perature of the amine (277°) but, since the critical temperature of the mixture is evidently higher than 277°, it may be possible that an upper critical solution temperature exists.

Results of the study of the three-component system are given in Table II and the solubility curve for this system at 25° is shown in Fig. 2. The broken part of the curve represents those compositions where the transition temperature was found to be indistinct. The composition corresponding to a maximum in the curve is approximately 31.5% amine, 26.5% ethanol, and 42.0% water.

TABLE II

MUTUAL SOLUBILITIES OF AMINE AND ETHANOL IN WATER

Weight, % amine	Weight, % ethanol	Weight, % amine	Weight, % ethanol
77.6	1.8	34.4	26.1
68.9	8.8	31.7	26.3
67.2	10.0	29.9	26.2
63.8	12.1	26.7	26.1
62.9	13.0	24.4	25.8
60.9	14.0	22.2	25.6
58.6	16.1	20.6	25.1
56.3	17.9	19.1	24.7
54.5	19.0	16.8	24.1
54.2	18.7	14.9	23.7
49.1	22.0	12.3	22.8
45.6	23.6	9.4	21.6
41.6	25.4	8.1	20.8
38.8	25.9	7.1	19.9
37.9	26.4	5.1	18.6
36.5	26.0	4.4	17.5

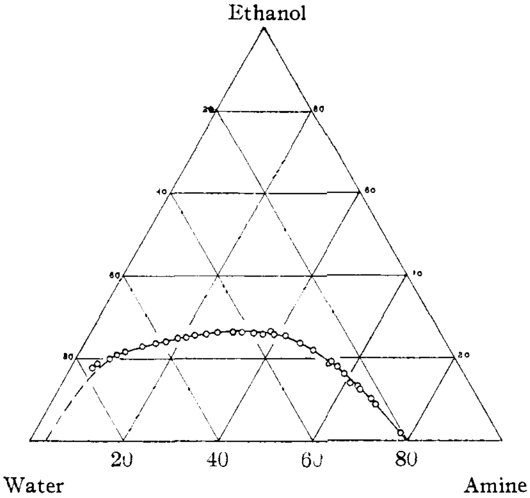

Fig. 2.—Solubility curve at 25° for the system di-*n*-propylamine–water–ethanol.

Summary

The mutual solubility of di-*n*-propylamine and water has been determined and the critical solution temperature found to be near −4.8°. The critical solution composition is approximately 34% amine and 66% water. No upper consolute temperature was found.

The solubility curve of the ternary system di-*n*-propylamine–ethanol–water has also been investigated at 25°.

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The Crystal Structure of *dl*-Alanine

BY HENRI A. LEVY AND ROBERT B. COREY

Introduction

The determination of the crystal structure of *dl*-alanine was undertaken as a continuation of X-ray diffraction studies which are a part of a program of research upon the constitution and configuration of proteins. In earlier investigations the structures of crystals of diketopiperazine[1] and of glycine[2] were determined and the interatomic distances and bond angles of their molecules thereby established. Definite data were thus made available for the construction of a tentative model of the polypeptide chain. In discussions of these data[1,2] and in a more recent consideration of their application to the problem of the configuration of the polypeptide chain[3] in protein molecules the presence of certain anomalies among the interatomic distances found in glycine and in its cyclic anhydride have been mentioned. Thus in both of these compounds a C–N distance near 1.40 Å. is found which is shorter than that predicted from the covalent radii (1.47 Å.). In diketopiperazine the C–C distance, 1.47 Å., is surprisingly short compared to that which might be anticipated (1.54 Å.); however, in glycine the distance 1.52 Å. is in agreement with the normal

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(1) R. B. Corey, THIS JOURNAL, **60**, 1598 (1938).

(2) G. Albrecht and R. B. Corey, *ibid.*, **61**, 1087 (1939).

(3) R. B. Corey, *Chem. Rev.*, **26**, 227 (1940).

value within the limits of error of the determination. A knowledge of corresponding atomic separations in the molecule of alanine, in which a hydrogen atom is replaced by a CH_3 "side chain," seemed a desirable extension of our information regarding these fundamental units of protein structure. For this reason the present determination of the crystal structure of *dl*-alanine was undertaken.

In a preliminary paper upon the crystal structures of some amino acids and related compounds, Bernal[4] reported that the unit cell of *dl*-alanine is orthorhombic with $a_0 = 6.0$ Å., $b_0 = 12.0$ Å., $c_0 = 5.8$ Å., containing four molecules of CH_3NH_2-$CHCOOH$. He found the space group to be $C_{2v}^9 - Pbn$. The crystals are optically negative with α parallel to the long axis, b. The general features of a suggested arrangement of the molecules within the unit cell were depicted, but no X-ray intensity data were given and no attempt was made to determine the positions of the atoms.

Preparation of Crystals.—The *dl*-alanine used was obtained from Amino Acid Manufactures, University of California at Los Angeles. The crystals, which were grown by slow evaporation of aqueous solutions, were small, well-formed needles elongated along the c axis, and characterized by the absence of any pronounced cleavage. For photographs involving rotations about this axis specimens about 0.1 mm. in diameter and 1 mm. long were used. For rotations about the a axis it became necessary to mount somewhat larger crystals (*ca.* 0.5 mm. diameter) horizontally on a firm glass fiber by means of shellac which was then thoroughly hardened by baking at about 70°. The orientation of the crystal was then adjusted by means of an optical goniometer and checked by X-ray photography, after which the ends of the needle were carefully dissolved away leaving a tiny portion in the form of a vertical cylinder of approximately uniform cross section which was used for the collection of X-ray intensity data.

The Unit Cell and Space Group.—Weissenberg photographs taken about the a and c crystallographic axes showed the unit cell of *dl*-alanine to be orthorhombic. Measurements of reflections from (200), (210), (310), (320), (002), and (011) observed on rotation photographs were used to obtain the dimensions $a_0 = 12.04$ Å., $b_0 = 6.04$ Å., $c_0 = 5.81$ Å., all $\pm$ 0.01 Å., based upon the wave length 1.539 Å. for the Cu Kα doublet. The density of the crystals, determined by the flotation method, was found to be 1.40, so that the unit of structure contains four molecules (calculated 4.00). The presence of all orders of (hkl) indicates a primitive lattice. Systematic absence of all $(h0l)$ reflections having h odd and of all $(0kl)$ reflections having $k + l$ odd establishes the space group as $D_{2h}^{16} - Pnam$ or $C_{2v}^9 - Pna$. Of the three sets of four equivalent positions provided by $D_{2h}^{16} - Pnam$, two require that the atoms lie at symmetry centers 000, $00\frac{1}{2}$, $\frac{1}{2}\frac{1}{2}0$, $\frac{1}{2}\frac{1}{2}\frac{1}{2}$, and $0\frac{1}{2}0$, $0\frac{1}{2}\frac{1}{2}$, $\frac{1}{2}00$, $\frac{1}{2}0\frac{1}{2}$, and the third requires that the atoms lie in mirror planes perpendicular to the c axis, at $xy\frac{1}{4}$; $\bar{x}\bar{y}\frac{3}{4}$; $\frac{1}{2} - x, \frac{1}{2} + y, \frac{3}{4}$; $\frac{1}{2} + x, \frac{1}{2} - y, \frac{1}{4}$. Since it is certain that an alanine molecule has neither a center nor a plane of symmetry, the atoms of the four alanine molecules cannot lie in these positions. Restrictions of this sort are not imposed by the symmetry elements of $C_{2v}^9 - Pna$, in which all atoms occupy the general positions xyz; $\bar{x}, \bar{y}, \frac{1}{2} + z$; $\frac{1}{2} - x, \frac{1}{2} + y, \frac{1}{2} + z$; $\frac{1}{2} + x, \frac{1}{2} - y, z$. *Pna* is thus the space group which is to be considered as a basis for this structure.

The symmetry elements present in the space group *Pna* are (1) two-fold screw axes at $xy = 00$, $\frac{1}{2}0$, $0\frac{1}{2}$, and $\frac{1}{2}\frac{1}{2}$, (2) n glide planes at $x = \frac{1}{4}$ and $\frac{3}{4}$, and (3) a glide planes at $y = \frac{1}{4}$ and $\frac{3}{4}$.

Axial ratios of *dl*-alanine calculated from our X-ray measurements are $a:b:c = 1.993:1:0.962$. Those based upon optical measurements reported by Groth[5] are 0.9971:1:0.4949, which, upon halving the length of the b axis, become 1.9942:1:0.9898. Difficulty in obtaining satisfactory optical signals from the terminal faces of the needle-like crystals is doubtless responsible for the discrepancy of about 3% in the $c:b$ ratio and also for the erroneous assignment of alanine to the point group D_{2h}. Upon interchanging the a and b axes both the size of the unit and the space group are seen to be in accord with the results previously reported by Bernal.[4]

Determination of the Structure

Disregarding the hydrogen atoms, which contribute too little to the X-ray scattering to permit the determination of their positions, a solution of the structure requires the assignment of values to three parameters, x, y, and z, for each of two oxygen atoms, three carbon atoms, and one nitrogen atom, with the exception that the symmetry of the space group *Pna* allows one z parameter to be arbitrarily assigned. Preliminary examination of the X-ray diffraction data shows that reflections from the planes (210) and (400) are strong, while that from (120) is weak. These data strongly suggest a high concentration of scattering matter in the neighborhood of $x =$

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(4) J. D. Bernal, *Z. Krist.* **78**, 363 (1931).

