

# HELICAL CONFORMATIONS OF POLYPEPTIDE CHAINS

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Received March 31, 1961

(Communicated by Dr. G. N. Ramachandran, F.A.Sc.)

## 1. INTRODUCTION

THIS paper deals with a study of the possible helical structures that can be built out of polypeptide chains, consistent with the demands of stereochemistry. The stereochemical restrictions in such structures may be divided into two types,

(a) those which demand that the bond distances and the bond angles between directly bonded atoms shall have specified values, and

(b) corresponding lengths and angles for secondary bonds, such as hydrogen bonds, shall lie within certain ranges, and similarly the contact distances between unbonded atoms shall not be less than certain limiting values.

In this paper, methods are developed whereby all possible simple helical structures satisfying the first condition (a) may be listed and described. It is assumed that the atoms in the peptide residue lie in a plane and that the configuration is that given by Corey and Pauling.<sup>1</sup> Once this is defined the only other restriction that enters the picture is the value of the 'tetrahedral' angle at the  $\alpha$  carbon atom. This is so if the so-called R-group specifying the type of amino-acid residue is neglected. Thus, the attempt has been essentially to describe the single helices that can be built out of peptide residues neglecting secondary bond formation or steric hindrance. When the formation of hydrogen bonds is also taken into account it can be shown that the well-known  $\alpha$  and  $\gamma$  helices of Pauling and others<sup>2</sup> come out. In fact, these are particular cases of slightly more general configurations. So also, it is found that the extended  $\beta$  structure and the pleated sheet structure of Pauling and Corey<sup>3</sup> are also only particular cases of a range of structures possible, in which every alternate residue has the same orientation (*i.e.*, digonal helices with two residues per turn). The method described here could also be utilised for finding out the co-ordinates of atoms when the elements of a helical structure are known from other data.

## 2. DESCRIPTION OF THE HELIX

In an arrangement of polypeptide residues in a regular helix, it should be possible to bring any residue into another equivalent residue by a rotation about the helix axis accompanied by a translation along that axis. We shall indicate the values of these two for the operation of bringing a residue to its neighbour by a rotation  $\psi$  (which we shall call the unit twist) and a translation  $h$ . This operation, if repeated a number of times, would lead to a helical structure. The translation  $h$  is always taken to be positive (say along  $OZ$ ) and so if  $\psi$  is +, *i.e.*, it is anti-clockwise looking from  $Z$  towards  $O$ , then it leads to a right-handed helix, and *vice versa*.

Since the peptide residue is a rigid planar structure, its position and orientation could be specified by the positions of the  $\alpha$  carbon atoms at which they are linked to one another and the orientation of the plane of the residue with respect to some standard plane passing through successive  $\alpha$  carbon atoms. Thus in Fig. 1 the group  $C_1(H_1R_1) \cdot C_1'O_1 \cdots N_1H_1 \cdot C_2(H_2R_2)$  joining at  $C_2$  with the next residue could be represented by the line  $C_1C_2$  forming one of the links of a chain of rods arranged in a helical fashion. Neglecting first the orientation of the plane of the residue with respect to the line  $C_1C_2$ , we shall consider the parameters required for specifying the configuration of the helical chain consisting of equal rods, each of length  $L$  equal to  $C_1C_2$ . The points  $C_1, C_2$ , etc., occur on a continuous helix (the thin line of Fig. 1) which may be considered to be wound on a cylinder of radius  $R$  and having a pitch  $P$ . Its projection on the basal plane perpendicular to the axis of the helix will be a circle of radius  $R$ . The points  $C_1, C_2$ , etc., occur at regular intervals on the continuous helix and in the projection the straight lines  $\bar{C}_1\bar{C}_2, \bar{C}_2\bar{C}_3$ , etc., all subtend the same angle  $\psi$  at  $O$ . Clearly the number of links per turn of the helix  $n$  is equal to  $2\pi/\psi$ . If  $\mu$  is the tilt of the rods  $C_1C_2$ , etc., *i.e.*, the angle made with the horizontal, and  $h$  and  $l$  are its vertical and horizontal components, then the following relations are obtained:

$$(i) \quad h = L \sin \mu; \quad l = L \cos \mu$$

$$(ii) \quad l = 2R \sin \left( \frac{\psi}{2} \right)$$

$$(iii) \quad h = \frac{P}{n}.$$

The number  $n$  defined above need not be integral for a discontinuous helix, like the one we are considering. Thus, given the length  $L$  of the links,

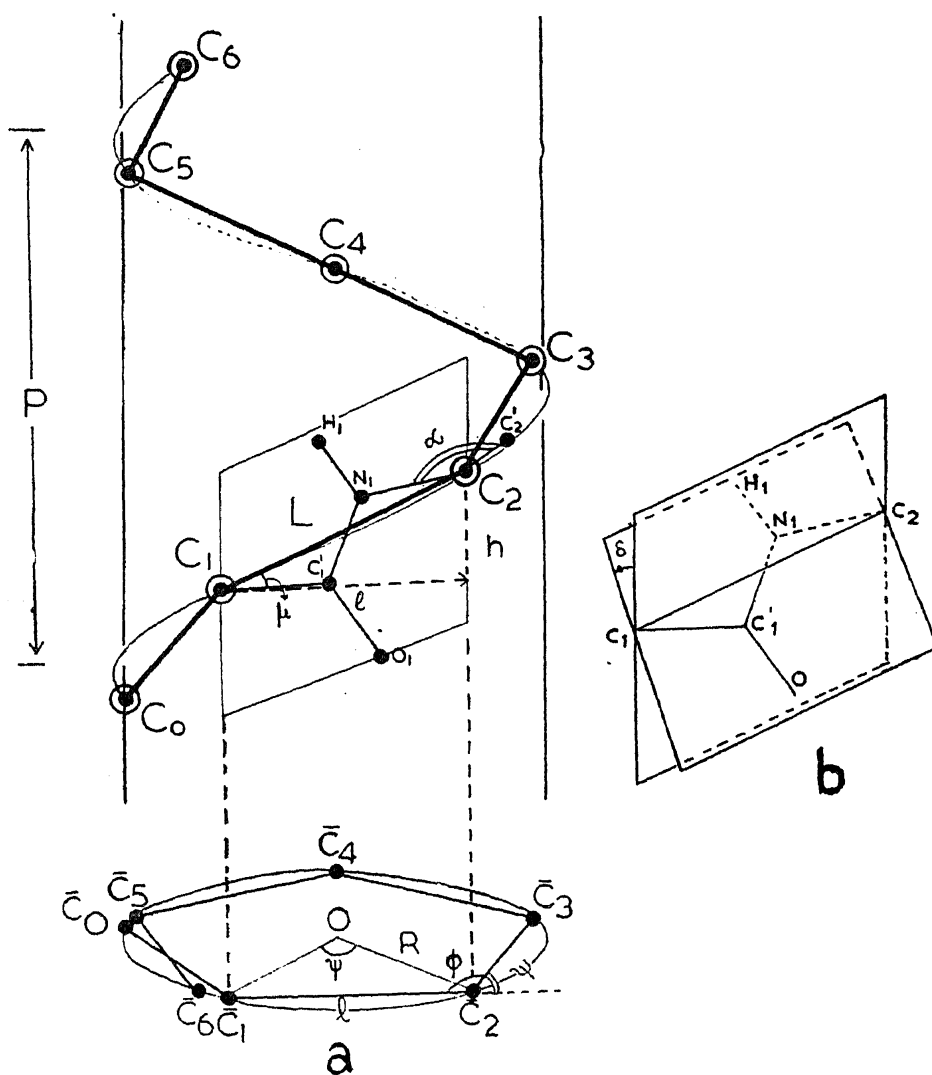


FIG. 1 a and 1 b. Polypeptide helix.

the helix requires two parameters for its specification. This could be, for instance, the pitch  $P$  and the radius  $R$  of the continuous helix associated with it or the tilt  $\mu$  and the unit twist  $\psi$ , which is the same as the angle subtended by it at the centre in the projection, or the tilt  $\mu$  and the number of links per turn  $n$ .

For discontinuous helices it is sufficient to consider the range 0 to  $\pi$  of the angle  $\psi$ , *i.e.*, the range  $\infty$  to 2 of  $n$ . This so because if  $\psi$  happens to be greater than  $\pi$ , it will be less than  $\pi$  when measured in the opposite sense. Consequently, it will be equivalent to a discontinuous helix of the opposite sense but with  $\psi$  less than  $\pi$ . Therefore, all possible helices made up of links of a definite length, say  $L$ , can be covered by considering the range 0 to  $\pi/2$  of the tilt  $\mu$  and the range 0 to  $\pi$  of the unit twist  $\psi$ . The range 0 to  $-\pi/2$

of the tilt only duplicates what is obtained in the range 0 to  $\pi/2$ . Reversing both  $\mu$  and  $\psi$  leads only to the same configuration.

Considering now the full residue with its constituent atoms, further restrictions are brought in. Thus the angle at an  $\alpha$  carbon atom, such as  $C_2$ , between the bonds  $N_1C_2$  and  $C_2C_2'$  cannot be arbitrary but must be equal to the tetrahedral angle, which is denoted here by  $\alpha$ . Consequently once the elements of the helix ( $\mu, \psi$ ) are fixed, the azimuth of the plane with respect to the line  $C_1C_2$  cannot have an arbitrary value. We shall define this azimuth by the angle  $\delta$  shown in Fig. 1 *b*, which is the angle by which the plane is rotated from a vertical position about the axis  $C_1C_2$ . The standard orientation is taken to be that in which the bond  $C'O$  points downwards and  $\delta$  is taken to be positive for anti-clockwise rotation looking from  $C_1$  to  $C_2$ . Actually it is found that, given the values of  $\mu$  and  $\psi$ , there are, in general, two orientations of the plane of the residue for which the angle  $\alpha$  takes the required value. It may of course happen that for certain ranges of  $\mu$  and  $\psi$ , the angle at the  $\alpha$  carbon atom can never be made equal to the required value, so that such helices cannot occur for polypeptide residues. When the two possibilities do occur for a definite ( $\mu, \psi$ ), these two are not equivalent and should, in fact, be considered as different possible structures. Consequently from the structural point of view the more important parameters are,  $\mu$  the tilt and  $\delta$  the azimuth of the plane of the residues. So also it is found more convenient to use the angle between the projection of two successive elements (for example, the angle  $\bar{C}_1\hat{C}_2\bar{C}_3$  in Fig. 1 *a*), rather than the angle  $\psi$  to specify the helix. The relation between these is  $\phi = \pi - \psi$ . Consequently  $n = 2\pi / (\pi - \phi)$ . Hereafter we shall only use  $\mu$  and  $\phi$  to specify the discontinuous helix. The sign of  $\phi$  is taken to be the same as that of  $\psi$ .

