Crystal and Molecular Structure of ω-Amino Acids, ω-Aminosulfonic Acids and Their Derivatives. VI. The Crystal and Molecular Structure of DL-γ-Amino-β-hydroxybutyric Acid (GABOB), A Nervous Inhibitory Chemical Transmitter

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DL-γ-Amino-β-hydroxybutyric acid (GABOB), $C_4H_9O_3N$, forms monoclinic plate crystals of space group $P2_1/c$, with $a=7.43$, $b=8.29$, $c=9.34$ Å, $\beta=110.9°$, and four molecules in the unit cell. Intensity data were collected by a film method. The structure was solved by the direct method with the symbolic addition procedure, and refined by least-squares methods to $R=0.096$. GABOB molecule having the zwitterionic structure, NH_3^+–CH_2–$CH(OH)$–CH_2–COO^-, forms *trans-zigzag* skeletal conformation with an intramolecular OH···O hydrogen bond of 2.773 Å, and contacts with each other by three dimensional network of NH···O and OH···O hydrogen bonds.

Using chloroxypropylphthalimide as a starting material, γ-amino-β-hydroxybutyric acid (GABOB) has been originally synthesized by M. Tomita[1] in 1923, and the optical and stereo-isomers were isolated by treatment with brucin and by difference in solubility. In order to characterize these isomers, some physicochemical investigations have been carried out and the hypothetical structures, an intramolecular hydrogen bonded form and an extended one, were proposed.[2] However, the crystal structure has not yet been determined. The chemical structure of vitamin B_T, L-carnitine, which acts as a growth factor for some insects,[3] was identified as L-γ-trimethyl-β-hydroxybutyrobetaine,[4] a trimethyl-derivative of GABOB, and the crystal structure of its hydrochloride is now solved in our laboratory.[5] Moreover, it is of most interest that GABOB is also a potent inhibitory chemical transmitter[6] in central nervous system as well as γ-aminobutyric acid (GABA) of which crystal structure was recently elucidated.[7]

In a previous paper,[8] we reported briefly about some structural features of GABOB, and this paper deals with the detailed structure analysis of this compound and the comparison of its molecular structure with those of other related compounds.

Experimental

A sample of DL-γ-amino-β-hydroxybutyric acid (GABOB) was kindly supplied by Prof. A. Musashi, Kobe Women's College of Pharmacy, Kobe. GABOB crystallizes as transparent plates from *N,N*-dimethylformamide solution by slow evaporation at room temperature. Weissenberg and precession photographs indicated the crystal to be monoclinic.

Table 1. CRYSTAL DATA FOR GABOB

$C_4H_9O_3N$	F.W.=119.1
Monoclinic	Space group $P2_1/c$
$a=7.43(1)$ Å	$Z=4$
$b=8.29(1)$	$D_m=1.45$ g cm^{-3}
$c=9.34(2)$	$D_c=1.47$ g cm^{-3}
$\beta=110.9(2)°$	

Unit cell dimensions were determined from zero-layer Weissenberg photographs about the a and b axes which were calibrated with superimposed aluminum powder photographs. The systematic extinctions ($h0l$, $l=2n+1$; $0k0$, $k=2n+1$) indicated the space group to be $P2_1/c$. The density was measured by flotation in a mixture of benzene and carbon tetrachloride. The crystal data are given in Table 1. Intensity data by a crystal of approximate dimensions, $0.15\times0.03\times0.5$ mm, were obtained from multiple-film equi-inclination Weissenberg photographs taken around the a axis. Another additional data were collected on a Rigaku-Denki four-circle computer-controlled diffractometer, using Ni-filtered Cu$K\alpha$ radiation, which were only used for the scaling purpose of the former data. Altogether, 930 independent reflections were measured. Lorentz and polarization corrections were applied but absorption correction was neglected. The observed structure factors were adjusted to their absolute values by the usual procedure, then the normalized structure factors were calculated.

Structure Determination and Refinement

The structure of DL-GABOB was solved by the symbolic addition method using a computer program DPD. After three cycles of the symbolic addition procedure for 124 reflections with $|E|\geqq1.5$ and with probability greater than 97%, signs of 97 reflections were determined. Possible two E-maps were calculated, and one of which revealed clearly the correct peaks of GABOB molecule.

Refinement of the structure was carried out by a block-diagonal least-squares procedure, using a program BLLS with unit weight for non-zero reflections. Five cycles of refinement with the isotropic temperature factors for the non-hydrogen atoms reduced an R index ($R=\Sigma||F_o|-|F_c||/\Sigma|F_o|$) to 0.18. After the

1) M. Tomita, *Z. Physiol. Chem.*, **124**, 253 (1923).
2) M. Tomita, T. Tomita, and K. Tomita, *ibid.*, **316** 121 (1959).
3) G. Fraenkel, M. Blewett, and M. Coles, *Nature*, **161**, 981 (1948).
4) M. Tomita and Y. Sendju, *Z. Physiol. Chem.*, **169**, 263 (1927).
5) K. Tomita, K. Urabe, Y. B. Kim, and T. Fujiwara, This Bulletin, to be published.
6) T. Hayashi and K. Nagai, Proc. 20th Internatl. Physiol. Cong. p. 410 (1956).
7) K. Tomita, H. Higashi, and T. Fujiwara, This Bulletin, **46**, 2199 (1973).
8) K. Tomita, *Tetrahedron Lett.*, **1971**, 2587.

