14	1 19 21	6 54 51	6 63 -69	6 13 -13	5 11 7	6* 0 5	K,L= 6 -8
3 28 -28	2 46 53	7* 0 -10	7* 0 -5	7* 0 -7	6 18 21	7 39 -38	1 33 -31
4* 0 -1	3 6 7	8 31 22	8 32 -28	8 37 38	7 17 -19	8 14 -11	2* 0 12
5 15 -14	4* 0 -4	K,L= 7 -3	K,L= 5 -4	K,L= 5 -5	8 48 38	K,L= 5 -7	3 24 28
6 3 -5	5* 0 19	1 86 -81	1 169 176	1 25 22	K,L= 4 -6	1 32 25	4* 0 -5
K,L= 10 -1	6 16 20	2 53 -44	2 67 58	2 123-129	1* 0 8	2 58 58	5 62 -54
1 20 18	7* 0 10	3 40 -36	3* 0 -5	3 91 94	2 139-142	3 114-108	6 29 -25
2 8 -12	K,L= 8 -2	4 32 30	4 12 -9	4 34 38	3 119-120	4* 0 10	K,L= 7 -8
3 24 15	1* 0 -3	5 44 -40	5 86 87	5 26 23	4* 0 2	5 20 -20	1* 0 0
4 20 -20	2 40 36	6 13 -12	6 97 89	6 19 -18	5 54 59	6 23 22	2 8 0
5 13 -11	3 41 -39	7 29 -25	7 18 16	7 13 -9	6* 0 -8	7* 0 2	3 26 -23
K,L= 11 -1	4 4 10	K,L= 8 -3	8 27 -21	8 16 -17	7 17 -18	K,L= 6 -7	4 21 23
1* 0 -5	5 13 13	1 32 -42	K,L= 6 -4	K,L= 6 -5	8* 0 -3	1 7 -12	5 32 -26
2 21 20	6 37 -40	2 25 -30	1 74 74	1 33 -35	K,L= 5 -6	2 33 -31	K,L= 1 -9
3 15 -8	7* 0 -5	3 88 -84	2 49 49	2 55 61	1 3 3	3 33 -36	1* 0 13
4 4 3	K,L= 9 -2	4 4 5	3* 0 12	3 79 77	2 53 -56	4 20 -22	2* 0 2
K,L= 12 -1	1* 0 13	5 11 2	4* 0 -19	4 40 40	3 73 -74	5 20 27	3 49 -53
1 24 -14	2* 0 -4	6 23 21	5 1 -8	5 75 -74	4* 0 -7	6 21 -20	4 26 -25
2 2 8	3 56 51	7 14 -14	6* 0 -12	6* 0 -8	5 25 -32	7 15 12	5 24 -17
3 25 -19	4 24 -21	K,L= 9 -3	7 36 39	7 14 18	6 12 -8	K,L= 7 -7	6 24 21
K,L= 13 -1	5 22 13	1 23 21	8* 0 -1	8 22 -19	7 9 -9	1 9 5	7 18 14
1 15 -13	6 14 -12	2* 0 7	K,L= 7 -4	K,L= 7 -5	8 25 -18	2* 0 -12	K,L= 2 -9
K,L= 0 -2	K,L= 10 -2	3 12 4	1 46 -40	1* 0 -3	K,L= 6 -6	3 30 -25	1 3 -4
1 378 306	1 37 33	4* 0 -1	2 83 77	2 42 36	1* 0 5	4 20 -13	2 36 -36
2 552-535	2 8 -13	5 30 31	3 26 -29	3 36 31	2* 0 25	5* 0 0	3 8 15
3 16 37	3 65 60	6* 0 10	4 44 -45	4* 0 0	3 33 22	6 38 32	4 64 -58
4 109-104	4 22 21	K,L= 10 -3	5 39 -42	5 64 63	4 9 10	K,L= 8 -7	5 20 -23
5 108-104	5* 0 8	1 8 -11	6 10 -1	6 10 4	5 8 7	1 52 50	6* 0 4
6 146-133	6* 0 -10	2 22 17	7 9 2	7 25 20	6 9 -5	2* 0 2	7* 0 4
7 38 -38	K,L= 11 -2	3 3 2	K,L= 8 -4	K,L= 8 -5	7 26 20	3* 0 -17	K,L= 3 -9
8* 0 -11	1* 0 7	4 15 19	1 17 16	1 17 10	K,L= 7 -6	4* 0 -5	1* 0 5