Now, if  $\mu$  and  $\delta$  are given, the elements of the helix ( $\mu, \phi$ ) are not uniquely fixed. In fact, two helices can be constructed, one of which is right-handed and the other is left-handed. However, we shall restrict ourselves to helices of one hand, say all right-handed, *i.e.*, corresponding to  $\phi$  positive. Then the complete range can be covered by considering the range 0 to  $\pi/2$  of the tilt  $\mu$  and the full range  $-\pi$  to  $+\pi$  of the azimuth  $\delta$ . All other possibilities of  $\mu, \delta$  and  $\phi$  are then either the duplicates of those contained in this range or only enantiomorphs of these, *i.e.*, left-handed helices. The relationship between these three parameters is shown in Fig. 2 which is a surface in three dimensions and whose equation is the relationship between  $\mu, \phi$  and  $\delta$ . The diagram has been drawn corresponding to the calculations made by the author for some sections of the surface taking the angle at the  $\alpha$  carbon atom ( $\alpha$ )

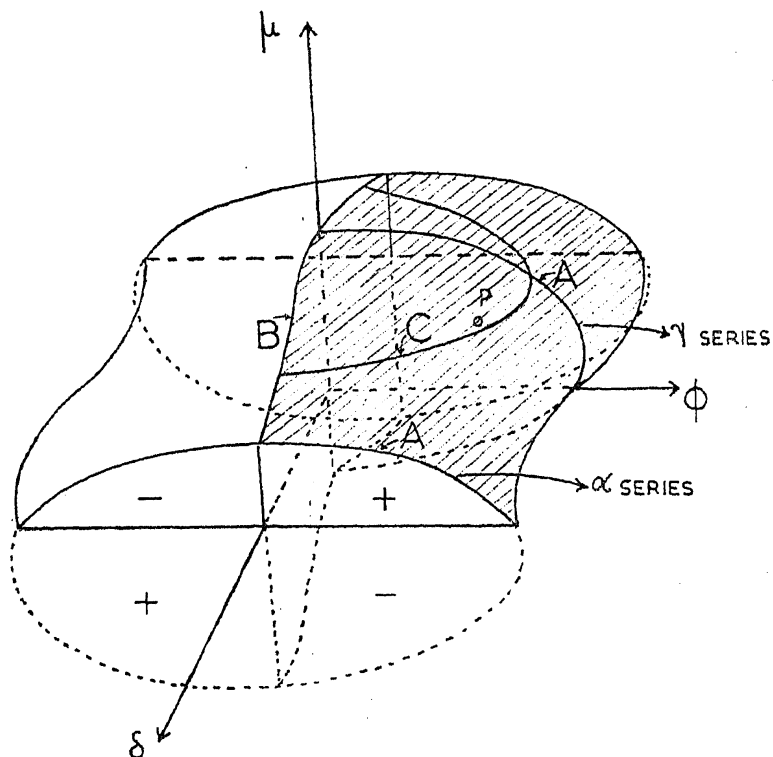


FIG. 2. A surface in three dimensions representing the relationship between the parameters  $\delta$ ,  $\phi$  and  $\mu$  of a helical structure.

to be  $110^\circ$ . It will be seen that the angle  $\phi$  has an upper limit namely  $119^\circ$  so that  $n$  should be less than  $360/61 \approx 6$ . Consequently, all helices composed of amino-acid residues must have their number of residues per turn between 2 and 6. So also there is an upper limit  $72^\circ 30'$  for the tilt  $\mu$ . In this diagram only the shaded quarter need be considered for working out the full range of configurations. All the helices in this range are right-handed ones. If either  $\phi$  or  $\mu$  is made negative, we get left-handed helices. The relation between equivalent helices in the different ranges is shown in Table I. Here the symbol

TABLE I  
*Relation between equivalent helices*

Sign of		Relation to helices in the positive range of $\mu$
$\mu$	$\phi$	
+ve	+ve	$H_+(\mu, \delta)$
-ve	+ve	$H_-(\mu, \pi + \delta)$
+ve	-ve	$H_-(\mu, -\delta)$
-ve	-ve	$H_+(\mu, \pi - \delta)$

$H(\mu, \delta)$  is used to denote a helix having the values  $\mu$  and  $\delta$  for tilt and azimuth, these two parameters occurring in the quarter shaded in Fig. 2. Since the helix is right-handed, *i.e.*, positive, it is denoted by  $H_+(\mu, \delta)$ . The symbol  $H_-(\mu, \delta)$  would mean that the co-ordinates of the atoms are the same, but they refer to a left-handed co-ordinate system, *i.e.*, it is a left-handed helix, which is the enantiomorph of  $H_+(\mu, \delta)$ .

In what we have discussed above, the residue itself has been considered to be a planar structure without asymmetry. Thus the orientation of the remaining two groups  $H$  and  $R$  at the  $\alpha$  carbon atoms is left unspecified. Both the configurations which are usually denoted by  $L$  and  $D$  could occur and they would obviously correspond to different structures, although  $\mu$ ,  $\delta$  and  $\phi$  are the same. To distinguish between these, we shall add another suffix  $L$  or  $D$  to the notation for the helix. Thus for a given  $\mu$  and  $\delta$  there are two right-handed helices  $H_{L+}(\mu, \delta)$  and  $H_{D+}(\mu, \delta)$  and two left-handed helices  $H_{L-}(\mu, \delta)$  and  $H_{D-}(\mu, \delta)$ . It is obvious that  $H_{D-}(\mu, \delta)$  is the enantiomorph of  $H_{L+}(\mu, \delta)$  and correspondingly  $H_{D+}(\mu, \delta)$  is the enantiomorph of  $H_{L-}(\mu, \delta)$ .

### 3. POSSIBLE HELICES SATISFYING THE FIRST CONDITION (a)

In Fig. 3 the dimensions of the backbone of a single residue ( $-C_1 \cdot C_1'O_1 \cdot N_1H_1 \cdot C_2-$ ) have been drawn to scale for the co-ordinates

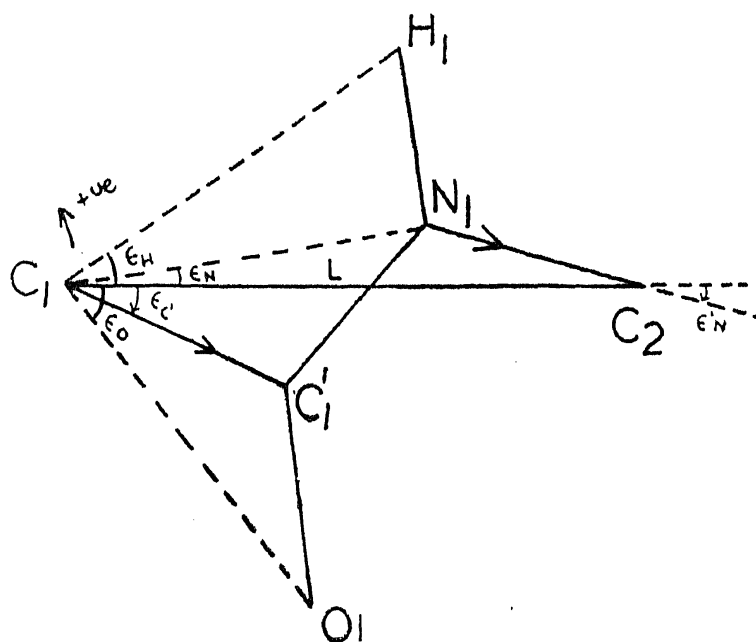


FIG. 3. Definition of various angles connected with the peptide residue.

given by Corey and Pauling<sup>1</sup>. The directly bonded atoms are jointed by lines. We are interested in the distances of the various atoms in the residue from the  $\alpha$  carbon atom  $C_1$  and angles between the lines joining them to  $C_1$  and the line  $C_1C_2$ . These are marked in Fig. 3 and their values are given in Table II

TABLE II

*Distances of the various atoms in the peptide residue (Fig. 3) from  $C_1$  and the angle made by these lines with the line  $C_1C_2$*

Sl. No.	Atoms	Lengths	Angles
1	$C_1C_2$	3.79 Å	..
2	$C_1C_1'$	1.53 Å	$\epsilon_{C'} = 22^\circ$
3	$C_1O_1$	2.41 Å	$\epsilon_O = 48^\circ 15'$
4	$C_1N_1$	2.39 Å	$\epsilon_N = 8^\circ$
5	$C_1H_1$	2.55 Å	$\epsilon_H = 31^\circ 15'$
6	$C_2N_1$	1.47 Å	$\epsilon_N' = 13^\circ$

(The angle  $\epsilon$  is taken to be positive if measured in the anti-clockwise direction from  $C_1C_2$ .)

It would, of course, be useful if the full range of  $\mu$  and  $\delta$  were covered in working out the co-ordinates of the various helices  $H(\mu, \delta)$ . However, this would be a laborious task, and therefore only certain sections of the surface in Fig. 2 have been worked out in full in this paper, and in doing so, the requisite techniques of calculation have been developed. The three types of sections studied are:

(A)  $\delta = \text{constant}$ , = 0 or  $180^\circ$ , which corresponds to the types of helices worked out by Pauling and others<sup>2</sup> and includes the  $\alpha$ ,  $\gamma$  and  $\pi$  helices;

(B)  $\phi = \text{a constant}$ , =  $0^\circ$ , which corresponds to the digonal helical structures. They have a two-fold screw axis of symmetry. Particular cases are the extended and the pleated sheet configuration of Pauling and Corey;<sup>3</sup> and

(C)  $\mu = \text{a constant}$ , =  $50^\circ$ . This value was chosen, as this corresponds to a residue repeat of 2.90 Å, close to the residue repeats of collagen and polyglycine II.

These three ranges studied are marked as the *A*, *B* and *C* series in Fig. 2.

#### 4. CYCLOGRAPHIC PROJECTION APPLIED TO THE PRESENT PROBLEM

In making the calculations, the cyclographic projection was found to be very useful. This projection is closely related to the stereographic projec-

tion. In a stereographic projection, a crystal face is represented by its pole (*i.e.*, the point at which the normal to the face intersects the unit sphere). In the cyclographic projection, on the other hand, it would be represented by the trace of the great circle, parallel to the crystal face (*i.e.*) by the great circle at right angles to the stereographic pole. Since a face is now represented by a great circle, the method is specially applicable to problems in which it is necessary to reproduce in projection, lines drawn on the crystal face. These would now be represented by points occurring on the great circle.

More generally, we may represent any plane (*e.g.*, the plane of the peptide residue) by a great circle and the orientation of the lines drawn in this plane (such as the lines  $C_1O_1$ , ...,  $C_1H_1$  and  $C_2N_1$ ) could then be represented by points on this great circle, the angular distance between representative points along the great circle in the cyclogram being equal to the angle between the corresponding lines on the plane.