Table 2. Final positional and thermal parameters

All values $\times 10^4$ for O, N, C atoms; for H, position parameters $\times 10^3$. 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}
C1	6372(6)	1025(7)	2719(6)	23(7)	39(11)	80(7)	−9(13)	32(11)	4(13)
C2	4511(6)	1350(8)	1390(5)	40(8)	82(13)	59(6)	44(15)	27(11)	26(13)
C3	2907(6)	1866(7)	1952(5)	37(8)	64(12)	55(6)	13(14)	36(11)	17(12)
C4	1123(6)	2364(7)	620(5)	53(8)	30(11)	48(6)	44(14)	29(11)	22(11)
N	−252(5)	3159(6)	1210(5)	44(7)	47(10)	66(5)	22(12)	35(10)	20(11)
O1	7873(4)	830(6)	2391(5)	27(6)	104(9)	131(6)	64(11)	99(10)	82(12)
O2	6330(5)	868(6)	4032(4)	56(6)	152(10)	59(5)	28(12)	9(9)	25(10)
O3	2359(4)	575(5)	2717(4)	51(6)	58(8)	85(5)	24(10)	59(9)	81(10)
H1	480(9)	250(9)	80(8)	1.6					
H2	402(9)	35(9)	57(8)	1.6					
H3	341(9)	299(9)	278(8)	1.4					
H4	335(9)	4(9)	375(8)	1.7					
H5	166(9)	316(9)	11(8)	1.3					
H6	36(9)	139(9)	−9(8)	1.3					
H7	55(9)	407(9)	189(8)	1.4					
H8	−67(9)	241(9)	169(8)	1.4					
H9	−165(9)	343(9)	24(8)	1.4					

refinement with the anisotropic temperature factors for all the non-hydrogen atoms, a difference Fourier synthesis was calculated. The peaks of all nine hydrogen atoms, including three attached to the amino-nitrogen atom, were found at their proper positions. The further least-squares refinement including the hydrogen atoms with isotropic temperature factors was continued until all shifts in the atomic coordinates became less than 10% of the estimated standard deviation. The final R index was 0.096 (0.123 including $F_o=0$). The final positional and thermal parameters are listed in Table 2. A list of the observed and calculated structure factors is presented in Table 3.

All the numerical computations were done on an NEAC 2200—500 computer in the Computing Center of this University and an FACOM 230-60 in the Data Processing Center of Kyoto University, using the program written by Dr. T. Ashida and by the authors.

Results and Discussion

The bond lengths and angles of DL-GABOB are shown in Fig. 1. The bond lengths and angles of the main chain are essentially the same as the corresponding ones of γ-aminobutyric acid (GABA).[7] The C3–O3 bond length of β-hydroxyl group, 1.425 Å, corresponds

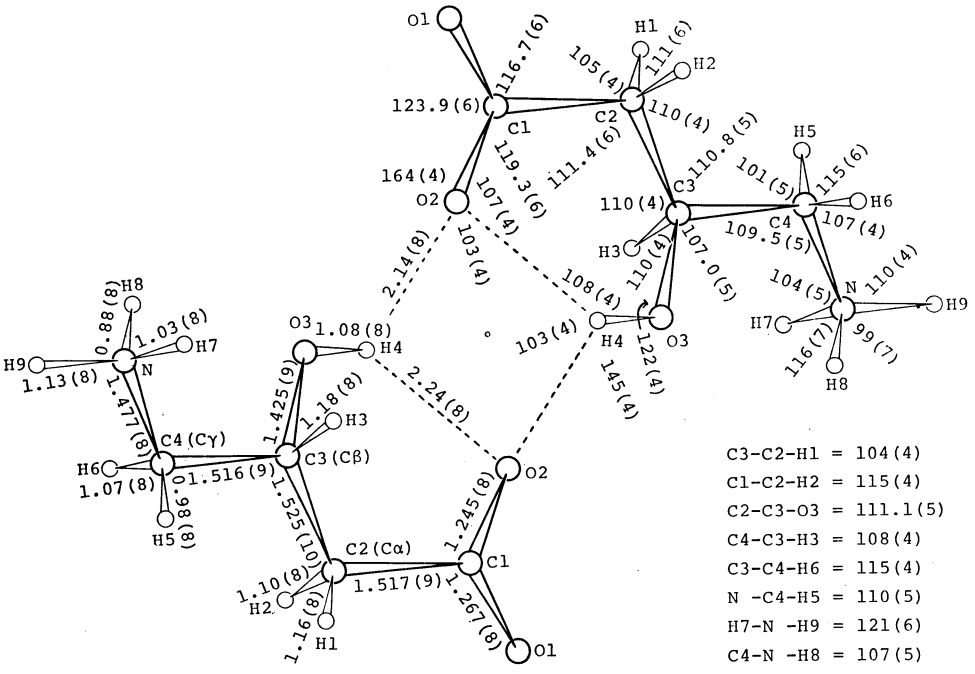

Fig. 1. Bond distances (Å) and bond angles (°). The estimated standard deviations are shown in parentheses. The broken lines indicate the hydrogen bonds.

