C

Chemistry

THE PLEATED SHEET, A NEW LAYER CONFIGURATION OF POLYPEPTIDE CHAINS

By Linus Pauling and Robert B. Corey

Gates and Crellin Laboratories of Chemistry*
California Institute of Technology, Pasadena, Calif.

Communicated March 1951

For many years it has been assumed that in silk fibroin, stretched hair and muscle, and other proteins with the β-keratin structure the polypeptide chains are extended to nearly their maximum length, about 3.6 Å per residue, and during the last decade it has been assumed also that the chains form lateral hydrogen bonds with adjacent chains, which have the opposite orientation. A hydrogen-bonded layer of this sort is represented diagrammatically in Figure 1.[1, 2, 3, 4]

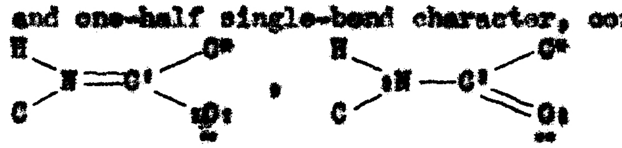
We have now discovered that there is another, rather similar hydrogen-bonded layer configuration of polypeptide chains, which differs from that of Figure 1 in several ways. In the new configuration, which we shall call the pleated-sheet configuration, the plane formed by the two chain bonds of the α carbon atom is perpendicular to the plane of the sheet, as shown in Figures 2 and 3, rather than being coincident with it. In this structure the successive residues in a chain are similarly oriented, directing their carbonyl groups in one direction and their imino groups in the ~~same way~~ opposite direction, and all of the chains are oriented in the same way, instead of adjacent chains being opposed in direction.

Let us assume that a polypeptide chain with the configuration indicated diagrammatically in Figure 2 is bent in such a way that the planes of the successive ~~residues~~ amide groups form dihedral angles whose edges are perpendicular to the plane formed by the axes of the ~~residues~~ groups (the lines connecting successive α carbon atoms). It is found that if the bond distances and bond angles are given the values that we have used in our recent considerations of protein configurations, the dihedral angle has the value 106.5°, and the vertical component of the axis of each residue is 3.07 A. It is also found that the carbonyl and imino groups are oriented in such a way that they can form satisfactory hydrogen bonds with corresponding groups in chains obtained by lateral translation. If the lateral translation is given the value 4.75 A, the N—H···O distance is 2.75 A; this is a normal hydrogen-bond distance. The N—H axis lies within 6° of the N···O axis, indicating that a stable hydrogen bond should be formed. The coordinates of atoms for the pleated-sheet configuration are given in Table 1, and a drawing of the configuration is shown as Figure 3.

It is to be noted that each imide group in the chain (neglecting the side chains) may be described as obtained from the preceding one by the operation of a glide plane of symmetry. Because of this, side chains of L amino acid residues are related differently to the structure when attached to one α carbon atom than when attached to the α carbon atom of an adjacent residue. The pleated-sheet configuration can accordingly be described as involving only one kind of glycine residue, in case that it were to be assumed by a polyglycine, but two kinds of residues for all optically active amino-acid polymers. These two kinds differ in that, for the $\underline{L}$ configuration, a residue of one kind points its β carbon atom in the C=O direction, and a residue of the other kind points its β carbon atom in the N—H direction.

We have found some evidence to support the belief that the pleated-sheet configuration is present in stretched muscle, stretched hair, feather keratin, and some other fibrous proteins that have been assigned the β-keratin structure. These proteins give x-ray diagrams on which there is a strong meridional reflection corresponding to spacing about 3.3 Å., which is a few percent larger than the fiber-axis distance per residue for the undistorted pleated sheet, but much smaller than the value 3.6 Å. for fully extended polypeptide chains. We have noticed that the pleated sheet can be subjected, without rupturing the hydrogen bonds, to a considerable distortion, in such a way as to increase the fiber-axis distance. This distortion is effected by rotating each imide group about its C—C* axis through a small angle. The rotation moves one of the two β positions of each carbon atom farther from the median plane and the other nearer, and the effective rotations for the two non-equivalent kinds of optically active residues are such as to permit each to be an $\underline{L}$ residue with its side chain farther from the median plane than in the undistorted structure. Presumably the van der Waals repulsion of the side chain atoms and the main chain atoms would be operating in proteins of normal chemical composition with the pleated-sheet configuration, and this would cause some distortion of the chain-lengthening sort. (It is to be noted that two kinds of pleated sheets can be constructed of $\underline{L}$ amino-acid residues, of which for one the

