drostene-17a-ol-3,11,17-trione, m.p. 238–242°; $[\alpha]^{23}D$ +121° (*c*, 0.48 in $CHCl_3$) and the known Δ^4-pregnene-17α-ol-3,11,20-trione,[10] m.p. 232–235°; $[\alpha]^{24}D$ +186° (*c*, 0.33 in $CHCl_3$). The conversion of VII into VI under conditions reported[11] to effect the expansion of ring D in 17α-hydroxyprogesterone served to establish the structure of VI.

(10) L. H. Sarett, THIS JOURNAL, **70**, 1454 (1948); T. H. Kritchevsky, D. L. Garmaise and T. F. Gallagher, *ibid.*, **74**, 483 (1952).
(11) J. van Euw and T. Reichstein, *Helv. Chim. Acta*, **24**, 879 (1941).

THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH
NEW BRUNSWICK, NEW JERSEY

JOSEF FRIED
RICHARD W. THOMA
JOHN R. GERKE
JOSEF E. HERZ
MILTON N. DONIN
D. PERLMAN

RECEIVED JUNE 30, 1952

POLYPEPTIDE HELICES IN PROTEINS

Sir:

About fifteen years ago[1] I discussed the principles underlying protein structure and proposed that the polypeptide chains in proteins, when not nearly fully extended, have folded or helical structures, with adjacent folds or turns of the helix connected by N–H ··· O hydrogen bonds. Considerable evidence has since accumulated in favor of these proposals and they are now generally accepted.

As the simplest examples illustrating these principles, I discussed a folded structure containing 7-atom rings

```
-C-NH-CHR-CO-N-
 O··············H
```

and helices containing 8-atom rings

```
-NCHR-CO-NH-CHR-C-
 H··················O
```

and 10-atom rings

```
-C-(NH-CHR-CO)2-N-
 O·················H
```

Bragg, Kendrew and Perutz[2] have recently considered similar 11-atom ring

```
-N-(CHR-CO-NH)2-CHR-C-
 H······················O
```

and 13-atom ring

```
-C-(NH-CHR-CO)3-N-
 O·················H
```

helices, assuming in both exactly four amino-acid residues per turn, and Pauling, Corey and Branson[3] have advocated the 13-atom ring helix with about 3.7 residues per turn. They pointed out, as I had done in the case of the 10-atom ring structure, that it is not necessary that this number be integral. (At the recent Chemical Conclave I mistakenly believed and stated that their model was merely a refinement of my 10-atom ring structure.)

An 11-atom ring structure is possible,[4] consistent with the published X-ray data and with all of Pauling and Corey's postulates regarding bond angles and distances, except that the N–C* bond is not in the C–C′O–NH plane, but makes an angle of about 30° with it. This is not unreasonable, on the basis of their estimate of about equal contributions of structures containing coplanar nitrogen and tetrahedral nitrogen. On the other hand, approximate coplanarity has been found in glycylglycine[5] and acetylglycine[6] crystals; this would seem to favor the 13-atom ring structure, which permits such coplanarity. However, since the energy difference associated with the difference in bond orientation is probably small and may be counteracted by environmental differences, this evidence is not very strong.

In neither the 11-atom ring structure nor the 13-atom ring structure is the C=O bond tilted with respect to the axis of the helix more than the N–H bond, unless the assumptions made are considerably in error. Hence, the infrared spectrum differences, tentatively and cautiously attributed by Bamford and co-workers[7] to such a difference in angle of tilt, should probably be interpreted in some other way.

In agreement with Bamford and his colleagues, I believe that, pending further experimental data, both of these structures should be considered possible for the alpha synthetic polypeptides, the alpha fibrous proteins and corpuscular proteins. Perhaps both types are sometimes present together, in fibrous natural proteins for example. All other types of structure seem to be definitely eliminated, at least for the alpha synthetic polypeptides, by the X-ray data.[7–9]