TABLE 3. OBSERVED AND CALCULATED STRUCTURE FACTORS ($\times 10$)
Reflections marked * were omitted from the least-squares refinement.

L FO FC	L FO FC	L FO FC	L FO FC	L FO FC	L FO FC	L FO FC	L FO FC
K,K= 0 0	2 262 -251	-11 35 39	5 41 -42	-3* 0 0	-11 30 -24	1 122 -116	0 59 -57	-8 87 -73
2 566 -584	3 112 111	H,K= 5 1	6* 0 -13	-4 50 64	H,K= 4 3	2 29 23	1 301 -336	-9 93 83
4 66 61	4 157 -138	-1 152 150	7 35 -50	-5 94 98	-1 62 -44	3 76 -74	2 89 -69	H,K= 7 5
6 288 -279	5 50 42	-2* 0 8	H,K= 6 2	-6 14 -21	-2 184 174	4* 0 -14	3 124 120	-1 22 -25
8 97 88	6 131 -71	-3 93 75	0 60 -57	-7 7 -58	-3 47 48	5 36 -35	4 83 -93	-2 40 -44
10* 0 5	7 119 -156	-4 23 -26	1 38 26	H,K= 0 3	-4 75 65	6 26 21	5 50 -55	-1* 0 -5
H,K= 1 0	8* 0 148	-5 44 50	2 69 -61	1* 0 5	-5 141 -147	H,K= 6 4	6 55 46	-4 83 78
0 71 -53	9* 0 13	-6 116 -126	3 43 -39	2 296 339	-6* 0 22	0 59 -55	7 69 69	-5 32 33
2 168 -147	H,K= 2 1	-7 68 -76	4 49 -54	3 82 88	-7 47 46	1 20 -15	8* 0 -7	-6 15 -13
4 81 -73	0 117 -107	-8 40 21	5 63 61	4 87 95	-8 71 -78	2 38 24	9 59 -48	-7 19 -20
6 27 18	1 73 -57	-9* 0 -17	H,K= 7 2	5 121 -110	-9 41 37	3 59 -63	H,K= 2 5	-8 38 -33
8* 0 -3	2 338 -369	-10 41 44	0 161 -175	6 83 95	-10 29 -22	4 37 28	0 177 -161	H,K= 8 5
10 41 32	3 104 -95	-11* 0 10	1 85 82	7 25 28	-11 41 -32	H,K= 7 4	1 52 -29	-1 33 25
H,K=2 0	4 78 -77	H,K= 6 1	2 38 30	8 135 -137	H,K= 5 3	0 72 70	2 16 -2	-2 11 22
0 316 -269	5 44 -42	-1 224 -226	3 32 23	9 53 41	-1* 0 -6	1* 0 192	3 105 101	-3 41 33
2 786 792	6 195 217	-2 81 -77	4 56 -54	10* 0 2	-2 62 58	2 28 15	4 76 71	-4 81 73
4 496 -494	7 57 65	-3 50 40	H,K= 8 2	H,K= 1 3	-3 175 -164	3 108 -126	5 19 16	-5 106 -112
6 63 54	8 38 38	-4 97 -81	0 37 36	0 339 358	-4 48 43	H,K= 8 0	6 54 -58	-6 10 -13
8 56 -53	9 34 44	-5* 0 3	1 24 -23	1 159 150	-5 114 110	0 24 23	7* 0 -23	H,K= 0 6
10 25 34	10* 0 -37	-6 91 -112	2 58 -96	2 15 8	-6 168 171	H,K= 1 4	8 67 56	1* 0 -13
H,K= 3 0	H,K= 3 1	-7 25 35	H,K= 1 2	3 83 -93	-7* 0 1	-1 109 99	H,K= 3 5	2 105 91
0 182 196	0 54 53	-8* 0 6	-1 549 -633	4 71 57	-8* 0 -9	-2 61 -64	0 40 28	3 77 90
2 200 -204	1 70 -51	-9* 0 1	-2 267 -279	5 143 -147	-9* 0 -3	-3 159 -151	1 30 22	4 144 -140
4 175 -181	2 98 -86	-10 24 29	-3 149 -137	6 147 -133	-10 38 -46	-4 23 -10	2* 0 -13	5 96 -100
6 79 -77	3 43 42	-11* 0 -2	-4 243 246	7 152 148	-11 23 -27	-5 101 100	3 132 -128	6 174 169
8 83 69	4 67 76	H,K= 7 1	-5 213 216	8 53 49	H,K= 6 3	-6* 0 -6	4 27 34	7 65 -55
H,K= 4 0	5 136 150	-1 62 71	-6 96 -87	9* 0 -6	-1 173 157	-7 94 -101	5 46 28	8* 0 15
0 93 75	6 36 30	-2 166 160	-7 97 88	10* 0 4	-2 133 -126	-8 29 29	6 17 16	9 49 46
2 194 -202	7 24 -16	-3 36 36	-8 19 28	H,K= 2 3	-3 116 -111	-9 59 64	7 34 -34	H,K= 1 6
4 97 101	8 14 2	-4 36 -34	-9 41 -30	0 144 -133	-4 17 22	-10 79 -59	H,K= 4 5	0 68 45
6 77 -73	9 82 -88	-5 97 -86	-10* 0 -1	1 61 48	-5 35 15	H,K= 2 4	0 59 -48	1 47 -49
8 145 126	H,K= 4 1	-6 47 -43	-11 65 -64	2 58 46	-6 30 -23	-1* 0 -3	1 171 -171	2 44 37
H,K= 5 0	0 28 13	-7 59 -60	H,K= 2 2	3 108 -49	-7 64 42	-2 189 183	2 58 60	3* 0 -15
0 195 182	1 82 67	-8 59 -61	-1 263 -238	4 108 115	-8 116 107	-3 219 228	3 33 -42	4 100 78
2* 0 0	2 90 -76	-9 44 45	-2 66 54	5 59 59	-9 20 15	-4 145 155	4 46 48	5* 0 -1
4 41 57	3 29 21	-10* 0 3	-3 77 57	6* 0 7	-10* 0 -9	-5 267 -285	5 112 119	6 95 -77
6 33 -29	4 47 -50	H,K= 8 1	-4 213 -204	7 60 -57	H,K= 7 3	-6 39 -27	6 34 31	7* 0 -23
