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RESIDUE ROTATIONS IN SMALL PEPTIDES

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The optical rotatory properties of a randomly oriented peptide have been regarded as depending additivily upon the contributions of the amino acid residues along the chain (1). In a polypeptide containing many residues of the same type, the residue rotation (1), [R], obtained by dividing the molecular rotation by the number of residues, remains very nearly constant as the chain length is altered. In short peptide chains, however, this does not hold (1, 2b, 5) and the rate of convergence of [R] to a constant value is variable (3). Therefore, in order to retain the notion of additivity, residue rotations have been divided into three classes, which are known experimentally to differ (1). It has then been assumed (2) that the molecular rotation can be expressed as the sum of contributions from these.

$$\phi_{Total} = \phi_{N\text{-terminal}} + n\phi_{internal} + \phi_{C\text{-terminal}}.$$

The claim has recently been made (4) that the equation has been shown to hold for all L-oligopeptides in the random-coil form. It is the purpose of this communication to show that it does not hold for all such peptides and that, if it is assumed to hold, valuable information may be lost. It has already been shown (5) that departure from additivity in terms of the equation does not always imply departure from the random-coil form in the peptide concerned.

It has long been known that below a certain chain length in peptides composed of a single amino acid type, not only is [R] variable

(1, 3) but the rotatory increment per added residue is not necessarily constant as the chain is extended (3). The L-lysine and L-alanine oligomers studied by Becker and Stahmann (6) and Brand (7) provide examples. This must mean that one or more of the three partial molecular rotations of the equation is, in fact, not constant.

Interaction between optically active neighbours (1) may be envisaged as a possible cause of the variation, since one may reasonably assume that a peptide chromophore joining two asymmetric residues will be perturbed by both and the mutual disposition of these may be affected by further substitution in the molecule. If this were the only source of variation, the N-terminal, internal and C-terminal residue rotations would be constant in randomly oriented peptides in which the optically active residues were separated by glycyls. To test the possibility, rotatory data have been obtained for several peptides of glycine containing a single L-leucyl residue. All gave satisfactory analysis figures and were re-crystallized to constant rotation. The molecular rotations in aqueous solution are tabulated below.

Values from the N-terminal L-leucyl peptides form a family of closely similar O.R.D. curves. However, in L-leugly$_4$ there is a small but definite decrease in rotatory magnitudes at all wavelengths. The reason for this is not evident.

The minima in the curves of gly-L-leugly$_2$ and gly-L-leugly$_3$ have been discussed previously (5). Gly-L-leugly$_4$ exhibits a similar feature. No minimum is observed in the curve from any other peptide containing internal L-leucine. Gly$_2$-L-leugly$_2$ and gly$_2$-L-leugly$_3$ give virtually identical rotatory magnitudes, which are slightly but significantly greater than those of gly-L-leugly. Those of gly$_3$-L-leugly differ only marginally from the gly-L-leugly values, but those of gly$_2$-L-leugly are considerably greater.

The di- and tri-peptides of the C-terminal L-leucine group show closely similar rotations in featureless O.R.D. curves, whereas those of gly$_3$-L-leu and gly$_4$-L-leu, similar to each other, are much more shallow and turn steeply positive below 248 mμ.

TABLE 1

Molar rotations x 10^{-1} at several wavelengths of peptides of L-leucine and glycine. Concentrations at 589 mμ were 0.1M, all others 0.01M, or *0.002M. T = 20 - 25°.

	ϕ_{589}	ϕ_{365}	ϕ_{265}	ϕ_{257}	ϕ_{248}	ϕ_{239}	ϕ_{236}	ϕ_{234}	ϕ_{230}
L-leugly	15.6°	57°	211°		318°	433°			
L-leugly$_2$	14.7	54	210		323	465			
L-leugly$_3$	14.6	55	202		316	457			
L-leugly$_4$	13.3	48	185		285	430			
gly-L-leugly	-10.8	-37	-122	-143	-179	-232			
gly-L-leugly$_2$	-8.1	-30	-90		-130	-155			
" " " *			-80		-110	-130	-125	-105	-50
gly-L-leugly$_3$	-7	-24	-66						
" " " *		-23	-50	-60	-68	-63		-37.5	0
gly-L-leugly$_4$	-7.9	-26	-71	-80	-97				
" " " *					-96	-97	-84	-65	$-48_{232\ m\mu}$
gly$_2$-L-leugly	-14	-51	-172		-256	-347			
gly$_3$-L-leugly	-11	-38	-127		-189	-247			
gly$_2$-L-leugly$_2$	-11.5	-40	-135		-205	-259			
gly$_2$-L-leugly$_3$	-12	-41	-138		-205	-256			
gly-L-leu	-6.6	-21	-73		-98	-109			
gly$_2$-L-leu	-7.2	-23	-74		-98	-111			
gly$_3$-L-leu	-3.9	-9	-19	-20	-21	+21			
gly$_4$-L-leu	-4.2	-10.8	-23		-25	+25			

If one takes L-leugly$_2$, gly-L-leugly and gly$_2$-L-leu as representative of the N-terminal, internal and C-terminal categories, the differences between their rotatory characteristics are obvious. The N-terminal curve is steeply positive, the internal is negative and the C-terminal also negative but of about half the magnitude. However, when the data from all the peptides are considered, it is apparent that the variations within the last two categories may be as great as the differences between them.

It is not the purpose here to discuss the origins (5) of these variations but merely to point out that they exist, even when only one asymmetric residue is included in the chain. It seems necessary to assume that they are potentially present in any group of peptides.

It is also worth noting that the O.R.D. differences and similarities in the compounds of L-leucine and glycine are suggested by the ϕ_{589} values and hence that the extensive existing data on monochromatic rotations may provide clues to the O.R.D. characteristics of peptides in other series.

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