(5) P. Groth, "Chemische Krystallographie." Vol. III, Leipzig, 1910, p. 214.

$^1/_8$, $y = {}^1/_4$, with an approximately symmetric distribution in the y direction about $y = {}^1/_4$. The optical data[4] suggest compression of the distribution in the x direction, with greater extension in the y and z directions.

Although these clues to the positions of the atoms together with knowledge of the size and shape of the glycine molecule[2] might be expected to provide a valuable guide in the determination of the atomic arrangement in crystals of *dl*-alanine, the presence of the methyl group introduces so many complications into the structure that any attempt at its solution by trial and error methods was soon found to be impracticable. X-Ray intensity data from a complete series of Weissenberg photographs taken about the a and c axes using Cu Kα radiation were therefore compiled and used in the calculation of sections through the Patterson diagram[6] as suggested by Harker.[7,2] The data employed in the evaluation of the various "F^2 series" may be obtained from Tables I, II, III, and IV.

Estimations of the relative intensities of reflections were made by comparing densities of spots on several negatives which differed only by known exposure ratios. In the case of the ($hk0$) spectra, photographs yielding intensity estimations believed to be especially reliable were obtained by a multiple film technique similar to that employed by deLange, Robertson, and Woodward.[8] Five Agfa non-screen X-ray films were placed one behind another in a Weissenberg camera and exposed simultaneously. The constant ratio of exposures of corresponding spots on adjacent films was found to be approximately 2.8 for Cu Kα radiation. Values of F^2 were obtained from the estimated intensities by dividing them by the Lorentz and polarization factor for equi-inclination Weissenberg data, $(1 + \cos^2 2\vartheta)/\sin 2\vartheta \sin \varphi$, in which ϑ is the Bragg angle and φ the azimuthal angle of the reflection.

The three-dimensional Patterson function

$$P(X, Y, Z) = \sum_h\sum_k\sum_l |F_{hkl}|^2 \cos 2\pi(hX + kY + lZ)$$

contains maxima at vector distances from the origin which correspond to vector distances between atoms in the crystal. (The symbols X, Y, and Z which represent the arguments of the Patterson function should not be confused with x, y, and z, the parameters of position in the unit cell.) The presence of two-fold screw axes perpendicular to the xy plane suggests that the diagram most useful for the determination of atomic positions should be the section $Z = \frac{1}{2}$ of the Patterson diagram, given by the series

$$P(X, Y, \tfrac{1}{2}) = \sum_h\sum_k\sum_l |F_{hkl}|^2 \cos 2\pi(hX + kY + \tfrac{1}{2}l)$$

which may be rewritten in the form

$$P(X, Y, \tfrac{1}{2}) = \sum_h\sum_k C_{hk} \cos 2\pi\,(hX + kY) \text{ in which}$$

$$C_{hk} = \sum_l (-1)^l\, |F_{hkl}|^2$$

In the present case the maxima of this function will arise from the following types of interatomic distances in the crystal.

(1) Two atoms related by a two-fold screw axis will have a separation of one-half unit in the z direction and will give rise to a peak in $P(X, Y, \frac{1}{2})$. As has been noted,[7,2] one-half of the vector from the origin to such a maximum may therefore be interpreted directly as the vector displacement of an atom from one of the screw axes of the crystal. If, then, a plot of $P(X, Y, \frac{1}{2})$ reduced to half scale is placed upon a projection of the unit cell so that the origin coincides with the positions of the screw axes, a maximum of this type might be expected to represent an atomic position. Since the function is unable to distinguish between the two non-equivalent sets of screw axes of the space group Pna, the number of maxima of this sort will be in general twice the number of atoms producing them.

(2) Any pair of atoms having a separation of about one-half unit in the z direction will give rise to a maximum in the function $P(X, Y, \frac{1}{2})$.

(3) Two atoms lying in or near the same xy plane will give rise not only to their respective peaks of type 1, but to an additional maximum half way between these two.[2] Fortunately the atomic distribution in crystals of *dl*-alanine is such that no maxima of this type are observed.

(4) Two atoms related by the n glide plane will have a separation of one-half unit in both the y and z directions and will therefore give rise to a maximum in the function $P(X, Y, \frac{1}{2})$ lying along the line $Y = \frac{1}{2}$. One-half the distance from the Y axis to a maximum along this line may thus represent the distance of an atom from the n glide plane.

The general features of the diagram, shown in Fig. 1, suggest a concentration of atoms near $x = \frac{1}{8}$, $y = \frac{1}{4}$ in the unit cell, in agreement with

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[6] A. L. Patterson, *Z. Krist.*, **90**, 517 (1935).

[7] D. Harker, *J. Chem. Phys.*, **4**, 381 (1936).

[8] J. J. deLange, J. M. Robertson, and I. Woodward, *Proc. Roy. Soc.* (London), **A171**, 398 (1939).

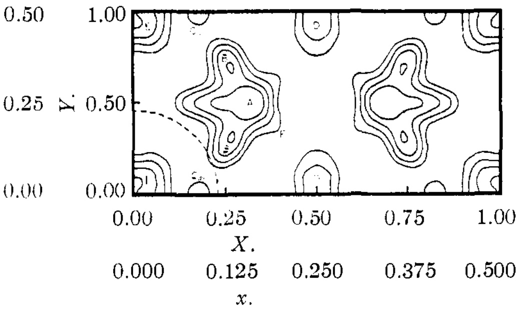

Fig. 1.—A half-scale plot of the Patterson section $P(X, Y, \frac{1}{2})$ superposed on a quarter of the unit cell. Contour lines are drawn at arbitrary equal intervals and negative contours are omitted. Letters identify corresponding peaks in succeeding Patterson plots. The scales labelled X and Y refer to the Patterson function; those labelled x and y to the unit cell.

the conclusions already drawn. The great spread in the X direction of the peak about A does not necessarily indicate extension of the molecule in this direction, since all maxima of type 4 will fall in this region. If peak D represents an atomic position, it means that an atom lies very close to the n glide plane at $x = \frac{1}{4}$. Inspection of the plot of the section $P(X, \frac{1}{2}, \frac{1}{2})$, Fig. 2, shows no maximum closer to the origin than $X = 0.15$, so that there can be no atom closer to the n glide plane than 0.075 a_0 or 0.84 Å., which excludes the presence of atoms much nearer $x = \frac{1}{4}$ than the general maxima about A of Fig. 1. Although peak D does not therefore represent an atomic position, its presence is readily accounted for as a peak of type 2, the result of interactions between two non-equivalent atoms in molecules related by the a glide plane and fortuitously having a separation of about one-half unit along the c axis. Peak E, if an atomic position, indicates an atom lying very close to a two-fold screw axis, a position which appears unlikely. Construction of the section $P(0, Y, Z)$, Fig. 3, reveals that this peak lies actually slightly above or below $Z = \frac{1}{2}$, and is therefore also to be considered to be of type 2.

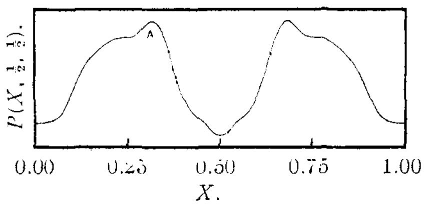

Fig. 2.—A plot of the Patterson diagram $P(X, \frac{1}{2}, \frac{1}{2})$. The absence of peaks near $X = 0$ and $X = \frac{1}{2}$ shows that no atoms are located close to $x = \frac{1}{4}$ and $x = 0$.

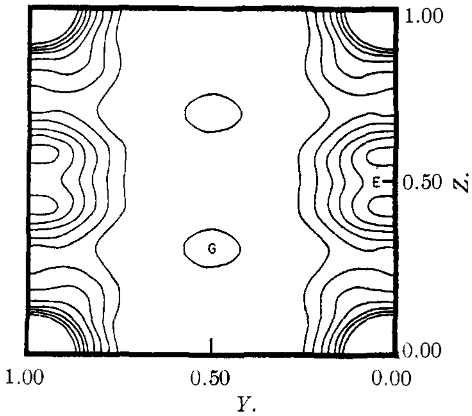

Fig. 3.—A plot of the Patterson section $P(0, Y, Z)$. Peaks correspond to pairs of atoms having about the same x parameters.

