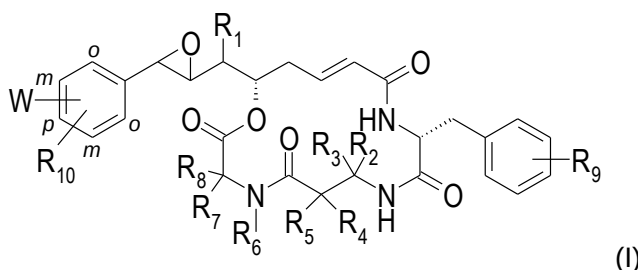


CLAIMS

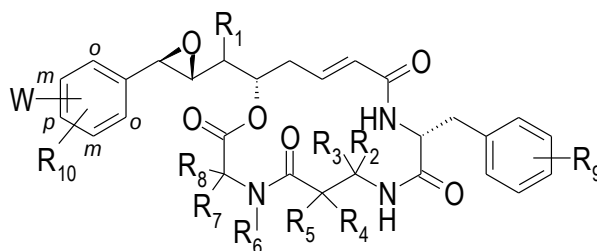
1. Cryptophycin compound of formula (I):



wherein:

- **R₁** represents a (C₁-C₆)alkyl group;
- **R₂** and **R₃** represent, independently of each other, a hydrogen atom or a (C₁-C₆)alkyl group; or alternatively **R₂** and **R₃** form together with the carbon atom to which they are attached a (C₃-C₆)cycloalkyl or a (C₃-C₆)heterocycloalkyl group;
- **R₄** and **R₅** represent, independently of each other, a hydrogen atom or a (C₁-C₆)alkyl group or a (C₁-C₆)alkyl-NH(R₁₂) group or a (C₁-C₆)alkyl-OH group or a (C₁-C₆)alkyl-SH group or a (C₁-C₆)alkyl-CO₂H group; or alternatively **R₄** and **R₅** form together with the carbon atom to which they are attached a (C₃-C₆)cycloalkyl or a (C₃-C₆)heterocycloalkyl group;
- **R₆** represents a hydrogen atom or a (C₁-C₆)alkyl group;
- **R₇** and **R₈** represent, independently of each other, a hydrogen atom or a (C₁-C₆)alkyl group or a (C₁-C₆)alkyl-CO₂H group or a (C₁-C₆)alkyl-N(C₁-C₆)alkyl₂ group; or alternatively **R₇** and **R₈** form together with the carbon atom to which they are attached a (C₃-C₆)cycloalkyl group or a (C₃-C₆)heterocycloalkyl group;
- **R₉** represents one or more substituents of the phenyl nucleus chosen, independently of each other, from: a hydrogen atom, -OH, (C₁-C₄)alkoxy, a halogen atom, -NH₂, -NH(C₁-C₆)alkyl or -N(C₁-C₆)alkyl₂ or -NH(C₁-C₆)cycloalkyl or (C₃-C₆)heterocycloalkyl;
- **R₁₀** represents at least one substituent of the phenyl nucleus chosen from a hydrogen atom and (C₁-C₄)alkyl;
- **W** represents
 - (C₁-C₆)alkyl-NH(R₁₁),
 - (C₁-C₆)alkyl-OH,
 - (C₁-C₆)alkyl-SH,
 - CO₂H or C(=O)NH₂;
 - (C₁-C₆)alkyl-CO₂H or (C₁-C₆)alkyl-C(=O)NH₂; or
 - (C₁-C₆)alkyl-N₃.
- **R₁₁** and **R₁₂** represent, independently of each other, a hydrogen atom or a (C₁-C₆)alkyl group.

