

FOURFOLD HELICAL STRUCTURES FOR SEQUENTIAL COPOLYMERS OF GLYCINE AND IMINO ACID RESIDUES PROLINE AND HYDROXYPROLINE

V. N. BALAJI AND V. SASISEKHARAN

Molecular Biophysics Unit, Indian Institute of Science, Bangalore 560 012, India

ABSTRACT

Regular fourfold helical structures have been proposed for copolymers of glycine and imino acid residues, proline and hydroxyproline, with two and four units in monomer. In these structures all the available NH groups are interchain hydrogen bonded. Energetically fourfold helical structures are as favourable as threefold helical structures. Stereochemically satisfactory fourfold helical structures are possible with unit height b ranging from 2.7 to 3.1 Å.

PROLINE and glycine are important constituents of collagen and related proteins¹. Sequential copolymers of proline and glycine are model systems, the physico-chemical studies of which can give information about the structure and conformation of proteins which are rich in these residues. Several sequential copolymers of glycine and proline with tri and hexapeptide units in the monomer and with glycine at every third position have been investigated in detail as model systems for collagen. In general these copolymers form triple helical structures². Recently, copolymers of glycine and proline with two and four peptide units in the monomer have been investigated in some detail³. For these types of copolymers, no satisfactory structures have been proposed though some of them are interpreted, under the conditions studied, to be ordered structures.

As a part of our programme of studies on regular fourfold helical structures for the backbone of polypeptides, we have investigated in detail the possibility of ordered structures for copolymers of glycine and imino acid residues, proline and hydroxyproline, with two and four units in the monomer. Our model building studies revealed that ordered structures are indeed stereochemically feasible for these copolymers. For poly(Gly-L-Pro), poly(Gly-L-Hyp), poly(Gly-Gly-L-Pro-Gly) and poly(Gly-Gly-L-Hyp-Gly) circular dichroism (CD) studies in solution have been carried out³. Under the conditions studied, poly(Gly-L-Pro) and poly(Gly-Gly-L-Pro-Gly) are interpreted as not ordered structures whereas poly(Gly-L-Hyp) and poly(Gly-Gly-L-Hyp-Gly) are ordered. However, no satisfactory structure has been proposed so far for any one of these. NMR studies on poly(Gly-