H,K= 6 0	5 63 -66	-1* 0 2	-5 171 -163	8 26 -18	-1 103 -98	-7* 0 4	H,K= 5 5	8 55 61
0 41 -33	6 77 73	-2 39 43	-6 83 65	9 41 37	-2 34 -27	-8 78 -79	0* 0 1	H,K= 2 6
2 153 159	7 29 -30	-3 46 43	-7 25 6	H,K= 3 3	-3 42 33	-9* 0 1	1* 0 8	0 185 164
4 114 -115	8 101 109	-4 23 -26	-8 53 -53	0 108 119	-4 110 105	-10 27 24	2 71 78	1 115 103
6* 0 21	H,K= 5 1	-5 39 42	-9 98 92	1 150 136	-5* 0 -7	H,K= 3 4	3 36 32	2 102 -96
H,K= 7 0	0 109 -99	-6* 0 -1	-10 58 55	2 186 182	-6* 0 -8	-1 16 -17	4 32 32	3* 0 -17
0 119 -124	1 266 -270	-7* 0 3	-11 47 -37	3* 0 -1	-7 95 81	-2 108 -103	5 12 12	4* 0 38
2 127 140	2 128 126	-8 68 74	H,K= 3 2	4* 0 -5	-8 31 -27	-3 345 339	H,K= 6 5	5* 0 17
4* 0 -2	3 44 33	-9 74 -81	-1 305 -265	5 97 -98	-9 37 -37	-4 84 81	0* 0 -22	6* 0 -35
H,K= 8 0	4* 0 -7	H,K= 9 1	-2 347 323	6 125 -124	H,K= 8 3	-5 197 -210	1 113 -128	H,K= 3 6
0 104 108	5* 0 0	-2 40 41	-3 191 175	7 16 -9	-1 37 -42	-6 123 130	2 69 74	0 63 66
2 91 77	6 78 89	-3 49 -46	-4 230 -228	8 101 -93	-2 81 -90	-7 51 52	3* 0 -6	1* 0 22
H,K= 1 0	7 91 88	-4 11 17	-5 117 110	H,K= 4 3	-3 20 -27	-8 51 54	4 61 58	2 90 94
-2 465 482	H,K= 6 1	-5 32 -32	-6* 0 6	0 37 35	-4 54 -57	-9 51 -56	H,K= 7 5	3* 0 -30
-4 240 225	0 332 324	-6 40 -40	-7 77 69	1 98 80	-5* 0 -2	-10 72 -63	0 98 80	4* 0 0
-6 37 -16	1 114 114	-7 18 6	-8 135 -137	2 99 -85	-6 53 59	H,K= 4 4	1 89 -64	5 38 52
-8 29 -21	2 48 -47	H,K= 0 2	-9 184 -190	3 24 -10	-7 46 49	-1 141 139	H,K= 1 5	6 47 67
-10 97 -92	3* 0 1	1 771 -803	-10 44 47	4 117 -135	-8 32 45	-2 52 -26	-1 156 162	7* 0 0
H,K= 2 0	4 22 -26	2 327 -320	-11 96 86	5 46 -44	H,K 9 3	-3 142 -127	-2 98 92	H,K= 4 6
-2 226 200	5 44 58	3 259 264	H,K= 4 2	6* 0 1	-2 36 56	-4 47 37	-3 14 17	0 132 130
-4 451 -437	6* 0 -19	4 215 203	-1 47 -31	7 44 36	-3 51 -75	-5 56 50	-4 61 -55	1 124 -145
-6 218 219	H,K= 7 1	5 199 -190	-2 41 -34	H,K= 5 3	-4 58 -78	-6 83 -80	-5 129 134	2 91 111
-8 179 165	0 50 53	6 122 -115	-3 232 -216	0 264 -267	-5 59 86	-7 29 -23	-6 72 74	3 142 195
-10 104 -106	1 53 48	7 110 102	-4 213 193	1 173 168	-6 39 -57	-8 82 86	-7 39 -31	4 30 -67
H,K= 3 0	2 75 -79	8 103 93	-5 23 -29	2 56 46	H,K= 0 4	-9 53 51	-8 18 19	5* 0 -59
-2 266 255	3 115 -119	9* 0 6	-6 116 -116	3* 0 -11	1 394 -414	-10 41 50	-9 119 -90	H,K= 5 6
-4 162 -166	4 29 31	10* 0 1	-7 180 182	4* 0 7	2 164 180	-11* 0 16	-10* 0 13	0 68 -66
-6 88 85	H,K= 8 1	11* 0 11	-8 60 -50	5 52 -48	3 88 76	H,K= 5 4	H,K= 2 5	1* 0 50
-8 92 -95	0* 0 7	H,K= 1 2	-9 45 -31	6 24 21	4 16 13	-1 385 368	-1 170 -166	2* 0 48
-10 157 167	1 107 -128	0 351 -317	-10 16 -24	H,K= 6 3	5 134 -134	-2 20 -7	-2 94 -89	3* 0 10
H,K= 4 0	2 93 101	1 140 150	-11 32 -33	0 117 102	6* 0 3	-3 197 -184	-3 146 145	H,K= 6 6
-2 347 -371	H,K= 1 1	2 87 -67	H,K= 5 2	1 55 -44	7 211 217	-4 54 -35	-4 53 47	0* 0 53
-4 35 26	-1 86 -89	3 298 275	-1 112 104	2 61 -65	8 94 84	-5 81 -19	-5 31 -39	1* 0 65
-6 301 311	-2 226 240	4 20 21	-2 121 -103	3 31 24	9 70 -63	-6 117 122	-6 132 147	2* 0 60
-8* 0 0	-3 54 54	5* 0 -13	-3 138 -120	4* 0 6	10 0 -16	-7 105 -123	-7 27 25	H,K= 1 6
-10 38 -38	-4 144 127	6 217 198	-4 205 188	5 31 -29	H,K= 1 4	-8 62 -65	-8 32 -23	-1 84 45
H,K= 5 0	-5 80 -87	7 76 -73	-5 206 208	H,K= 7 3	0 222 221	-9 82 100	-9* 0 3	-2 36 -30
-2 293 -315	-6 101 -91	8 37 -30	-6 150 -165	0 61 -63	1 50 -42	-10 31 34	-10* 0 0	-3 57 -39
-4 48 33	-7* 0 -5	9 23 19	-7 259 -282	1 64 64	2 64 57	H,K= 6 4	H,K= 3 5	-4 194 -199
-6 224 -235	-8 36 36	10* 0 3	-8* 0 4	2 110 -118	3 130 -119	-1 66 -60	-1 42 32	-5 67 52
