The Crystal Structure of Alpha-amino Isobutyric Acid*

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Introduction

Since the war, crystal structures of some amino acids have been determined by several authors[1],[2],[3],[4] using the three-dimensional Fourier method. These works have revised several points of older knowledge; for example, the value of C—N distance has now turned out to be nearly equal to the sum of covalent radii of carbon and nitrogen atoms. Still it is desirable to collect more X-ray data extended to other amino acids in order to study the nature of chemical bonds as well as protein structure. Thus the present authors have carried out the investigation on the crystal structure of α-amino isobutyric acid, of which an account will be given below.

Crystallographic and Other Data

Alpha-amino isobutyric acid $(CH_3)_2C(NH_2)COOH$ was for the first time found by T. Yabuta[5] in 1938 in the decomposition products of a protein. The melting point of this new substance is 319~320°C. and it sublimes already fairly below the melting point like many other amino acids. The reaction of this substance with thymol-hypobromite is shown to be positive.

Single crystals used in this investigation were prepared from aqueous solution by slow evaporation. These show monoclinic symmetry, and cleavage parallel to (110) is very perfect and that cleavage parallel to (001) is fairly perfect. Specimens were cut into cylindrical shape being not more than 0.05 mm. in diameter. From the oscillation photographs of a-, b- and c-axes respectively, the unit cell of this crystal was determined to be of the following dimensions; $a=10.59\pm0.04$ kx, $b=8.97\pm0.01$ kx, $c=11.34\pm0.03$ kx and $\beta=94\pm0.5°$, the number of molecules in this unit being calculated to be eight from the density $\rho=1.27_5$ measured by the flotation method. The determined space group is $C^6_{2h}-C2/c$.

Determination of the Structure

The eight molecules in the unit cell should be arranged so that every set of eight atoms all occupy the eight-fold general positions of $C2/c$. The Patterson and Harker series were synthesized along a-, b- and c-axes, of which $P(x, y)$, $P(y, z)$ and $H(x, 1/2, z)$ were especially useful to find the atomic parameters. These are shown in Figs. 1, 2 and 3.

Using the results of the trial and error

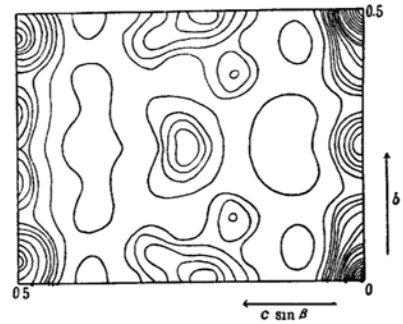

Fig. 1.– $P(y, z)$. The contour lines are drawn at equal intervals of an arbitrary scale.

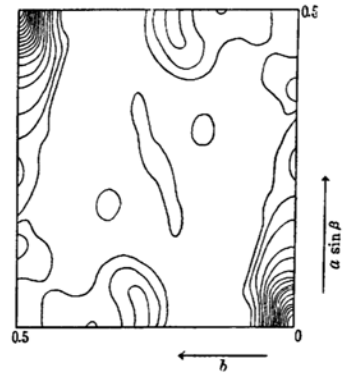

Fig. 2.—$P(x, y)$. The contour lines are drawn at equal intervals of an arbitrary scale.

* A preliminary study of this problem was reported at the anual Meeting of the Chemical Society of Japan in April, 1950.

(1) E. W. Hughes and W. T. Moor, *J. Am. Chem. Soc.*, **71**, 2618 (1949).

(2) J. Donohue, *J. Am. Chem. Soc.*, **72** 949 (1950)

(3) G. B. Carpenter and J. Donohue, *J. Am. Chem. Soc.*, **72**, 2315 (1950).

(4) D. Shoemaker, J. Donohue, V. Schomaker and R. B. Corey, *J. Am. Chem. Soc.*, **72**, 2328 (1950).

(5) T. Yabuta, *Gakuj yutsu Kyokai (Japanese Scientific Association) Ho*, **13**, 80 (1938).