2. Cryptophycin compound of formula (I) according to claim 1, having the following structure:



- 5 3. Cryptophycin compound of formula (I) according to any one of claim 1 or 2, characterized in that **R₁** represents a methyl group.
4. Cryptophycin compound of formula (I) according to any one of claims 1 to 3, characterized in that:
 - 10 - each of **R₂** and **R₃** represents a hydrogen atom, or
 - one of **R₂** and **R₃** represents a methyl group and the other one represents a hydrogen atom, or
 - **R₂** and **R₃** form together with the carbon atom to which they are attached a cyclopropyl group.
5. Cryptophycin compound of formula (I) according to any one of claims 1 to 4, characterized in that each of **R₄** and **R₅** represents a methyl group.
- 15 6. Cryptophycin compound of formula (I) according to any one of claims 1 to 5, characterized in that **R₆** represents a hydrogen atom.
- 20 7. Cryptophycin compound of formula (I) according to any one of claims 1 to 6, characterized in that **R₇** and **R₈** represent independently of each other a hydrogen atom or a (C₁-C₆)alkyl group.
8. Cryptophycin compound of formula (I) according to any one of claims 1 to 7, characterized in that **R₉** represents two substituents selected from a methoxy group and a chlorine atom.
- 25 9. Cryptophycin compound of formula (I) according to any one of claims 1 to 8, characterized in that **R₁₀** represents a hydrogen atom.
10. Cryptophycin compound of formula (I) according to any one of claims 1 to 9, characterized in that:
 - 30 ▪ **R₁** represents a (C₁-C₆)alkyl;
 - each of **R₂** and **R₃** represents a hydrogen atom;
 - **R₆** represents a hydrogen atom;
 - **R₉** represents two substituents selected from a methoxy group and a chlorine atom; and

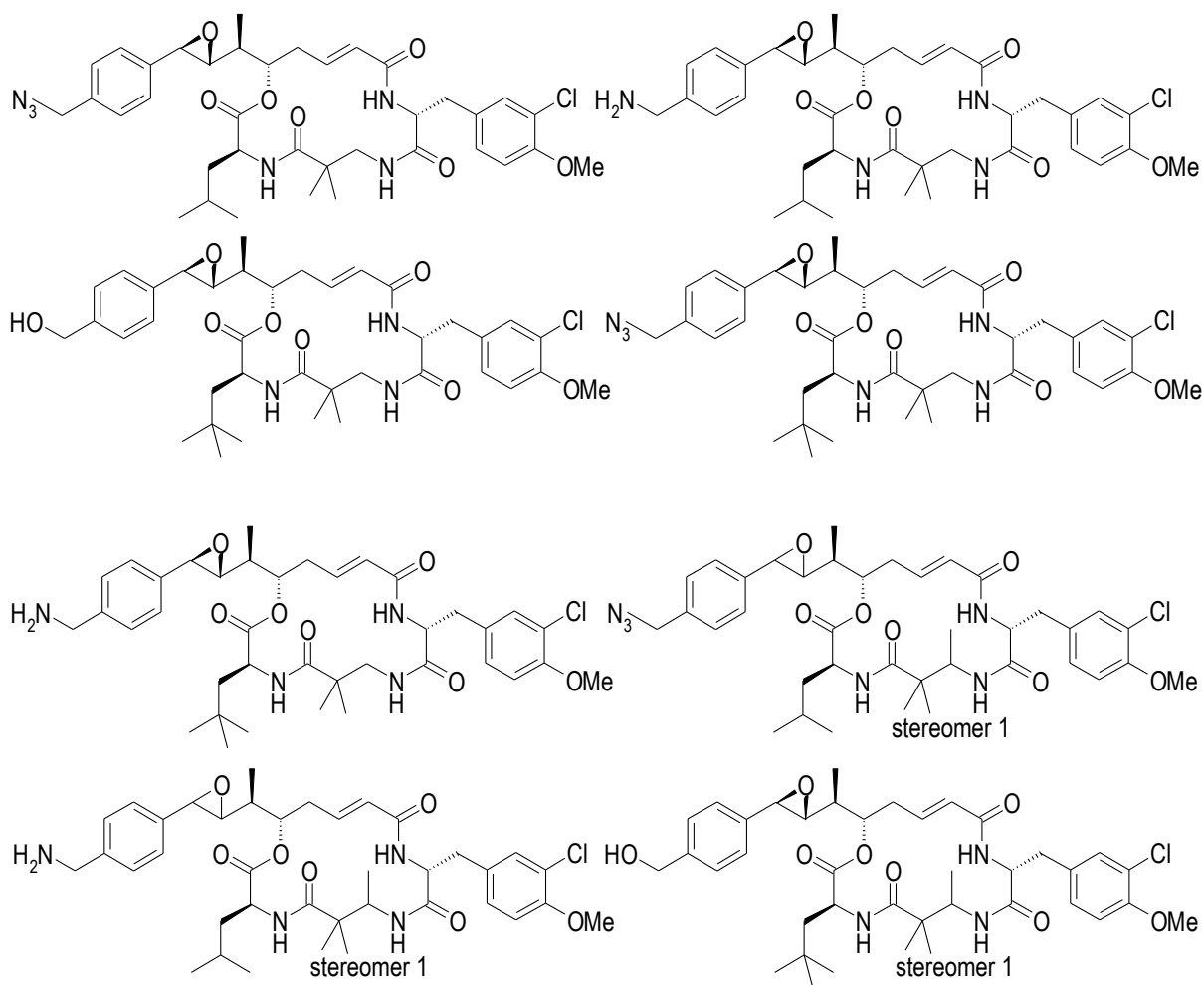
R_{10} represents a hydrogen atom.

