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BBA Report

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The non-planar peptide unit^{*}

II. Comparison of theory with crystal structure data^{**}

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SUMMARY

The theoretical results derived in Part I (Ramachandran, G.N., Lakshminarayan, A.V. and Kolaskar, A.S. (1973) *Biochim. Biophys. Acta* 303, 8–13) that the three bonds of the peptide unit meeting at N can have a pyramidal structure is confirmed by an analysis of 14 published crystal structures of small peptides. It is shown that the dihedral angles θ_N and $\Delta\omega$ are correlated, while $\theta_{C'}$ is small and is uncorrelated with $\Delta\omega$, showing that the non-planar distortion at C' is generally small.

In Part I (ref. 1), it was shown that quantum chemical theory predicts the ready occurrence of non-planar distortions of the peptide unit and that the most facile deformation is a distortion of the three bonds N–C', N–C₂^α and N–H meeting at the N atom (Fig. 1a) which make them have a pyramidal structure (Fig. 1b). On the other hand, the four atoms C₁^α, C', O and N are expected to be very nearly planar (Fig. 1c). In terms of the dihedral angles $\Delta\omega$, θ_N and $\theta_{C'}$ (which have been defined in ref. 1), shown in Figs 1b and 1c, variation of $\Delta\omega$ up to about 15° are possible, and correspondingly, θ_N is most likely to have a value equal to -1.5 to $-2.0 \Delta\omega$; while $\theta_{C'}$ would be small. These predictions of the theory have been verified by an analysis of crystal structure data of a number of peptides for which accurate atomic co-ordinates are available.

The structures chosen for the analysis are either those published during the last three years or are unpublished, in which hydrogen atom positions have also been located. The dihedral angles were calculated from fractional co-ordinates listed in the respective

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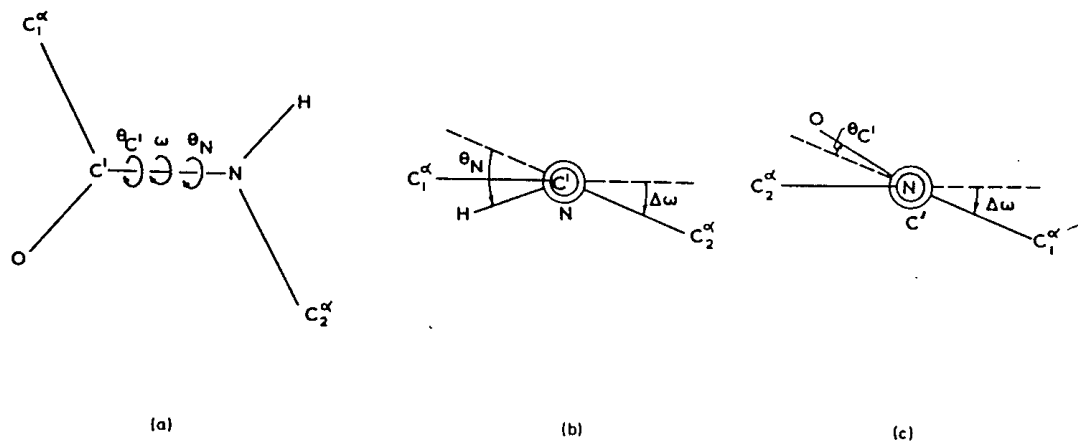


Fig. 1. (a) The nomenclature of the atoms in a peptide unit. All the three dihedral angles $\theta_{C'}$, θ_N and ω , mentioned in the text, refer to rotations about the bond $C'-N$. (b) The angles $\Delta\omega$ and θ_N are marked in the figure, which is a projection of the relevant atoms down the bond $C'-N$. The angle is positive if clockwise, and negative if anticlockwise. Note that the bonds $N-C'$, $N-C_2^\alpha$ and $N-H$ have a pyramidal conformation, and that θ_N is approx. $-2 \Delta\omega$ in the example shown. (c) Projection, similar to (b), down the bond $N-C'$. The angles $\Delta\omega$ and $\theta_{C'}$ are marked, whose signs follow the same convention as in (b). Note that $|\theta_{C'}|$ is small, and the atoms N , C' , C_1^α and O are very nearly coplanar in the example shown, which is typical.

papers, by using a simple program. These are listed in Table I with the values rounded off to 0.1° . From the reported standard deviations, these angles are expected to be accurate to about 0.5° for $\Delta\omega$ and $\theta_{C'}$, and only to about 2° for θ_N . It will be readily seen from Table I that, in the case of open peptides, $\Delta\omega$ can be either positive or negative for L-peptide units, with approximately equal facility. For small values of $\Delta\omega$, under 5° in magnitude, θ_N is mostly variable between $\pm 10^\circ$. On the other hand, when $\Delta\omega$ is larger than 10° in magnitude, θ_N is invariably of the opposite sign and larger than $\Delta\omega$. On the other hand, in all structures, $\theta_{C'}$ is small and always less than 5° .

Although a few cyclic peptides have been solved, only one has hydrogen coordinates listed, for which the data are given in Table I. It will be seen that, even with the strains imposed by cyclisation, $\Delta\omega$ does not exceed 10° , while the magnitude of θ_N is quite large. However, $\theta_{C'}$ does not exceed 2° in most cases, and is equal to 4° only for one peptide unit.

All these data confirm the two predictions of the theory of Part I, namely:

- (1) $\Delta\omega$ and θ_N are correlated, with θ_N approx. $-1.5 \Delta\omega$; and
- (2) $|\theta_{C'}|$ is small.

