Circular Dichroism Evidence for a Stereospecific Complexation Reaction in Copper(II) Chelates of Poly-α-amino-acid Ligands

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Summary Evidence is presented for the stereospecific formation of the Cu^{II} derivatives of *NN'*-bis(salicylaldiminato) poly-L-ornithine and poly-L-lysine where the two diastereotopic faces of the square planar metal chelates are alternately bridged to the α-helical polypeptide matrix.

IT is known that copper(II) chelates of salicylaldimine derived from amino-acid esters show rapid transesterification and amidation reactions.[1] The proposed mechanisms are similar to those suggested for a large group of essential amino-acid reactions catalysed by pyridoxal-phosphate enzymes. In an attempt to reproduce some features of enzymatic activity, such as stereoselectivity, using simpler systems, we have prepared the Cu^{II} derivatives of *NN'*-bis(salicylaldiminato)-poly-L-ornithine and -poly-L-lysine. The polypeptides were suspended in the minimum amount of water and then methanol was added to effect dissolution. In these solutions the existence of the polypeptide chains in the right-handed α-helix conformation was

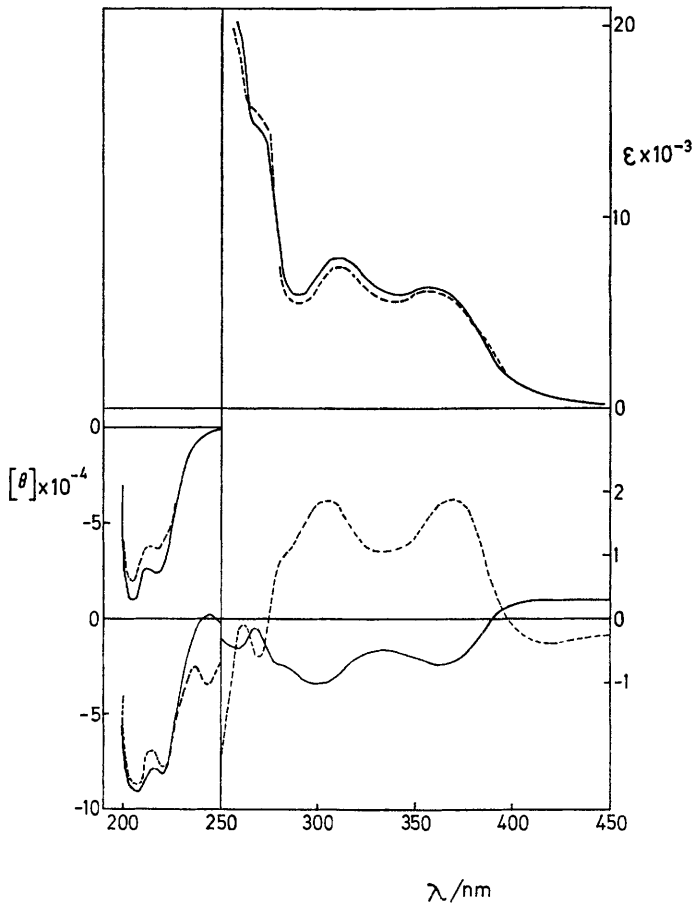

FIGURE. Absorption and c.d. spectra of the Cu^{II} derivatives of *NN'*-bis(salicylaldiminato) -poly-L-ornithine (– – – – – –) and -poly-L-lysine (————) in methanol (polypeptide concentration 3×10^{-4}M). The c.d. spectra of the poly-L-α-amino-acids in the same solvent and concentration are on the left hand side.

checked by c.d. spectra (Figure). Salicylaldehyde and copper acetate were added in stoicheiometric amounts and the solution refluxed until the u.v. spectra remained unchanged. They are very similar for both systems and are characteristic of Cu^{II} bis(salicylaldimine) chelates[2] (Figure).

Possible structures of the complexes were studied by model building, with the polypeptide chain fixed in the right-handed α-helical conformation. The asymmetric distribution of the side chains strongly suggests stereospecific formation of the complexes, dictated by the need to avoid either eclipsed conformations along chemically bonded bridges or disallowed contacts between non-bonded atoms. In the case of poly-L-ornithine, the only structure allowed is the one in which a stereotopic face (the *R*-face) of the square-planar copper chelate 'sees' the polypeptide chain. A similar situation arises for poly-L-lysine but a minor stereospecificity should be expected. Here, however, the opposite *S*-face of the chelate is 'seen' by the polypeptide chain. As a consequence, opposite Cotton effects are detected in the two cases for the electronic transitions of the copper chelate chromophore (Figure). Opposite trends in the range between visible region and 250 nm, where peptide electronic transitions do not contribute, are observed, whereas at shorter wavelengths the typical c.d. spectrum of the right-handed α-helix is still easily recognizable.

These findings are fully consistent with the explanation previously put forward by us on the 'solvent effect' found in the case of the Cu^{II} salicylaldiminato- complex of the cyclodecapeptide antibiotic Gramicidin S.[3]

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