Journal of Macromolecular Science, Part A
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597274

Conformational Study of Dipeptides

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To cite this Article Kumbar, Mahadevappa and Windwer, Stanley(1972) 'Conformational Study of Dipeptides', Journal of Macromolecular Science, Part A, 6: 7, 1403 — 1409
To link to this Article: DOI: 10.1080/10601327208056904
URL: http://dx.doi.org/10.1080/10601327208056904

J. MACROMOL. SCI.—CHEM., A6(7), pp. 1403-1409 (1972)

Conformational Study of Dipeptides

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ABSTRACT

Steric maps for various dipeptides have been studied by 1° rotations. The studied dipeptides have been tabulated. Only the maps for gly-L-gly and gly-L-ala have been reproduced and are included in this work. From this study two important features have emerged; the rotation by 1° smooths the boundaries between allowed and disallowed regions, and it expands the sterically allowed regions.

INTRODUCTION

In the last few years great progress has been achieved in computer determination of the stable conformations of polypeptides and proteins. The methods commonly used for such determinations are broadly classified into two catagories; the empirical methods [1-3] and the quantum mechanical calculations [4, 5]. The empirical methods have gained more popularity due to their simplicity and the short computer time of the energy minimization procedure. These methods have often yielded satisfactory results. The quantum mechanical treatment of the problem is more rigorous, less empirical, and probably takes more computer time than the empirical methods. These methods are more likely to yield better results and may lead to a better understanding of the stable conformations.

These methods are gaining more support and becoming more common due to their rewarding nature [4, 5].

A polypeptide chain has an extremely large number of conformational possibilities because of the rotations about the single bonds of the backbone and side chains. However, there exist a limited number of conformations due to steric interactions. The conformations may be further limited by the introducing of a bulky side chain. The problem of polypeptide conformation is a complex matter. Due to this very reason, all the workers in this field have introduced various assumptions and approximations so that tractable computer programs can be developed and the polypeptide conformation can be simulated. Among the various assumptions, the most important ones are:

1. The atoms are assumed to have hard core rather than soft core. Even though this assumption is not realistic, it reduces the computational labor.
2. In a polypeptide unit there are only two rotational possibilities about two single bonds, $N-C^{\alpha}$ and $C^{\alpha}-C'$. This limits the number of conformations, and hence the computer time.

In order to understand the conformational status of any polypeptide or protein, it is natural and usual to study its fundamental unit in detail. Such a unit is chosen as the peptide unit, which is derived by linking two amide groups at the C^{α}-atom. Another very important assumption utilized here is that the amide group is a planar trans (or occasionally cis) conformation which retains its planarity under various circumstances. Thus the investigation of the peptide unit is further facilitated by the study of dipeptides. The overall conformation of a polypeptide depends upon two types of interactions: the short-range interactions, which exist in adjacent peptide units, and the long-range interactions, which exist in nonadjacent peptide units. The short-range interactions only limit the number of conformations and in no way predict the stable or the most probable conformation. It seems that the long-range interactions are the deciding factor in obtaining the stable or the most probable conformation.

The task of the present work is to explore the short-range interactions in more detail than has previously been done. Leach et al. [6] have studied the various dipeptides and obtained steric maps. However, these authors have used the 10° increment for the ϕ and ψ angles for two reasons. First, the steric maps can be directly printed from the memory of the machine on an output sheet, and second, the computation can be carried out in a relatively short time. Rotation of ϕ and ψ by less than 10° presents some difficulties: the steric maps cannot be printed directly, and computation takes a much longer time, the time depending on the nature of the side chain. We have surmounted

these difficulties and obtained steric maps for various dipeptides by rotation ϕ and ψ by a 1° increment.

