The Conformation of Bovine Pancreatic Ribonuclease *S*-Peptide

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WHETHER co-operative intramolecular interactions are responsible for the conformation of a particular segment of the polypeptide backbone in a protein has not yet been established. The *S*-peptide–*S*-protein system[1] represents a model for investigating this problem. The *X*-ray structure of RNase S, recently elucidated by Wyckoff *et al.*,[2] shows that 50% of the *S*-peptide (residues 2—12) is in an α-helical conformation.

To determine whether the *S*-peptide can retain such a structure in the absence of the partner *S*-protein, we studied its conformational features by optical rotatory dispersion and circular dichroism techniques. The o.r.d. curves of *S*-peptide are shown in Figure 1 and the corresponding c.d. curves in Figure 2. The o.r.d. in phosphate buffer shows two troughs, one at *ca.* 205 mμ (typical of fully random polypeptides) and the other at *ca.* 230 mμ. Similar features are shown by the corresponding curve in 8M-urea, within the wavelength limit fixed by the absorbancy of the solution. The first trough still persists although shifted to *ca.* 233 mμ; such persistence eliminates the possibility that in this region the observed dispersion arises

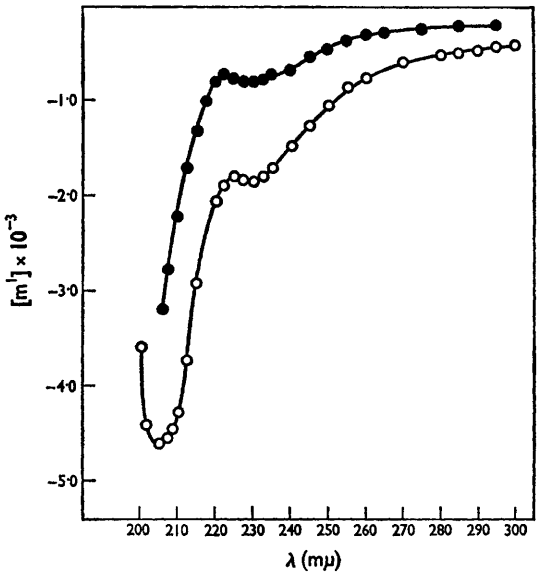

FIGURE 1. *Optical rotatory dispersion of* S-*peptide in* 0·01 M-*phosphate buffer* (pH 6·8) *with* 0·9% *sodium chloride* (—○—○—) *and in* 8M *urea* (—●—●—). [m'] is reduced mean residue rotation.

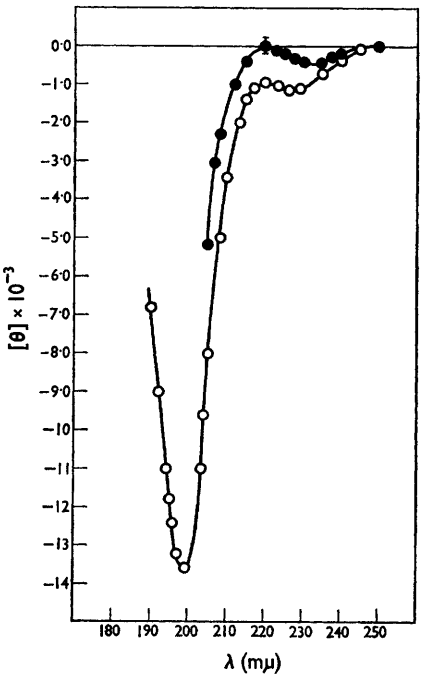

FIGURE 2. *Circular dichroism of* S-*peptide in* 0·01 M-*phosphate buffer* (pH 6·8) *with* 0·9% *sodium chloride* (—○—○—) *and in* 8M-*urea* (—●—●—). [θ] is mean residue molecular ellipticity.

from the amide n–π^* transition of some of the residues in an α-helical conformation. It is highly unlikely that an α-helix, including at most ten residues,[2] and therefore unstable by itself, can exist in a strong hydrogen-bonding medium such as 8M-urea solution.

Similar conclusions can be drawn from the c.d. curves, which show a large negative band centred at *ca.* 198 mμ associated with the amide π–π^* transition of disordered polypeptides,[3] and another band, much weaker, at *ca.* 227 mμ, which is shifted to about 231 μm in 8M-urea solution. Although the origin of the latter band, corresponding to the trough at longer wavelengths in the o.r.d. curves, is as yet unknown, it is possible to conclude from our results that the *S*-peptide is essentially randomly coiled in agreement with the lack of rotatory thermal transition observed by Sherwood and Potts.[4]

Comparing our findings with the *X*-ray data, it is obvious that in the binding process the *S*-peptide undergoes a coil-to-helix transition, which facilitates the largest hydroprophobic interactions with the *S*-protein. But for the *S*-peptide, the presence of the protein is equivalent to a decrease in the dielectric constant of the solvent, a change which is known to cause helix formation.

Conformational studies on some synthetic compounds, analogous[5] to the *S*-peptide, show that these also assume a similar randomly coiled form. A possible explanation of the varied capacity of such synthetic eicosapeptides to activate the *S*-protein might be sought in their differing tendency to undergo the coil-to-helix conformational transition.

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