Protected Decapeptide *ortho*-Nitrophenylsulphenyl–(L-leucyl–L-alanyl)$_5$–ethyl Ester [Nps–(L-Leu–L-Ala)$_5$–OEt]. Shortest Critical Peptide Size for Development of the α-Helix in the Solid State

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Summary Conformational studies of a series of oligopeptides having the sequence of alternate L-leucyl and L-alanyl residues in the solid state have revealed that the α-helical conformation begins forming at the decapeptide level, which may be considered as the shortest critical peptide chain length for development of the α-helical conformation in the solid state.

THE problem of critical chain length for development of secondary structures in linear oligopeptides is of current interest in peptide chemistry.[1] Our studies of the conformations of a number of oligopeptides having a variety of known repeating sequences of amino-acids have shown that there is a critical peptide size for development of the α-helix in every peptide system in the solid state, and the critical size depends on the composition and the repeating sequence of the amino-acids.[2] Here we have focussed our interest on finding a peptide system having the shortest critical chain length for development of the α-helix, and chose a peptide system consisting of alternate L-leucyl and L-alanyl residues. The choice of these amino-acids is based on experimental results[3] which suggest that the strongest α-helical conformation is formed in peptides consisting of these two amino-acids.

A series of oligopeptides protected by *o*-nitrophenylsulphenyl (Nps) and ethyl ester (OEt) groups were mainly prepared by the fragment condensation method using dicyclohexylcarbodi-imide and *N*-hydroxysuccinimide.† The samples prepared were dissolved in hexafluoropropan-2-ol and reprecipitated by addition of diethyl ether. Shear stress was then applied to the treated samples.‡ Conformation of the oligopeptides in the solid state was studied by far-i.r. spectroscopy and *X*-ray powder diffraction measurements.

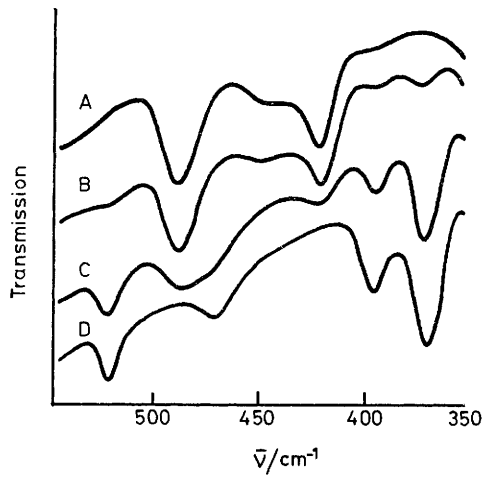

FIGURE 1. The far-i.r. spectra of octa- (A), nona- (B), deca- (C), and dodeca-peptides (D).

† A full account of the method and the results of the syntheses of these oligopeptides will be reported elsewhere.

‡ We have found that the application of shear stress to oligopeptides induces the conformational transformation from a non-equilibrium to an equilibrium conformation in the solid state.

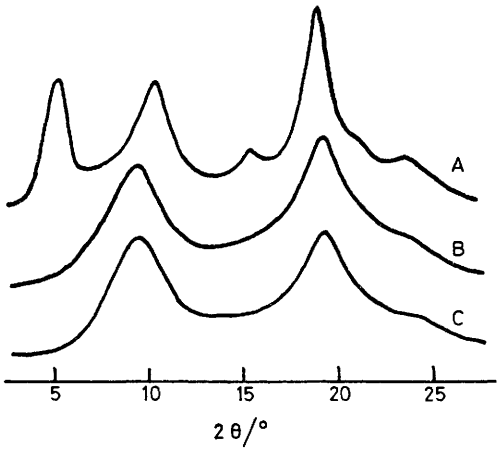

FIGURE 2. *X*-ray diffraction measurements on octa (A), nona- (B), and deca-peptides (C).

Figure 1 shows the far-i.r. spectra of the octa- (A), nona- (B), deca- (C), and dodeca-peptides (D). The first two peptides showed bands at 488 and 424 cm^{-1}, characteristic of L-leucyl residues, and at 451 cm^{-1}, characteristic of L-alanyl residues associated with the β-structure. In contrast, the deca- and dodeca-peptides showed bands at 526 and 369 cm^{-1} characteristic of L-alanyl residues, and at 393 cm^{-1} characteristic of L-leucyl residues with the α-helix. This result suggests that the nona- and lower oligopeptides take the β-structure, but the deca- and higher oligopeptides take the α-helical conformation in the solid state. This result was supported by *X*-ray diffraction measurements (Figure 2). The nonapeptide showed the characteristic prominent peaks at $2\theta = 10{\cdot}3°$ (020) and $18{\cdot}9°$ (110) of the orthorhombic unit cell of a peptide with the β-structure, while the deca- and dodeca-peptides showed the prominent peak at $2\theta = 9{\cdot}0°$ which can be assigned to the (100) plane of the hexagonal unit cell of a peptide with the α-helix.

This evidence suggests that the α-helical conformation begins at the decapeptide level and that the nona- and lower peptides take the β-structure. Thus it can be concluded that the decapeptide level is the critical peptide size for development of the α-helix in the solid state. Considering the nature of the amino-acids of this peptide system, we believe that the critical length, the decapeptide, may be the shortest one.

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[1] G. M. Bonora and C. Toniolo, *Biopolymers*, 1974, **13**, 2197; J. M. Becker and F. Naider, *ibid.*, 1747; C. Toniolo and G. M. Bonora, *Bio-org. Chem.*, 1974, **3**, 114; *Makromol. Chem.*, 1974, **175**, 1665, 2203; M. Palumbo, S. D. Rin, G. M. Bonora, and C. Toniolo, *ibid.*, 1976, **177**, 1477.

[2] R. Katakai, *J. Amer. Chem. Soc.*, 1977, **99**, 232; R. Katakai and Y. Nakayama, *Polymer*, 1977, **18**, 755; R. Katakai, *J.C.S. Perkin I*, 1977, 1193.

[3] G. D. Fasman in 'Poly-α-Amino Acids,' ed. G. D. Fasman, Marcel Dekker, New York, 1967, p. 499.