9* 0 -4	2 18 -14	5 24 -20	2 30 -31	2* 0 8	1 22 -25	5 18 15	2 20 19
K,L= 1 -2	3 22 -21	6 14 -10	3 11 -9	3* 0 11	2 81 -76	6 37 32	3 26 22
1 287 253	4 12 13	K,L= 11 -3	4 24 -29	4 42 -42	3 87 84	K,L= 9 -7	4 30 32
2 394 397	5 5 -12	1* 0 -8	5 48 39	5* 0 -1	4 40 43	1 10 -10	5* 0 0
3 36 101	K,L= 1 -3	2* 0 -5	6* 0 11	6 1 4	5 27 22	2 4 2	6 7 7
4 75 73	1 22 -33	3 31 27	7 12 -17	7* 0 7	6 26 -26	3 23 23	7 30 -22
5 182-181	2 335-336	4 4 -7	K,L= 9 -4	K,L= 9 -5	7 4 -8	4* 0 9	K,L= 4 -9
6* 0 5	3 169-169	5 16 13	1* 0 8	1 8 15	K,L= 8 -6	K,L= 0 -8	1* 0 2
7 85 84	4 26 24	K,L= 12 -3	2 8 -16	2 64 53	1 3 -11	1 34 -43	2 12 -12
8 21 16	5 177 173	1* 0 7	3* 0 -32	3 17 -21	2* 0 7	2 131-133	3 25 -21
9* 0 -2	6 90 -88	2* 0 3	4* 0 18	4 51 -50	3 29 26	3 5 21	4 30 30
K,L= 2 -2	7 84 -85	3 41 30	5 2 -39	5 46 -40	4 36 28	4* 0 6	5 55 52
1 309-281	8 23 -25	K,L= 0 -4	6* 0 6	6 20 17	5 27 -29	5 54 -54	6* 0 -1
2 38 62	9 25 25	1 73 61	K,L= 10 -4	K,L= 10 -5	6* 0 9	6 23 -38	K,L= 5 -9
3 227 227	K,L= 2 -3	2 337 342	1 9 -16	1 11 9	K,L= 9 -6	7 25 -21	1* 0 -7
4 66 87	1 11 25	3 272-260	2* 0 -12	2* 0 2	1 15 -12	8 6 -9	2 3 -1
5 22 25	2 420-424	4 118-130	3 3 -41	3 6 -3	2* 0 1	K,L= 1 -8	3 10 16
6 75 -93	3 45 56	5 23 -16	4* 0 29	4 11 -12	3 12 15	1 27 -31	4 8 -20
7 40 47	4 57 56	6 154 155	5* 0 9	5 14 12	4 17 14	2 24 -24	5 52 50
8 14 14	5* 0 -1	7 86 82	K,L= 11 -4	K,L= 11 -5	5 28 26	3 33 27	6 6 -12
9 17 17	6 141-137	8* 0 1	1* 0 -2	1* 0 5	K,L= 10 -6	4 52 47	K,L= 0-10
K,L= 3 -2	7 55 -57	9 9 -7	2* 0 -12	2* 0 5	1 34 -28	5 10 9	1* 0 -13
1 17 -10	8 15 -20	K,L= 1 -4	3* 0 -9	3 15 -14	2* 0 -3	6 10 -12	2 7 20
2 228 229	9* 0 -9	1 149-153	K,L= 1 -5	4 6 0	3 2 11	7 23 -16	3* 0 2
3 94 108	K,L= 3 -3	2 106-105	1 22 -28	K,L= 0 -6	4 12 -8	8 52 -51	4 71 73
4 79 -83	1 349 350	3 51 -53	2 40 43	1 70 65	K,L= 1 -7	K,L= 2 -8	5 19 -22
5 119-121	2 120 125	4 78 -86	3 35 37	2 214 211	1 46 -44	1 8 -4	6 29 -28
6 11 13	3 14 16	5 5 16	4 109 105	3 149 149	2 37 -38	2* 0 -7	
7 37 37	4 45 50	6 159-155	5 8 -2	4 100 -91	3 67 63	3 20 -19	
8 40 37	5 20 -23	7 19 -23	6 57 61	5 24 18	4 9 -17	4 16 24	
K,L= 4 -2	6 100 100	8 10 -6	7 27 -26	6 19 7	5* 0 -4	5 47 46	