In this study the axis of the helix is taken perpendicular to the plane of projection. If  $\mu$  is known, the direction  $C_1C_2$  is fixed, while the plane of the peptide is a great circle passing through this point. The previous residue is obtained by rotating the whole configuration through an angle  $-\psi$  about the centre (*e.g.*,  $C_0C_1$  of Fig. 4). For different values of  $\psi$ , it is possible to

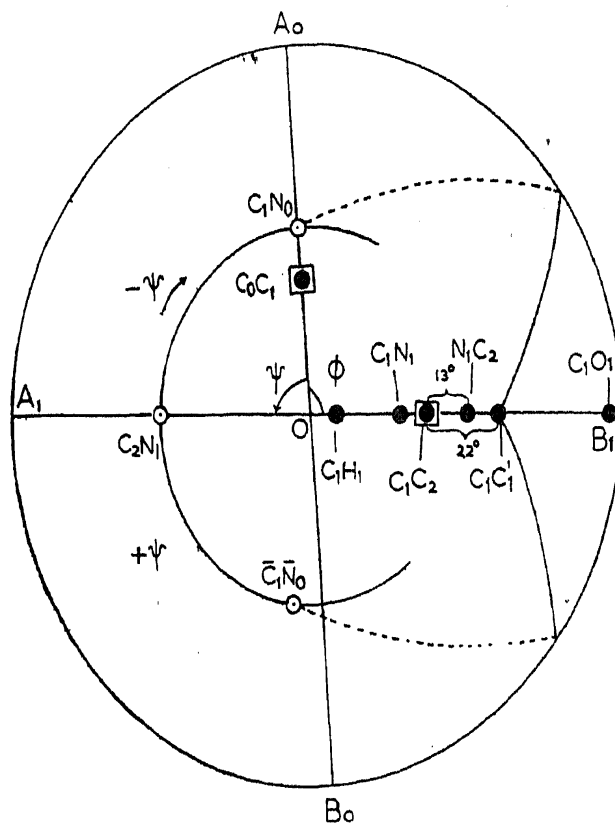


FIG. 4. Cyclogram for  $\delta = 0^\circ$ .

read off the angle between the bonds  $N_0C_1$  and  $C_1C_1'$  which should be equal to the tetrahedral angle  $\alpha$ . Constructions were made with a 30 cm. Wulff net. Angles could be measured accurate to a quarter of a degree,



## 5. RESULTS

*Configurations with Peptide Plane Parallel to the Helical Axis (Series A with  $\delta = 0$  and  $180^\circ$ )*

(a) *Determination of  $\phi$  for various tilts.*—Here  $\delta = 0^\circ$  corresponds to the C = O group pointing down and  $\delta = 180^\circ$  to the group pointing up. Taking the first series, measurements were started with  $C_1C_2$  horizontal; which was then tilted up at intervals of  $5^\circ$  and measurements were made for each tilt. Figure 4 is the cyclogram of a typical case with  $\mu = 50^\circ$ . The directions of all the lines ( $C_1N_1, C_1C_1' \dots$ ) in the first residue would now occur on the meridian through  $C_1C_2$  represented by the horizontal line  $A_1B_1$  in the stereogram. In particular, the bonds  $N_1C_2$  and  $C_1C_1'$  occur at latitudes  $\mu - \epsilon_{N'} = \mu - 13^\circ$  and  $\mu - \epsilon_{C'} = \mu - 22^\circ$  on this line. Considering the residue  $C_0C_1$  previous to  $C_1C_2$ , its plane would be represented by another meridian  $A_0B_0$  at an angle  $-\psi$  to  $A_1B_1$ . We are interested in the "tetrahedral" angle between  $C_1N_0$  and  $C_1C_1'$  and this angle should be equal to  $110^\circ$ .  $C_1N_0$  can be obtained from the corresponding bond  $C_2N_1$  (which is in the direction exactly opposite to  $N_1C_2$ ) in the first residue, by rotating it through an angle  $-\psi$ . Thus the method of fixing  $\psi$  (or  $\phi$ ) is as follows. A circle is drawn with  $O$  as centre and radius equal to the distance  $C_2N_1$  from  $O$  and the angular distance (along a great circular arc) of the various points on it from  $C_1C_1'$  is measured. That point for which this is equal to  $\alpha$  gives the orientation  $A_0B_0$  of the previous residue. It is obvious that there will be two settings  $C_1N_0$  and  $\bar{C}_1\bar{N}_0$  symmetrically situated with respect to the plane  $A_1B_1$  for which the angle  $\alpha$  is equal to the required value. These correspond to right-handed and left-handed helices respectively. Since we shall be dealing exclusively with right-handed helices for which  $\psi$  is positive or anti-clockwise, only the setting  $C_1N_0$  which is to the left of  $C_1C_2$  need be considered.

Thus for different values of  $\mu$  the plane  $A_0B_0$  is determined and the angle between  $A_1B_1$  and  $A_0B_0$  (i.e., the angle  $B_1\hat{O}A_0$ ) is measured. This gives  $\phi = \pi - \psi$ , and hence the number of residues per turn  $n = 2\pi/\pi - \phi$ .

This process was carried out, starting from  $\mu = 0^\circ$  and increasing the tilt until  $\phi = 0^\circ$ , i.e.,  $n = 2$ . A value of  $110^\circ$  was first taken for the "tetrahedral" angle and for this angle the maximum possible value of  $\mu$  was  $72\frac{1}{2}^\circ$ . The same procedure was repeated with two other values of  $\alpha$ , viz.,  $105^\circ$  and  $115^\circ$ . The relation between the tilt  $\mu$  and angle  $\phi$  is shown graphically in the three upper curves of Fig. 5 corresponding to the three values of  $\alpha$ . Similar measurements were also made with the peptide turned through  $180^\circ$ , i.e.,

with  $C=O$  pointing up. But they were made only for  $\alpha = 110^\circ$ . The data thus obtained are shown in the lower curve of Fig. 5.

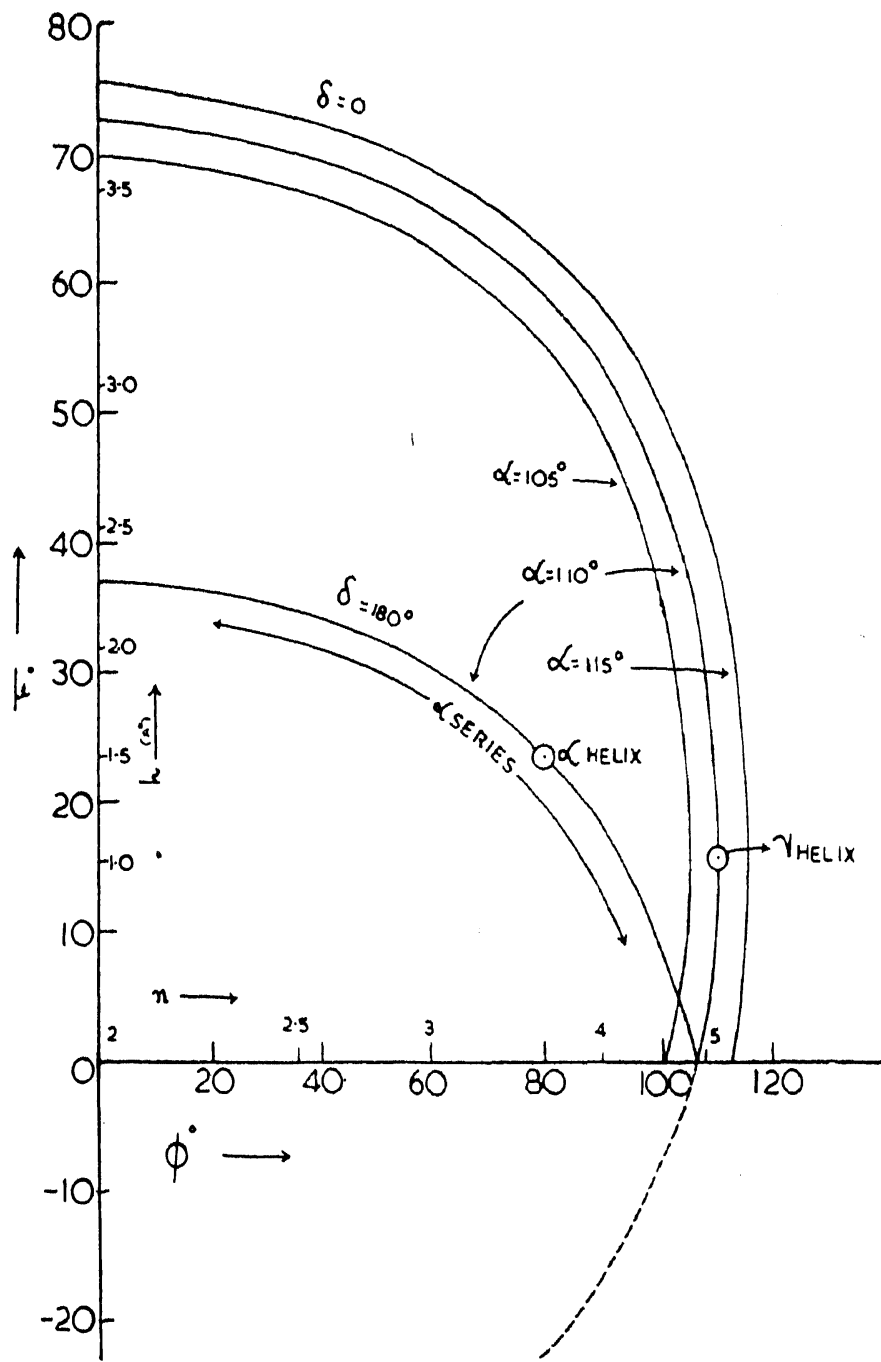


FIG. 5. Variation of  $\phi$  with  $\mu$  for  $\delta = 0$  and  $180^\circ$ .

Along the co-ordinates of Fig. 5 are also marked  $n$ , the number of residues per turn, and  $h$ , the vertical height of the residue.

(b) *Discussion of the curves.*—It will be noticed from Fig. 5 that the turn ratio  $n$  for the same value of the tilt depends on the bond angle at the  $\alpha$  carbon atom. In general,  $n$  decreases as  $\alpha$  is decreased. The three curves for values of  $\alpha$  changing by  $5^\circ$  are seen to be closely similar, the separation between any

two being practically a constant. It is because of this that for the second range, calculations were made only for one value of  $\alpha$ . In fact, for all the results described in the succeeding sections, only one value of  $\alpha$ , viz.,  $110^\circ$  was used.

It will be noticed that for both  $\delta = 0^\circ$  and  $180^\circ$ , the maximum tilt occurs when  $\phi = 0^\circ$ , i.e.,  $n = 2$ . In the first case this maximum value of  $\mu$  is  $72\frac{1}{2}^\circ$  while for the second case it is only  $37\frac{1}{2}^\circ$ . The former corresponds to the fully extended  $\beta$ -structure with a length of  $7.23 \text{ \AA}$  for two residues and the atomic positions are drawn to scale in Fig. 6 a. The latter may be obtained

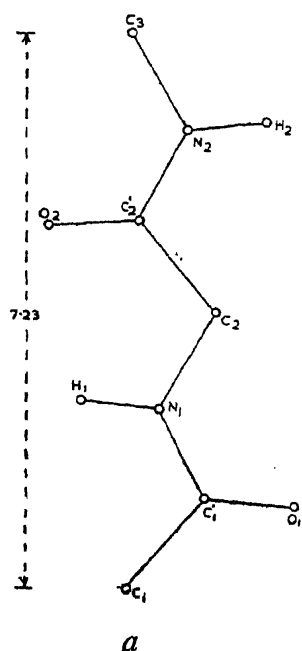


FIG. 6 a. Fully extended  $\beta$  structure.