the deformation that relieves the strain of side-chain van der Waals repulsion increases the fiber-axis length, and for the other it decreases it.) It might well occur that the magnitude of the deformation would be such as to give the fiber-axis residue length observed for the β-keratin proteins, about 3.3 Å. This deformation results from a 20° rotation of the imide groups, which gives 3.32 Å. as the residue length. Coordinates for the structure with 20° rotation and also for a less deformed structure, with 7° rotation, are given in Table 1.

The deformed structures require some distortion of the hydrogen bonds, in that if the hydrogen atom is kept coplanar with the imide group the N—H direction deviates from the N···O axis by an angle somewhat greater than the distorting angle of rotation. The nature of the distortion is such, however, as to suggest that not much strain energy is involved. Let us consider the effect on the stability of the imide group of moving the hydrogen atom onto (or nearly onto) the N···O axis. This motion would keep the hydrogen atom nearly in a plane normal to the  plane; that is, it involves moving the hydrogen atom towards one of the tetrahedral corners of the nitrogen atom. If the nitrogen atom were forming a pure double bond with the carbonyl carbon C' there would be strong resistance to this motion of the hydrogen atom. However, it forms a bond with about one-half double-bond character and one-half single-bond character, corresponding to the resonance  ; and for the second of the structures the tetrahedral position for the hydrogen atom would be the normal one, whereas for the first the planar position is stable. Accordingly we would predict that this rotational distortion of the pleated sheet would not involve so much strain as if the bonds were double bonds.

We may now ask to what extent distortion of the imide group from the planar configuration, through rotation of the two ends $\begin{matrix}\mathrm{H}\diagdown \\ \mathrm{C}\diagup\end{matrix}\!\mathrm{N}$ $\overset{---}{=}$ and $\overset{---}{=}$ $\mathrm{C'}\!\begin{matrix}\diagup\mathrm{C''} \\ \diagdown\!\!\diagdown\mathrm{O}\end{matrix}$ in opposite directions about the $\mathrm{N}\overset{---}{=}\mathrm{C'}$ axis, might be expected to occur. The strain energy of this distortion, which is essentially also the strain energy of distortion of the hydrogen atom out of the plane, can be estimated in the following way. With δ the dihedral angle formed by the planes of the two end groups, the imide resonance energy may be taken equal to $-\underline{A}\sin^2(\delta-\pi/2)$, and the strain energy to $\underline{A}\sin^2\delta$. The factor $\underline{A}$ is the imide resonance energy for the planar configuration. This may be estimated as about 30 kcal mole^{-1}. (The experimental value for the carboxylate ion, in which each of the two C — O bonds has 50 percent double-bond character, is 36 kcal mole^{-1}, and somewhat smaller values are found for amides, esters, and related substances.[5]) We thus find about 0.9 kcal mole^{-1} strain energy for 10° distortion of the imide group, 3.5 kcal mole^{-1} for 20° distortion, and so on, and we may predict that distortions as large as 20° might well occur, in structures in which these distortions would relieve a larger strain, but that in general the polypeptide chain would avoid structures involving such strains. In any case, we would expect the distortion to be divided between the imide residue and the hydrogen bond. In calculating the coordinates of Table 1 we have not taken account of these distortions.

The discussion of the pleated sheet in β-keratin and other proteins will be presented in following papers. In this discussion we make use of the x-ray scattering form factor for the sheet. The form factor, calculated for reflections from planes parallel to the median plane of the undistorted sheet, is for convenient later reference given here, in Figure 4, as calculated from the equation $F = \sum_i f_i \cos(2\pi y_i \sin\theta/\lambda)$. The sum has been taken over the atoms of one residue of the undistorted structure, including also a β carbon atom, with $y = 2.04$, the f_i values given in the International Tables for the Crystal Structure Determination having been used.