These considerations, if correct, suggest that atomic positions lie close to peaks A, B, and C. Although the isolated position and regular shape of peak C should make it useful for the definite location of an atom, the poor resolution around peaks A and B renders them of little significance with regard to atomic positions. An attempt was made to increase the resolution of these peaks, following a method outlined by Patterson in his original paper,[6] by plotting a new "F^2 series"

$$P'(X, Y, \tfrac{1}{2}) = \sum_h\sum_k\sum_l |F_{hkl}|^2/f(hkl) \cos 2\pi (hX + kY + \tfrac{1}{2}l)$$

in which $f(hkl)$ represents the square of the average scattering power of all the atoms in the unit cell for the value of the scattering angle at which the reflection (hkl) occurs. The resulting plot showed increased intensity in peak C, the virtual disappearance of peaks D and E, and apparent sharpening of peaks A and B, but failed completely to clarify the poorly resolved area surrounding them. Although the results were a confirmation of the conclusions already drawn from the original plot of $P(X, Y, \frac{1}{2})$, they failed to be of any additional assistance toward the assignment of tentative atomic positions.

The next step was an attempt to fit a molecule of reasonable dimensions into the unit cell in a manner consistent with the optical and X-ray data and the suggestions furnished by the Patterson sections. Certain assumptions regarding the size and shape of this molecule may safely be made from data obtained from other crystals, especially those from glycine.[2] Thus the group composed of the carboxyl radical and the α carbon atom must be coplanar, with the bond lengths close to C–O = 1.25 Å. and C–C = 1.54 Å., and bond angles

O–C–O = 125° and O–C–C = $117\frac{1}{2}$°. The methyl and amino groups may be expected to be arranged tetrahedrally about the α carbon atom at distances 1.54 and 1.40 Å. to 1.47 Å., respectively, but with an undetermined orientation with respect to the plane of the carboxyl group. Separations between atoms in different molecules will be governed largely by the length of a hydrogen bond between carboxyl oxygen and amino nitrogen atoms (2.7 Å. to 3.0 Å.), and by the van der Waals radii[9] of oxygen (1.35 Å.), carbon (1.5 Å.), amino radical (1.85 Å.) and methyl radical (2.0 Å.). A scale model with these dimensions was constructed and manipulated over the half-scale plot of $P(X, Y, \frac{1}{2})$ in order to find orientations in which projections of all atoms occupied positions close to peaks A, B, C, and the "extension" F. Each of these positions was further examined for steric conflicts between atoms in neighboring molecules.

Of the many arrangements considered, the one finally selected as being structurally much superior to all others resulted from placing an oxygen atom over peak $C_{(1)}$ and the methyl carbon atom near peak $C_{(2)}$. If the methyl group is placed on peak $C_{(2)}$, as is suggested by the Patterson section, the two methyl radicals related by the adjacent two-fold screw axis at the origin are separated by about 3.6 Å., considerably under the minimal separation, about 4.0 Å., of such groups in previously determined structures. If the restriction is imposed that the methyl groups maintain a separation of at least 4.0 Å., they must lie outside a cylinder of radius 1.37 Å. about the screw axis, the trace of which is shown by the dotted circle in Fig. 1. We deemed it essential that all arrangements complying with this restriction be examined before considering structures requiring methyl–methyl distances shorter than the accepted minimal values. That the methyl group may nevertheless lie close to peak $C_{(2)}$ is suggested by the appearance on $P(0, Y, Z)$, Fig. 3, of a maximum at G, indicating the presence of two atoms about 3.5 Å. apart which lie in or near the same *yz* plane with a separation in the *y* direction of about one-half unit. The molecular model which we have assumed permits this relative orientation of an oxygen atom and the methyl carbon atom if they are placed close to peaks $C_{(1)}$ and $C_{(2)}$, respectively. In accordance with these arguments, the methyl radical was placed on the circle of Fig. 1 as close as possible to peak $C_{(2)}$. The atomic parameters describing this preliminary structure, which are listed in columns A of Table V, yielded calculated intensities for the simpler (*hk*0) reflections in approximate, though by no means close, agreement with those observed. Calculation of some simple (0*kl*) and (*h*0*l*) intensities showed agreement of the same order, strongly indicating that the structure described was not far from the correct one.

Before embarking upon the exhaustive series of calculations necessary to the complete determination of atomic parameters based upon this tentative model, we thought it best to make certain that no radically different configuration could be found which would yield a plausible structure and equally good intensity agreement. A thorough and systematic study of all possible interpretations of the Patterson diagrams failed to reveal any other structurally acceptable arrangement giving even approximate agreement between calculated and observed intensities. The parameters listed were therefore used as the starting point in the determination of the atomic positions.

Refinement of Atomic Parameters.—The method which most readily suggests itself for the straightforward refinement of the preliminary structure is the calculation of a Fourier series using the observed amplitudes of all reflections the phases of which could be considered to be established by the preliminary model. The only Fourier projection which may be calculated using real structure factors for a crystal having the symmetry of the space group *Pna* is $\rho(x,y)$, corresponding to projection along the *c* axis. Inspection of our preliminary structure shows that such a Fourier series based upon the data available could not establish the atomic centers, since peaks representing most of the atoms would fall too close together to be resolved. Furthermore, on account of the relatively poor intensity agreement in the case of certain planes, structure factors whose signs were known with reasonable certainty were too few to yield a Fourier projection of any significance. The Fourier method consequently was abandoned until a closer approach to the correct structure had been attained by a trial and error procedure.

For each (*hk*0) plane a plot was prepared showing values of the trigonometric part of the struc-

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[9] L. Pauling, "The Nature of the Chemical Bond," 2nd ed., Cornell University Press, Ithaca, N. Y., 1940, p. 189.

ture-factor term as a function of the atomic parameters. By the use of these plots in a manner already described,[2] significant improvement in the structure factors was gradually accomplished, until a point was reached at which it appeared clear that no further progress could be made without relinquishing to some extent the restriction placed upon the methyl carbon atom. In fact, it was evident almost at the outset that several serious conflicts among the F-values could readily be resolved by altering the parameters of this atom so as to bring it closer to the peak $C_{(2)}$ in Fig. 1, and hence nearer the two-fold screw axis, but a change of this nature, resulting in an unprecedented approach of methyl groups, seemed unjustifiable as long as it could not be convincingly demonstrated that it was the only solution to the problem. To provide further evidence regarding a move of this sort, a Fourier projection, $\rho(x,y)$, was calculated, using 65 non-vanishing structure factors whose signs were then known with reasonable certainty. A plot of this projection, Fig. 4, shows a symmetrical, well-resolved peak corresponding to the methyl carbon atom at $x = 0.099$, $y = 0.019$, which represents a methyl-methyl approach of 3.7 Å. In the face of these considerations, we were compelled to relinquish the preconceived restrictions on the position of the methyl radical. It was therefore placed in accordance with the peak of $\rho(x,y)$, and the resulting structure became a new point of departure for further refinement by the methods described above. The signs of only two of the structure factors used in this series were reversed by subsequent changes in the atomic positions; their correction served to reduce still further the methyl-methyl separation.

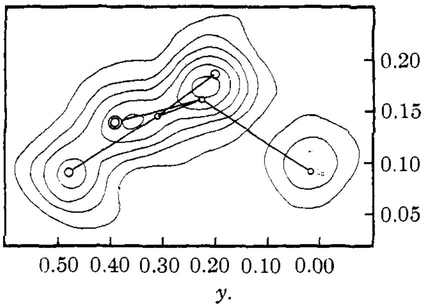

Fig. 4.—A Fourier projection $\rho(x,y)$ which showed that the carbon atoms of adjacent methyl groups must approach closer than 4.0 Å., the distance in the trial structure upon which it was based. The position of the methyl carbon atom in this trial structure is indicated by a cross; its correct position is shown by the small circle CIII.