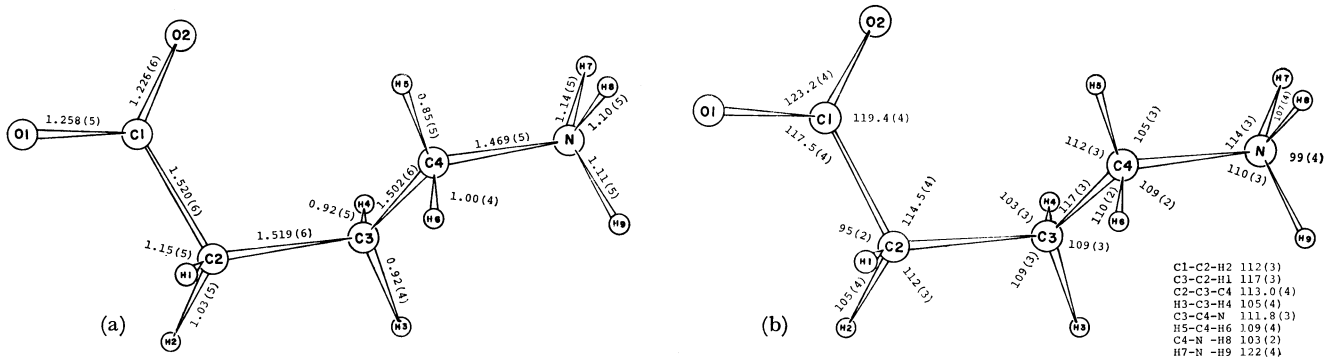

Fig. 1. (a) Bond distances (Å) and (b) Bond angles (°). The estimated standard deviations are shown in parentheses.

(Table 3. continued)