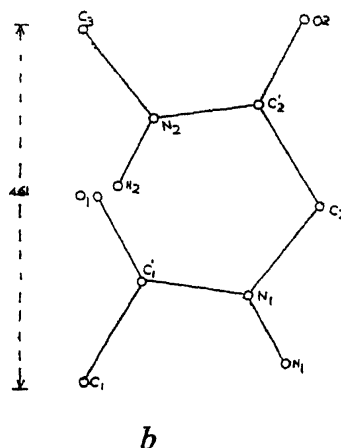


FIG. 6 b. Bent  $\beta$  structure.

from this by rotating both the residues at the  $\alpha$  carbon atom through  $180^\circ$ . This is a highly bent structure (Fig. 6 b) with a repeat of only  $4.61 \text{ \AA}$  for two residues. It has very short contacts between atoms in the neighbouring residues and is therefore not possible for an actual structure. The entire range of configurations for  $n = 2$  lies between  $\mu = 37\frac{1}{2}^\circ$  to  $72\frac{1}{2}^\circ$ . In the next section the stereochemically possible ranges and the co-ordinates of the atoms for this type of digonal structure will be discussed.

The maximum possible value for  $\phi$  when  $\delta = 0^\circ$  or  $180^\circ$  is  $\alpha$ , the "tetrahedral" angle. Therefore  $\psi$  minimum is  $70^\circ$  and the maximum possible number of residues per turn is  $n_{\text{max.}} = 5.14$ . The lower curve for  $\delta = 180^\circ$  does not really have a maximum value, for it could be considered as a continuation of the upper curve for negative values of  $\mu$ .

It is likely that actual structures do not take up all the configurations contained in the two curves in Fig. 5. We shall on the other hand consider which of these would be favoured if the condition that a hydrogen bond of length about 2.75 Å should be formed between NH and CO groups. The range is then considerably reduced.

Considering first the curve for  $\delta = 180^\circ$ , the configurations in this case are all closely similar to the  $\alpha$  helix. The  $\alpha$  helix itself has a value 3.6 for  $n$  with  $\alpha = 110^\circ$  and has a practically straight hydrogen bond with the N—H ... O length equal to 2.75 Å. However, if a slight variation in the "tetrahedral" angle from  $105^\circ$  to  $115^\circ$  is allowed and a short range in the neighbourhood of 2.75 Å for the hydrogen bond length is also permitted, then the range  $n = 2$  to 4.4 of the lower curve can be utilised to form a helical structure in which a residue is hydrogen-bonded to its 1st, 2nd, 3rd, or 4th neighbour. The helices with  $n = 4.3$  and 4.4 have been described, and are known as  $\pi$ -helices.<sup>4</sup> Other helices in the neighbourhood of  $n = 2.2$  and 3.0 have also been described by Donohue,<sup>5</sup> who has also compared the stability of these helices.

Considering the upper curve ( $\delta = 0^\circ$ ), the  $\gamma$  helix of Pauling and others<sup>2</sup> belongs to this range with  $n = 5.14$ . Since  $n$  is nearly 5 for most of the region in the curve ( $\delta = 0^\circ$ ), it is not possible to have other helices of this type with an internal hydrogen bond and this is the only possible helix with probably a small possible change in  $n$  by varying the "tetrahedral angle"  $\alpha$ . By the time  $n$  approaches 4, the pitch of the helix is larger than 12 Å and so no hydrogen bonds can be formed.

It may be mentioned that the discussion here is restricted to configurations with  $\delta = 0^\circ$  or  $180^\circ$  (*i.e.*, with the peptide plane exactly vertical). There is no stereochemical reason why this should be so, and if this restriction is removed, it may perhaps be possible to have hydrogen-bonded helical structures over a wider range of values of  $n$  than what has been stated above. This aspect has not yet been fully studied.

(c) *Derivation of the co-ordinates.*—Once the elements of the helix  $\mu$  and  $\phi$  are known, it is only necessary to know the co-ordinates of the atoms in any one residue to completely specify the structure. The position of any atom, *e.g.*, N is given in terms of its cylindrical polar co-ordinates  $r_N$ ,  $\theta_N$  and  $z_N$  with *OZ* as *z* axis and *OC* as the initial position in the perpendicular basal plane (Fig. 7), where C is the corresponding  $\alpha$  carbon atom (*e.g.*,  $C_1$  for the residue  $C_1C_2$ ). Figure 7 is actually drawn for a general orientation of the peptide ( $\delta$  other than  $0^\circ$  or  $180^\circ$ ). When  $\delta = 0^\circ$  or  $180^\circ$  all the atoms

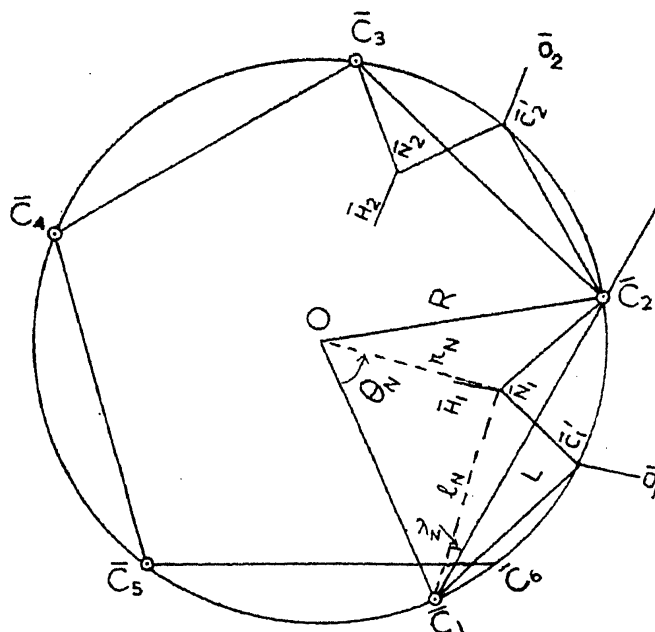


FIG. 7. Basal projection of polypeptide helix.

will lie in the projection on the line  $\bar{C}_1\bar{C}_2$  (projected line of  $C_1C_2$ ). The letters with bars over them indicate the positions of the atoms in the projection. If  $l_N (= \bar{C}_1\bar{N}_1)$  is the projected length of  $C_1N_1$  in the basal plane for a particular  $\mu$ , then

$$l_N = L_N \cos(\mu + \epsilon_N) = L_N \cos \mu_N$$

where  $\mu_N = \epsilon_N + \mu$  and  $L_N$  is the actual distance between  $C_1$  and  $N_1$  in the peptide plane, given in Table II. The three cylindrical co-ordinates can then be obtained in terms of  $R$ , the radius of the cylinder on which the  $\alpha$  carbon atoms lie,  $l_N$  the projected length of  $C_1N_1$  and  $L$ , the projected length of  $C_1C_2$ . Thus  $r_N$  is given by

$$r_N = \sqrt{l_N^2 + R^2 - l_N \cdot L}$$

The angle  $\theta_N$  measured from  $O\bar{C}_1$  in the projection is given by

$$\theta_N = \sin^{-1} \left[ \frac{l_N \sin \frac{\phi}{2}}{r_N} \right]$$

The height  $z_N$  is given by

$$z_N = L_N \sin \mu_N$$

Similarly the co-ordinates of the other atoms can be obtained. The values of  $r$ ,  $\theta$  and  $z$  for all the atoms in the peptide residue are plotted in Figs. 8 (a and b) against the tilt for a range covered by the curve for  $\delta = 180^\circ$ . They correspond to the  $\alpha$  series of helices with the range 4.5 to 2 for  $n$ .