These two results are most markedly demonstrated by the plots in Fig. 2. It will be seen from Fig. 2a that there is a correlation between the variation of $\Delta\omega$ and of θ_N . The observed correlation corresponds to a pyramidal arrangement of the three bonds $N-C'$, $N-C_2^\alpha$ and $N-H$, as shown in Fig. 3a of Part I (ref. 1). On the other hand, the best fit to the data in Fig. 2b is a horizontal straight line, showing that $\theta_{C'}$ is uncorrelated with $\Delta\omega$. Also, as shown by the broken lines in Fig. 2a and Fig. 2b, the spread of θ_N is much larger than that of $\theta_{C'}$, showing that the bonds at the N atoms are much more easily deformed than those at the C' atom.

TABLE I

X = X-ray, N = neutron diffraction, N.L. = not listed in the reference.

| Compound | R value (%) | $\Delta\omega$ (degrees) | θ_N (degrees) | $\theta_{C'}$ (degrees) | Techn and re |
|---|-------------|--------------------------|----------------------|-------------------------|--------------|
| <i>Open peptides</i> | | | | | |
| Gly-L-Leu | 4.0 | -11.4 | +24.1 | +0.2 | X,* |
| Gly-Gly,HCl,water | 6.8 | -3.2 | -3.5 | -2.4 | N, 2 |
| α -Gly-Gly | 6.0 | +3.6 | +8.2 | +3.3 | N, 3 |
| L-Ala-Gly | 4.7 | -6.1 | +2.5 | -2.0 | X, 4 |
| L-Ala-L-Ala | 6.6 | -4.3 | -3.9 | -1.6 | X, 5 |
| Gly-L-Ala,HCl | 9.8 | -10.7 | +17.2 | +4.5 | X, 6 |
| Acetyl-L-Pro-L-methylamide | 9.8 | -8.4 | +11.4 | +1.3 | X, 7 |
| Glutathione | 4.0 | +2.7 | -8.6 | +1.2 | X,** |
| <i>N</i> -Methyl-DL-Leu-Gly,HBr | 10.3 | +13.7 | -13.4 | +3.7 | X,** |
| L-Ala-Ala,HCl | | +2.6 | +6.4 | +1.2 | |
| L-Ala-Ala,HCl | 7.9 | -1.1 | -17.9 | +2.2 | X, 8 |
| L-Ala-Gly,LiBr | 3.7 | +0.8 | -21.1 | -2.7 | X, 9 |
| Gly-Gly phosphate monohydrate | 3.7 | +7.2 | +2.0 | -2.5 | X, 10 |
| Gly-Gly phosphate monohydrate | 2.4 | -4.5 | -9.7 | +0.2 | X, 11 |
| DL- <i>N</i> -Chloroacetyl-Ala | 6.4 | -4.9 | +8.7 | -0.5 | X, 12 |
| <i>Cyclic peptide</i> | | | | | |
| \square -Gly-Gly-D-Ala-D-Ala-Gly-Gly- | 6.5 | +1.4 | -13.1 | -0.9 | X, 13 |
| | | -2.8 | +28.5 | -1.1 | |
| | | +3.7 | -9.2 | +1.5 | |
| | | +8.2 | N.L. | +4.2 | |
| | | +3.0 | +5.8 | -0.7 | |
| | | -7.4 | +13.1 | +1.0 | |

*Venkatesan, K., personal communication.

**Cole, F.E., personal communication to Venkatesan, K.

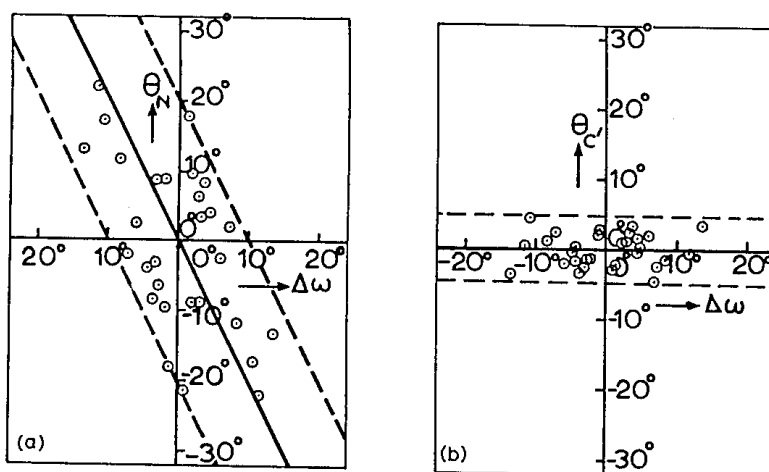


Fig. 2. Plot of (a) θ_N vs $\Delta\omega$ and (b) $\theta_{C'}$ vs $\Delta\omega$, of the crystal structure data. The broken lines enclose the available data, while the solid line in the middle indicates the correlation between θ_N and $\Delta\omega$ in (a), and the absence of correlation between $\theta_{C'}$ and $\Delta\omega$ in (b).

It may be mentioned that our analysis is fully consistent with the general observation of crystallographers, who find that the deviations of the atoms, from the best plane through C_1^α , C' , O, N and C_2^α , is small for the first four atoms and is large only for C_2^α . In their terminology, we would say that the H atom is also appreciably out of plane and is on the same side of the plane as C_2^α .

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