H	FO	FC
K,L=	0	0
1	114	94
2	130	-124
3	192	-214
4	192	196
5	125	135
6	77	79
7	28	23
8	41	40
K,L=	1	0
1	52	50
2	42	-50
3	262	264
4	73	-61
5	15	-13
6	96	103
7	30	20
8	10	8
K,L=	2	0
0*	0	-30
1	45	-49
2	173	-144
3	160	-162
4	116	115
5	65	-74
6*	0	0
7	33	-27
8*	0	4
K,L=	3	0
1	436	-401
2*	0	-2
3	86	90
4	68	65
5	6	6
6*	0	20
7	41	32
8	19	-24
K,L=	4	0
0	409	-413
1	160	-161
2	1	-25
3	45	35
4	72	-80
5*	0	14
6	77	-78
7	43	-42
8*	0	-7
K,L=	5	0
1	154	-164
2	121	-117
3	30	35
4	63	60
5	23	-26
6	79	-75
7	29	-30
8*	0	4
K,L=	6	0
0*	0	21
1	112	118
2*	0	17
3	82	87
4	13	-12
5	94	94
6*	0	0
7	17	10
K,L=	7	0
1	98	99
2	13	15
3	24	20
4	31	-28
5	35	-36
6	10	-9
7	12	6
K,L=	8	0
0*	0	-15
1	48	44
2*	0	-9
3*	0	2
4	17	11
5	37	-36
6	19	14
K,L=	9	0
1	15	-10
2	64	55
3*	0	-4
4*	0	3
5*	0	-3
6	2	-2
K,L=	10	0
0	20	20
1	59	-55
2*	0	19
3	24	-17
4	25	-23
5	12	-18
K,L=	11	0
1	24	-27
2	46	-39
3	8	16
4	5	9
K,L=	12	0
0*	0	8
1*	0	3
2*	0	12
3	27	-20
K,L=	1	1
0	112	-88
1	355	-321
2	83	79
3	249	283
4	80	80
5	57	-60
6	41	50
7	50	41
8	5	7
K,L=	2	1
0	971	-991
1	334	-336
2	84	-81
3	105	98
4	48	-53
5*	0	7
6	43	-46
7	34	-30
8	57	-51
K,L=	3	1
0*	0	7
1	201	-191
2	22	-41
3	166	-163
4	67	-67
5	6	9
6	58	-62
7	25	-22
8	29	-19
K,L=	4	1
0	14	-13
1	276	279
2	93	95
3	112	113
4	130	-129
5	78	78
6	17	21
7	18	14
K,L=	5	1
0	149	-160
1	184	197
2*	0	10
3	34	36
4	37	-34
5	31	-39
6	14	-11
7*	0	-12
K,L=	6	1
0	61	49
1	146	144
2	57	53
3	91	-88
4*	0	15
5	28	-27
6	19	21
7	33	28
K,L=	7	1
0	35	29
1	19	12
2	67	69
3	50	47
4	23	19
5	9	10
6	11	-9
7	34	30
K,L=	8	1
0	14	17
1	81	-83
2*	0	-10
3	39	-41
4*	0	0
5	19	-23
6	5	7
K,L=	9	1
0	59	54
1	35	-31
2	72	-71
3	30	-29
4	24	18
5	24	20
K,L=	10	1
0*	0	6
1	18	-12
2	24	33
3*	0	2
4	10	-6
5*	0	-3
K,L=	11	1
0*	0	-2
1*	0	2
2	19	-16
3	14	-16
4*	0	1
K,L=	12	1
0	23	-21
1	15	9
2*	0	8
3	6	9
K,L=	13	1
0*	0	-3
K,L=	0	2
0	395	-370
1	131	-107
2	159	-161
3	45	-49
4	5	4
5	79	72
6	7	-10
7	10	0
K,L=	1	2
0	5	14
1	60	-44
2	37	37
3	161	-152
4	183	-183
5	9	14
6	46	-46
7	6	-9
K,L=	2	2
0	69	-67
1	258	277
2*	0	15
3	78	79
4	91	-92
5	43	40
6*	0	13
7	3	-7
K,L=	3	2
0	135	-143
1	186	185
2	96	-87
3	24	-15
4	50	-45
5	17	-14
6	23	-23
7	17	-16