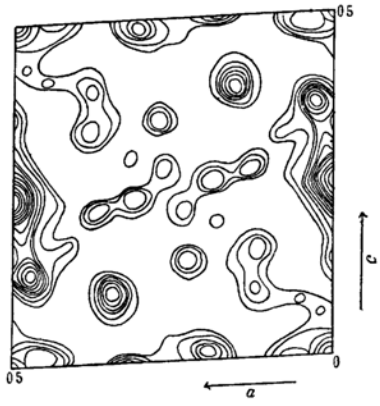

Fig. 3.—H $(x, 1/2, z)$. The contonr lines are drawn at equal intervals of an arbitrary scale.

method, the two-dimensional Fourier series were synthesized along the three principal axes. As the resolution of the obtained projections for the whole unit cell was rather poor, the part-cell projections were prepared. However, in these projections the atoms were not yet sufficiently resolved. Thus we proceeded to the three-dimensional Fourier analysis, which was done by the method of the Beevers-Lipson strips. The result is shown in Fig. 4.

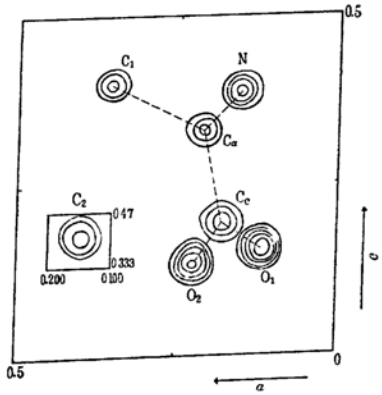

Fig. 4.—Composite drawing of electron density which were made from a section of $\rho(x, y, z)$ at several values of y. The contour lines are drawn at equal intervals of an arbitrary scale.

The refined locations of peaks were calculated by the method proposed by G. B. Carpenter and J. Donohue[3] in the paper on *N*-acetylglycine. Final parameter values obtained are listed in Table 1. Another table of comparison between observed and calculated *F*-values is omitted because of scarcity of space. Copies of this table will be available if required. In calculting structure factors a temperature factor with B=2.25 A.^{2} was used. For the accuracy of determination expressed in the usual way as

$$\Sigma(|F_{obs.}| - |F_{calc.}|)/\Sigma|F_{obs.}|$$

a figure of 0.199 was obtained for 1110 (*hkl*) reflections. It is to be added that this determination neglects the contributions of the hydrogen atoms.

Table 1

Parameter Values of Atoms

	N	C_c	C_α	C_1	C_2	O_1	O_2
x	0.154	0.178	0.212	0.355	0.148	0.112	0.224
y	0.100	−0.025	−0.031	−0.027	−0.167	0.083	−0.121
z	0.388	0.199	0.331	0.365	0.382	0.159	0.138

Discussion of the Structure

The determined atomic configuration and dimensions of the α-amino isobutyric acid molecule in the crystal are shown in Fig. 5. as well as in Table 2.

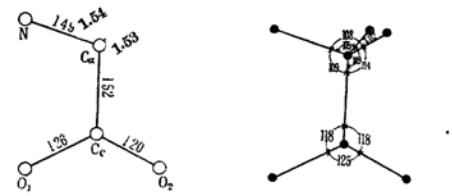

Fig. 5.—The molecule of the α-amino isobutyric acid, showing interatomic distances and bond angles. The hydrogen atoms are not drawn.