GENERATION OF BACKBONE AND SIDE-CHAIN CONFORMATION

The backbone conformation has been generated by using the standard convention [7]. Residue number 1 is placed at the origin of the cartesian coordinate system and the residue number 2 is attached to it at the C^{α} atom in such a way that $\phi = \psi = 0$ in the standard notation [7]. The coordinates of residue 1 are computed by using the bond angles and bond lengths given by Scheraga [1]. The method described by Nemethy and Scheraga [8] has been used to obtain the various conformations as functions of rotational angles ϕ and ψ. In a new convention, the transformation matrix from unit 2 to 1 is

$$T_{2-1} = T_{\alpha} T_{\phi} T_{\beta} T_{\psi_1} T_{\gamma} \tag{1}$$

where all the matrices are defined by Nemethy and Scheraga [8]. The values of the angles α, β, and γ are taken as -13.1, 70.5, and 22.1°, respectively. The C^{β} atom is considered as a part of unit 2, whose position in space depends only on rotation around ϕ_1. Hence a transformation matrix for C^{β} is

$$T_{C^{\beta}} = T_{\alpha} T_{\phi_1} \tag{2}$$

The side chain is considered to be attached to the C^{β} atom and generated by the same procedure as given by Nemethy and Scheraga. The local coordinates of the side-chain atoms are computed using the bond angles and bond lengths given by Scherago [1].

1° ROTATION

Since the steric maps rotated by 10° can be easily printed out from the memory of the computer, we have first obtained steric maps by rotating a 10° interval. These maps are printed out on an output sheet and traced directly into figures. If the maps are to be obtained in 1° interval, one should be able to store a 361 × 361 matrix in the machine.

Even if it is possible to synchronize the printed 361 × 361 map into figures of size 11 × 9 in., it is impossible to store the 361 × 361 matrix in the machine (at least for CDC 3600) and print out in a symmetric way as is possible for 10° rotation. Due to this difficulty, we have introduced an alternative method. By examining the 10° rotated figures it is seen that a rotation by 1° effects only the boundary between the allowed and disallowed regions, and in no way alters the inside regions. The boundary is defined as the region enclosed by the last points in the allowed regions and the first points in the disallowed regions. For example (see Fig. 1), ϕ = 130° and ψ = 100-140° (last points in the allowed region) are allowed, while ϕ = 140° and ψ = 100-150° (the first points in the disallowed region) are not allowed. The area encompassed by these points is defined as the boundary. Thus there is a 10°-wide boundary between the two regions, which extends mainly inside the disallowed region. Therefore, it is not necessary to rotate the angles ϕ and ψ by 0 to 360°, but it is sufficient to investigate only the boundary by rotating a 1° interval. In a separate program we have done so and printed out the allowed angles. Then we have transcribed these allowed regions onto 10° rotated steric maps. However, the accuracy in transcribing is not that great due to very fine unsketchable boundaries. The small details which appear in 1° rotation have been omitted, and the boundaries have been drawn much smoother.

DISCUSSION

The steric maps for the various dipeptides presently generated are listed in Table 1. The maps for gly-L-gly and gly-L-ala are reproduced in Figs. 1 and 2, respectively. The allowed regions are enclosed by lines. The areas that are allowed by 1° rotation are indicated by lines,

TABLE 1. Dipeptides Studied by 1° Rotation

gly-L-gly, gly-L-ala, gly-L-cys, gly-L-ser,
gly-L-met, gly-L-lys, gly-L-val, gly-L-thr,
gly-L-iso, gly-L-leu, gly-L-asp, gly-L-asn,
gly-L-glu, gly-L-gln, gly-L-arg, gly-L-his,
gly-L-phen, gly-L-tyr, gly-L-try