K,L=	4	2
0	103	101
1	186	207
2	123	131
3	108	-115
4	12	-17
5	34	-29
6*	0	9
7*	0	10
K,L=	5	2
0	117	115
1*	0	18
2	29	-28
3	108	106
4	134	124
5	29	30
6	17	-16
7*	0	9
K,L=	6	2
0	48	45
1	101	-106
2*	0	-20
3	85	-92
4	31	27
5*	0	-12
6	21	18
K,L=	7	2
0	150	149
1	58	-46
2	64	-70
3	64	-67
4	15	15
5	27	28
6*	0	4
K,L=	8	2
0	13	-12
1	55	-51
2*	0	3
3	80	74
4*	0	-7
5	10	-13
6	9	13
K,L=	9	2
0	21	-21
1	3	12
2	20	-20
3	50	-44
4*	0	-3
5	21	-14
K,L=	10	2
0	48	-51
1*	0	-3
2	12	23
3	25	28
4	10	10
K,L=	11	2
0*	0	-7
1	12	-8
2	40	36
3	21	15
K,L=	12	2
0*	0	1
1	8	6
2	29	-30
K,L=	1	3
0	103	-124
1	45	-67
2	53	-54
3	61	60
4	96	-98
5	43	-34
6	47	-42
7	7	5
K,L=	2	3
0	109	-113
1*	0	4
2	101	98
3*	0	-20
4	42	-39
5	64	-55
6*	0	7
7	32	-25
K,L=	3	3
0	206	211
1	54	58
2	89	-96
3	2	14
4	183	184
5	49	49
6	12	7
7	2	-6
K,L=	4	3
0	68	78
1	99	-102
2	93	82
3	79	-88
4*	0	-3
5	15	-10
6	27	19
K,L=	5	3
0	176	172
1	54	-49
2	33	-37
3	62	-59
4	16	15
5	39	32
6	5	3
K,L=	6	3
0	33	-31
1	46	-46
2	34	-39
3	109	110
4	21	19
5	19	-19
6	17	12
K,L=	7	3
0	69	-74
1*	0	1
2	31	28
3	68	-60
4	35	-30
5	40	-37
6	21	20
K,L=	8	3
0	71	-69
1	48	-49
2	6	2
3	60	61
4	14	17
5	2	-7
K,L=	9	3
0	17	-13
1	13	13
2	29	29
3	23	25
4	5	-7
K,L=	10	3
0	11	1
1	18	16
2	11	-13
3	23	-21
4*	0	-11
K,L=	11	3
0*	0	-3
1	18	19
2*	0	5
3	17	16
K,L=	12	3
0	25	21
1	27	18
K,L=	0	4
0	172	-172
1	60	-55
2*	0	20
3	42	-44
4	62	-66
5	55	-51
6	34	33
K,L=	1	4
0	172	180
1	150	150
2	21	18
3	127	-120
4	94	96
5	50	50
6	36	35
K,L=	2	4
0	5	-4
1	33	-29
2	122	128
3	22	-24
4	29	-32
5*	0	-5
6*	0	8
K,L=	3	4
0	169	168
1	37	34
2	18	-12
3	110	-103
4	24	26
5	51	45
6	31	24
K,L=	4	4
0*	0	9
1	22	19
2*	0	0
3	85	88
4	46	42
5	5	-6
6*	0	-4
K,L=	5	4
0	107	-117
1	36	-40
2	29	28
3	11	-4
4	41	-40
5	35	-39
6*	0	-1
K,L=	6	4
0	51	-56
1	70	-67
2	79	-80
3	46	46
4	36	38
5*	0	0
K,L=	7	4
0	25	-23
1	56	57
2	25	33
3	14	16
4	5	-13
5	9	-1
K,L=	8	4
0	15	17
1	19	-17
2*	0	10
3	29	-30
4	26	-24
K,L=	9	4
0	4	6
1	35	34
2	12	-2
3	24	24
4	30	-23
K,L=	10	4
0	24	24
1	50	43
2*	0	1
3*	0	-11
K,L=	11	4
0	36	-30
1	8	-8
2*	0	-2
K,L=	12	4
0	10	14
K,L=	1	5
0	134	135
1	77	79
2	27	31
3	125	-123
4	12	18
5	30	34
6	32	31
K,L=	2	5
0	34	33
1	7	2