-8 318 383	-9 40 32	H,K= 2 2	-9 104 106	3 64 55	4 124 -111	-2 29 -21	-2 157 -147	-6 34 33
-10 69 -74	-10* 0 4	0 379 -365	-10 38 -42	H,K= 8 3	5 230 239	-3 135 122	-3 79 60	-7* 0 -5
H,K= 6 0	-11 34 36	1 574 582	-11 23 -30	0 82 -88	6 72 -95	-4 39 -41	-4 107 -95	-8 67 61
-2 90 -66	H,K= 2 1	2 233 235	H,K= 6 2	1 76 95	7 66 -59	-5 72 -62	-5 93 93	-9 88 72
-4 37 -5	-1 170 169	3 340 -357	-1 123 -95	H,K= 1 3	8 38 -32	-6 41 -31	-6* 0 -3	H,K= 2 6
-6* 0 -19	-2 68 77	4 105 89	-2 272 226	-1 147 161	9 21 -18	-7 55 40	-7 108 -106	-1 207 -228
-8* 0 -1	-3 128 106	5 112 106	-3 37 -38	-2 77 -64	H,K= 2 4	-8 89 72	-8 109 109	-2 119 -101
-10* 0 6	-4 29 27	6 134 141	-4 18 15	-3 266 -286	0 38 36	-9* 0 12	-9* 0 12	-3 66 57
H,K= 7 0	-5 99 99	7 123 -116	-5 144 122	-4 25 -4	1 256 273	-10 28 35	H,K= 4 5	-4 22 -8
-2 82 79	-6* 0 -7	8 123 -112	-6* 0 10	-5 50 23	2 209 -196	H,K= 7 4	-1 73 -44	-5 82 60
-4 317 -305	-7 112 -103	9 39 40	-7 26 22	-6 115 -111	3 206 -219	-1 125 -130	-2 109 -100	-6 91 -80
-6 245 238	-8 51 56	H,K= 3 2	-8 80 -67	-7* 0 14	4* 0 10	-2 95 -99	-3 136 121	-7 41 43
-8 87 -81	-9 70 -59	0 64 -46	-9 86 -79	-8 83 -94	5 0 -12	-3 78 84	-4 75 73	-8 30 26
-10 60 56	-10 67 67	1 144 -147	-10 36 -33	-9 84 78	6 72 -65	-4 47 42	-5 47 -44	-9 25 -23
H,K= 8 0	-11 23 -21	2 67 53	-11 35 -36	-10 14 15	7 93 -85	-5 163 -174	-6 51 -50	H,K= 3 6
-2 83 -77	H,K= 3 1	3 98 81	H,K= 7 2	H,K= 2 3	8* 0 3	-6 99 -83	-7 51 44	-1 62 -54
-4 76 -79	-1 291 -305	4 105 94	-1 169 -175	-1 73 65	9 85 77	-7 111 108	-8 31 -24	-2 168 -168
-6* 0 0	-2 187 -184	-6	-2 160 158	-2 165 160	H,K= 3 4	-8 36 -30	-9 74 -79	-3 60 -34
-8 59 -43	-3 241 234	6 42 -41	-3 161 154	-3 195 -192	0 90 -88	-9 43 39	-10 24 18	-4 47 -25
H,K= 9 0	-4 159 -144	7 17 2	-4* 0 -21	-4 67 -52	1 65 -39	H,K= 8 4	H,K= 5 5	-5 59 -47
-2 44 -48	-5 45 49	8 36 34	-5 180 -155	-5 54 -43	2 45 19	-1 112 129	-1 106 -102	-6 91 -89
-4 74 81	-6 38 -36	9* 0 14	-6 113 103	-6 110 99	3 98 -90	-2 47 52	-2 27 -19	-7 110 98
-6 70 -81	-7 45 41	H,K= 4 2	-7 113 103	-7* 0 -17	4 78 -81	-3 69 -64	-3 55 48	-8 91 76
H,K= 0 1	-8 25 26	0 53 36	-8 82 -41	-8 71 -73	5 51 -45	-4 44 -48	-4 126 -116	-9 25 -19
1 204 -194	-9* 0 -3	1 60 -45	-9 68 -74	-9 48 45	6* 0 13	-5 14 -20	-5 73 -63	H,K= 4 6
2 435 -458	-10 106 104	2 72 -76	-10* 0 3	-10 55 -60	7 151 153	-6 19 -22	-6 82 64	-1* 0 16
3 111 86	-11* 0 -1	3 209 195	H,K= 8 2	-11 21 16	8 26 16	-7 12 -10	-7 26 31	-2 33 14
4* 0 0	H,K= 4 1	4 144 134	-1 30 26	H,K= 3 3	H,K= 4 4	H,K= 0 5	-8 24 -20	-3 83 -73
5 76 82	-1 136 116	5 70 -50	-2 32 -24	-1* 0 9	0* 0 0	1 70 55	-9 25 19	-4 149 -127
6 32 26	-2 279 248	6* 0 -2	-3* 0 13	-2 125 -110	1 34 -36	2 123 119	-10 25 -25	-5 64 66
7 98 94	-3 132 -116	7* 0 14	-4 61 61	-3 158 -143	2 87 -99	3 52 -36	H,K= 6 5	-6 24 -16
8 63 -71	-4 285 -279	8 25 -21	-5 42 35	-4 81 77	3 47 41	4 108 -112	-1 117 104	-7 32 -28
9 102 -100	-5* 0 -13	H,K= 5 2	-6 26 -16	-5 119 -113	4* 0 24	5 92 94	-2 50 52	-8* 0 4
10* 0 8	-6 84 -88	0 240 203	-7* 0 -7	-6 75 -75	5 34 -42	6 67 -75	-3* 0 -4	-9 28 -24
11* 0 -2	-7 17 -30	1 83 -77	-8 21 13	-7 125 127	6* 0 2	7 138 -156	-4* 0 -13	H,K= 5 6
H,K= 1 1	-8 44 34	2 46 -46	-9 74 -72	-8 31 28	7 34 29	8* 0 -6	-5 49 46	-1 42 -44
0 115 -120	-9 18 9	3 87 93	H,K= 9 2	-9 54 -48	H,K= 5 4	9* 0 5	-6 51 -38	-2 174 211
1 68 57	-10 36 34	4* 0 14	-2 40 -50	-10 36 -40	0 148 -140	H,K= 1 5	-7 150 -156	-3 24 -47