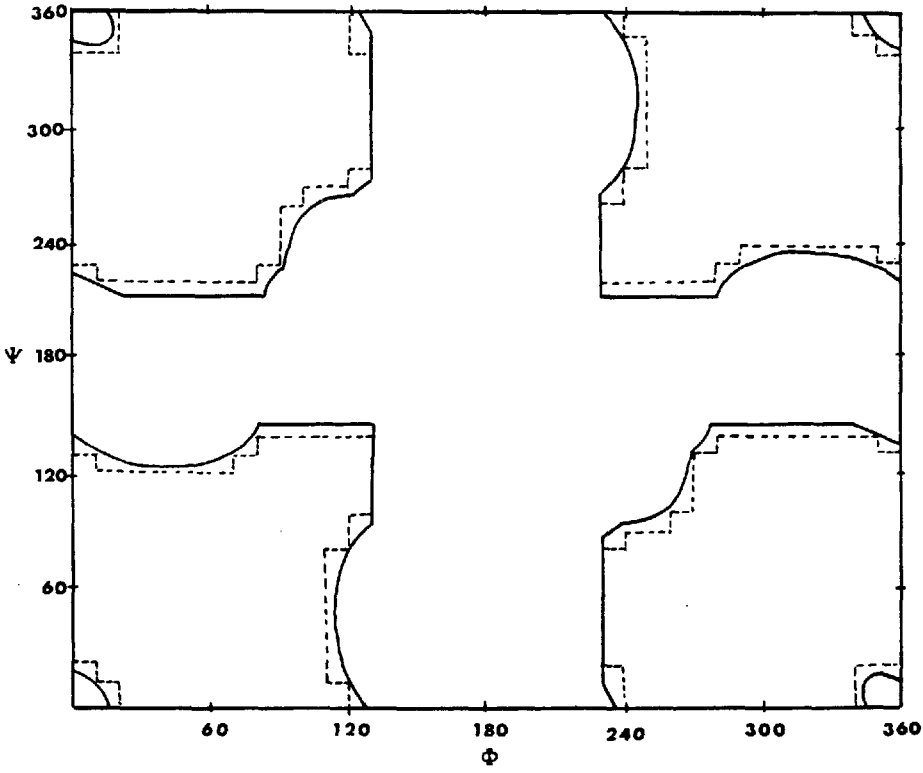

FIG. 1. Steric map for gly-L-gly. (--) 10° rotation and (—) 1° rotation.

and 10° rotation by dotted lines. From the examination of the maps, two important features emerge: The rotation by 1° smooths the boundaries between the allowed and disallowed regions, and the 1° rotation expands the sterically allowed regions. The physical appearance of the maps depends upon many factors; contact distances, bond angles, bond lengths, whether atoms are considered to be hard or soft core, etc. In our computation we have used the hard core contact distances described by Scheraga [1]. The $-CH$, $-CH_2$, and $-CH_3$ which occur in backbone and side chains are treated as single atoms having a spherical appearance. In order to account for the steric interactions, the contact distances are increased by 0.3 due to hydrogen atoms. The other groups which occur in side chains, such

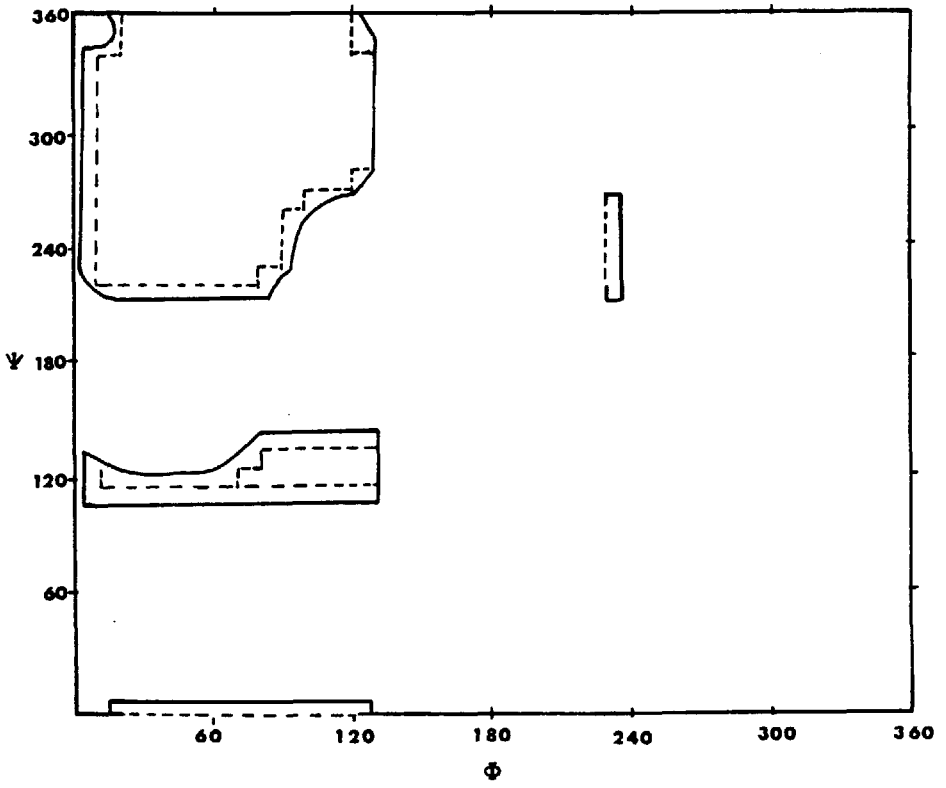

FIG. 2. Steric map for gly-L-ala. (--) 10° rotation and (—) 1° rotation.