This investigation was aided by a grant from The Rockefeller Foundation, The National Foundation for Infantile Paralysis, and The United States Public Health Service.

Table 1

Coordinates of Atoms in the Polypeptide Pleated-sheet Configuration

	Unrotated			7° Rotation			20° Rotation		
Atom	X	Y	Z	X	Y	Z	X	Y	Z
C_1	0.00	1.15	0.00	0.00	1.09	0.00	0.00	0.96	0.00
N_1	-0.36	0.30	1.14	-0.36	0.46	1.17	-0.36	0.35	1.29
C_1'	0.53	-0.28	1.91	0.53	-0.31	1.96	0.50	-0.40	1.98
O_1	1.74	-0.14	1.73	1.72	-0.31	1.75	1.63	-0.64	1.58
C_2	0.00	-1.15	3.07	0.00	-1.09	3.15	0.00	-0.96	3.32
N_2	-0.36	-0.30	4.21	-0.36	-0.39	4.31	-0.34	-0.14	4.49
C_2'	0.53	0.28	4.98	0.53	0.22	5.12	0.50	0.08	5.49
O_2	1.74	0.14	4.80	1.72	-0.04	4.95	1.63	-0.39	5.50
C_1^*	0.00	1.15	6.14	0.00	1.09	6.30	0.00	0.96	6.64

References

*Contribution No.

[1]Astbury, W. T., Trans. Faraday Soc., 29, 193 (1933).

[2]Huggins, M. L., J. Org. Chem., 1, 407 (1936); Chem. Rev., 32, 195 (1943).

[3]Pauling, L., J. Am. Chem. Soc., 62, 2643 (1940).

[4]Lotmar, W., and Picken, L. E. R., Helv. Chim. Acta, 25, 538 (1942).

[5]Pauling, L., The Nature of the Chemical Bond, Cornell University Press, Ithaca, New York, 1939.

c

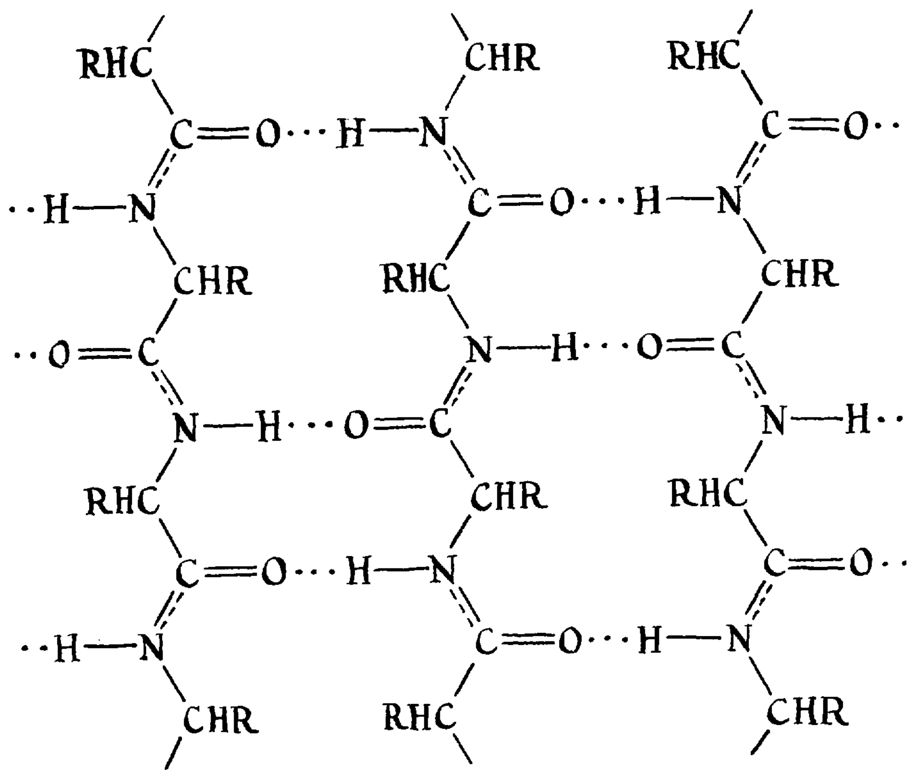


Fig. 1. Diagrammatic representation of a hydrogen-bonded layer structure of polypeptide chains, with alternate chains oppositely oriented.