to the normal C–O single bond length. DL-GABOB molecule has the ziwtterionic structure, NH_3^+–CH_2–$CH(OH)$–CH_2–COO^-, by the protonation to the γ-amino group. D and L molecules are related by a center of symmetry as shown in Fig. 1, and the hydrogen atom attached to the O3 atom takes part in the intra- and intermolecular bifurcated hydrogen bond to form DL dimer. GABOB molecule forms the expected *trans-zigzag* conformation in crystalline state. The Cα(C2), Cβ(C3), Cγ(C4) and N atoms which compose the skeletal structure of GABOB are in a plane (plane I), and the O1, O2, and C1 atoms of the carboxyl group including the Cα(C2) atom are in another plane (plane II). Deviations of the atoms from each plane are listed in Table 4. The dihedral angle of 11.5° between these two planes indicates that all the atoms in main chain are roughly in one plane. Deviations of each atom from the best plane including all the atoms except O3 are as follows; O1: −0.19, O2: 0.06, C1: −0.03, C2: 0.17, C3: 0.10, C4: 0.14, and N: −0.20 Å. Newman projections of atoms in respect to the C1–C2, C2–C3, and C3–C4 bonds with the torsion angles are shown in Figs. 2a and 2b for GABOB and GABA, respectively. The largest conformational difference between GABOB and GABA in crystalline state is found in their torsion angles in respect to the C2–C3 bond, which are *trans* (173.7°) in GABOB and *gauche* (73.6°) in GABA, respectively. The intramolecular hydrogen