The best agreement between calculated and observed ($hk0$) structure factors thus eventually achieved is presented in columns 2 and 3 of Table I. The values of $F_{\text{obsd.}}$ (cor.) there listed are obtained from the estimated intensities after correcting them for extinction according to the approximation of Darwin[10]:

$$I_{\text{cor.}} = I_{\text{obsd.}}/(1 - 2g\, I_{\text{obsd.}}),$$

in which the coefficient $2g$ was given the value 0.00005. The values of $F_{\text{calcd.}}$, given by the general expression

$$F_{hkl} = \sum_j f_j \exp\,[-2\pi i(hx_j + ky_j + lz_j)],$$

TABLE I

STRUCTURE FACTORS F_{hk0} OBSERVED AND CALCULATED WITHOUT AND WITH THE CONTRIBUTIONS OF THE HYDROGEN ATOMS

$hk0$	Obsd. (cor.)	Calculated Without hydrogen	Calculated With hydrogen	$hk0$	Obsd. (cor.)	Calculated Without hydrogen	Calculated With hydrogen
200	14.4	−17.1	−17.2	10·2·0	11.0	11.3	11.8
110	14.5	−19.4	−16.9	930	3.9	2.4	2.4
210	66.2	−65.5	−65.6	11·1·0	6.2	5.4	5.6
310	10.6	9.9	12.5	840	7.4	−7.7	−8.0
020	5.1	− 1.7	3.4	550	6.8	6.8	6.8
400	59.8	−59.5	−60.3	650	<2.1	−0.1	−0.3
120	6.7	6.6	8.8	10·3·0	4.1	−5.2	−5.0
220	34.8	31.8	35.0	11·2·0	2.5	−2.2	−2.2
410	35.9	34.6	35.7	060	4.3	5.9	5.9
320	19.5	16.0	20.9	12·0·0	9.1	9.4	9.6
510	13.6	16.7	14.5	940	4.8	−6.0	−5.9
420	8.9	− 7.3	− 7.9	160	7.2	−6.9	−7.0
600	9.4	8.9	8.6	260	2.4	2.8	2.4
130	3.7	− 3.9	− 3.7	12·1·0	4.1	2.3	2.5
230	<1.5	− 1.0	0.6	750	<2.1	1.4	1.3
610	4.1	4.9	4.1	360	<2.1	1.6	1.9
520	10.8	− 9.9	−11.4	11·3·0	9.7	−9.1	−9.1
330	5.2	3.6	3.5	460	3.2	−2.5	−2.4
430	16.7	−16.5	−17.0	12·2·0	1.9	2.9	2.7
620	31.7	−36.1	−35.7	10·4·0	7.4	7.0	7.1
710	5.7	− 6.7	− 5.2	850	2.1	3.2	3.2
530	7.7	− 7.4	− 7.5	560	3.9	4.7	4.7
040	16.7	17.6	17.5	13·1·0	3.6	−3.1	−3.1
140	11.0	11.7	12.4	660	4.5	−6.2	−6.1
720	7.6	− 9.3	− 9.5	12·3·0	2.2	1.2	1.5
800	4.4	− 5.6	− 4.8	950	3.4	−2.8	−2.9
240	2.0	3.0	2.7	11·4·0	<1.7	0.7	0.7
810	15.9	−13.2	−14.1	13·2·0	7.1	−6.0	−6.0
630	6.9	8.8	7.8	760	3.3	−4.6	−4.6
340	2.1	− 1.7	− 1.1	170	1.5	−1.8	−2.0
440	4.8	− 5.9	− 5.5	14·0·0	2.8	2.5	2.4
820	5.8	5.5	5.1	270	2.6	−3.6	−3.7
730	11.3	11.0	12.0	10·5·0	5.1	4.2	4.3
910	<2.0	− 2.2	− 0.5	14·1·0	1.7	−1.6	−1.6
540	3.3	− 3.0	− 2.1	370	3.1	3.9	4.0
920	11.6	12.6	12.4	13·3·0	2.9	3.4	3.5
640	7.4	− 7.8	− 7.7	860	<1.5	−1.6	−1.7
150	4.0	4.0	3.5	12·4·0	6.1	8.3	8.2
830	4.1	7.2	6.8	470	2.0	−2.5	−2.6
10·0·0	<2.1	2.0	2.2	14·2·0	<1.4	0.2	0.2
250	6.1	− 6.6	− 6.3	570	2.0	−3.3	−3.3
10·1·0	6.3	5.7	5.8	11·5·0	<1.3	2.3	2.3
350	10.3	−10.4	−10.1	960	<1.3	1.2	1.2
740	6.8	6.4	5.7	15·1·0	2.6	−2.5	−2.5
450	3.6	− 3.0	− 3.3				

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[10] C. G. Darwin, *Phil. Mag.*, **43**, 800 (1922).

are based upon the x and y parameters for the carbon, nitrogen, and oxygen atoms listed in columns (B) of Table V. For the atomic scattering factors, f_j, in all calculations, the values of Hartree[11] were used combined with a temperature correction, $\exp(-B \sin^2 \theta/\lambda^2)$, in which B was given the value 2.23×10^{-16}.

The structure upon which these calculated F-values are based is consistent with the optical and cleavage properties of the crystal, and involves no features not in accord with accepted structural principles. Furthermore the agreement throughout most of the 89 (*hk*0) reflections is as good as could be desired. It is probable therefore that within the limits of error imposed by the data this structure is correct. Nevertheless, there are a few serious and apparently insoluble conflicts, particularly among planes of large spacing. Especially disturbing is the pair of planes (320) and (510), which are observed to have F-values of 19.5 and 13.6, respectively, while the calculated quantities are approximately 16 for both. The plots of the structure factors for these planes show conclusively that it is impossible to move any atom in such a way as to improve the agreement of one plane without causing that of the other to become even worse. It was likewise impossible to improve the agreement of (020) either positively or negatively. It occurred to us that these discrepancies might arise from neglect of the contributions to the X-ray scattering made by the seven hydrogen atoms of each alanine molecule. In some cases it has been the practice to compensate for the scattering of hydrogen atoms in methyl and amino radicals by making small alterations in the atomic scattering function for carbon and nitrogen. Inspection of the contributions of these atoms to (320), (510), and planes with similar spacing showed that this conflict could not be resolved by any adjustments of this sort. Although, as already stated, the locations of the hydrogen atoms cannot be determined from X-ray data, in this crystal they can be placed with considerable confidence from purely structural considerations, as discussed in a later section, once the positions of the other atoms are known. Contributions of the hydrogen atoms may therefore be estimated directly using the scattering function for atomic hydrogen.[11] Structure factors including these contributions, based upon the assumed parameters for hydrogen listed in Table V, are presented in the final column of Table I. The significant improvement in agreement obtained, not only for planes of large spacing but for many reflections throughout the assemblage, is confirmatory evidence for both the excellence of the (*hk*0) data and the correctness of the structure determined.

Having established the x and y parameters, the refinement of the z parameters was carried out by similar methods, using agreement of the (0*kl*) intensities as the criterion for improvement. For this purpose plots of both the real and imaginary parts of the complex structure factors were necessary. The final assignment of z parameters is confirmed by the intensity agreement of the (*h*0*l*) reflections. Comparison of observed and calculated F-values for the (0*kl*) and (*h*0*l*) planes is shown in Tables II and III. Agreement among 238 nonprism reflections, shown in Table IV, substantiates the assignment of all the parameters. Calculated structure factors including the contributions of the hydrogen atoms for the 36 (*hkl*) planes having $\sin \vartheta < 0.5$ are also listed in Table IV. As in the case of the (*hk*0) reflections, many of these planes show decided improvement in their intensity agreement. The significance of

TABLE II

OBSERVED AND CALCULATED VALUES OF THE STRUCTURE FACTORS $|F_{0kl}|^a$

0*kl*	Obsd.	Calcd.	0*kl*	Obsd.	Calcd.	0*kl*	Obsd.	Calcd.
011	22	18	024	9	10	062	3	4
002	54	50	051	6	6	026	9	8
022	18	17	015	20	16	071	9	9
031	18	15	044	11	12	055	2	2
013	10	7	053	6	8	064	5	5
004	17	14	035	5	5	017	10	9
033	16	13	006	6	6	046	4	5
042	6	7						

[a] Calculated values include contributions of the hydrogen atoms. Values of F_{0k0} are given in Table I.

TABLE III

OBSERVED AND CALCULATED VALUES OF THE STRUCTURE FACTORS $|F_{h0l}|^a$

*h*0*l*	Obsd.	Calcd.	*h*0*l*	Obsd.	Calcd.	*h*0*l*	Obsd.	Calcd.
201	34	34	603	16	14	605	7	5
401	12	13	802	12	11	12·0·1	6	7
202	18	14	404	14	13	206	5	4
402	26	22	803	8	8	12·0·2	3	4
601	18	17	10·0·1	8	9	406	4	4
203	16	15	604	8	6	12·0·3	5	6
602	10	10	205	20	15	606	10	7
403	24	20	10·0·2	5	5	14·0·1	5	7
801	10	9	405	17	13	207	14	13
204	9	8	10·0·3	11	9	407	4	3

[a] Calculated values include contributions of the hydrogen atoms. Values of F_{h00} and $|F_{00l}|$ are given in Tables I and II, respectively.

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(11) "International Tables for the Determination of Crystal Structures," Gebrüder Borntraeger, Berlin, 1935, Vol. II, pp. 571–574.

this improvement is discussed in a later section. The final assignment of all parameters is listed in columns (B) of Table V.