c

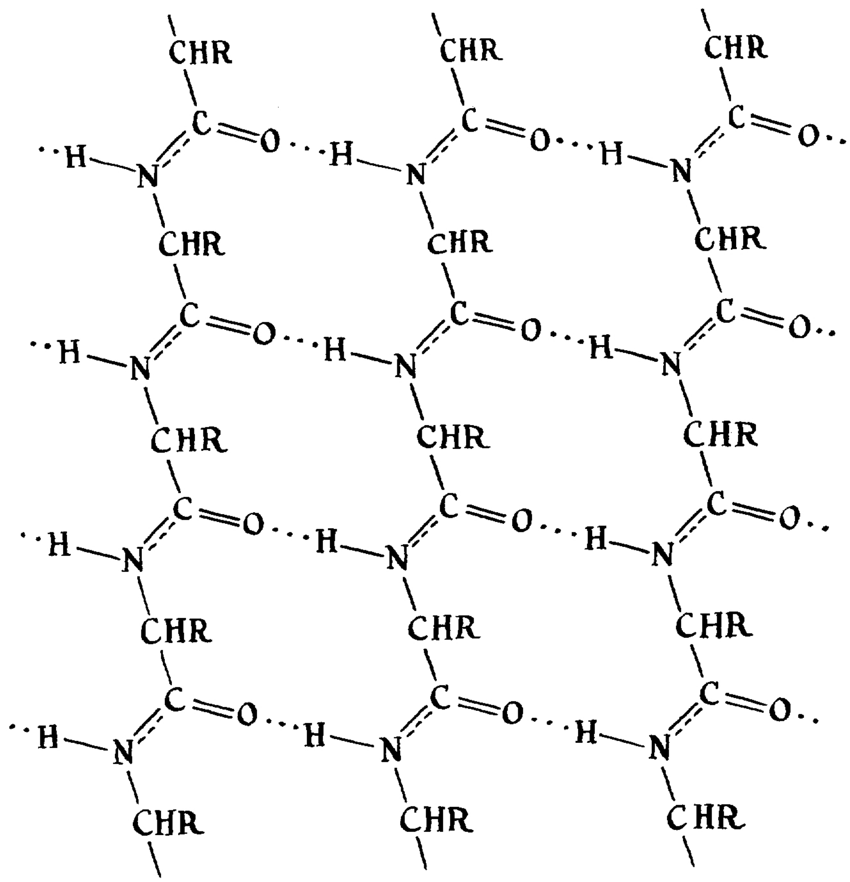


Fig. 2. Diagrammatic representation of a hydrogen-bonded layer structure of polypeptide chains, with all chains similarly oriented (the pleated sheet).

