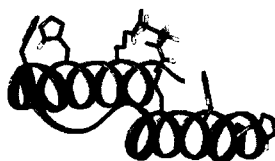


Abstract

Interhelical bridges with 5 and 8 carbons have been introduced into a number of designed 42mer helix-loop-helix polypeptide motifs with catalytic activity using site selective, self-catalysed reactions. For example, the bridged polypeptide DSG-PE42Dcap has been synthesised.



DSG-PE42Dcap

The interhelical bridges have been proved to have strong helix promoting effects and the catalytic activity of the polypeptide in aqueous solution has been shown to be enhanced by the bridging.

The bridging reaction has been optimised, and the catalysis of the site selective reaction has been investigated in detail.

Computer modelling shows that interhelical bridging of helix-loop-helix motifs may result in polypeptide structures with cavities. The novel bridging reaction may be used to introduce bridges with additional functional groups, which can be used to increase the catalytic efficiency and induce chiral discrimination.

Keywords: *de novo* design, bridged polypeptides, interhelical bridging, self functionalisation, self-catalysed acylation, *N*-hydroxysuccinimide esters, NHS-esters, catalysis, CD spectroscopy.

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