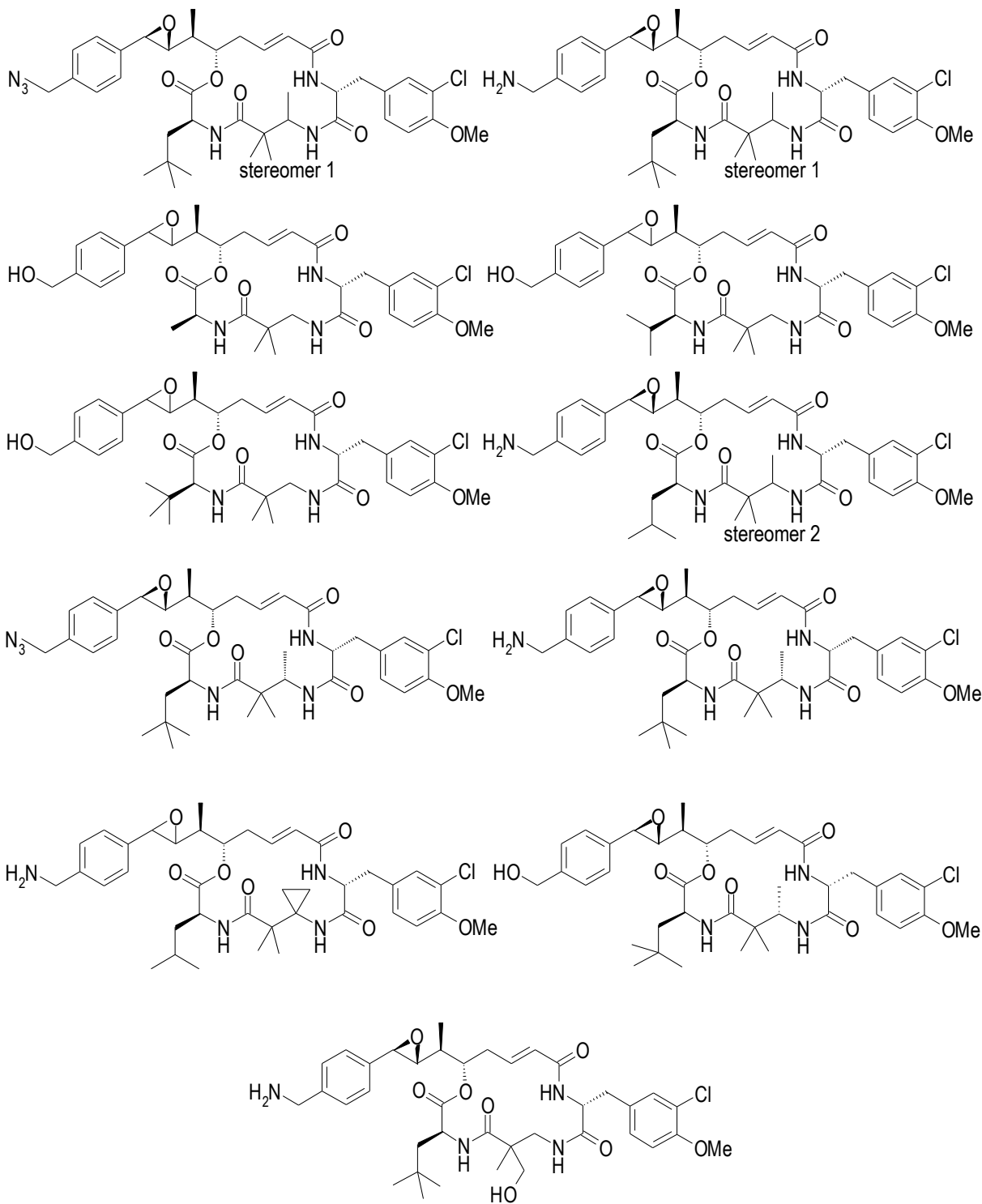
11. Cryptophycin compound of formula (I) according to any one of claims 1 to 9, characterized in that:

- R_1 represents a (C1-C6)alkyl;
- R_2 and R_3 represents a (C1-C6)alkyl, and the other one represents a hydrogen atom;
- R_6 represents a hydrogen atom;
- R_9 represents two substituents selected from a methoxy group and a chlorine atom; and
- R_{10} represents a hydrogen atom.

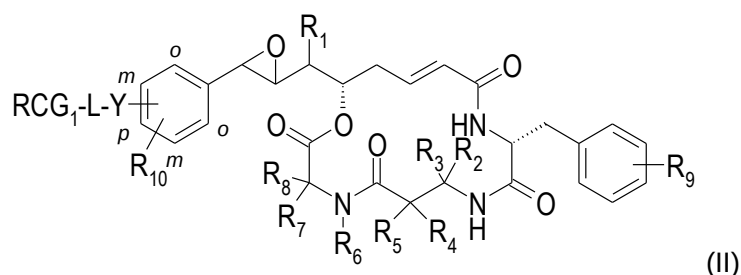
12. Cryptophycin compound of formula (I) according to any one of claims 1 to 11, characterized in that **W** is selected from (C₁-C₆)alkyl-NHR₁₁, (C₁-C₆)alkyl-OH, (C₁-C₆)alkyl-SH and (C₁-C₆)alkyl-CO₂H, preferably **W** represents a CH₂-NH₂ or a CH₂-OH group.

13. Cryptophycin compounds of formula (I) according to claim 1 which are selected from the following list:





10 14. Cryptophycin payload of formula (II):

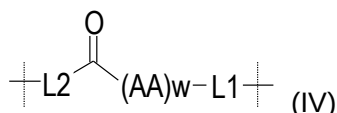


wherein

R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₉ and R₁₀ are as defined in claim 1 to 11, and

- **Y** is selected from (C₁-C₆)alkyl-NR₁₁, (C₁-C₆)alkyl-O, (C₁-C₆)alkyl-S, C(=O)O, C(=O)NH, (C₁-C₆)alkyl-C(=O)O, (C₁-C₆)alkyl-C(=O)NH or (C₁-C₆)alkyl-triazole group;
- **R₁₁** represents a hydrogen atom or a (C₁-C₆)alkyl group;
- **L** represents a linker;
- **RCG1** represents a reactive chemical group present at the end of the linker,

L being of formula (IV):



in which:

- **L1** represents
 - a single bond or a NR₁₆(hetero)aryl-CR₁₅R₁₄-O-C(=O) group if Y = (C₁-C₆)alkyl-N(R₁₁);
 - a NR₁₈-(C₂-C₆)alkyl-NR₁₇-C(=O) group or a NR₁₆(hetero)aryl-CR₁₅R₁₄-O-C(=O)-NR₁₈-(C₂-C₆)alkyl-NR₁₇-C(=O) group if Y = (C₁-C₆)alkyl-O or (C₁-C₆)alkyl-S;
 - a NR₁₆(hetero)aryl-CR₁₅R₁₄- group if Y = C(=O)O, C(=O)NH, (C₁-C₆)alkyl-C(=O)O or (C₁-C₆)alkyl-C(=O)NH;
- **R₁₁, R₁₄, R₁₅, R₁₆, R₁₇ and R₁₈** represent, independently of each other, a hydrogen atom or a (C₁-C₆)alkyl group;
- **(AA)_w** represents a sequence of **w** amino acids **AA** connected together *via* peptide bonds;
- **w** represents an integer ranging from 1 to 12;
- **L2** represents a single bond or a (C₁-C₆)alkyl group or a (C₁-C₆)alkyl-(OCH₂CH₂)_i group or a (C₁-C₆)alkyl-(OCH₂CH₂)_i-O(C₁-C₆)alkyl group or a (CH₂CH₂O)_i(C₁-C₆)alkyl group or a CH(SO₃H)-(C₁-C₆)alkyl group or a (C₁-C₆)alkyl-CH(SO₃H) group or a (C₁-C₆)alkyl-cyclohexyl group or a NR₁₉-(C₁-C₆)alkyl group or a NR₂₀-(CH₂CH₂O)_i(C₁-C₆)alkyl group or a NR₂₁-aryl group or a NR₂₁-heteroaryl group or a (C₁-C₆)alkyl-NR₂₂C(=O)-(C₁-C₆)alkyl group or a (C₁-C₆)alkyl-NR₂₂C(=O)-(C₁-C₆)alkyl-(OCH₂CH₂)_i group;
- **R₁₉, R₂₀, R₂₁ and R₂₂** represent, independently of each other, a hydrogen atom or a (C₁-C₆)alkyl group;
- **i** represents an integer between 1 and 50;

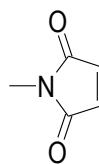
AA denotes a natural or unnatural amino acid, of configuration D or L, chosen from: alanine

(Ala), β -alanine, γ -aminobutyric acid, 2-amino-2-cyclohexylacetic acid, 2-amino-2-phenylacetic acid, arginine (Arg), asparagine (Asn), aspartic acid (Asp), citrulline (Cit), cysteine (Cys), α,α -dimethyl- γ -aminobutyric acid, β,β -dimethyl- γ -aminobutyric acid, glutamine (Gln), glutamic acid (Glu), glycine (Gly), histidine (His), isoleucine (Ile), leucine (Leu), lysine (Lys), ϵ -acetyl-lysine (AcLys), methionine (Met), ornithine (Orn), phenylalanine (Phe), proline (Pro), serine (Ser), threonine (Thr), tryptophan (Trp), tyrosine (Tyr), valine (Val);

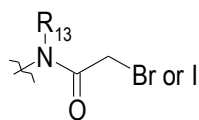
RCG1 being chosen from:

- C(=O)-Z_aR_a group for which

- 10
- Z_a represents a single bond, O or NH, and
 - R_a represents H or a (C₁-C₆)alkyl, (C₃-C₇)cycloalkyl, (C₅-C₁₀)aryl, (C₅-C₁₀)heteroaryl or (C₃-C₇)heterocycloalkyl group or a succinimidyl group;

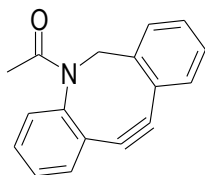


- one of the following reactive groups: the maleimido group; the haloacetamido



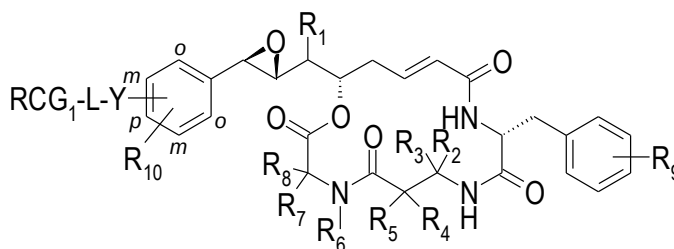
group with R₁₃ representing a hydrogen atom or a (C₁-C₆)alkyl group; -Cl; -N₃; -

OH; -SH; -NH₂;



- 15 -C≡CH, a group or a O-(C₁-C₆)alkyl hydroxylamine group.