2	36	32
3	93	88
4	69	66
5	23	23
K,L=	3	5
0	57	-54
1	52	-52
2	67	-67
3	60	50
4*	0	-7
5	18	-16
K,L=	4	5
0	16	-14
1	40	-31
2	109	-113
3	1	-5
4	40	40
5*	0	-4
K,L=	5	5
0	41	-51
1	41	48
2	40	44
3	37	31
4	13	-12
5*	0	-12
K,L=	6	5
0	39	52
1	58	-53
2	6	-13
3	20	-22
4	42	-37
5*	0	6
K,L=	7	5
0	14	-11
1	59	56
2	16	11
3	18	17
4	43	-35
K,L=	8	5
0*	0	17
1	47	41
2	29	25
3	11	4
4*	0	-1
K,L=	9	5
0	28	-26
1	42	-39
2*	0	-7
3*	0	-12
K,L=	10	5
0	13	13
1	4	9
2	1	-9
K,L=	11	5
0	7	13
K,L=	0	6
0	9	6
1	48	-44
2	31	27
3	91	84
4	64	62
5	39	38
K,L=	1	6
0	23	-21
1	17	18
2	70	-70
3	51	46
4	10	8
5*	0	0
K,L=	2	6
0	15	-24
1	13	-12
2	35	-41
3	6	-14
4	11	16
5	6	-11
K,L=	3	6
0	65	-61
1	30	31
2	20	14
3	46	44
4*	0	-4
5*	0	-5
K,L=	4	6
0	35	45
1	17	-19
2	30	-31
3	26	-25
4	49	-44
K,L=	5	6
0	63	-59
1	20	15
2	57	56
3*	0	12
4	43	-35
K,L=	6	6
0	26	37
1	17	13
2	18	16
3	26	23
4*	0	4
K,L=	7	6
0*	0	-3
1	36	-38
2	16	-18
3	16	-16
K,L=	8	6
0*	0	-13
1	33	31
2*	0	0
3	24	-18
K,L=	9	6
0	35	25
1	32	-30
2	13	9
K,L=	1	7
0	29	-34
1	83	78
2*	0	-5
3*	0	16
4	1	-1
K,L=	2	7
0*	0	8
1	22	23
2	18	-16
3	26	-27
4	31	-29
K,L=	3	7
0	38	-39
1	62	-63
2	41	40
3*	0	8
4	14	-18
K,L=	4	7
0	69	73
1	19	18
2	19	-14
3	12	17
K,L=	5	7
0*	0	6
1	32	-28
2	12	-14
3	9	-15
K,L=	6	7
0	20	-22
1*	0	16
2	11	13
3	25	-21
K,L=	7	7
0	47	43
1*	0	-10
2*	0	8
K,L=	8	7
0	18	-17
1*	0	-6
K,L=	9	7
0	13	-11
K,L=	0	8
0*	0	-9
1	9	14
2	4	-7
3*	0	-11
K,L=	1	8
0	24	25
1	88	-81
2	5	-12
3*	0	0
K,L=	2	8
0	35	46
1	13	24
2	22	-18
3*	0	4
K,L=	3	8
0	8	18
1	49	-46
2*	0	-15
K,L=	4	8
0	5	2
1*	0	-4
2	13	11
K,L=	5	8
0	11	14
1	26	24
2	19	19
K,L=	6	8
0	38	-39
1	24	-24
K,L=	7	8
0*	0	-5
K,L=	1	9
0	31	36
1	40	-38
K,L=	2	9
0	6	7
1*	0	-5
K,L=	3	9
0	33	-32
1	30	24
K,L=	4	9
0	17	-20
1	34	-33
K,L=	5	9
0	4	-5
K,L=	1	-1
1	249	252
2	333	325
3	37	-48
4	10	-20
5	93	-95
6	25	-32
7	8	21
8	7	15
K,L=	2	-1
1	194	-172
2	38	39
3	29	-44
4	166	203
5	104	108
6	90	105
7	17	24
8	6	13
K,L=	3	-1
1	82	68
2	11	-24
3	58	-65
4	163	-167
5	66	84
6	105	110
7*	0	-14
8	18	-19
K,L=	4	-1
1	74	101
2	82	-81
3	204	-212
4	27	-27
5	80	-90
6	51	54
7	39	-35
8*	0	0
K,L=	5	-1
1	81	-98
2*	0	11
3	13	-13
4	49	40
5	36	37
6	14	13
7	13	9
8	36	-39