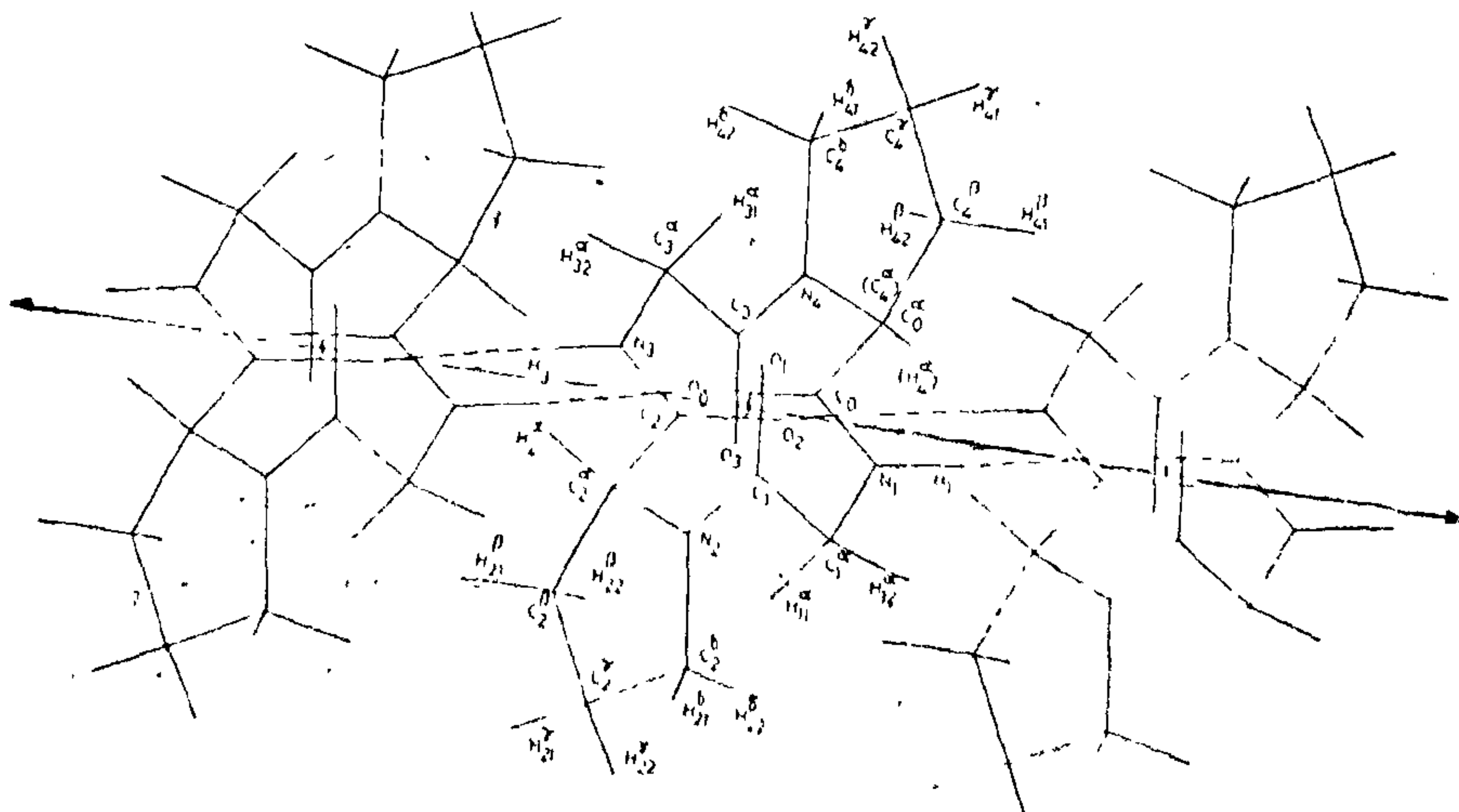


FIG. 1. Projection down the helix axis of a fourfold structure of poly(Gly-L-Pro). The hydrogen bonds denoted by (- - -) are roughly perpendicular to the chain axis and are confined to sheets. The sheets can be arranged in space such that the pyrrolidine rings are closely packed (not shown here). Individual chains have a twofold screw and the backbone four-fold screw.