TABLE IV

OBSERVED AND CALCULATED VALUES OF THE STRUCTURE FACTORS $|F_{hkl}|$

		Calculated				Calculated	
hkl	Obsd.	Without hydrogen	With hydrogen	*hkl*	Obsd.	Without hydrogen	With hydrogen
111	4	6	3	113	19	13	15
211	11	11	11	611	6	6	6
311	31	27	27	521	6	8	6
121	5	5	6	213	12	9	9
112	44	33	35	512	20	20	19
221	15	9	12	331	13	13	14
411	9	11	8	422	8	8	8
212	23	20	20	313	10	8	8
321	18	14	15	132	4	6	6
312	14	15	14	123	12	10	10
511	15	14	14	431	9	7	7
122	23	18	20	621	4	5	5
421	23	21	21	232	13	12	12
222	13	11	12	711	14	13	15
412	19	17	16	612	12	9	9
131	16	18	16	413	7	6	6
322	14	12	12	223	18	15	15
231	7	8	6	522	12	12	11

hkl	Obsd.	Calcd.[a]	*hkl*	Obsd.	Calcd.[a]	*hkl*	Obsd.	Calcd.[a]
332	14	12	215	10	7	625	2	2
323	17	15	922	6	8	435	<3	2
531	5	4	642	7	9	162	7	9
513	9	8	741	9	12	461	2	5
432	7	8	823	11	16	216	2	1
721	4	4	443	6	8	553	4	5
141	3	3	832	5	4	11·1·3	<3	1
622	8	11	152	11	12	316	2	2
423	16	14	315	14	12	12·1·2	4	5
712	5	7	451	<3	3	644	2	3
241	14	15	10·2·1	4	3	535	8	6
811	9	10	252	4	4	126	3	2
114	17	14	624	13	12	154	4	4
631	8	10	434	4	6	561	5	8
133	12	11	931	9	13	254	2	4
341	2	4	714	3	3	725	5	5
214	7	5	733	6	7	145	3	2
532	15	17	913	4	4	10·3·3	5	7
613	7	6	10·1·2	7	7	653	<2	2
233	5	6	125	8	6	245	<2	3
523	5	3	352	10	12	226	4	3
314	8	7	543	4	6	416	3	2
722	5	6	225	10	9	354	2	5
142	13	11	415	8	8	635	2	3
333	5	5	551	7	5	326	<2	1
821	14	15	534	10	9	744	3	5
441	<2	3	742	6	9	345	8	5
242	4	5	724	2	2	516	4	3
124	12	10	325	7	6	661	2	3
812	2	2	144	5	5	163	2	4
731	3	4	452	3	5	263	4	6
414	4	5	10·2·2	<3	2	426	3	4
224	7	6	923	<3	3	454	<2	1
433	6	7	515	4	3	12·1·3	2	4
342	3	5	244	2	2	753	3	3
632	6	8	425	5	6	445	2	4
911	9	12	643	4	6	13·1·2	3	4
623	5	5	651	<3	3	735	6	7
713	<3	1	833	3	5	363	3	5
324	3	3	153	8	9	136	<2	2
541	4	3	634	4	5	236	4	3
514	10	8	552	3	5	616	<2	2
442	3	4	344	6	5	554	<2	0
822	8	9	10·1·3	5	6	761	2	4
533	11	10	11·1·2	5	8	545	6	5
424	2	2	253	2	2	526	<2	1
732	14	15	135	3	1	654	<2	1
921	<2	1	842	3	5	645	<2	3
723	6	7	353	<3	2	626	5	5
912	<2	3	235	2	3	716	3	2
831	4	3	525	8	5	155	7	7
641	4	5	615	12	9	255	<2	1
143	6	4	444	6	8	164	<2	3
151	7	8	161	5	7	264	<2	2
134	3	4	261	9	8	355	3	5
251	<2	2	743	3	3	117	2	2
542	10	10	734	4	4	754	5	6
813	12	10	751	5	8	217	4	3
243	14	16	11·2·2	2	3	745	3	4
10·1·1	7	9	335	7	7	364	<2	1
614	9	9	453	3	4	146	3	1
234	8	8	10·2·3	6	7	317	5	3
524	6	5	361	<2	3	455	2	2
633	8	10	933	2	3	246	<2	2
343	10	10	544	5	4	346	2	2
351	14	15	116	1	2	464	3	4
115	14	10	715	5	6	417	4	5
334	6	6						

[a] These calculated values do not include contributions of the hydrogen atoms.

TABLE V

PARAMETERS OF THE ATOMS IN THE PRELIMINARY AND FINAL STRUCTURES OF *dl*-ALANINE

		(A) Preliminary structure			(B) Final structure		
		x	*y*	*z*	*x*	*y*	*z*
Atoms whose parameters are experimentally established							
O_I	Carboxyl	0.09	0.50	0.14	0.090	0.481	0.134
O_{II}		.17	.21	.00	.186	.201	.000
C_I		.14	.33	.17	.145	.312	.161
N		.13	.42	.57	.139	.393	.576
C_{II}	Alpha	.17	.26	.42	.161	.227	.408
C_{III}	Methyl	.12	.03	.47	.091	.017	.444
Hydrogen atoms, whose parameters are assumed							
H_I	Amino				.060	.447	.566
H_{II}					.192	.521	.548
H_{III}					.157	.332	.733
H_{IV}	Alpha				.249	.185	.428
H_V	Methyl				.004	.063	.448
H_{VI}					.114	.940	.607
H_{VII}					.105	.900	.305

Description of the Structure

The Alanine Molecule.—In Fig. 5 are shown three projections of the alanine molecule, one perpendicular to a plane passing through O_I, O_{II}, and C_{II}, and the other two parallel to this plane. The departure of the carboxyl carbon atom from this plane, 0.016 Å., is without significance since it is within the limit of error of the determination of atomic positions. The nitrogen atom is distant 0.390 Å. from the carboxyl plane and the methyl carbon 1.375 Å. in the opposite direction. The bond lengths and bond angles in the alanine molecule, shown in the figure, are listed in Table VI, together with corresponding distances and angles found in molecules of glycine[2] and diketo-

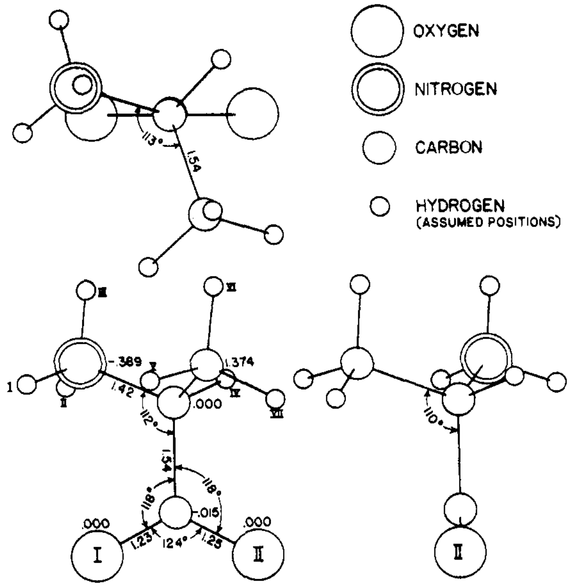


Fig. 5.—Three projections of the alanine molecule. Figures given to three decimal places represent the departures in angstrom units of the atoms from the plane of the α carbon and oxygen atoms; those to two decimal places represent bond lengths in angstrom units.

piperazine.[1] We believe it to be highly improbable that any of the distances reported for alanine is in error by as much as 0.03 Å. or any of the angles by as much as 3°.

TABLE VI

BOND LENGTHS AND BOND ANGLES FOUND IN MOLECULES OF *dl*-ALANINE, GLYCINE AND DIKETOPIPERAZINE

		dl-Alanine	Glycine	Diketo-piperazine,
C—O	$\mathrm{C_I}$—$\mathrm{O_I}$	1.23 Å.	1.25 Å.	1.25 Å.
	$\mathrm{C_I}$—$\mathrm{O_{II}}$	1.25	1.27	. .
C—N	$\mathrm{C_{II}}$—N	1.42	1.39	1.41
C—C	$\mathrm{C_I}$—$\mathrm{C_{II}}$	1.54	1.52	1.47
	$\mathrm{C_{II}}$—$\mathrm{C_{III}}$	1.54	. .	. .
∠O—C—O	$\mathrm{O_I}$—$\mathrm{C_I}$—$\mathrm{O_{II}}$	124°	122°	
∠O—C—C	$\mathrm{O_I}$—$\mathrm{C_I}$—$\mathrm{C_{II}}$	118	119	
	$\mathrm{O_{II}}$—$\mathrm{C_I}$—$\mathrm{C_{II}}$	118	119	
∠C—C—N	$\mathrm{C_I}$—$\mathrm{C_{II}}$—N	112	112	
	$\mathrm{C_{III}}$—$\mathrm{C_{II}}$—N	113	. . .	
∠C—C—C	$\mathrm{C_I}$—$\mathrm{C_{II}}$—$\mathrm{C_{III}}$	110	. . .	

Molecular Environment.—Each alanine molecule has twelve neighbors—four related to it by the *b* and *c* translations, four by the *n* glide planes, and four by the two-fold screw axes. These relationships are indicated in Table VII in which interatomic distances between neighboring molecules are summarized. Analogous distances in glycine and diketopiperazine are included for comparison.

