

COMMUNICATION TO THE EDITORS

*Conformation of Side Groups in Amino Acids and Peptides**

The conformation of a pair of peptide units in a polypeptide chain can be denoted in terms of a pair of dihedral angles ϕ , ϕ' .¹ [The two angles should be denoted by ϕ and ψ ($\psi = 180^\circ + \phi'$), according to the latest conventions² agreed to by the workers in this field at the 1965 Gordon Conference on Proteins (New Hampton, June 27th to July 2nd, 1965) and the IOPAB symposium on Some Biological Systems at the Molecular Level held in Naples from September 8-11, 1965. As these angles are not specifically discussed in this paper, the new conventions are not discussed further here.] All the conformations allowed by the exclusion of short contacts have been plotted on the (ϕ, ϕ') diagram when the alpha carbon atom at which the peptide units are linked belongs to a glycyl or an alanyl residue.³ The restrictions of the allowed regions for some of the other amino acids have also been discussed recently,⁴ making use of certain assumptions about the orientation of the C^γ and other atoms with respect to the backbone of the chain. We have for some time been making a survey of the known facts (contained in the published x-ray structure determinations) regarding the conformation of the side groups in various examples. A detailed report is in preparation and this note is a short résumé of the main results.

1. The length of the bond $C^\beta C^\gamma$ is not sensibly different from the standard value of 1.54 Å. for a single bond. However, the angle $C^\alpha C^\beta C^\gamma$ is significantly larger than the tetrahedral value and was found to have a mean value of 114° in 27 cases. (The authors are grateful to Professor Shneior Lifson of the Weizman Institute of Science for pointing out this possibility from a similar behavior in hydrocarbon chains, which led to their looking for the actual value of this angle. The earlier authors (e.g., Ref. 4) used a value of 110° for this angle. The larger value has been used in examining the effect on the theoretically possible conformations of the type studied in ref. 4 (C. M. Venkatachalam and G. N. Ramachandran, in preparation).) The angles at the alpha carbon atom (such as $NC^\alpha C^\beta$, $C' C^\alpha C^\beta$, and $NC^\alpha C'$) were however found to be not significantly different from 109.5° in a systematic way.

2. The C^γ atom was found to occur close to one of three possible positions, one *trans* and two *gauche* about the $C^\alpha C^\beta$ bond, with respect to the amino nitrogen. We may define an angle χ_1 , by which C^γ has to be rotated about the $C^\alpha C^\beta$ direction from its position when it is *cis* to N, in a clockwise sense looking from C^α to C^β . (This follows the standard conventions, mentioned above.) The three positions are then close to $\chi_1 = 60, 180$, and 300° , which may be denoted by I, II, and III (Fig. 1).

3. The three positions were found to be fairly well represented in different side groups. Neglecting examples in which the gamma position in the side chain is occupied by an oxygen or sulfur atom, the position I was found to occur in ten cases, position II in 11 cases, and position III in 17 cases. However, oxygen and sulfur were found to occur mostly in position I (6 cases) as against zero for position II and 4 for position III. Taking into account all the atoms, the mean values of χ_1 for the three positions were 66° for I, 184° for II, and 294° for III. The deviations from $60, 180$, and 300° , respectively, seem to be significant, although the data are not large enough to attach a standard deviation to these values. Thus, for position I, only three examples had χ_1 less than 60° , while 13 had χ_1 greater than 60° .

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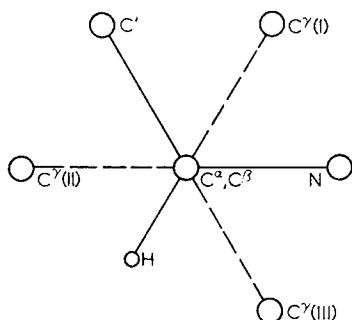


Fig. 1. The orientation of the C^γ atom, looking down the $C^\alpha-C^\beta$ bond. The atoms N, C' , and H come from the C^α atom down below, while C^γ is attached to the C^β atom up above. The three approximate positions of C^γ are indicated by I, II, and III.

4. As will be seen from Figure 1, position I may be expected to be the most difficult one for a gamma atom to occur, as it would be placed in between the big atoms N and C' as viewed along $C^\alpha C^\beta$. Yet, this position is favored by such a large atom as sulfur, and this conformation occurs in cysteine·HCl, hexagonal cystine, cystine·2HBr, cysteinylglycine·NaI, and the cysteinyl residue in glutathione. The gamma carbon atom along with the ring of histidine also goes to position I in three crystals.

5. Among branched side groups, the γ atoms in valine go to I and II and I and III in two different crystals, of isoleucine·HBr to I and II and of isoleucine·HCl to I and III, i.e., position I seems to be favored in these cases also. However, the γ atoms in threonine go to II and III.

6. Tyrosine and phenylalanine side groups, both of which contain benzene rings, go only to position II in five cases. On the other hand, the side group of tryptophan goes to I or III in two cases.

7. Unlike the above cases, which seem to show some sort of a regularity in their behavior, the arginine γ -carbon atom has been found to go to all the three positions in three different crystals. The detailed stereochemistry of the arginine molecule in the different crystals is being published.⁵

In order to conserve space, detailed references are not given in this paper, but a full report giving the atomic coordinates of the atoms in all the side groups in a standard coordinate system is expected to be prepared shortly (A. V. Lakshminarayanan, V. Sasisekharan, and G. N. Ramachandran, in preparation). The main purpose of this note is to draw the attention to such studies and to the need to study in detail the side group conformations in proteins such as myoglobin and lysozyme in order to bring out regularities of the type discussed above. They will be valuable in building up the structures of polypeptides and proteins. There is also a need to work out the crystal structures of more simple peptides. We have worked out programs for standardizing the coordinates of the structures from the usual data and would appreciate receiving data on new and unpublished structures from those who have them.

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