(1) M. L. Huggins, Abstracts, Rochester Meeting, American Chemical Society, B10 (1937); see also Abstracts, Memphis Meeting, A.C.S., P4 (1942); *Annual Review of Biochemistry*, **11**, 27 (1942); *Chem. Revs.*, **32**, 195 (1943).
(2) W. L. Bragg, J. C. Kendrew and M. F. Perutz, *Proc. Roy. Soc. (London)*, **A203**, 321 (1950).
(3) L. Pauling and R. B. Corey, THIS JOURNAL, **72**, 5349 (1950); *Proc. Nat. Acad. Sci.*, **37**, 235, **241**, 256, 261, 282 (1951); L. Pauling, R. B. Corey and H. R. Branson, *ibid.*, **37**, 205 (1951).
(4) M. L. Huggins, THIS JOURNAL, **74**, 3963 (1952).
(5) E. W. Hughes and W. J. Moore, *ibid.*, **71**, 2618 (1949).
(6) G. B. Carpenter and J. Donohue, *ibid.*, **72**, 2315 (1950).
(7) C. H. Bamford, L. Brown, A. Elliott, W. E. Hanby and I. F. Trotter, *Nature*, **169**, 357 (1952).
(8) M. F. Perutz, *ibid.*, **167**, 1053 (1951); **168**, 653 (1951); H. E. Huxley and M. F. Perutz, *ibid.*, **167**, 1054 (1951).
(9) W. Cochran and F. H. C. Crick, *ibid.*, **169**, 234 (1952).

RESEARCH LABORATORIES
EASTMAN KODAK COMPANY
ROCHESTER 4, NEW YORK

MAURICE L. HUGGINS

RECEIVED JUNE 23, 1952

COÖRDINATES OF THE 11-ATOM RING POLYPEPTIDE HELIX

Sir:

In order to facilitate comparison of the 11-atom ring helical polypeptide structure[1,2] with other structures and with experimental data, I have calculated atomic coördinates, on the following assumptions: (1) the translational and rotational shifts per amino-acid residue are 1.47Å. and 100°, as observed[2–4] in poly-(methyl glutamate); (2) the bond distances and bond angles are those assumed by Pauling and Corey,[5] except that some

(1) M. L. Huggins, THIS JOURNAL, **74**, 3963 (1952).
(2) C. H. Bamford, L. Brown, A. Elliott, W. E. Hanby and I. F. Trotter, *Nature*, **169**, 357 (1952).
(3) L. Pauling and R. B. Corey, *Proc. Nat. Acad. Sci.*, **37**, 241 (1951); *Nature*, **169**, 494 (1952).
(4) M. F. Perutz, *ibid.*, **167**, 1053 (1951).
(5) L. Pauling and R. B. Corey, *Proc. Nat. Acad. Sci.*, **37**, 235 (1951).

departure of the N–C* bond from the C–C′O–N plane is allowed; (3) no distances between non-bonded atoms are unreasonably short; and (4) the configuration around each alpha carbon atom is *levo*, with the Fischer convention correct.[6]

These assumptions are insufficient to determine the coördinates uniquely, the values obtained depending on the postulates made with regard to the hydrogen bond length and the minimum permissible distance between the β carbon atom and neighboring oxygen atoms. Nevertheless, the following set of coördinates is presented, with certain other pertinent magnitudes derived from them.

	x, Å.	y, Å.	z, Å.	ρ, Å.	ϕ, deg.
Axis	0	0		0	
C	0.00	−2.245	0.00	2.245	0.0
C′	1.21	−1.30	0.00	1.78	42.9
O	1.70	−0.90	−1.06	1.92	62.1
N	1.69	−0.95	1.18	1.94	60.7
C*	2.21	0.39	1.47	2.245	100.0
C_β	0.28	−3.48	−0.88	3.51	4.2
H_N	1.18	−1.36	1.96	1.80	41.0

Hydrogen bond distance	2.88Å.
Angle between N–C* and C–C′O–N plane	30°
Angle H–N · · · O between N–H bond and hydrogen bond axis	5°
Angle C′=O · · · N between C′=O bond and hydrogen bond axis	140°
Angle between C=O and helical axis	31°
Angle between N–H and helical axis	39°
Angle N–C–C_β	116°
Angle C′–C–C_β	112°

To obtain the coördinates of the hydrogen atom of the NH group, it was assumed that the N–H bond has a length of 1.014Å., that it lies in the C–C′O–N plane, and that it makes equal angles (113°) with the N–C′ and N–C* bonds. In computing the C_β coördinates, this atom was assumed to be 2.97Å. from each of the two neighboring carbonyl oxygen atoms. This leads to the slightly large value given for the N–C–C_β angle.