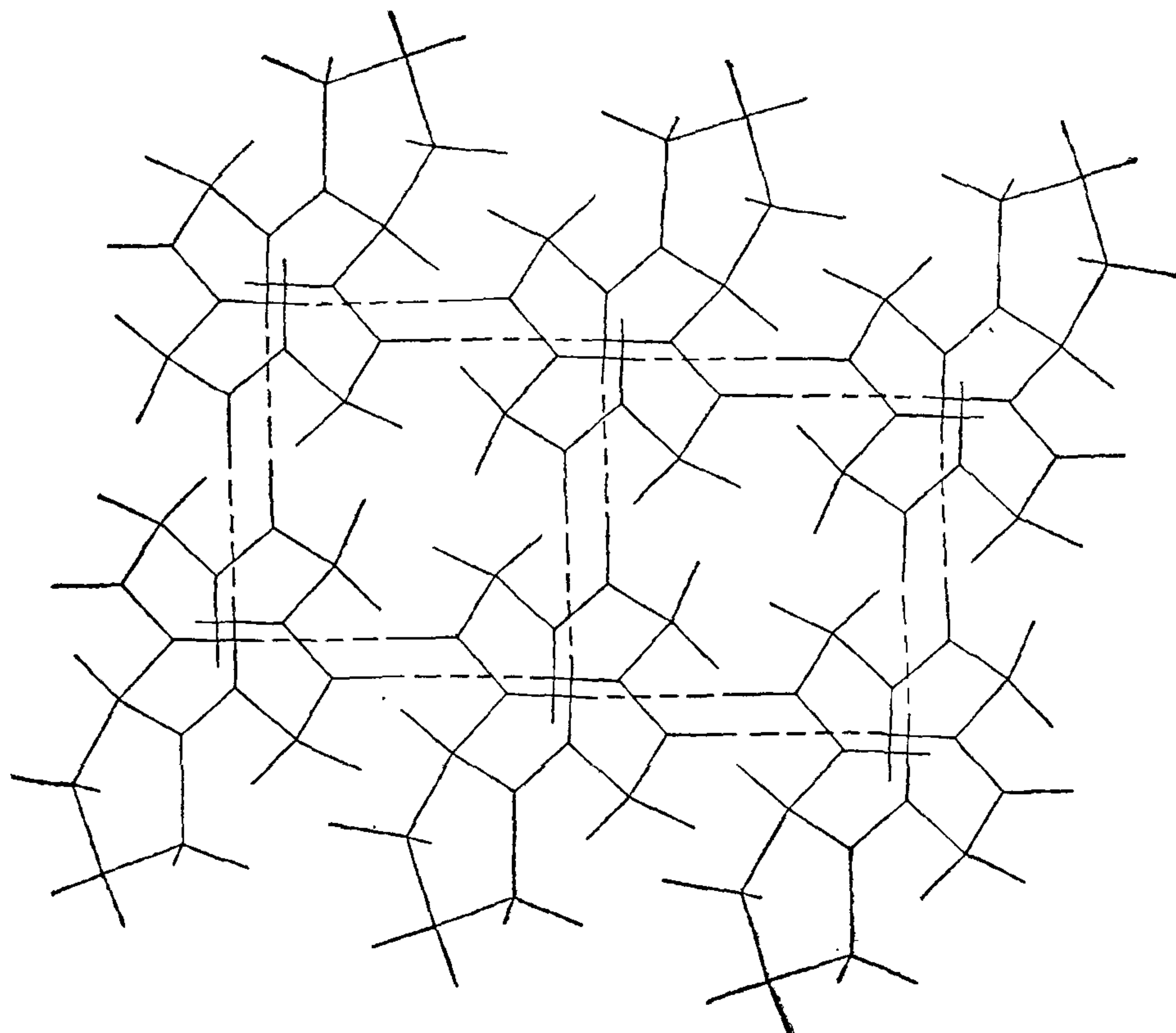


FIG. 2. Projection down the helix axis of a fourfold structure of poly(Gly-Gly-L-Pro-Gly) with interchain hydrogen bonds. As in Figure 1, the hydrogen bonds are roughly perpendicular to the chain axis and form sheets in one direction. The sheets form a bilayer which are held together by hydrogen bonds that are roughly perpendicular to the layers.

L-Pro) and poly(Gly-Gly-L-Pro-Gly) have also been carried out⁴. The NMR data have been interpreted in terms of *cis-trans* isomerization of the peptide bond. For poly(Gly-L-Pro) using CD and NMR data the possibility of isomerization about ψ angle of the prolyl residue has been suggested⁵. Because of imino acid residues both α -helix and beta structure are ruled out. Further, triple chain association with a network of hydrogen bonds is also not possible because of the sequence of residues. On the other hand, stereochemically satisfactory fourfold helical structures for the backbone of all the four copolypeptides can be built. In these structures all the available NH groups are interchain hydrogen bonded.

In general fourfold helical structures with interchain hydrogen bonds are possible depending upon the unit height b and the criteria applied for the hydrogen bond formation; the unit height b was found to be restricted from 2.7 to 3.1 Å, for hydrogen bond length (N...O) of 2.8 to 3.0 Å and the angle $\widehat{HNO} < 30^\circ$. For all the copolymers mentioned in this paper we have chosen as examples fourfold helical structures corresponding to $n = -4$ and $b = 2.8$ Å, where n is the number of peptide units per turn of the helix.

For poly(Gly-L-Pro) an arrangement is given in Fig. 1, which is a projection down the helix axis. For the example shown in Fig. 1, the chain to chain

distance is 4.75 Å and the corresponding hydrogen bond parameters are $N...O = 2.9$ Å and $\widehat{HNO} = 14^\circ$. The hydrogen bonds are roughly perpendicular to the chain axis and are confined to sheets. These sheets can be arranged in space such that the pyrrolidine rings are closely packed. Such a packing arrangement leads to a monoclinic or pseudo orthorhombic unit cell. In the case of poly(Gly-L-Hyp) the interaction between sheets will be further stabilized by the participation of the hydroxyl group of hydroxyproline in hydrogen bond formation.