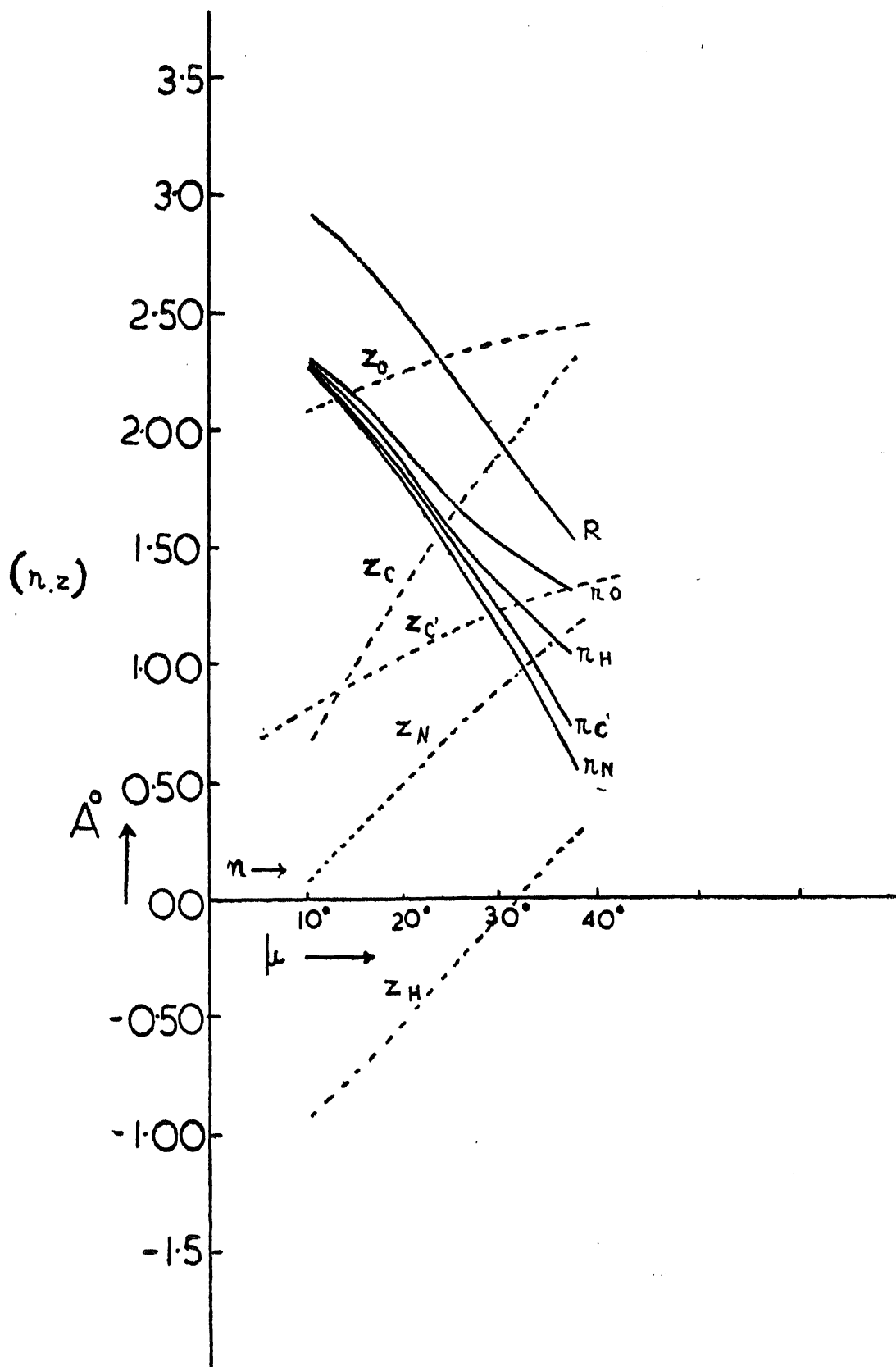


FIG. 8 a

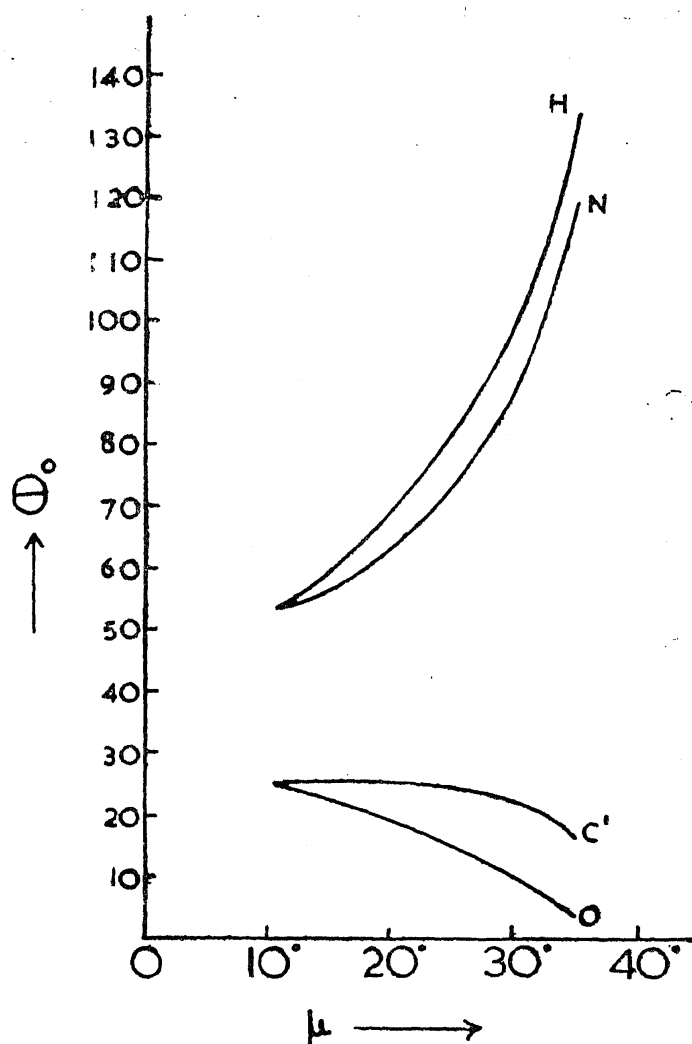


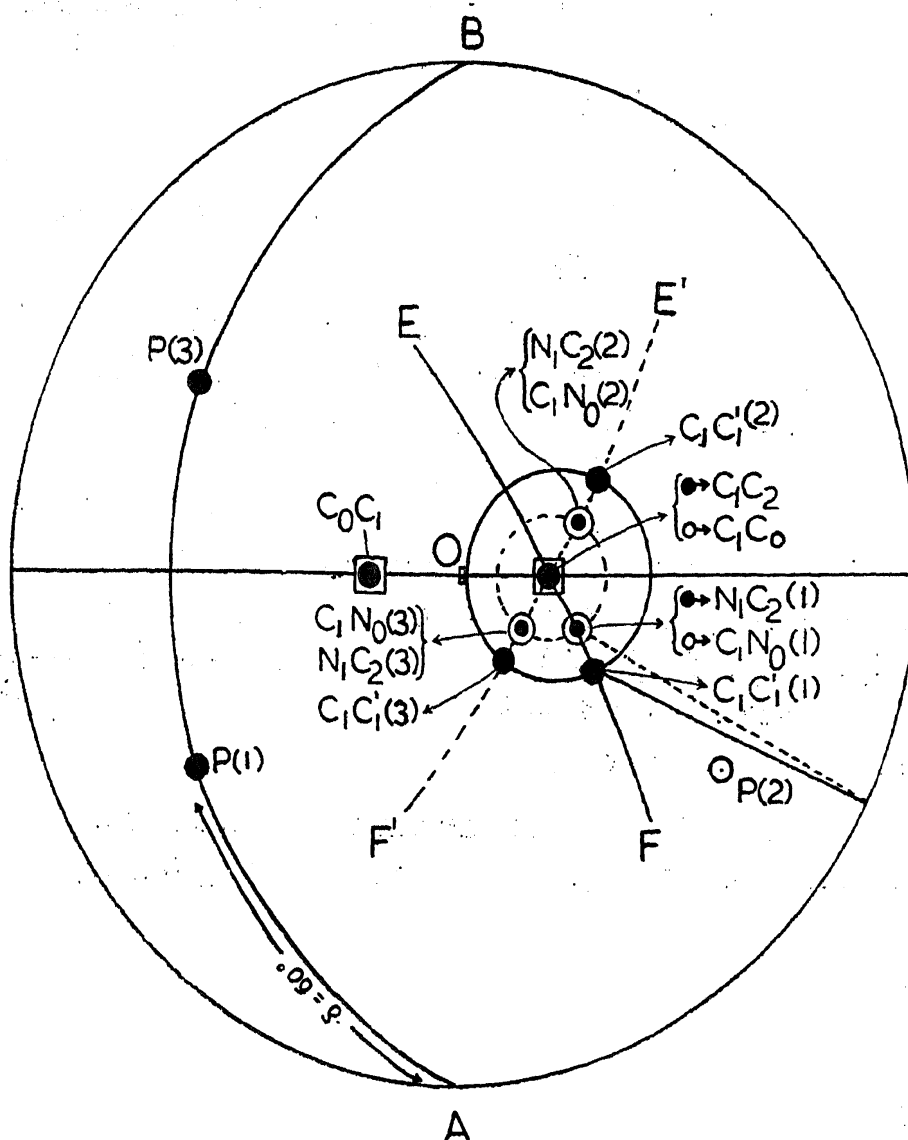
FIG. 8 b

Figs. 8 a and b. Variation of  $r$ ,  $\theta$  and  $z$  with  $\mu$  for the  $\alpha$  series.

## 6. CONFIGURATIONS FOR $n = 2$ ; $\beta$ STRUCTURES

(a) *Determination of  $\delta$  for various tilts.*—For  $\phi = 0^\circ$ , i.e.,  $n = 2$ , it has been pointed out in the previous section, that the tilt ranges from  $\mu = 37\frac{1}{2}^\circ$  to  $72\frac{1}{2}^\circ$ . Over this range the azimuth  $\delta$  would continuously change from  $180^\circ$  to  $0^\circ$ . Corresponding to a tilt  $\mu$ , there will be a definite value of  $\delta$  which can be determined as follows:

Corresponding to a particular value of  $\mu$ , the pole of the peptide residue is on the great circle  $AB$  of Fig. 9, the angle  $\delta$  being measured from the point  $A$ . The line  $C_1C_2$  is represented by the point  $C_1C_2$ . For the different azimuths the two directions  $C_1C_1'$  and  $N_1C_2'$  would lie on small circles with  $C_1C_2$  as pole and radii equal to  $\epsilon_{C'}$  and  $\epsilon'_{N'}$ . For  $\delta = 0^\circ$  they lie on the meridian through  $C_1C_2$ . For a value of  $\delta = 60^\circ$  (say), the pole of the peptide plane


 FIG. 9. Cyclogram for  $\phi = 0^\circ$ .

is represented by  $P(1)$  in Fig. 9. The great circle corresponding to the peptide plane is  $EF$  whose pole is  $P(1)$  and the lines  $C_1C_1'$  and  $N_1C_2$  are now represented by points on this great circle, and are marked as  $C_1C_1'(1)$  and  $N_1C_2(1)$ . Since we have definitely assumed that  $\phi = 0^\circ$  (or  $\psi = 180^\circ$ ) the previous residue would have its pole  $C_0C_1$  on the same meridian as  $C_1C_2$  but on the opposite side. Therefore  $C_1C_0$  would occur at the same point as  $C_1C_2$  but below the plane of the paper. Consequently the direction  $C_1N_0$  will also lie on the dotted circle shown in Fig. 9 with  $C_1C_2$  as pole, and it would coincide with  $N_1C_2$ , but would lie below the plane of the paper.

The problem is to determine the value of  $\delta$  for which the angle between  $C_1N_0(1)$  and  $C_1C_1'(1)$  is equal to  $110^\circ$ . As  $\delta$  is varied, the angle between  $C_1N_0$  and  $C_1C_1'$  will change and for the particular example shown in the diagram (*i.e.*, for  $\mu = 67^\circ$ ), the angle is  $110^\circ$  when  $\delta = 60^\circ$ , as indicated.



More generally, for each value of  $\mu$ , the position of the pole of the peptide on the great circle is determined for which  $C_1C_1'$  and  $C_1N_0$  (which correspond to the intersection of the corresponding peptide plane with the two small circles) are at an angle of  $110^\circ$ .

If  $P$  is taken at  $-\delta$ , which is equivalent to choosing the pole  $P$  (2), the relevant directions in the plane are now represented by  $C_1C_2$  (2),  $N_1C_2$  (2),  $C_1N_0$  (2) in the great circle  $E'F'$ .

Once again it will be seen that the angle between  $C_1C_1'$  (2) and  $C_1N_0$  (2) will be the same as the angle between  $C_1C_1'$  (1) and  $C_1N_0$  (1), considered earlier. Since  $\phi = 0^\circ$  or  $\psi = 180^\circ$ , this is not a different helix, but may be seen to be equivalent to the former one, but going in the opposite direction. However, this second great circle has its other pole at  $P$  (3) which is opposite to  $P$  (2). Corresponding to this, the bond directions  $C_1C_1'$  and  $C_1N_0$  occur at  $C_1C_1'$  (3) and  $C_1N_0$  (3), and the angle between them is not the same as that between  $C_1C_1'$  (1) and  $C_1N_0$  (1). This shows that  $\delta$  and  $180 - \delta$  are not equivalent, although  $+\delta$  and  $-\delta$  are. Hence, the whole range  $0^\circ$  to  $180^\circ$  of  $\delta$  will have to be studied.

The above method was used to determine the values of  $\delta$  corresponding to various values of the tilt  $\mu$ . The graph connecting  $\delta$  and  $\mu$  is shown in Fig. 10.