Table 4. Deviations (Å) of atoms from the least-squares planes[a)]

Plane I;	
$-0.39310X-0.91866Y-0.03919Z+2.14576=0$,	
C2	−0.065
C3	+0.064
C4	+0.078
N	−0.069
Plane II;	
$-0.13800X-0.98032Y-0.14116Z+1.67365=0$,	
C1	−0.023
C2	+0.007
O1	+0.008
O2	+0.008

a) X, Y, and Z are orthogonal coordinates in Å parallel to a, b, and c*.

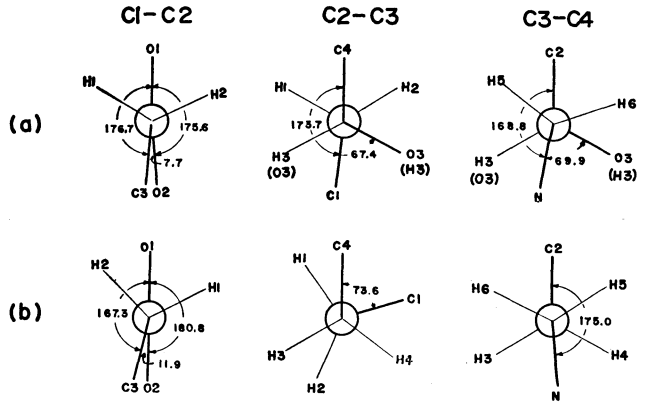

Fig. 2. Molecular conformations of DL-GABOB (a), and GABA (b).[7] Torsion angles are in degree.

bond between the O3 and the O2 atom in GABOB molecule is thought to play an important role in restricting the rotational freedom around the C2–C3 bond and keeping the extended *trans-zigzag* conformation of the molecule.

GABOB is well known as a potent inhibitory chemical transmitter in central nervous system as well as GABA, and it is of most interest that the skeletal conformation of GABOB is just the same as that of GABA hydrochloride,[9] but is different from that of GABA.[7] It is still obscure why these chemical transmitters may be released from the membrane of nerve ganglion into synapse and inhibit the transmitting of the stimulus to neighboring nerve cell, however, it may be postulated that GABA may be induced the change of its molecular conformation by binding to an ion (probably potassium or chlorine ion) due to the increase of ion concentration in presynaptic membrane by the stimulus and may be selectively released through the channel of membrane into synapse with the ion. On the other hand, the molecular conformation of GABOB is fixed as the extended *trans-zigzag* one due to the OH···O intramolecular hydrogen bond of 2.773 Å and probably released into synapse without any affection by ion concentration. GABA or GABOB in synapse may bind to the postsynaptic receptor site at neighboring nerve cell membrane in order to decrease the membrane resistance, chiefly attributable to an increase in Cl^- permeability. The nature of the interactions between the chemical transmitter and its receptor molecule is electrostatic, hydrogen bonding and van der Waals, and the resulting force between the molecules depends on the mutual orientation and conformation of the molecules. The zwitterionic form of GABA or GABOB may affect on the electrostatic interaction with the receptor and the amino group may participate in the hydrogen bonding with the receptor as a donor while the carboxyl group acts as an acceptor of hydrogen bond. In this case, the important intramolecular distances between the amino nitrogen atom and the carboxyl oxygen atoms are equal within the standard deviations; N–O1=6.052, 6.11 Å, N–O2=5.027, 5.15 Å for DL-GABOB and GABA hydrochloride, respectively. This important role of the extended *trans-zigzag* conformation for the inhibitory action may be also supported by the fact that muscimol, an isoxazole betaine isolated from *Amanita muscaria*, having a restricted similar backbone conformation, acts as a GABA-like depressant.[10] In addition, the O3 atom of GABOB is engaged in OH···O intramolecular hydrogen bond of 2.773 Å and this atom seems to interact with extra active sites of a receptor in nervous system than the GABA molecule does.

