# COMMUNICATION TO THE EDITORS

## *Determination of the Possible Conformations of the Residues Linked in a Polypeptide Chain*

Recently, Nemethy and Scheraga[1] have reported a study of polypeptide conformations using computer methods. This is based on Pauling-Corey parameters for the peptide residue and on criteria for van der Waals contacts analogous to the data reported by Ramachandran and coworkers.[2,3] An extension of the matrix method developed at Madras[4] has been used for specifying the conformation of a polypeptide chain consisting of any number of residues, besides having side chains, and these have been fed into an electronic computer for working out the conformations. Such an extension has also been made by the present authors employing the CDC 3600 computer and the results are in the process of being written up in detail for publication.

Specifically, the following studies have been made: *1.* The effect of the angle $N\hat{C}\alpha C'$ (denoted by $\tau$) on the allowed region of the $\phi$–$\phi'$ plane (in the notation of references 2 and 3) has been worked out, and it is found that the allowed region increases appreciably with $\tau$ both for a glycyl as well as a nonglycyl alpha carbon atom. The values of the percentage of the allowed area, with outer limit contact distances, are 57% for $\tau = 110°$ and 67% for $\tau = 115°$ for the glycyl case and 13, 20, and 24%, respectively, for $\tau = 105$, 110, 115, for the nonglycyl case.

*2.* A thorough review of the observed conformations ($\phi$, $\phi'$) at an alpha carbon atom in simple peptides and cyclic peptides shows that they invariably occur within the outer limit in the ($\phi$–$\phi'$) diagram for $\tau = 110°$. Wherever they occur outside, the value of $\tau$ in the particular structure is found to be larger than 110°, and it is found to lie within the outer limits for the actually observed angle. Incidentally, the values of $\phi'$ (1) and $\phi'$ (2) for amino acids are found to be not always close to 180 and 0°, but to occur up to 50° away in either direction (mostly within ±30°).

*3.* The effect of the presence of a $\gamma$-carbon atom on the allowed regions of the ($\phi$–$\phi'$) plane has also been studied, with the $\gamma$-carbon atom at the three energetically most favored positions [at azimuthal angles ($\psi$) of 60, 180, and 300° from the position in which the atoms N and C$\gamma$ are *cis* with respect to the C$\alpha$—C$\beta$ bond]. In all the three cases, there are further restrictions in the allowed range than without the $\gamma$-carbon atom, but the reduction is only a few per cent (Fig. 1). Similar studies have also been made by Scheraga and coworkers.[5]

*4.* Numerical data have been obtained for the contact distances between neighboring residues at intervals of 5° for $\phi$ and $\phi'$, for the region of the ($\phi$–$\phi'$) plane between the fully allowed and outer limit boundaries. This will be useful in working out these boundaries with slightly different sets of allowed contact distances than those used in the earlier work.

*5.* Mathematical methods and computer programmes have been worked out for studying the allowed ranges of the conformations ($\phi_i$, $\phi_i'$) at a series of alpha carbon atoms ($i = 1, 2, 3 \ldots$) along a chain. Attempts are being made to work out the types of restrictions which occur in ($\phi_2$, $\phi_2'$) when ($\phi_1$, $\phi_1'$) is specified.

*6.* The type of study mentioned in the previous paragraph has been extended up to 5 successive residues in the case of *helical* chains, that is those in which all ($\phi_i$, $\phi_i'$) are the same. In this way, all the types of hydrogen-bonded helices that are possible, subject to the limiting contact distances, have been worked out, along with data on the hydrogen bond lengths and angles and the residue heights and number of residues per turn. It is found that, along with helices topologically similar to the alpha helix (right- and left-handed), those *similar* to the $3 \cdot 0_{10}$ helix (i.e., hydrogen bonded to the third residue ahead)

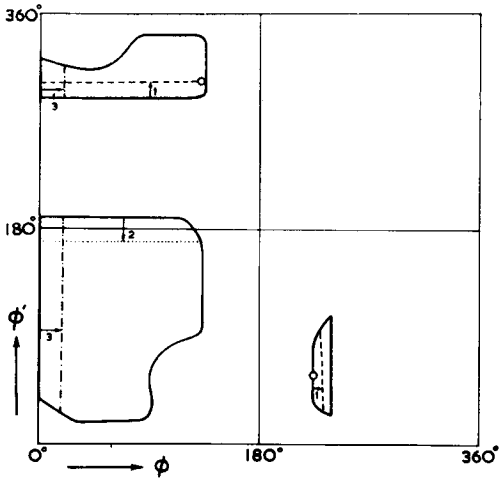


Fig. 1. The shift in the outer limit boundaries of the allowed conformations when a $\gamma$-carbon is present in addition to a $\beta$-carbon atom. The shift is marked by an arrow (→) and the shifts for the three positions taken for the $\gamma$-carbon atom are indicated as follows: —, $C_\beta$ alone; – –, $C_\gamma$ in position 1; . . . , $C_\gamma$ in position 2; –·–, $C_\gamma$ in position 3. The conformations ($\phi$,$\phi'$) for the right and left-handed $\alpha$-helices are also marked.

(both right- and left-handed), can also have very good hydrogen bonds, still being within the outer limits. The $\pi$-helix cannot be formed for $\tau = 110°$, but is just possible for $\tau = 115°$ (the actual angle reported in the literature is 113°). Helices similar to the $2{\cdot}2_7$ helix have large hydrogen bond angles (HN̂O) greater than 20° and are therefore rather unlikely. The $\gamma$-helix and the $4{\cdot}3_{14}$ helices are not possible. For these calculations, the ($\phi$–$\phi'$) plane was generally scanned at intervals for 5° for $\phi$ and $\phi'$, and for the $\pi$-helix at intervals of 2°.

7. Studies are now in progress for finding out, if possible, the simplest types of cyclic conformations and those involving S—S bridges.

We are deeply grateful to Dr. R. Narasimhan and his colleagues at the Tata Institute of Fundamental Research, Bombay, for making available the CDC 3600 computer for these studies and for assistance with programming. One of the authors acknowledges the award of an U.S. N.S.F. Senior Visiting Scientist award and the others financial assistance from the C.S.I.R., India.

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Received June 21, 1965