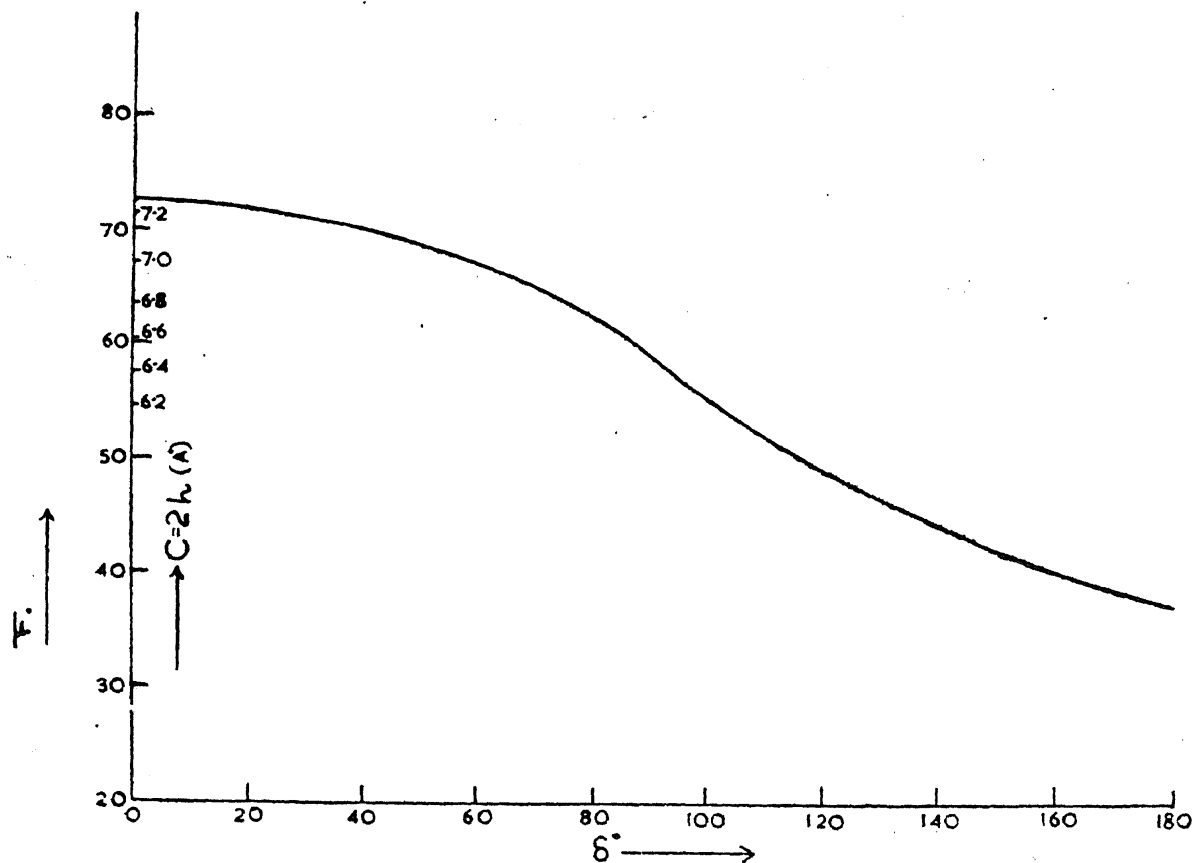


FIG. 10. Variation of  $\delta$  with  $\mu$  for  $\phi = 0^\circ$ .

(b) *Discussion of the  $\beta$  structures.*—As already pointed out in the previous section, the polypeptide chain is fully extended when  $\mu = 72\frac{1}{2}^\circ$  (for  $\delta = 0^\circ$ ) and is buckled when  $\mu = 37\frac{1}{2}^\circ$  (for  $\delta = 180^\circ$ ). The latter position is obviously impossible (Fig. 6 b). The fully extended chain is quite satisfactory so long as only a single chain is considered. But if hydrogen bonds of the type N—H...OC have to be formed between chains arranged side by side, then if the chains are all parallel, the bonds cannot be straight, the angle between NH and NO being more than  $30^\circ$ . Even then only glycine can be accommodated in the side-chain. On the other hand if alternate chains go in opposite directions, as in the so-called anti-parallel structure, then good hydrogen bonds can be formed, but there are short contacts between the  $\alpha$  carbon atoms if  $\delta$  has a value  $0^\circ$ , *i.e.*, the chains are completely flat. If the chains are allowed to buckle slightly ( $\delta$  is allowed to have values in the range  $0^\circ$  to  $90^\circ$ ), hydrogen bonds can be formed between either parallel or anti-parallel chains. Thus for example, when  $\delta = 67^\circ$  (or  $h = 3.5 \text{ \AA}$ ) for polyglycine, there is no steric hindrance between parallel or anti-parallel chains and good hydrogen bonds can be formed in both cases with anti-parallel chains giving a more linear hydrogen bond.

Thus the steric hindrance between the side-chains may be relieved by allowing the chains to buckle according to the size and chemical nature of the side-chains and an appreciable range of repeat distances can be obtained with acceptable hydrogen bond configuration for both parallel and anti-parallel chain configurations. Actually this range of repeat distances was found to be  $c = 6.25$  to  $7.00 \text{ \AA}$  for both the parallel and anti-parallel arrangements. These may be defined as the  $\beta$  type of structures. The corresponding change in  $\mu$  is from  $55^\circ$  to  $67^\circ$  and in  $\delta$  from  $60^\circ$  to  $100^\circ$ .

The ideal pleated sheet configuration described by Pauling and Corey<sup>3</sup> corresponds to  $\delta = 90^\circ$  and  $c = 6.5 \text{ \AA}$ . The other pleated sheet configuration described by them is  $c = 7.0 \text{ \AA}$  for  $\delta = 60^\circ$ .

(c) *Derivation of the co-ordinates.*—In each case the positions of the poles  $C_1O_1$ ,  $C_1C_1'$ , etc., were noted. These could be obtained by drawing small circles corresponding to  $\epsilon_0$ ,  $\epsilon_{C'}$ , etc., about  $C_1C_2$ . The inclinations ( $\mu_0$ ,  $\mu_{C'}$ , etc.) of the lines  $C_1O_1$ ,  $C_1C_1'$ , etc., to the basal plane could be directly read off from the net. Thus for example if  $\mu_N$  is the inclination of  $C_1N_1$ , then the projected length of  $C_1N_1$  on the basal plane is given by

$$\bar{C}_1\bar{N}_1 = l_N = L_N \cos \mu_N.$$

The height above the basal plane is given by

$$z_N = L_N \sin \mu_N.$$

The azimuthal angle between  $\bar{C}_1\bar{N}_1$  and  $\bar{C}_1\bar{C}_2$  (Fig. 7) can also be measured from the net and is denoted by  $\lambda_N$ . Similarly, these three quantities  $l$ ,  $z$  and  $\lambda$  were obtained for the other atoms.

When  $\phi = 0^\circ$  ( $n = 2$ ), the structure is a digonal helix and therefore it is convenient to obtain the positions of the atoms referred to a rectangular co-ordinate system. The  $z$ -axis is taken to be parallel to the axis of the helix and passing through  $\bar{C}_1$ . The  $x$ -axis is taken to be along  $\bar{C}_1\bar{C}_2$ . The  $y$ -axis is perpendicular to  $\bar{C}_1\bar{C}_2$  at  $\bar{C}_1$  such that  $x, y, z$  form a right-handed system. Then the rectangular co-ordinates of any atom (say  $N_1$ ) are then given in terms of  $z_N, l_N$  and  $\lambda_N$  by  $x_N = l_N \cos \lambda_N, y_N = l_N \sin \lambda_N, z_N = z_N$ .

The  $x, y$  and  $z$  co-ordinates for the range from  $\mu = 50^\circ$  to  $72\frac{1}{2}^\circ$  are given in Fig. 11. The co-ordinates of the atoms of the backbone are given in Table III for some  $\beta$  structures. The hydrogen-bond lengths, angles and the stereochemically possible  $\beta$  structures, both for the parallel and anti-parallel arrangements, are being worked out and will be reported later.

## 7. CONFIGURATIONS FOR CONSTANT TILT AND VARYING $\delta$

(a) *Determination of  $\phi$  for various  $\delta$  ( $\mu = 50^\circ$ ).*—In this case the peptide link  $C_1C_2$  was maintained at  $\mu = 50^\circ$  and the peptide plane was rotated about  $C_1C_2$  over a full range, viz.,  $-180^\circ \leq \delta \leq 180^\circ$ . The variation of the number of residues per turn  $n$  (or  $\phi$ ) with the azimuth  $\delta$  of the peptide plane was calculated. The plane was initially kept parallel to the helical axis and then rotated about  $C_1C_2$  both in the anti-clockwise ( $+\delta$ ) and clockwise ( $-\delta$ ) directions. For this particular value of  $\mu$ , the magnitude of  $\delta$  has an upper limit  $117^\circ$ . So, measurements were made for values of  $\delta$  at intervals of  $10^\circ$  over the range  $-117^\circ < \delta < 117^\circ$ . As will be seen from Fig. 5,  $\delta$  can have the full range  $-180^\circ$  to  $+180^\circ$  only for values of  $\mu$  less than  $37\frac{1}{2}^\circ$ . The method of obtaining the angle  $\phi$  for given  $\mu$  and  $\delta$  is as follows:

With  $\mu = 50^\circ$ , the pole of  $C_1C_2$  is plotted first (Fig. 12). Small circles corresponding to the angular values of  $\epsilon_C$  and  $\epsilon'_N$  can be drawn about the pole  $C_1C_2$ . For convenience, the small circle  $\epsilon'_N$  is drawn about the pole opposite to  $C_1C_2$  in Fig. 12. The locus of the pole of the peptide for various values of  $\delta$  will be the great circle  $AB$ . The great circle is divided into intervals of  $10^\circ$ . For each of these poles, the corresponding great circle of the peptide plane is traced. In each case the intersections of the small circles with the great circle of the peptide plane should give the points representing  $C_1C_1'$  and  $C_2N_1$  for the azimuth  $\delta$  of the peptide.