For the copolymer of poly(Gly-Gly-L-Pro-Gly), the projection down the helix of a fourfold helical structure for the backbone is given in Fig. 2. Note that all the NH groups are interchain hydrogen bonded. As in poly(Gly-L-Pro), the hydrogen bonds are roughly perpendicular to the chain axis and form sheets in one direction. The structure in fact is a bilayer of two such sheets held together by hydrogen bonds which are roughly perpendicular to the layers. Such bilayers can be packed in space involving close packing of pyrrolidine rings. In the case of poly(Gly-Gly-L-Hyp-Gly) further stability is achieved by hydrogen bond formation of the hydroxyl group of hydroxyproline residue.

It is well known that the regular conformations the polypeptides can have are the α -helix, the beta form and the triple helix¹. Each of these structures can aggregate to form a fibre, the α -helix and the triple helix by close packing of approximately cylindrical protofibrils and the beta form by stacking of sheets. Incidentally, α -helix, beta form and triple helix are single, double and triple chain hydrogen bonded arrangements. The single chain α -helix have intrachain hydrogen bonds nearly parallel to the helix axis. Each chain in the beta form is a twofold helix and the chains are aggregated in the form of sheets with hydrogen bonds nearly perpendicular to the chain axis. In polyglycine II⁶, which is a typical example for threefold arrangement, the chains are packed in a hexagonal array, each chain being hydrogen bonded to its six neighbours. These hydrogen bonds lie roughly perpendicular to the chain axis, and run in several directions. In the fourfold helical structures which are altogether different from the above three types of conformations, the hydrogen bonds are also nearly perpendicular to the helix axis. The α -helix, the beta form and the triple helix are plotted in the (ϕ, ψ) -map and shown in Fig. 3. A typical fourfold structure is also plotted and is shown by (\square). The ranges in (ϕ, ψ) values within which fourfold helical structures can occur for copolymers

of glycine and imino acids cited in this paper are also shown in this figure, along with the conformational energy contours for polyglycine and poly-L-proline^{7,8}. We note that the fourfold type conformations presented here lie close to the threefold structures in the conformational energy space and the energy difference between the two types of structures is small. This would therefore indicate that the copolymers mentioned in this paper can take up regular fourfold helical structures for the backbone. In addition, our investigations revealed that these types of fourfold structures are also possible for other copolymers of