Table 2

Interatomic Distances and Bond Angles

Distances kx	Angles
$O_1-C_c=1.26$	$O_1-C_c-O_2=125.3°$
$O_2-C_c=1.20$	$O_1-C_c-C_\alpha=117.9°$
$C_c-C_\alpha=1.52$	$O_2-C_c-C_\alpha=117.7°$
$C_\alpha-N=1.49$	$C_c-C_\alpha-N=108.8°$
$C_\alpha-C_1=1.53$	$C_c-C_\alpha-C_1=114.0°$
$C_\alpha-C_2=1.54$	$C_c-C_\alpha-C_2=108.7°$
	$N-C_\alpha-C_1=107.5°$
	$N-C_\alpha-C_2=104.9°$
	$C_1-C_\alpha-C_2=112.2°$

The two $C_\alpha-C$ (methyl) distances and the $C_\alpha-N$ distance were found to be 1.53, 1.54 and 1.49 kx, respectively, in agreement with the sum of the covalent radii of Pauling. Among the bond angles of carbon atoms which are mostly nearly equal to the standard tetrahedral angle, there are observed some appreciable

deviations, for example, $C_c-C_\alpha-C_1=114.0°$ and $N-C_\alpha-C_2=104.9°$. As for the structure of the carboxylic group it was found that the bond distances $C-O_1$ and $C-O_2$ are somewhat

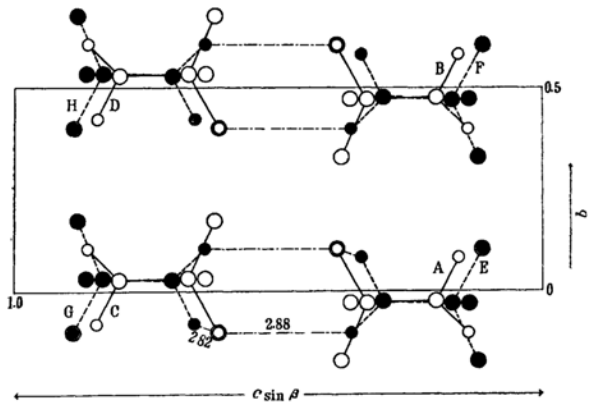

Fig. 6a.—Projection of molecules upon the (100) plane of the crystal, showing some significant interatomic distances. To distinguish molecules which superpose one another, atoms of one kind are drawn in white circles and those of the other kind are drawn in black circles.

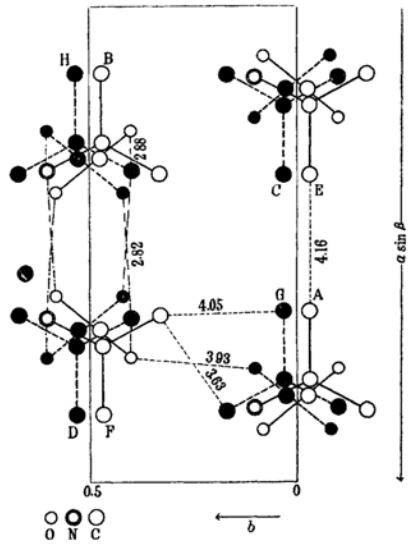

Fig. 6b.—Projection of molecules upon the (001) plane of the crystal, showing some significant interatomic distances. To distinguish molecules which superpose one another, atoms of one kind are drawn in white circles and those of the other kind are drawn in black circles.

different, 1.26 and 1.20 kx. respectively. It is to be noted that in the case of DL-alanine $C-O_1=1.21$ Å. is shorter than $C-O_2=1.27$ Å. Like all the amino acids hitherto analysed, the *N* atom lies approximately in the same plane as the carboxylic group. The value of the interatomic distance between N and O_1 in the molecule was calculated to be 2.61 kx.

The projections of the molecules along *a* and *b* axes respectively are given in Figs. 6a and 6b. The principal intermolecular interatomic distances between molecules are listed in Table 3. In these, the letters A to H refer to equivalent points in the space group as follows:

A: x, y, z; B: $1/2+x, 1/2+y, z$; C: $-x, -y, -z$; D: $1/2-x, 1/2-y, -z$; E: $-x, y, 1/2-z$; F: $1/2-x, 1/2+y, 1/2-z$; G: $x, -y, 1/2+z$; H: $1/2+x, 1/2-y, 1/2+z$.