Distances and angles of the hydrogen bonds are listed in Table 5. The crystal structure of DL-GABOB is shown in Fig. 3. DL-GABOB molecules are connected by three-dimensional networks of NH···O and OH···O type hydrogen bonds, in which O3H···O2 hydrogen bond holds D-antipode of GABOB with its L-form related by a center of symmetry. There are

Table 5. Hydrogen bond distances and angles in GABOB

Distances (Å)	
donor (original) acceptor	
N ···O2 (I)	2.749 (0.007)[a)]
N ···O1 (II)	2.825 (0.007)
N ···O1 (III)	2.844 (0.007)
O3···O2 (IV)	3.080 (0.008)
O3···O2	2.773 (0.008)[b)]

Angles (degree)	
C4–N ···O2 (I)	115.7 (0.4)
C4–N ···O1 (II)	110.1 (0.4)
C4–N ···O1 (III)	96.9 (0.3)
C3–O3···O2 (IV)	137.7 (0.4)
C3–O3···O2	73.0 (0.4)[b)]

original	x	y	z
I	$-1+x$	$1/2-y$	$-1/2+z$
II	$-1+x$	y	z
III	$1-x$	$1/2+y$	$1/2-z$
IV	$1-x$	$-y$	$1-z$

a) Estimated standard deviations are in parentheses.
b) Intramolecular hydrogen bonding.

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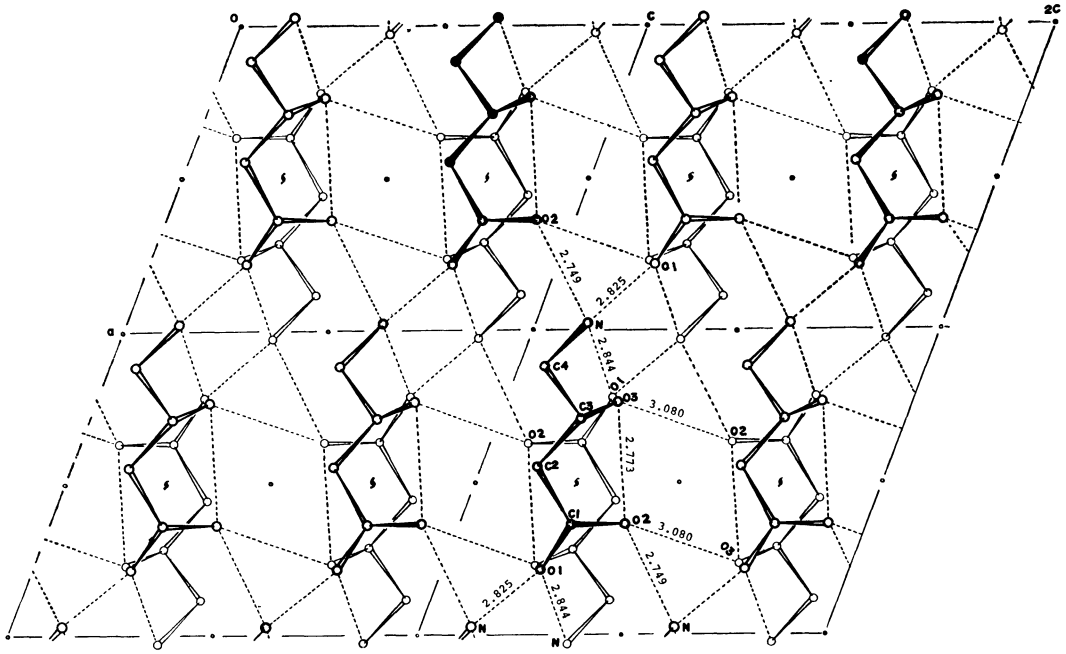

Fig. 3. The crystal structure of DL-GABOB projected along the b axis. The broken lines indicate the hydrogen bonds.

no unusual short contacts in this crystal.

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