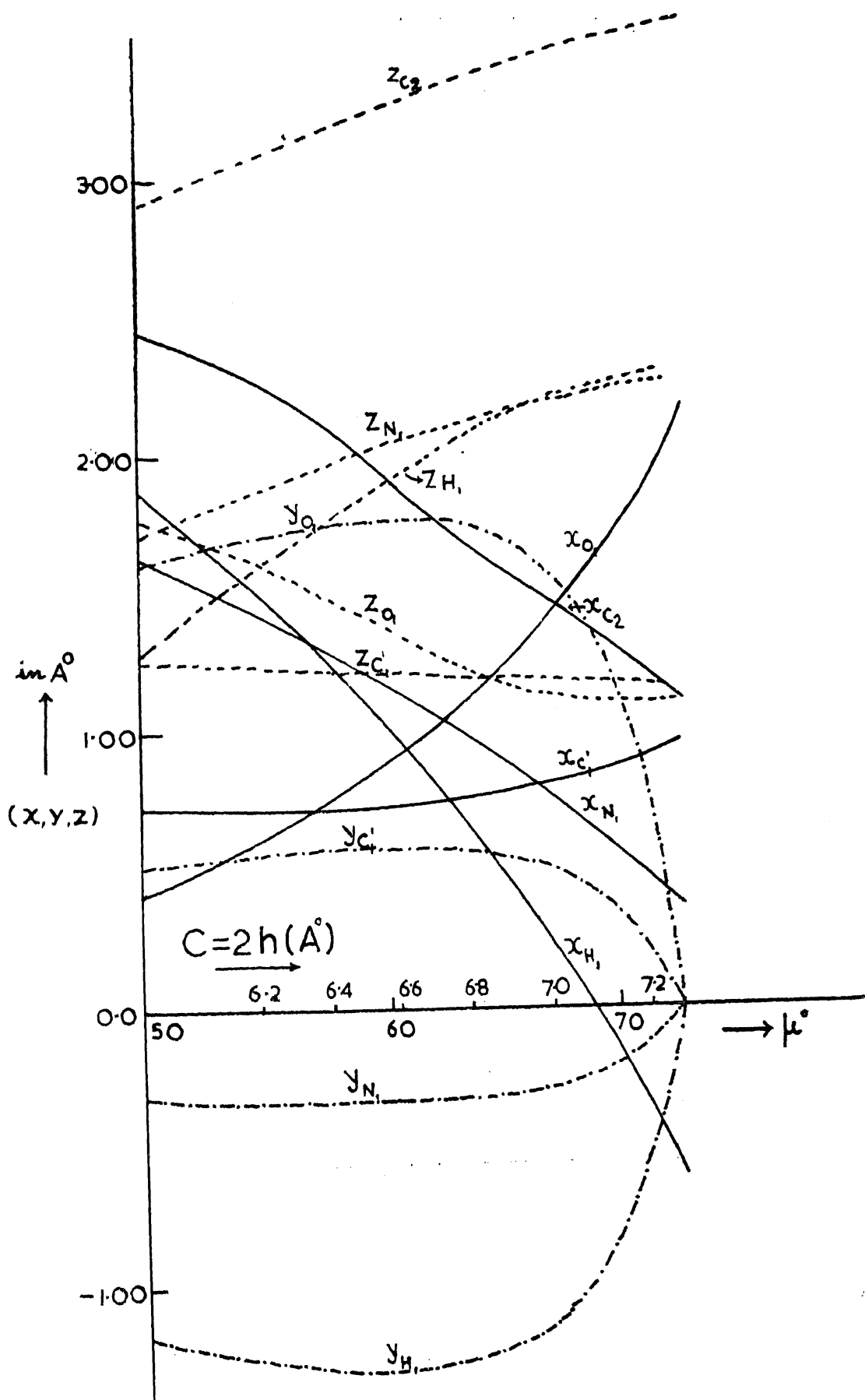


FIG. 11. Variation of  $x$ ,  $y$  and  $z$  with  $\mu$  for the  $\beta$  series.

TABLE III

*Atomic co-ordinates for the backbone of some  $\beta$  structures  
(These have been calculated from the value of  $c$  for an ideal structure)*

(a) *Stretched pig bristle: Fibre repeat  $c = 6.62 \text{ \AA}$  ( $\delta = 86^\circ$ )*

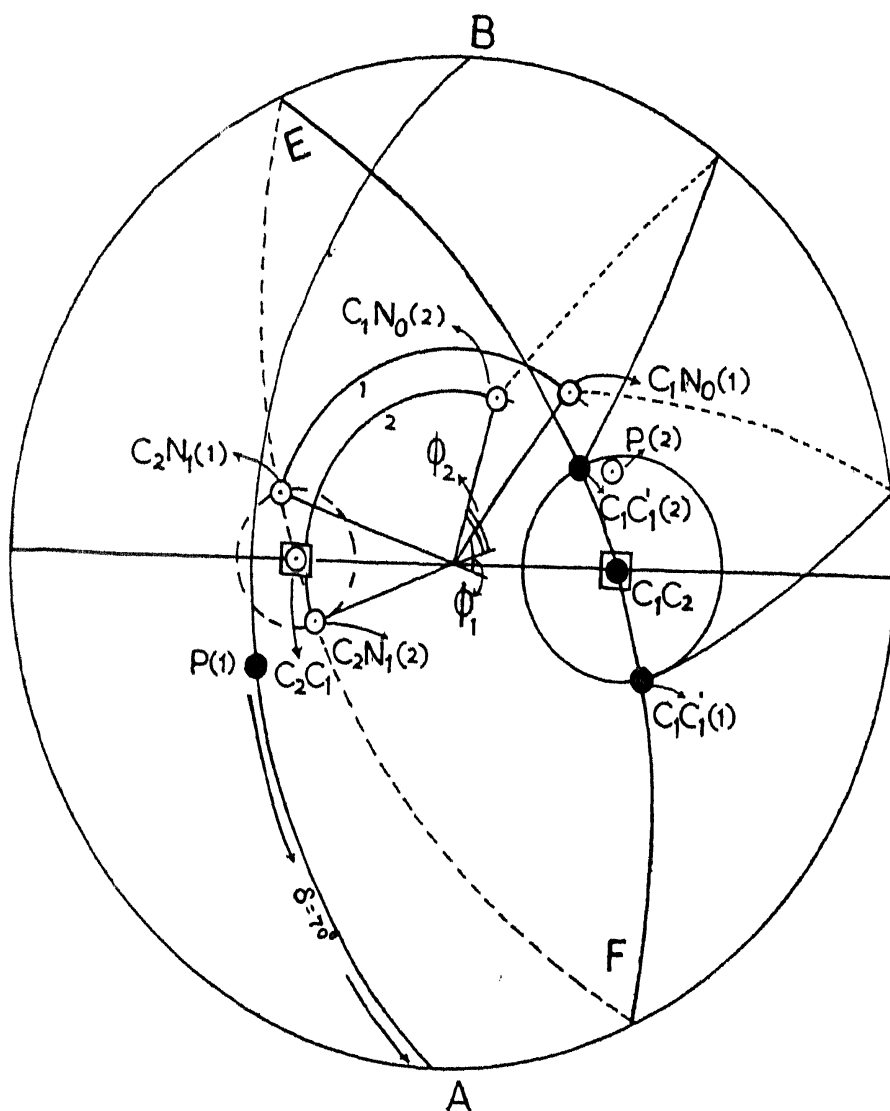
Atom	$x$	$y$	$z$
C <sub>1</sub>	0.00	0.00	0.00
C <sub>1</sub> '	0.74	0.58	1.22
O <sub>1</sub>	0.95	1.78	1.35
N <sub>1</sub>	1.15	-0.35	2.06
H <sub>1</sub>	0.95	-1.34	1.95
C <sub>2</sub>	1.90	0.00	3.31

(b)  *$\beta$ -poly- $\gamma$ -methyl-L-glutamate: Fibre repeat  $c = 6.84 \text{ \AA}$  ( $\delta = 73^\circ$ )*

Atom	$x$	$y$	$z$
C <sub>1</sub>	0.00	0.00	0.00
C <sub>1</sub> '	0.75	+0.55	1.20
O <sub>1</sub>	1.125	+1.65	1.20
N <sub>1</sub>	0.99	-0.35	2.15
H <sub>1</sub>	0.65	-1.30	2.13
C <sub>2</sub>	1.70	0.00	3.42

(c)  *$\beta$ -polyglycine: Fibre repeat  $c = 7.00 \text{ \AA}$  ( $\delta = 60^\circ$ )*

Atom	$x$	$y$	$z$
C <sub>1</sub>	0.00	0.00	0.00
C <sub>1</sub> '	0.82	0.50	1.20
O <sub>1</sub>	1.46	1.58	1.15
N <sub>1</sub>	0.77	-0.30	2.24
H <sub>1</sub>	0.23	-1.15	2.24
C <sub>2</sub>	1.49	0.00	3.50


 FIG. 12. Cyclogram for  $\mu = 50^\circ$ .

As an example, let us consider the plane rotated through  $\delta = 70^\circ$  (Fig. 12) the pole being at  $P$ ,  $70^\circ$  from  $A$ . The great circle representing the peptide plane for this pole  $P$  is  $EF$ . There are two sets of points  $C_1C_1'$  (1)  $C_2N_1$  (1) and  $C_1C_1'$  (2) and  $C_2N_1$  (2) given by the intersections of this great circle with the two small circles. These two sets correspond to the positions obtained by rotating the plane through  $\delta$  ( $= 70^\circ$ ) and  $180 + \delta$  ( $= 250^\circ$ ) which is the same as taking  $\delta = 70^\circ$  in the anti-clockwise direction and  $\delta = -110^\circ$ , *i.e.*,  $110^\circ$  in the clockwise direction. One is obtained from the other by turning the plane through  $180^\circ$  about  $C_1C_2$ . The corresponding pole of the peptide plane in the second position is  $P$  (2) at  $\delta = -110^\circ$ .

The problem now is to find how much the previous residue  $C_0C_1$  is to be rotated away from  $C_1C_2$  so that the angle  $\alpha$  becomes equal to  $110^\circ$ . As already pointed out, if the peptide planes should form a helical structure then the normals to these planes should make the same angle with the axis of the helix,

Therefore the plane  $C_0C_1$  should also be rotated through  $\delta = 70^\circ$  or  $-110^\circ$  as the case may be from the vertical position.

Therefore  $C_1N_0$  will lie on a small circle with  $O$  as centre and passing through the representative point of  $C_2N_1$  as shown in Fig. 12, *i.e.*, it must lie on the small circle 1 for  $\delta = 70^\circ$  and on the small circle 2 for  $\delta = -110^\circ$ . Now it is only necessary to find the points on these two small circles 1 and 2 which are at  $110^\circ$  from  $C_1C_1'$  (1) and  $C_1C_1'$  (2) respectively. These are marked in Fig. 12 and the values of  $\phi$  in each case can also be directly read off on the Wulff net.

The above procedure was repeated for the whole range of  $\delta$  and in each case the value of  $\phi$  was noted. The graph connecting the azimuth  $\delta$  with  $\phi$  (and  $n$ ) is shown in Fig. 13.

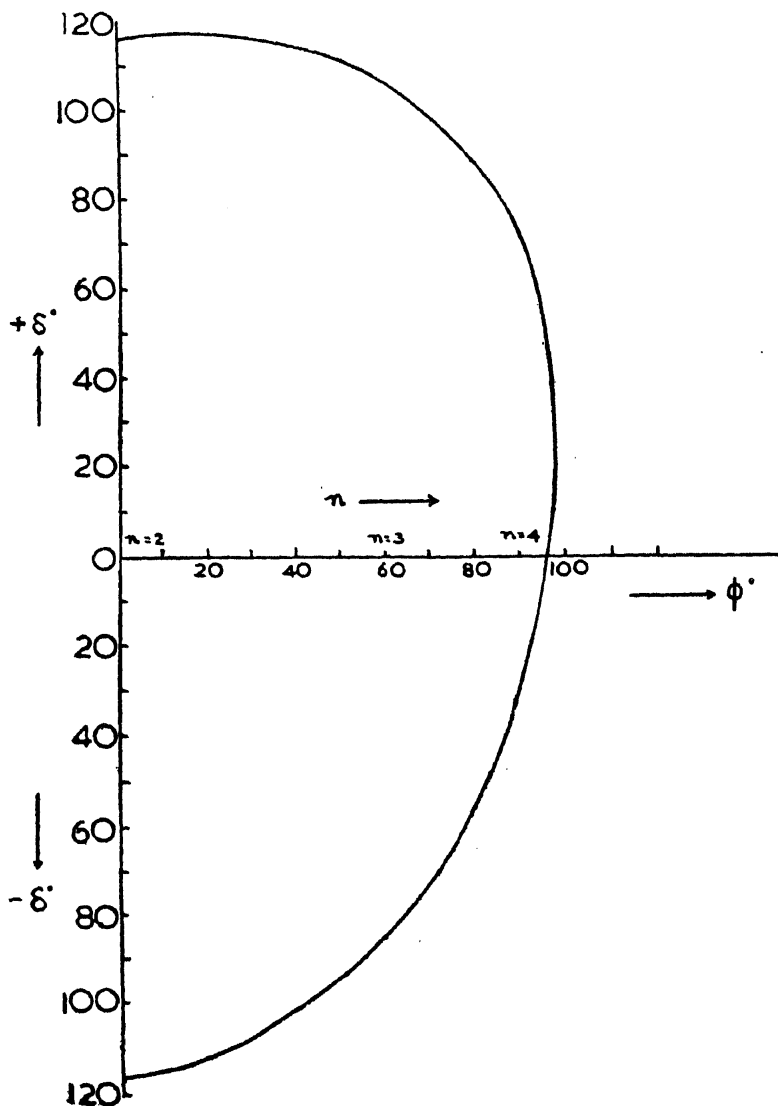


FIG. 13. Variation of  $\delta$  with  $\phi$  for  $\mu = 50^\circ$ .