TABLE VII

INTERMOLECULAR INTERATOMIC DISTANCES FOUND IN CRYSTALS OF *dl*-ALANINE, GLYCINE AND DIKETOPIPERAZINE

dl-Alanine, Å.			Glycine, Å.	Diketo-piperazine, Å.
$\mathrm{NH_3}$—O			$\mathrm{NH_3}$—O	NH—O
N—$\mathrm{O_I}$	2_1[a]	2.88	2.93	2.85
N—$\mathrm{O_{II}}$	*n*	2.84	3.05	
N—$\mathrm{O_{II}}$	c_0	2.78	2.88	
			2.76	
$\mathrm{CH_3}$—O			$\mathrm{CH_2}$—O	$\mathrm{CH_2}$—O
$\mathrm{C_{III}}$—$\mathrm{O_I}$	b_0	3.70	3.65	3.32
$\mathrm{C_{III}}$—$\mathrm{O_{II}}$	2_1	3.58	3.41	3.33
$\mathrm{C_{III}}$—$\mathrm{O_{II}}$	*n*	3.30	3.27	
$\mathrm{C_{III}}$—$\mathrm{O_{II}}$	c_0	3.59	3.34	
CH—O			3.52	
$\mathrm{C_{II}}$—$\mathrm{O_I}$	*n*	3.59	3.35	
$\mathrm{C_{II}}$—$\mathrm{O_{II}}$	*n*	3.44		
$\mathrm{CH_3}$—$\mathrm{NH_3}$			$\mathrm{CH_2}$—$\mathrm{NH_3}$	$\mathrm{CH_2}$—NH
$\mathrm{C_{III}}$—N	b_0	3.88	3.87	3.55
			3.87	
$\mathrm{CH_3}$—$\mathrm{CH_3}$			$\mathrm{CH_2}$—$\mathrm{CH_2}$	$\mathrm{CH_2}$—$\mathrm{CH_2}$
$\mathrm{C_{III}}$—$\mathrm{C_{III}}$	2_1	3.64	4.22	3.96
			4.05	3.96
$\mathrm{CH_3}$—CH				
$\mathrm{C_{III}}$—$\mathrm{C_{II}}$	*n*	4.38		
$\mathrm{CH_3}$—C				
$\mathrm{C_{III}}$—$\mathrm{C_I}$	*n*	3.64		
$\mathrm{C_{III}}$—$\mathrm{C_I}$	2_1	3.68		
CH—C				
$\mathrm{C_{II}}$—$\mathrm{C_I}$	*n*	3.73		

[a] Symbols in this column indicate the symmetry element or unit translation by which the molecules are related in the crystal.

Significant interatomic distances between a molecule and six of its neighbors are shown in Fig. 6. Between a nitrogen and adjoining oxygen

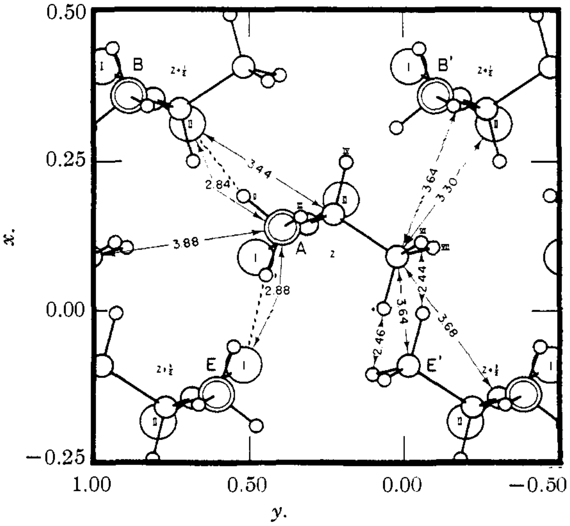


Fig. 6.—A projection of several molecules upon the *c* face of the crystal, showing some significant interatomic distances. The capital letters identify the molecules in succeeding drawings.

atoms distances of 2.88 Å. and 2.84 Å. clearly indicate the locations of two hydrogen bonds. A third hydrogen bond, not shown in this figure, connects the nitrogen atom to an oxygen atom (O_{II}) of the molecule directly above.

General Features of the Structure.—In crystals of *dl*-alanine the molecules are linked together by hydrogen bonds into a closely knit framework. For convenience in description the structure may be considered as an array of interconnected chains of molecules extending in the direction of the *c* axis. These chains are shown in Fig. 7. Each chain is surrounded by six other chains, two related to it by the *b* translation, two by the *n* glide plane, and two by non-equivalent two-fold screw axes. For example, chains A and A″, related by *b* translation, are so placed as to maintain normal van der Waals contacts (3.88 Å.) between amino and methyl groups. The pair A and B′, related by the *n* glide plane, are connected by one hydrogen bond (2.84 Å.) on each molecule. Chains A and E, related by one of the non-equivalent screw axes (near an oxygen atom), are connected by two hydrogen bonds (2.88 Å.) on each molecule, whereas chains A′ and E, related by the other screw axis (near a methyl radical), are not bonded together at all. Here are found the short methyl-methyl distances, 3.64 Å. The three last types of relationship are also shown in Fig. 8, which is a packing diagram of the structure viewed along the *b* axis. Thus chains A and B exemplify the first of these, A and E the second, B and C the third. The abnormally short methyl-methyl distances are indicated by the intersections of the large line-shaded spheres.

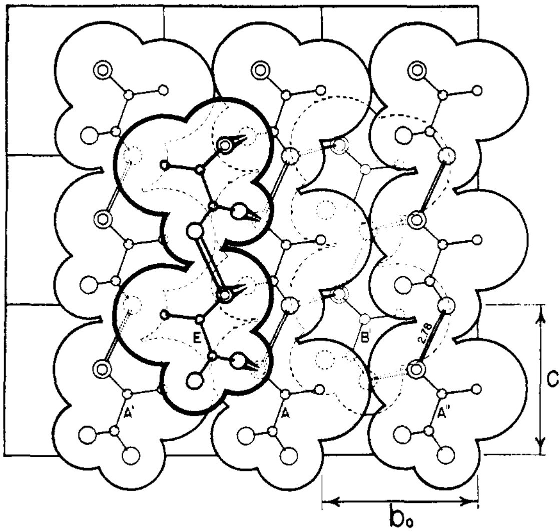


Fig. 7.—A packing diagram of several molecules projected upon the *a* face. Double lines between atoms represent hydrogen bonds.

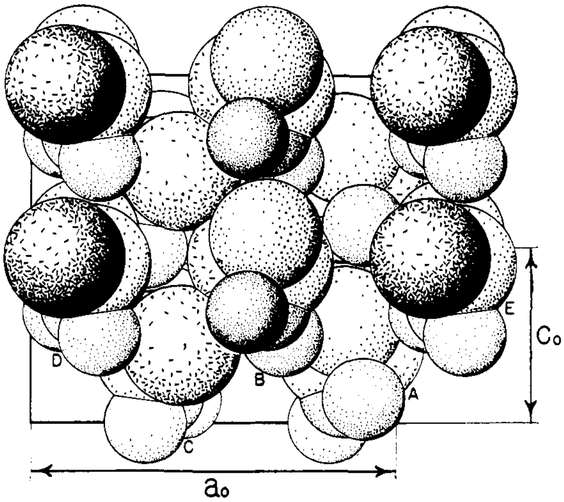


Fig. 8.—A packing diagram of several molecules projected upon the *b* face. The groups of three adjacent small spheres represent carboxyl radicals; the large, line-shaded spheres, methyl radicals.

Further packing relations between adjacent molecules are brought out in Fig. 9, which is a diagram of the structure viewed in the direction of the *c* axis. The staggered arrangement of the molecules of alanine, expressed by the screw axes and glide planes, is of a nature to bring the car-

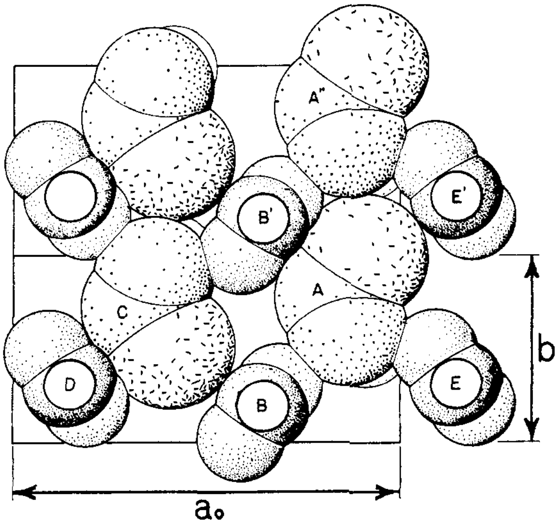


Fig. 9.—A packing diagram of several molecules projected upon the *c* face. The α carbon atom and the methyl and amino radicals have been omitted from molecules B, D, E, etc.

boxyl radical of one molecule close to the amino and methyl groups of four others. In order to show these relationships the α carbon atoms of molecules B, D, E, etc., and the large groups attached to them have been omitted in this figure. The hydrogen bonds formed by the nitrogen atom of molecule A with the oxygen atoms of molecules B and E are clearly indicated. Each methyl group is almost completely surrounded; thus the methyl radical of molecule A makes contacts with the oxygen atom (II) of B′ (3.30 Å.), with the amino group of A″ (3.88 Å.), and of course with methyl groups of molecules E′ above and below it, not shown in this figure.