GABA molecule has the zwitterionic structure as well as γ-amino-β-hydroxybutyric acid[13] or α-amino acids so far investigated. The molecular projections of GABA around the C2–C3 (C_α–C_β) and C1–C2 bonds are shown in Fig. 2. Three hydrogen atoms attached to the amino nitrogen atom are shown clearly in the difference Fourier map. This indicates that the rotation around the N–C4 bond is so restricted as having the most stable *trans* configuration (Fig. 2). The GABA molecule has no planar zigzag configuration but a somewhat twisted structure, *i.e.*, the C3–C4 bond has the *gauche* configuration to the C1–C2 bond with respect to the C2–C3 bond, the torsion angle around the C2–C3 bond being 73.6°. On the other hand, the carboxyl C1–O1 and C1–O2 bonds have nearly the *trans* and *cis* configuration to the C2–C3 bond with respect to the C1–C2 bond, and the torsion angles are 167.3 and 11.9°, respectively. It is of particular interest that the twisted molecular structure of GABA in the present work and the extended *trans*-zigzag one

13) K. Tomita, T. Fujiwara, H. Higashi, and M. Harada, presented at the Anual Meeting of Pharmaceutical Society of Japan (1971). Full detail will be published in the near future in this Bulletin.

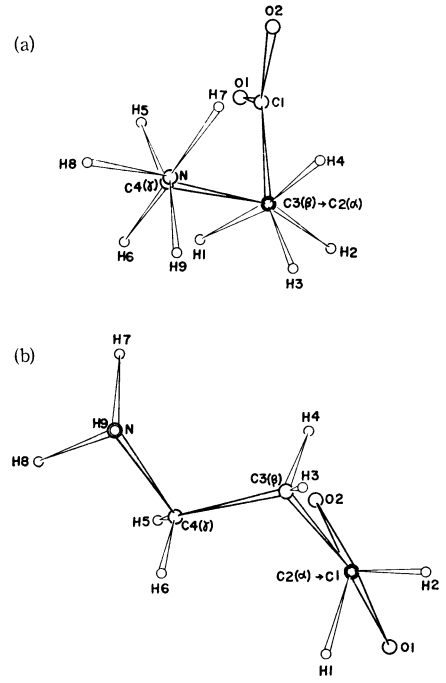

Fig. 2. Projections of the molecule. (a) around the C3–C2 (C_β–C_α) bond, (b) around the C2–C1 bond.

in GABA hydrochloride[14] are also found in bis(γ-aminobutyrato)copper(II)[15] and its dihydrate,[15] respectively. Three atoms, C1, O1, and O2, of the carboxyl group and the C2 atom are exactly in one plane (mean deviation from the least-squares plane is 0.001 Å), another plane being formed by the C2, C3, C4, and N atoms with the mean deviation of 0.03 Å. The dihedral angle between these two planes is 79.1°, which coincides well with 68.4° in bis(γ-aminobutyrato)-copper(II). Similar dihedral angles between the plane of carboxyl group and that containing C_α, C_β, and N atoms have been observed in β-alanine (83.8°),[16] bis-β-alaninatocopper(II) hexahydrate (about 70°)[17] and bis(β-amino-*n*-butyrato)copper(II) dihydrate (about 67°).[18]

The GABA molecule is thought to be like a chemical condenser which is composed of the amino terminal with a positive charge, the carboxyl end with a negative charge and three non-conductive methylene linkages connecting both ends. It is also of interest to assume that the GABA molecule is a biological on-off switch which works with the change of surrounding environments such as pH, the concentration of Na^+ and Cl^- ions and so on. GABA is well-known as a chemical transmitter in the central nervous system. Which of the two observed configurations around the C2–C3 bond is the active form is not yet certain but correlation between configuration and charge of the GABA molecule, such as monovalent cationic, monovalent anionic and zwitterionic, is probably substantial for the interaction to its receptor. The intramolecular distances between the nitrogen and oxygen atoms are listed in Table 4 together with those of the related compounds.

The crystal structure of GABA is shown in projection along the crystallographic *b* and *c* axes in Figs. 3 and 4, respectively. Distances and angles about the hydrogen

Table 4. Intramolecular distances in GABA and related compounds

From atom	To atom	Distance (in Å)	Compound
O1	N	5.612 (0.006)[a]	GABA (this work)
O2	N	4.238 (0.007)	
O1	N	6.052 (0.007)	γ-Amino-β-hydroxybutyric acid[13]
O2	N	5.027 (0.007)	
O1	N	6.11 (0.02)	GABA·HCl[14]
O2	N	5.15 (0.02)	

a) Estimated standard deviations are in parentheses.