It is seen that there are two types of hydrogen bonds in intermolecular contacts, one of which is formed between N and O_1, *e. g.* N in (B) and O_1 in (F) and its dimension is 2.82kx, and the other is between N and O_2, *e. g.* N in (B) and O_2 in (H) and its dimension 2.88 kx. It can be said that the molecules are tied to one another with hydrogen bonds in two dimensions between amino groups and carboxylic groups. There is seen considerably short intermolecular contact with respect to methyl groups, *e. g.* C_2 in (F) and C_2 in (G). The dimension of this contact is 3.63 kx. still shorter than that 3.79 A. in L-threonine crystal.

Considering the intermolecular contacts observed, the cleavages parallel to (110) and to (001) are interpreted quite naturally. For reference molecular dimensions found in some crystals of amino acids are listed in Table 4, where those of α-amino isobutyric acid are given in the last column.

Table 3

Principal Intermolecular Atomic Distances (kx)

N (B) – O (F) = 2.82	N (A) – O (B) = 5.56
N (B) – O (H) = 2.88	N (A) – O (G) = 4.20
O (A) – O (B) = 3.20	C (F) – C (G) = 3.63
N (A) – N (C) = 4.61	C (F) – C (G) = 4.05
N (A) – N (D) = 4.14	C (A) – C (E) = 4.16
N (A) – N (E) = 4.23	O (F) – O (G) = 3.93
N (A) – O (E) = 4.50	C (F) – O (G) = 5.86
N (A) – O (F) = 4.75	

Summary

X-ray examination of crystals of α-amino isobutyric acid shows them to be built upon a composite monoclinic unit having $a=10.59$ kx, $b=8.97$ kx, $c=11.34$ kx, and $\beta=94°$, containing eight molecules. The space group is $C2/c$ with all atoms being in the general positions with the following parameters which were determined by the three-dimensional

Table 4

A Comparison of Dimensions found in Some Crystals of Amino Acid.

	N-acetyl-glycine.	β-glycyl-glycine.	DL-alanine.	L-threonine.	α-amino isobutyric acid.
C_c-O	1.19	1.21	1.21	1.24	1.26
	1.31	1.27	1.27	1.25	1.20
C_c-C_α	1.51	1.53	1.54	1.52	1.52
$C_\alpha-N$	1.45	1.48	1.50	1.49	1.49
$C_\alpha-C$	—	—	1.51	1.54	1.53
	—	—	—	—	1.54
$C_\beta-C$	—	—	—	1.50	—
$O_1\cdots N$	—	—	2.69	2.67	2.61
Hydrogen Bond;					
O...N	3.03	2.80	2.88	2.90	2.88
	—	2.81	2.84	2.80	2.82
Bond Angles;					
$O-C_c-O$	124	125	125	127	125
$O-C_c-C_\alpha$	124	123	121	117	118
	112	112	113	116	118
$C_c-C_\alpha-N$	110	111	108	110	109
$C_c-C_\alpha-C$	—	—	111	113	114
	—	—	—	—	109
$N-C_\alpha-C$	—	—	110	108	108
	—	—	—	—	105
$C-C_\alpha-C$	—	—	—	—	112
$C_\alpha-C_\beta-O_H$	—	—	—	104	—
$O-C_\beta-O_H$	—	—	—	111	—

Fourier analysis; nitrogen: $x=0.154$, $y=0.100$, $z=0.388$; carboxylic carbon: $x=0.178$, $y=-0.025$, $z=0.199$; α-carbon: $x=0.212$, $y=-0.031$, $z=0.331$; methyl carbon 1: $x=0.355$, $=-0.027$, $z=0.365$; methyl carbon 2: $x=0.148$, $y=-0.167$, $z=0.382$; oxygen 1: $x=0.112$, $y=0.083$, $z=0.159$; oxygen 2: $x=0.224$, $y=-0.121$, $z=0.138$. Bond distances are 1.26 and 1.20 kx. for carbon-oxygen, 1.52, 1.53 and 1.54 kx. for carbon-carbon and 1.49 kx. for carbon-nitrogen. There are observed a considerably close intramolecular approach between nitrogen and oxygen atoms and also close contact between two methyl groups.

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