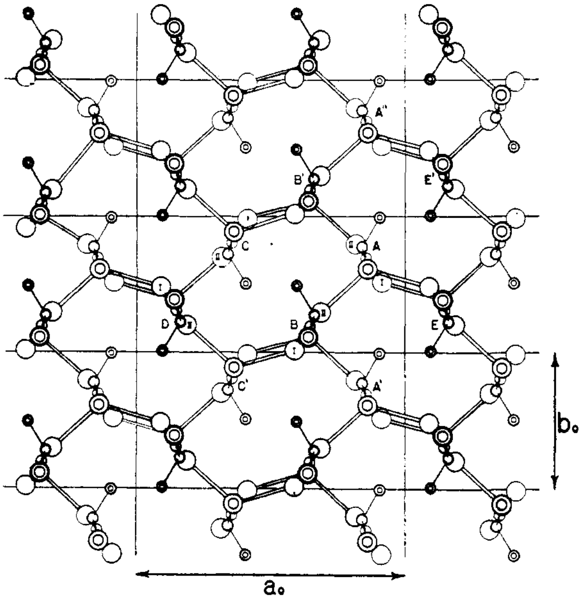


Fig. 10.—A projection of a portion of the structure, including several unit cells, upon the *c* face of the crystal. The location of the methyl groups inside hydrogen bond "tubes" is clearly shown.

A more complete picture of the hydrogen bond framework is obtained by viewing several adjacent unit cells projected upon the *xy* plane. Thus in Fig. 10 the hydrogen bonds are seen to bind the molecular chains into an array of "cylindrical tubes," each "tube" involving six molecular strings, and each string being common to three "tubes." The methyl radicals of two chains project toward each other inside each tube. A three-dimensional view of the single "tube" formed by chains A, B, C′, D. C, and B′ is shown in Fig. 11.

Discussion

Dimensions of the Molecule.—The configuration of the alanine molecule is not greatly differ-

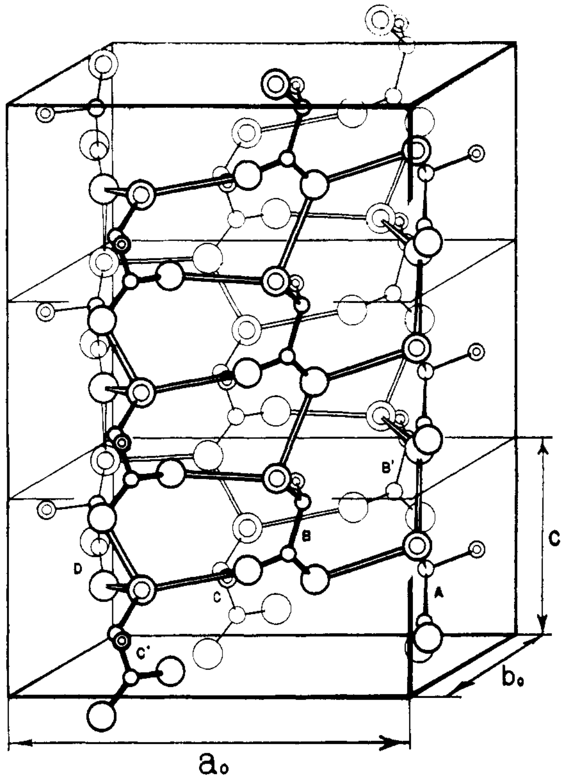
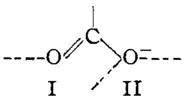
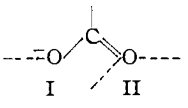


Fig. 11.—An oblique projection of one of the "tubes" shown in Fig. 10.

ent from that predicted for it. The coplanarity of the α carbon atom with the carboxyl radical and the values of the bond angles around the carboxyl carbon atom are in accord with the structures found for formic acid,[12] oxalic acid dihydrate[13] and glycine.[2] The carbon to oxygen bond lengths, 1.23 and 1.25 Å., tend to be slightly shorter than those in glycine (1.25 and 1.27 Å.), but are in excellent agreement with those (1.24 Å.) in the oxalic acid dihydrate structure recently proposed by Robertson.[13] Although the two C–O bond lengths are substantially equal within the limits of error of this determination, a small difference (0.02 Å.) seems to be indicated by the X-ray data. A difference of this sort appears not unreasonable upon consideration of the two principal electronic configurations which contribute to the structure of the carboxyl radical, namely



A



B

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[12] L. Pauling and L. O. Brockway, *Proc. Natl. Acad. Sci.*, **20**, 336 (1935).

[13] J. M. Robertson, *Trans. Faraday Soc.*, **36**, 917 (1940).

The involvement of oxygen II in the formation of two hydrogen bonds should tend to stabilize structure A in which this atom carries a negative formal charge; accordingly the C–O_{II} bond should have a little less double-bond character than the C–O_I bond and should therefore be slightly longer.

The C–N bond length (1.42 Å.) is close to the corresponding values found in glycine (1.39 Å.) and diketopiperazine (1.41 Å.). It is not yet clear why these distances are so much shorter than those found for C–N single bonds in CH_3NO_2,[14] $N(CH_3)_3$,[15] CH_3NC,[16] CH_3N_3,[17] $(CH_3)_2NH$,[18] $C(NO_2)_4$,[19] and $(CH_3)_2NCl$,[20] all of which are close to 1.47 Å., which is also the value computed from the covalent radii[21] of nitrogen and carbon. The C–C–N angle (112°), like the corresponding angle in glycine (112°), appears to be distorted slightly from the tetrahedral value. In both cases the distortion doubtless results from the steric interaction of the amino and carboxyl groups.

Positions of the Hydrogen Atoms.—Much of the difficulty encountered in the course of the work leading to the determination of the structure of *dl*-alanine arose from certain wholly unpredictable features of the structure itself. Thus, much effort was expended throughout the determination in attempting to bring certain simple reflections into completely satisfactory intensity agreement. These conflicts were finally found to be irreconcilable without the introduction of calculated contributions of the hydrogen atoms, based upon specific assumed positions for them in the structure. When the positions of the other atoms had been established, those of the hydrogen atoms could be inferred from the hydrogen bond angles and generally accepted atomic dimensions. If the N–H distance is taken to be 1.00 Å. and the C–H distance to be 1.09 Å.[22] and all bond angles are assumed to be approximately tetrahedral, the position of hydrogen IV on the α carbon atom is completely fixed, and the positions of the other hydrogen atoms are partially described, the orientations of the amino and methyl radicals about their respective bonds to the α carbon atom only remaining unspecified.

In the case of the amino group, the six angles formed by the three hydrogen bonds and the C–N bond about each nitrogen atom range between 102 and 126°. This angular distribution of hydrogen bonds, which approximates a tetrahedral arrangement, strongly suggests that the amino radical assumes an orientation in which the three hydrogen atoms covalently bonded to the nitrogen atom do not lie far from positions on straight lines between the nitrogen and oxygen atoms. The positions assumed for hydrogens I, II, and III are such as to satisfy this condition. Hence it appears that in *dl*-alanine, as in glycine,[2] the significant factors determining the molecular arrangement in the crystal are directed forces exerted by hydrogen bonds having definite orientation with respect to the molecules.

Acceptable orientations of the methyl radical are limited by the abnormally short methyl–methyl distance in this crystal. Although this approach of methyl radicals on different molecules is closer than any which has been observed heretofore, it is possible to assign an orientation to the groups in which distances between hydrogen atoms are not less than 2.4 Å., twice the van der Waals radius for hydrogen given by Pauling.[9] Only one such orientation consistent with the symmetry requirements of the space group appears possible. The parameters assigned to hydrogen atoms V, VI, and VII are those for this arrangement, in which the shortest intermolecuar hydrogen—hydrogen distances are 2.44 and 2.46 Å. These contacts between hydrogen atoms are shown in Fig. 12, from which it is clear that even a small rotation of the radical would result in serious conflict between hydrogen spheres, representing an approach closer than 2.4 Å.

The question may arise as to whether hydrogen atoms necessarily occupy positions in the crystal which satisfy the symmetry requirements deduced from absences in the X-ray reflections. It seems to us that in the present instance the validity of this assumption is demonstrated by the striking improvement obtained in the intensity agreement on inclusion of the hydrogen terms in the structure factors. It should be emphasized that the parameters describing the positions of the hydrogen atoms have not been evaluated directly from the X-ray data. Nevertheless the improvement in the agreement of the structure

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(14) L. O. Brockway, J. Y. Beach and L. Pauling, THIS JOURNAL, **57**, 2693 (1935).