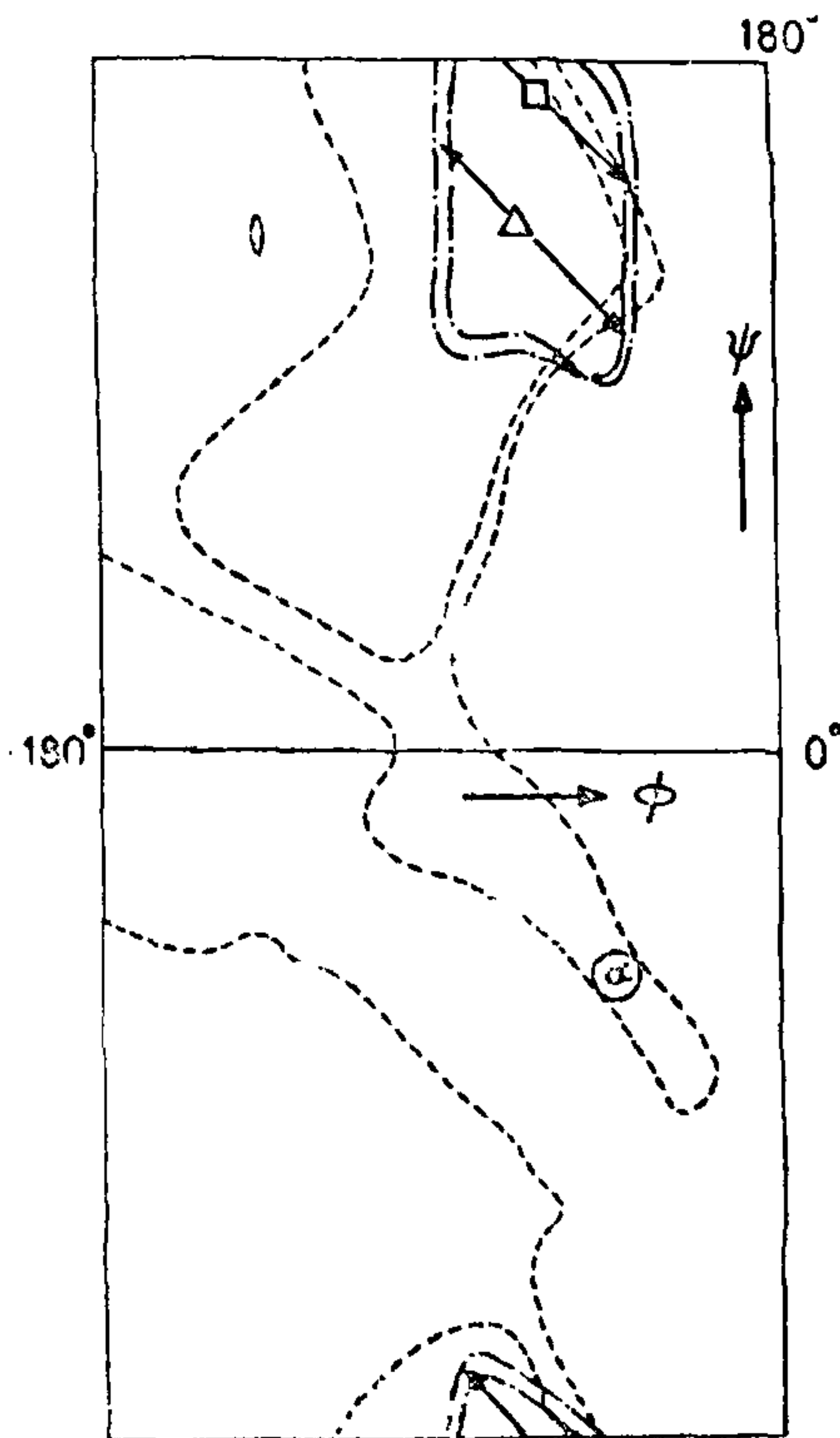


FIG. 3. (ϕ, ψ) -map to show α -helix (α), beta form (O), a triple helix (Δ) and a typical fourfold structure (\square). Energy contours for polyglycine and poly-L-proline are shown by (---) and (-·-·-) respectively. For polyglycine the energy corresponds to 4 and 5 kcal/mole and for poly-L-proline the energy corresponds to 5 and 10 kcal/mole. The allowed range for the fourfold and threefold structures are denoted by (\square) and (Δ) respectively.

glycine and imino acid residues with two and four residues in the monomer unit and also for polyglycine and poly-L-proline. The details of these will be reported elsewhere.

ACKNOWLEDGEMENT

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BIOISOMERISM IN CYCADS

BIR BAHADUR, N. PRATAP REDDY AND P. VIJAYA KUMAR

Department of Botany, Kakatiya University, Warangal 506 009, A. P.

ABSTRACT

Left and right handedness in *Cycas revoluta* Thunb., and *C. circinnalis* L. (Cycadaceae) with regard to spirality of scale and foliage leaves are described. Left and right handed plants occur at random in almost equal ratio, although the left handers are in slight excess. The phyllo-taxy is symmetrical and multijugate in both the species.

INTRODUCTION

HANDEDNESS in gymnospermous plants though known for over hundred years since Beal⁵ first observed in cones of *Picea* (Pinaceae), this phenomenon has been recorded during this century in *Pinus austriaca*⁷. In this communication, we describe observations on handedness in *Cycas revoluta* Thunb., and *C. circinnalis* L. (Cycadaceae).

MATERIAL AND METHODS

Mature plants of *C. revoluta* and *C. circinnalis* growing at different places in Hyderabad, Secunderabad, Warangal (A.P.) and Agra (U.P.) have been examined. A cycad is regarded as right handed (dextro-rotatory) when the spirality of the leaves is counter-clockwise and a mirror image with clockwise spiral constitute a left handed (levo-rotatory) plant. Regular observations for several years confirmed that handedness is not a sporadic phenomenon but a regular feature of the species, for a right handed plant produces even the foliage leaves in counter-clockwise spiral and the left handed plant in clockwise spiral. Observations as to the spirality of the mega and microsporophylls further confirm the handedness in both the species.

OBSERVATIONS

Mature plants of *C. revoluta* and *C. circinnalis* have a branched or unbranched stout columnar and woody

trunk with a crown of large palm like leaves at the summit. The leaves are dimorphic. In Plate 1, left (L) and right (R) handed plants of *C. revoluta* are shown. Both the L and R plants look alike but a close examination reveals that they are different the way the scale leaves show spirality.

