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OPTICAL ROTATORY MINIMA IN SOME SIMPLE PEPTIDES

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Current theories of optical rotation (1) indicate a very steep dependence of rotational strength on the distances separating the chromophore concerned from the groups imparting asymmetry to its environment. Glycyl-L-leucylglycine contains two peptide chromophores, each of which, presumably, is asymmetrically perturbed by the substituents on the α-carbon atom of the leucine residue, so that the observed rotation contains contributions from both these chromophores and each of these contributions is the sum of the partial rotations of all the conformational states adopted by the chromophore. Since the peptide group is planar, such conformations are specified by the dihedral angles, ϕ_{NC} and ϕ_{CC}, between the peptide planes and the N - C_α - C plane of the leucyl residue. Factors governing the values of the dihedral angles defining peptide conformations are currently under discussion (2).

In addition to the two peptide groups, gly-L-leugly contains an ionized carboxyl group absorbing at similar wavelengths, but this is remote from the centre of asymmetry of the molecule and hence its rotational contribution is likely to be small. If the peptide chain is extended from

either end, the added peptide groups are similarly remote from the leucyl residue and their direct contributions to the total rotation will similarly be small. They may, however, affect this quantity indirectly by their influence on the rotational strengths of the peptide groups flanking the leucyl α-carbon atom. Three ways in which this may occur are as follows.

1. By direct interaction, which would imply special conformational states favouring such interaction. The α-helix is one of these.

2. By the change in the electron energy levels within the groups resulting from the conversion of the adjacent $^{+}NH_3$- and $-COO^{-}$ groups to peptide linkages.

3. By a change in the balance between steric and minimum rotational free energy requirements within the molecule, with a consequent change in the values of ϕ_{NC} and ϕ_{CC} .

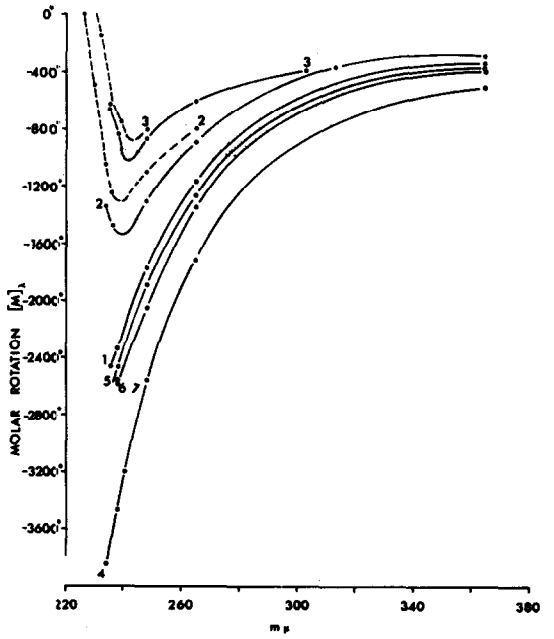
As reported recently (3) the molar rotations of some peptides containing leucyl residues separated by glycyls could be obtained with reasonable accuracy by summing the rotations of appropriate model compounds. This would suggest that none of the foregoing factors was having an appreciable effect. However, the molar rotation of gly-L-leugly$_2$-L-leugly, $[M]_D$ = -164° , was smaller than expected from values for the two available model compounds, gly-L-leugly, $[M]_D$ = -108°, and gly$_2$-L-leugly$_3$, $[M]_D$ = -120° The O.R.D. curve of gly-L-leugly$_2$-L-leugly included a sharp minimum at 237mμ which persisted with pH or concentration change, whereas that of gly-L-leugly was smooth. The α-helix could be eliminated as the source of this feature, despite the coincidence in wavelength between the minimum associated with that conformation and the one obtained in the hexapeptide curve.

All the possible tetra- and penta- and one of the hexapeptides of glycine and leucine containing a single internal L-leucyl residue have

now been prepared * Their O.R.D. curves in aqueous solution are reproduced in the Figure.

FIG. 1

The O.R.D. in aqueous solution of, 1, gly-L-leugly; 2, gly-L-leugly$_2$; 3, gly-L-leugly$_3$; 4,gly$_2$-L-leugly; 5, gly$_3$-L-leugly; 6, gly$_2$-L-leugly$_2$; 7, gly$_2$-L-leugly$_3$. Concentrations are - - - - 0.002M and ——— 0.01M.



*Satisfactory analysis figures were obtained for all compounds. They were recrystallized to constant rotation.

Two of the compounds, gly-L-leugly$_2$ and gly-L-leugly$_3$ give rotational minima similar in position and magnitude to that of gly-L-leugly$_2$-L-leugly. These, too, persist as pH or concentration is changed and, as with the hexapeptide (3), the dependence of rotational magnitudes upon concentration is similar to that in gly-L-leugly. None of the other peptides shows such a minimum. The feature is, therefore, to be associated with a leucine occupying the residue position second from the amino end in these peptide chains and, presumably, it is this residue, or, more properly, one or both of its flanking peptide chromophores, which produces the minimum in the O.R.D. curve of gly-L-leugly$_2$-L-leugly.

Goodman (4) has recently extended into the α-helix Cotton effect region his observations on rotational effects in non-aqueous solutions of peptide derivatives. Certain of his oligomers show O.R.D. minima at about 238 mμ under solvent conditions which render secondary structure unlikely. Both magnitude and position make it probable that the features are to be identified with the one reported here, in which case it is not specific to a particular side chain.

As has already been suggested for the hexapeptide (3), the minima in these curves may result from the superposition of a positive Cotton effect on a negatively tending curve, such as is observed in polypeptides in the random coil form. However, the peptide chromophores flanking the asymmetric carbon atom of the second residue cannot be solely responsible for the effect in the polymers. The contributions to the total rotation from these groups would be a small part of the whole. If a relationship exists between the features in the O.R.D. curves of the short chain and the long chain compounds, it is probable that special values of the dihedral angles are involved, since these might occur many times in a long chain.

Apart from the minima, the differences in rotational magnitudes between the curves in the figure are striking. These suggest the need for caution in estimating peptide rotations from those of model compounds. They also suggest that further rotational data from simple peptides will be of value. It may be possible in favourable cases to relate the rotatory characteristics of a single peptide chromophore to the average spatial disposition of the groups around it and thus provide a further line of approach to the problem of peptide chain conformations.

REFERENCES

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