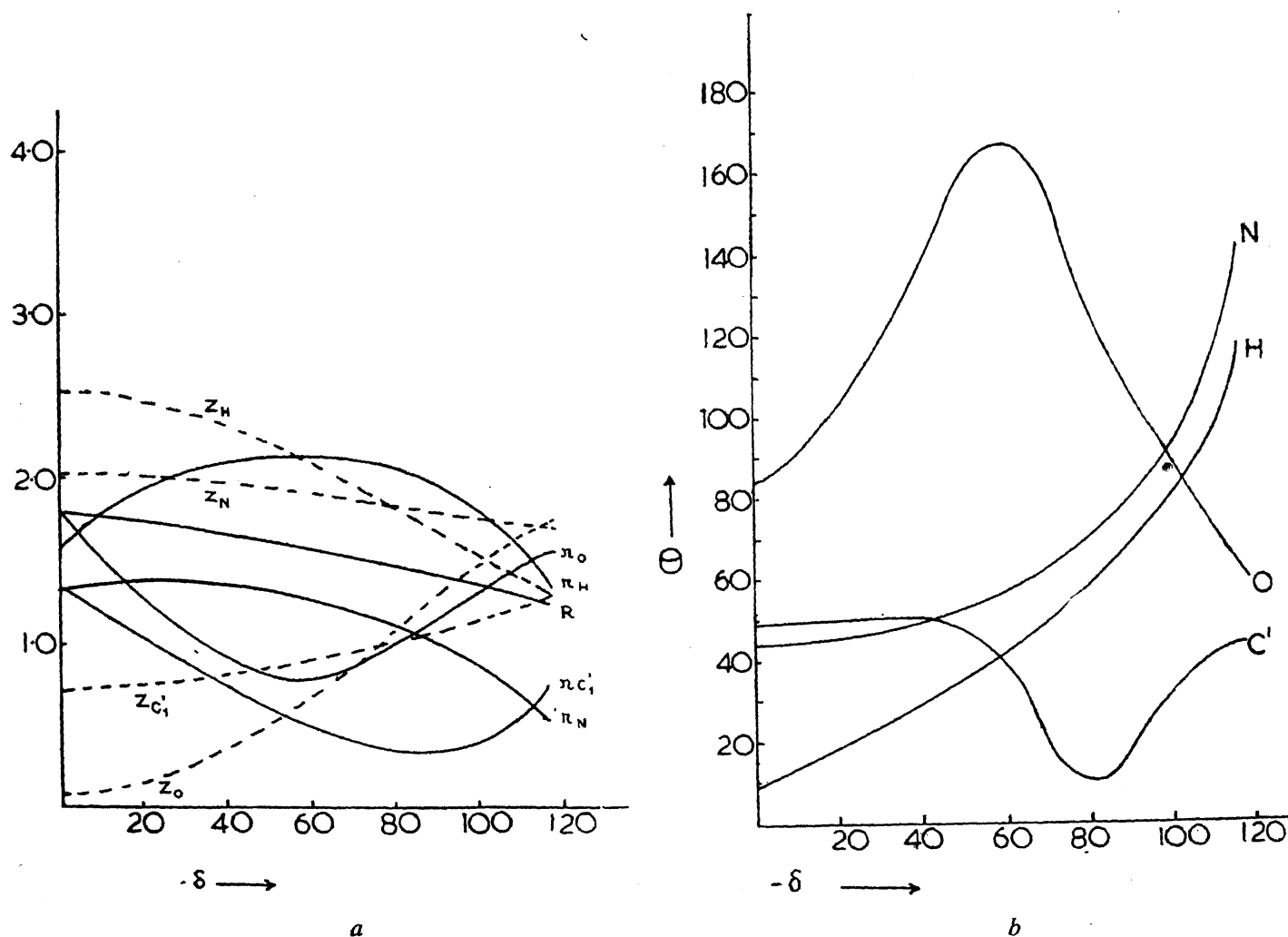
(b) *Discussion of the graph.*—The upper part corresponds to positive values of  $\delta$ , *i.e.*, to anti-clockwise rotations of the peptide plane from the vertical standard position with  $C=O$  pointing down, whereas the lower part corresponds to clockwise rotations. In the helices corresponding to the upper part ( $\delta$  positive) the  $C=O$  group points away from the axis of the helix, while in the case of helices with  $\delta$  negative, the  $C=O$  groups point inwards towards the axis. Thus for a particular tilt  $\mu$ , there are two helices with the same number of residue per turn corresponding to the clockwise and anti-clockwise rotations of the peptide with respect to  $C_1C_2$ , in one of which the CO groups are turned inwards, while in the other, the NH groups are pointing inwards.

This means that, in general, for a particular orientation of the peptide with respect to the helical axis there are two different helical configurations one with C' atoms near the axis and the other with N atoms near the axis of the helix. These correspond to two values of  $\delta$  separated by  $180^\circ$ . The two configurations mentioned by Crick and Rich<sup>6</sup> for polyglycine II, which correspond to  $\mu = 54^\circ 30'$  and  $\delta = 90^\circ$ , have this type of relationship. If imino-acid residues like proline or hydroxyproline residues occur, the configurations with N atoms near the axis are not possible. The polypeptide chain configurations in poly-L-proline II,<sup>7</sup> poly-L-hydroxyproline A<sup>8</sup> and polyglycine II<sup>9</sup> are very similar and the point *P* marked in Fig. 2 is close to the above structures.

The maximum possible value of  $\delta$  for a given value of  $\mu$  is determined by the value of the angle  $\alpha$ . In the present case where  $\alpha = 110^\circ$ , the maximum value for  $|\delta|$  is  $117^\circ$ . Because of this, it may not always be possible to have two structures in which the peptide is reversed with respect to each other, *e.g.*, in the above case of  $\mu = 50^\circ$ , if  $|\delta| < 60^\circ$ , the second corresponds to  $|\delta| > 120^\circ$  and is therefore not possible.

(c) *Derivation of the co-ordinates.*—For each value of  $\delta$ , the positions of the points  $C_1O_1$ ,  $C_1C_1'$ , etc., were noted as in Sec. 6 (c) and the inclinations of the lines  $C_1O_1$ ,  $C_1C_1'$ , etc., were directly read off, on the Wulff net. As mentioned in Sec. 6 (c) the values of  $l$ ,  $\lambda$  and  $z$  for each atom were also obtained. The absolute values of  $l$ ,  $\lambda$  and  $z$  will be the same for both positive and negative values of  $\delta$ . But in the projection the positions of the atoms in the two cases will be related by a reflection about a vertical plane through  $C_1C_2$ . The three cylindrical co-ordinates  $r$ ,  $\theta$  and  $z$  can then be obtained in terms of  $R$  (the radius of the cylinder on which the  $\alpha$  carbon atoms lie)  $l$ ,  $\lambda$  and  $z$  from equations similar to the ones given in Sec. 5 (c). As an example, the values of  $r$ ,  $\theta$  and  $z$  for all the atoms in the peptide residue are plotted in Figs. 14 (a and b)





Figs. 14<sup>a</sup> and <sup>b</sup>. Variation of  $r$ ,  $\theta$  and  $z$  with  $\delta$  for  $\mu = 50^\circ$ .

against the azimuth  $-\delta$ . These correspond to the series of helices in which the CO groups point inwards.

## 8. CONCLUSIONS

We have considered above methods whereby, when the tilt  $\mu$  and one other variable (either  $\delta$  or  $\phi$ ) is given, the remaining parameter can be determined. This method could be extended to cover the complete range of possible values for these quantities, but this is not reported here, since the attempt has been essentially to develop the methods for such a study. We have, however, obtained a knowledge of the nature of the relation between the three variables, *viz.*, the surface shown in Fig. 2. This corresponds to a value of  $110^\circ$  for  $\alpha$ . For  $\alpha = 105^\circ$  and  $115^\circ$  two similar surfaces one within, and the other enclosing the surface for  $\alpha = 110^\circ$ , will be obtained.

As was mentioned in the introduction, the attempt here has been mainly to list the possible configurations of single helices. Some ranges of these are immediately ruled out because of short contacts between atoms in the single chain itself. The next step is to consider the formation of stabilizing secondary bonds. These could be between residues within the chain itself or with other chains. Restricting ourselves to the former type, the bonds  $\text{NH} \dots \text{OC}$  (hydrogen bonds) may be nearly parallel to the helical axis or they may go across the centre of the helix and link with a group on the opposite side. A consideration of the former leads to the whole  $\alpha$  series for which  $n$  may range from 2.2 to 4.4 and  $\gamma$  series with  $n$  near about 5. The latter seems to be impossible if only helices with every residue identical in its relation to the helical axis are considered for all the  $\text{N-H}$ 's or all the  $\text{C=O}$ 's will be pointing in, so that an  $\text{N-H}$  cannot link with a  $\text{C=O}$  across the axis of the helix. It will be worthwhile therefore to consider helices with a "helix repeat" of 2 residues. The particular case of such helices are the series of  $\beta$  structures, with residue repeat ranging from  $c = 6.25$  to  $7.00 \text{ \AA}$ .

So also, if interchain bonds are considered with other than digonal structures, once again two classes arise, *viz.*, between helices wound on the same cylinder, that is with coincident axes, and helices with non-coincident axes. The former is not very difficult to work out and it appears that for polypeptides it is practically ruled out except perhaps for the extreme limit  $n \approx 5$ ,  $h \approx 2 \text{ \AA}$  which is possible only if the tetrahedral angle is everywhere made about  $115^\circ$ . The latter would lead to coiled coil structures in general if  $n$  is non-integral. Some of these considerations are under study in this laboratory but they are beyond the scope of this paper.

The author wishes to express his grateful thanks to Prof. G. N. Ramachandran for the invaluable suggestions he gave during the course of this study. His thanks are also due to the Government of India, for the award of a research fellowship, during the tenure of which the work was carried out.

#### SUMMARY

It is shown in this paper, how simple polypeptide helices for all possible orientations of the peptide residue with respect to the helical axis can be obtained by the method of cyclographic projection. The cyclographic projection is actually applied to three cases and the results are described. It is also shown that the celebrated  $\alpha$  helix and the other helices, described so far, are particular cases of slightly more general ones. So also it is found that the extended  $\beta$  structure, and the pleated sheet structure of Pauling and Corey, are also particular cases of a range of structures possible, in which every

alternate residue has the same orientation (*i.e.*, digonal helices with two residues per turn). The method described here can also be used to find out the co-ordinates of atoms when the elements of a helical structure are known from other data.

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