(15) L. O. Brockway and H. O. Jenkins, *ibid.*, **58**, 2036 (1936).

(16) L. O. Brockway, *ibid.*, **58**, 2516 (1936).

(17) L. Pauling and L. O. Brockway, *ibid.*, **59**, 13 (1937).

(18) S. H. Bauer, *ibid.*, **60**, 524 (1938).

(19) A. J. Stosick, *ibid.*, **61**, 1127 (1939).

(20) D. P. Stevenson and V. Schomaker, *ibid.*, **62**, 1913 (1940).

(21) (a) Ref. 9, p. 164; (b) V. Schomaker and D. P. Stevenson, *ibid.*, **63**, 37 (1941).

(22) Ref. 9, p. 168.

factors for several (*hkl*) reflections, as well as for such variously oriented prism planes as (110), (020), (220), (320), (510), (810), and (630), obtained upon inclusion of the hydrogen terms is too pronounced to be accidental. There can be little doubt therefore that the hydrogen atoms occupy positions in the neighborhood of those assigned.

The van der Waals Radius of Hydrogen.—It is interesting to compare the hydrogen contact distances in *dl*-alanine (2.44 and 2.46 Å.) with those deduced from the structures of other crystals. Mack[23] has shown that in hexamethylenetetramine probable positions for the hydrogen atoms result in contacts at 2.58 Å. In diketopiperazine[1] the positions postulated for hydrogen atoms are such as to bring those on adjacent CH_2 groups into contact at 2.68 Å. and 2.64 Å. In crystalline hydrogen,[24] if adjacent molecules are rotating independently, the minimal distance of approach is 3.00 Å. These distances vary in a reasonable manner, being greatest in the hydrogen crystal, where attractive forces between molecules are extremely small, and least in *dl*-alanine, where the hydrogen bond framework brings about relatively large intermolecular attraction.

Rotation of Methyl Groups.—In crystals in which larger methyl–methyl contact distances (*ca.* 4.0 Å.) are found, it is probable that the groups are undergoing rotational motion. Pauling[25] has suggested that this is the case in crystalline methane and in hexamethylbenzene at temperatures above their transition points, 20°K. and 151°K., respectively. In methane[26] the distance between carbon atoms is 4.16 Å., and in hexamethylbenzene[27] the distances between methyl carbon atoms on different molecules range upward from 3.87 Å. It has been assumed in previous discussions[23,27] of these crystals that the rotation of adjacent groups is completely independent. If this is so in methane, hydrogen atoms on different molecules reach a minimal separation of 1.98 Å. Likewise for the hexamethylbenzene crystal Brockway and Robertson[27] calculate a minimal intermolecular hydrogen separation of 1.78 Å. for tetrahedral methyl groups but point out that with slight distortion of the radicals this separation can be made about 2.00 Å.

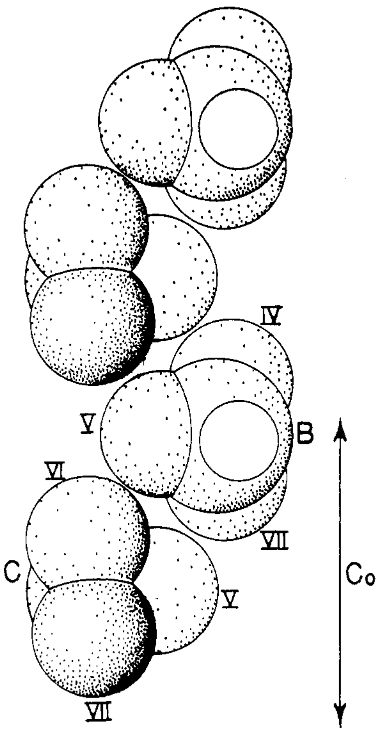

Fig. 12.—A packing diagram of the methyl groups of adjacent molecules, showing the assumed positions for the hydrogen atoms.

This approach of hydrogen atoms to within 2.0 Å. of each other seems to us extremely unlikely when compared to the much greater contact distances which appear to exist between hydrogen atoms in the hydrogen crystal and in groups having fixed orientations. It seems more reasonable to assume that the groups in methane and hexamethylbenzene do not rotate with complete independence, but rather that the rotation of adjacent groups involves an approximate phase dependence so that hydrogen atoms on different molecules remain at least 2.4 Å. apart. (The possibility of some such "cog-wheel" rotation was mentioned although not urged by Mack.[23]) Thus it appears that in these crystals intermolecular forces, although not sufficient to prevent rotation of the methyl groups, are large enough to compel them to rotate synchronously. In crystals of *dl*-alanine, however, contacts between adjacent methyl groups take place within the tubular cells of the hydrogen bond framework, and it seems to us that the forces resulting from this peculiar arrangement are sufficient to prevent even synchronized rotation of the methyl groups and to compel them to assume preferred orientations with respect to one another. According to this picture, dis-

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(23) E. Mack, Jr., THIS JOURNAL, **54**, 2141 (1932).

(24) W. H. Keesom, J. de Smedt and H. H. Mooy, *Proc. Acad. Amsterdam*, **33**, 814 (1930).

(25) L. Pauling, *Phys. Rev.*, **36**, 430 (1930).

(26) H. H. Mooy, *Proc. Acad. Amsterdam*, **34**, 550, 660 (1931).

(27) L. O. Brockway and J. M. Robertson, *J. Chem. Soc.*, 1324 (1939).

tances between adjacent methyl groups on different molecules as short as those observed in *dl*-alanine are to be expected only in crystals whose structures involve especially strong intermolecular attractive forces, such as those resulting from hydrogen bonds, and distances significantly shorter than these are not to be expected in any crystal.

The Structure of Proteins.—The determination of the crystal structure of *dl*-alanine provides information which confirms and extends our present concepts regarding the atomic arrangement in a polypeptide chain and the way in which these chains may be held together in natural proteins. The introduction of the methyl side chain has been found to cause no appreciable alteration in the length of the bond between the nitrogen and the α carbon atoms from that observed in glycine, 1.39 Å. However, since its departure from the normal bond distance, 1.47 Å., is as yet not understood, conclusions regarding this distance in proteins can scarcely be made without additional experimental evidence. Many attempts have been made to arrive at satisfactory models of the ways in which polypeptide chains are folded or packed together in natural proteins, and it has been generally recognized that the formation of hydrogen bonds between the NH and CO groups probably plays an important part in determining the configuration of the chain and its relation to its neighbors. At the present time our knowledge of the constitution of protein molecules and of the many factors which govern their interaction with one another is inadequate for selecting the most probable model from the many which may be considered. The crystal structures of both glycine and *dl*-alanine demonstrate the importance of the directional properties of hydrogen bonds between nitrogen and oxygen atoms in determining atomic and molecular arrangements. It is therefore probable that in proteins also these directional properties of the hydrogen bond play an important role in determining the most stable arrangements of their atoms. The methyl–methyl approach of 3.64 Å. found in *dl*-alanine suggests that if the molecules of a protein are strongly bonded together the side chain radicals may take up positions somewhat closer to one another than that which might be expected from the normal contact distances which they exhibit under conditions permitting rotation about interatomic bonds. It is probable, however, that short intermolecular distances of this kind occur only occasionally, when the structure is such as to involve unusually strong bonding forces, and that the 10% shortening found in alanine is close to the limit to be expected.

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Summary

Weissenberg X-ray data using Cu Kα radiation show that crystals of *dl*-alanine are built upon an orthorhombic unit having $a_0 = 12.04$ Å., $b_0 = 6.04$ Å., and $c_0 = 5.81$ Å., and containing four molecules of $CH_3NH_2CHCOOH$. The space group is $C_{2v}^9 - Pna$, with all atoms in general positions, given by the following parameters: oxygen I, $x = 0.090$, $y = 0.481$, $z = 0.134$; oxygen II, $x = 0.186$, $y = 0.201$, $z = 0.000$; carboxyl carbon, $x = 0.145$, $y = 0.312$, $z = 0.161$; nitrogen, $x = 0.139$, $y = 0.393$, $z = 0.576$; alpha carbon, $x = 0.161$, $y = 0.227$, $z = 0.408$; methyl carbon, $x = 0.091$, $y = 0.017$, $z = 0.444$. Interatomic distances within the molecule are carbon–oxygen, 1.25 and 1.23 Å., carbon–carbon, 1.54 Å., and carbon–nitrogen, 1.42 Å., each correct within 0.03 Å. The structure consists of alanine molecules linked together by a three-dimensional framework of hydrogen bonds, which is responsible for an abnormally close approach (3.64 Å.) of methyl radicals of adjacent molecules. Consideration of the X-ray intensity data shows that they can be satisfied only by the assignment of structurally plausible positions to the hydrogen atoms and the inclusion of their contributions to the X-ray scattering. Special features of the structure are discussed and their implications in the solution of certain problems of protein structure are briefly mentioned.

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