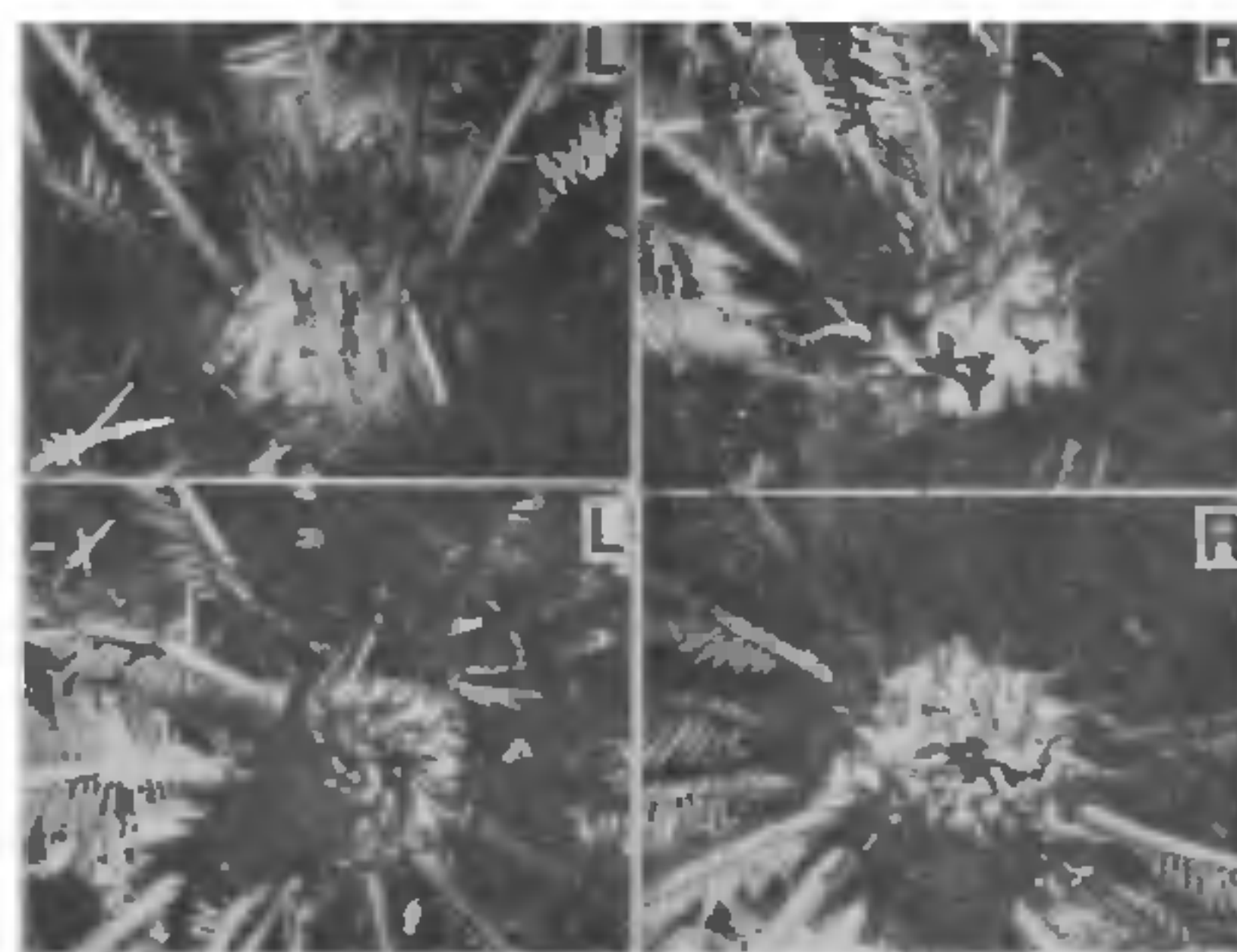


PLATE 1—L: Left handed plant of *Cycas revoluta* showing clockwise spirality of scale leaves in side and top view. R: Right handed plant of *Cycas revoluta* showing counter-clockwise spirality of scale leaves in side and top view.

The scale leaves are small, brown felted, cover the foliage leaves in bud condition and exhibit clear