as —SH, —OH, $-NH_2$, and —NH, are also treated as single atoms, and increases in the steric interactions due to hydrogen atoms have been accounted. Treating these groups as single units is not realistic, but the computational problem becomes less laborious.

Figure 1 describes the steric interactions in gly-L-gly. When 1° rotation is carried out, the boundaries are much smoother than 10° rotation, especially the boundaries enclosed by ϕ = 110-130°, ψ = 0-100°; ϕ = 0-80°, ψ = 120-140°; and ϕ = 230-280°, ψ = 80-150°. The boundaries that are not affected by 1° rotation are those enclosed by ϕ = 130°, ψ = 100-150°; and ϕ = 230°, ψ = 20-80°. Since the map is symmetric through the center, a similar explanation also holds for the upper two allowed regions. The sterically disallowed regions are

centered around ϕ = 180°, ψ = 0-360°; and ψ = 180°, ϕ = 0-360°; and also near ϕ,ψ = 0,0; 0,360; 360,0; and 360°,360°. The maximum overlap occurs when two residues are coplanar or nearly coplanar due to the steric interactions between the O,H of residue 1 and the O,H to residue 2.

When the C^{β}-atom is attached to the C^{α}-atom as in gly-L-ala, the sterically allowed region is much restricted (Fig. 2). The lower right area which is allowed in gly-L-gly completely disappears. Out of the upper right region, only a small portion is allowed. Two small portions remain in the lower left region. The upper left region retains much of its area except the small region enclosed by ϕ = 0-10° and ψ = 220-340°. The dotted lines correspond to ϕ = 230°, ψ = 210-270°; ϕ = 20-120°, ψ = 0°; and ϕ = 10-70°, ψ = 120° do not describe the area but simply represent the sterically allowed conformations when 10° rotation is performed. Again here, as in the gly-L-gly, the 1° rotation brings a smooth boundary to the 10° rotated boundary. From the map it is clear that only two areas are dominant as observed previously [6], and most of the stable conformations of gly-L-ala fall in these two regions [9]. The effect of 1° rotation on other steric maps of the most common dipeptides has also been investigated. An effect similar to the cases of gly-L-gly and gly-L-ala has been found.

From the above discussion it can be concluded that the sterically allowed conformations are considerably restricted if the branch is very close to the backbone and if the branch atoms are bigger. The rotation by 1° reveals the detail nature of the boundaries between the allowed and disallowed areas, and makes the boundaries much smoother.

REFERENCES

[1] H. A. Scheraga, Advan. Phys. Org. Chem., 6, 103 (1968).
[2] G. N. Ramachandran, Int. J. Prot. Res., 1, 5 (1969).
[3] P. J. Flory, Statistical Mechanics of Chain Molecules, Wiley (Interscience), New York, 1969.
[4] B. Pullman, Colloq. Int. Cent. Nat. Rech. Sci., 301, 261 (1971).
[5] H. A. Scheraga, Chem. Rev., 71, 195 (1971).
[6] S. J. Leach, G. Nemethy, and H. A. Scheraga, Biopolymers, 4, 369 (1966).
[7] J. T. Edsall, P. J. Flory, J. C. Kendrew, A. M. Liquori, G. Nemethy, G. N. Ramachandran, and H. A. Scheraga, J. Mol. Biol., 15, 399 (1966).
[8] G. Nemethy and H. A. Scheraga, Biopolymers, 3, 155 (1965).
[9] C. M. Venkatachalam and G. N. Ramachandran, in Conformation of Biopolymers (G. N. Ramachandran, ed.), Academic, New York, 1967, p. 83.

Received for Publication June 15, 1972