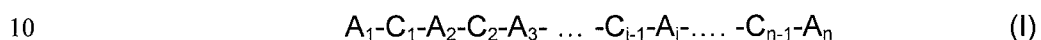


ABSTRACT

METHOD FOR PREPARING PEPTIDES BY ASSEMBLING MULTIPLE PEPTIDE FRAGMENTS

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Method for preparing a peptide assembly of n fragments and $n-1$ amino acids bearing a thiol function, represented by the formula:



in which $A_1, A_2, A_3, \dots, A_i, \dots, A_n$ are peptide fragments, $C_1, C_2, C_3, \dots, C_{i-1}, \dots, C_{n-1}$ are amino acid residues bearing a thiol function, n is comprised between 3 and 50, and i is 2 to n , in which a peptide-thioester is prepared of formula: A_1-SR (II) in which A_1 is a peptide fragment and SR is an alkyl thioester residue, R being alkyl optionally substituted, starting from a
 15 bis(2-sulphanylethyl)amino peptide: $A_1-SEAoff$ in which $SEAoff$ is a cyclic bis(2-sulphanylethyl)amino group, by action of a thiol $R-SH$, in the presence of a cyclic disulphide reducing agent, followed by condensation with a peptide fragment of structure: $H-C_1(SR')-A_2-SEAoff$ (III) in which (SR') represents a disulphide residue on the thiol of the amino acid C_1 , in the presence of an aromatic thiol $ArSH$, followed by conversion of the obtained new
 20 peptide, of structure: $A_1-C_1-A_2-SEAoff$ (IV), to a peptide-thioester of formula: $A_1-C_1-A_2-SR$ (II'), by action of a thiol $R-SH$, in the presence of a cyclic disulphide reducing agent, and condensation with a peptide fragment of structure $H-C_2(SR')-A_3-SEAoff$ (III') in the presence of an aromatic thiol $ArSH$, in order to produce a peptide fragment of structure $A_1-C_1-A_2-C_2-A_3-SEAoff$ (IV') and reiteration of these 2 operations up to $n-2$ times, in order to obtain a peptide
 25 fragment of structure $A_1-C_1-A_2-C_2-A_3- \dots -C_{i-1}-A_i- \dots -C_{n-2}-A_{n-1}-SEAoff$ (IV^m), then implementation of a native ligation reaction of this obtained peptide fragment (IV^m), with a peptide of formula: $H-C_{n-1}-A_n$ (Vⁿ) by reduction in the presence of a cyclic disulphide reducing agent, in order to produce the multiple peptide assembly of general formula (I).

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