C

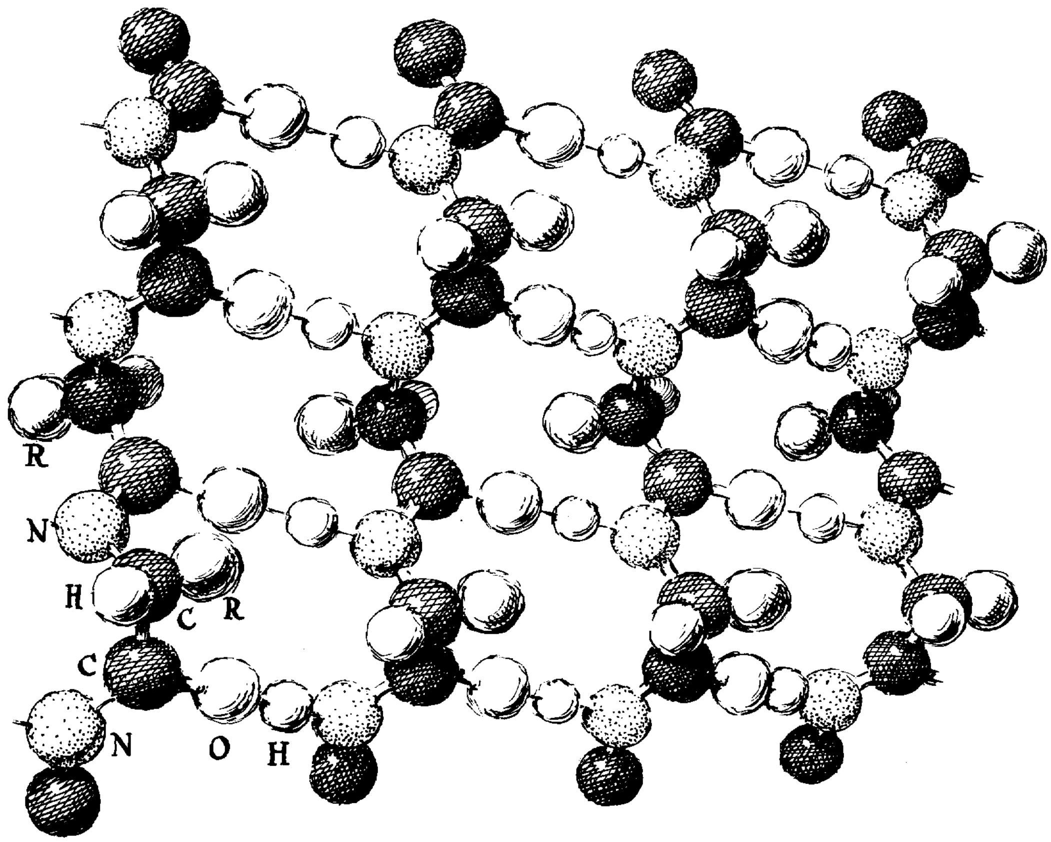


Fig. 3. Drawing representing the pleated-sheet configuration of polypeptide chains.

C

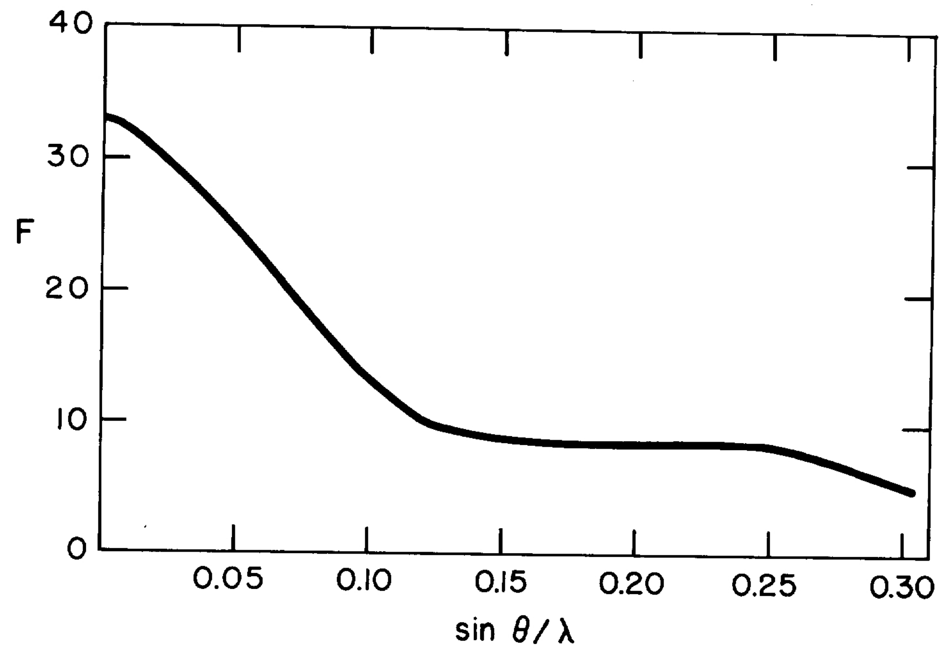


Fig. 4. Calculated x-ray form factors for the pleated sheet, for planes parallel to the plane of the sheet.