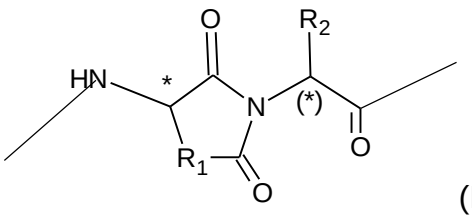
Claims

1. A method of synthesizing a peptide product comprising at least one cyclic imide group of formula (I) or a salt or solvate thereof:



(I)

wherein

R_1 is a bridge of one or two atoms lengths,

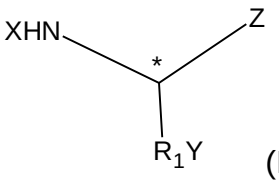
R_2 is an amino acid side chain,

* denotes an asymmetric C atom, and

(*) denotes an optionally asymmetric C atom,

comprising the steps:

(a) coupling a synthesis building block of formula (II):



(II)

wherein

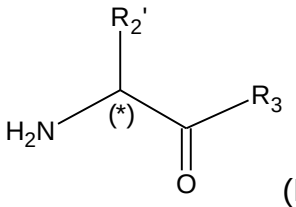
X is a base-labile amino protecting group,

Y is an unprotected carboxy or carboxamido group,

* denotes an asymmetric C atom, and

Z is a carboxy group,

to a peptide product of formula (III)



(III)

wherein

$R_{2'}$ is an optionally protected amino acid side chain,

R_3 is a peptidic residue, and

(*) denotes an optionally asymmetric C atom

under conditions wherein the cyclic imide group of formula (I) is formed and wherein the coupling conditions comprise a reaction time of at least 12 h, a temperature of between 15 and 40°C, repeated addition of coupling reagents such as TBTU or HBTU with DIPEA or HOBt/DIC and dimethylformamide (DMF) as organic solvent

(b) cleaving off the amino protecting group X, wherein said step (b) is not carried out with piperidine as deprotecting agent,

(c) optionally continuing the peptide synthesis, and

(d) optionally purifying the peptide product (I).

2. The method of claim 1, wherein R_1 is $-CH_2-$.

3. The method of claim 1, wherein R_1 is $-CH_2-CH_2-$.

4. The method of any one of claims 1-3, wherein Y is a carboxy group.

5. The method of any one of claims 1-4, wherein Y is a carboxamido group.

6. The method of any one of claims 1-5, wherein X is an Fmoc amino protecting group.

7. The method of any one of claims 1-6, wherein coupling step (a) is carried out on resin.

8. The method of any one of claims 1-7, wherein the yield of a cyclic imide product in coupling step (a) is ≥ 50%, ≥ 60%, ≥ 70%, ≥ 80% or ≥ 90% based on the amount of the total yield of a coupling product in step (a).

9. The method of any one of claims 1-8, wherein cleaving step (b) is carried out with the deprotecting agent 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).

10. The method of any one of claims 1-9, wherein the cyclic imide group of formula (I) is selectively introduced at at least one predetermined position of the peptide product.