Reasonable minor changes in the assumptions would lead to some variations from the coördinates given. They would not, however, reduce the angle between the N–C* bond and the C–C′O–N plane significantly, nor would they change greatly the angles of tilt of the C=O and N–H bonds.

The coördinates listed are for a right-handed spiral, since (assuming the Fischer convention correct) a left-handed spiral would lead to much too small a distance between the β carbon atom and a carbonyl oxygen atom in the next turn of the helix. It may be noted that Pauling and Corey's second alternative set of C_β coördinates for the 13-atom ring structure, which are the ones to use (according to the Fischer convention) for *levo* polypeptides in their left-handed spiral, give a $C_\beta \cdots$ O distance of only 2.64Å. I conclude that *levo* polypeptides form right-handed spirals and *dextro* polypeptides left-handed spirals, whichever of these two types of structure is correct.

Some of the conclusions to be drawn from the results of these calculations are discussed briefly in another communication.[1]

(6) A. F. Peerdeman, A. J. Van Bommel and J. M. Bijvoet, *Proc. Acad. Sci. Amsterdam*, **B54**, 3 (1951).

RESEARCH LABORATORIES
EASTMAN KODAK COMPANY
ROCHESTER 4, NEW YORK
MAURICE L. HUGGINS

RECEIVED JUNE 23, 1952

THE PLANARITY OF THE AMIDE GROUP IN POLYPEPTIDES

Sir:

Dr. M. L. Huggins has kindly sent us copies of his Letters,[1,2] in which he has proposed a helical configuration of polypeptide chains as an alternative to the α helix described in our earlier publications.[3,4,5] In his configuration the amide group is not planar. The deformation of the amide group from the planar configuration can be described as a rotation of 17.5° of the NHC* plane about the C′–N axis plus a bending of 15° of the N–C* bond and the N–H bond out of the rotated plane, to the same side. The part of the strain energy due to the rotation of the π orbital of the nitrogen atom can be calculated by the formula[6,7] $A \sin^2 \delta$ with A = 30 kcal. mole^{-1} and δ = 17.5°; this calculation gives 2.7 kcal. mole^{-1}. The strain energy of deformation of the N–C* bond and the N–H bond can be calculated by the assumption that the bond energy is proportional to the strength of the bond orbital of the nitrogen atom in the bond direction, which is for these bonds 15° from the the direction of maximum strength. With use of the bond energies of the bonds (48.6 and 83.7 kcal. mole^{-1}, respectively), this calculation leads to 3.3 kcal. mole^{-1} for the bending energy of the two bonds. The total strain energy for the distorted amide group is thus found to be 6 kcal. mole^{-1}. This strain energy, which in the structure proposed by Huggins applies to every residue, is so great as to make the structure unacceptable in comparison with the α helix, which is just as satisfactory in every other respect, so far as we are aware, and which involves planar amide groups.

(1) M. L. Huggins, THIS JOURNAL, **74**, 3963 (1952).
(2) M. L. Huggins, *ibid.*, **74**, 3963 (1952).
(3) L. Pauling and R. B. Corey, *ibid.*, **72**, 5349 (1950).
(4) L. Pauling, R. B. Corey and H. R. Branson, *Proc. Nat. Acad. Sci.*, **37**, 205 (1951).
(5) L. Pauling and R. B. Corey, *ibid.*, **37**, 235 (1951).
(6) L. Pauling and R. B. Corey, *ibid.*, **37**, 251 (1951).
(7) R. B. Corey and L. Pauling, *Proc. Roy. Soc.* (*London*), to be published; presented at the Discussion Conference of the Royal Society of London, May 1, 1952.

GATES AND CRELLIN LABORATORIES OF CHEMISTRY
CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA 4, CALIFORNIA
LINUS PAULING
ROBERT B. COREY

RECEIVED JULY 7, 1952

LIPOTHIAMIDE PYROPHOSPHATE: COENZYME FOR OXIDATIVE DECARBOXYLATION OF α-KETO ACIDS

Sir:

It has been reported[1] recently that lipothiamide (LT), the amide of α-lipoic acid (α-LA) and thiamin, is required for oxidation of pyruvate and α-ketoglutarate by resting cell suspensions of an *Escherichia coli* mutant. The organism lacks the

(1) L. J. Reed and B. G. DeBusk, THIS JOURNAL, **74**, 3457 (1952).