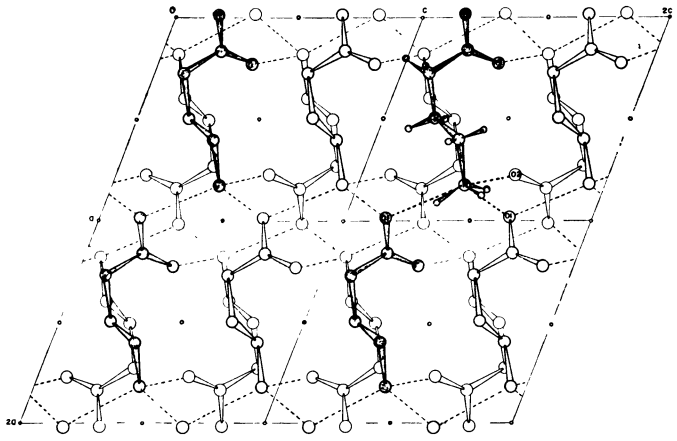

Fig. 3. The crystal structure projected along *b* axis. The broken lines indicate the hydrogen bonds.

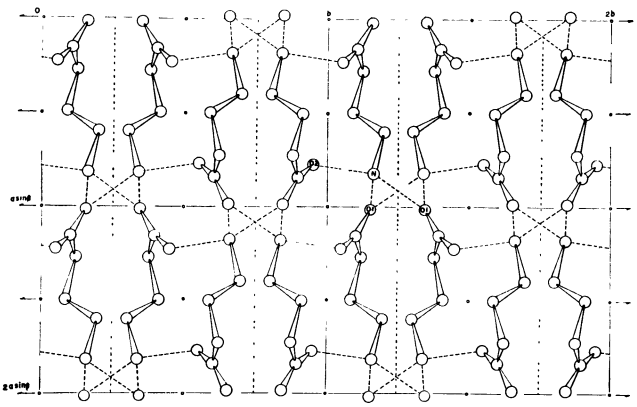

Fig. 4. The crystal structure projected along *c* axis. The broken lines indicate the hydrogen bonds.

14) K. Tomita, *Jap. J. Brain Physiol.*, **61**, 1 (1965).
15) A. Takenaka, E. Oshima, S. Yamada, and T. Watanabé, *Acta Crystallogr.*, **B29**, 503 (1973).
16) J. Jose and L. M. Pant, *ibid.*, **18**, 806 (1965).
17) K. Tomita, This Bulletin, **34**, 397 (1961).
18) B. R. Bryan, R. J. Poljak, and K. Tomita, *Acta Crystallogr.*, **14**, 1125 (1961).

Table 5. Hydrogen bond distances and angles in GABA

Distance (in Å)				Angle (in degrees)	
donor (original) acceptor					
N···O1 (I)	2.768 (0.006)[a]			C4–N···O1 (I)	103.0 (0.3)[a]
N···O1 (II)	2.726 (0.006)			C4–N···O1 (II)	107.9 (0.3)
N···O2 (III)	2.746 (0.007)			C4–N···O2 (III)	101.9 (0.3)
	original	x	y	z	
	(I)	$1+x$	y	z	
	(II)	$1+x$	$1/2-y$	$1/2+z$	
	(III)	$1-x$	$-y$	$1-z$	

a) Estimated standard deviations are in parentheses.

Table 6. Intermolecular distances less than 4.0 Å in GABA

From (original)	To	Distance (in Å)
N	O2 (I)[a]	3.346 (0.007)[b]
N	C1 (I)	3.436 (0.007)
C3	O1 (I)	3.624 (0.007)
C4	O1 (I)	3.413 (0.007)
N	C1 (II)	3.664 (0.007)
N	C2 (II)	3.836 (0.007)
C4	O1 (II)	3.471 (0.007)
N	C1 (III)	3.807 (0.007)
C4	O2 (III)	3.372 (0.007)
O2	C3 (III)	3.598 (0.007)
O2	O2 (III)	3.867 (0.010)

a) See symmetry codes in Table 5.
b) Estimated standard deviations are in parentheses.

bonds are listed in Table 5 and intermolecular distances less than 4.0 Å in Table 6. GABA molecules in the crystal are connected by three-dimensional networks of NH···O hydrogen bonds. Each hydrogen bond has nearly equal distance, three C4–N···O angles being also almost tetrahedral. The O2 atom is the acceptor of two hydrogen bonds whereas the O1 atom accepts only one hydrogen bonding. There are no unusual short contacts in this crystal, the shortest one of 3.346 Å being found between the N and O2 atoms.

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