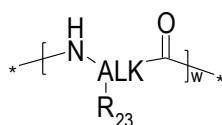
15. Cryptophycin payload of formula (II) according to claim 14, having the following structure:



- 20 16. Cryptophycin payload of formula (II) according to any one of claim 14 or 15, characterized in that Y represents (C₁-C₆)alkyl-NR₁₁ in which R₁₁ represents a hydrogen atom or a (C₁-C₆)alkyl group, preferably Y represents CH₂-NH.

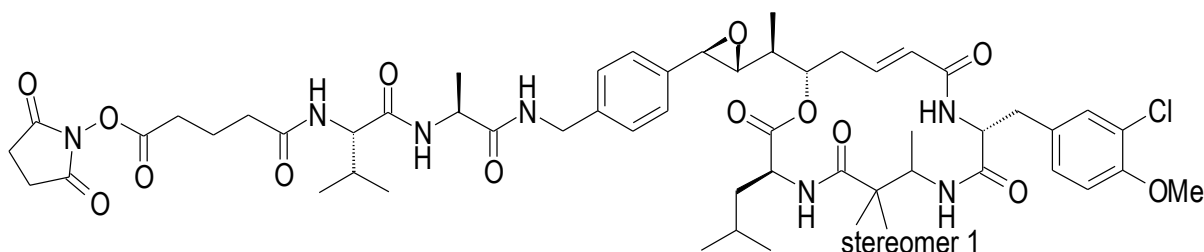
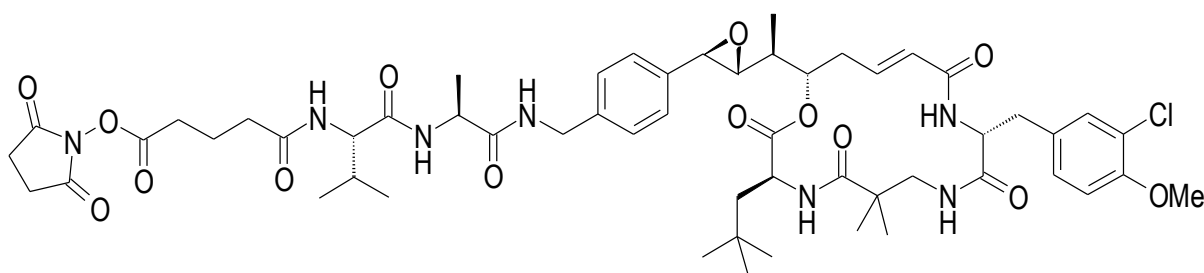
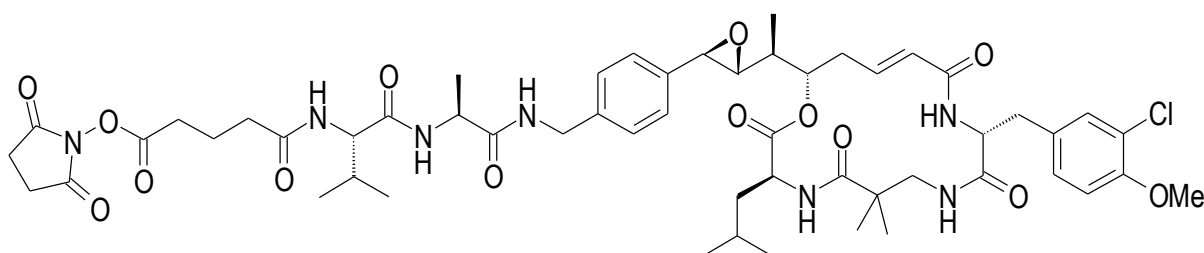
- 25 17. Cryptophycin payload of formula (II) according to claim 14, characterized in that the

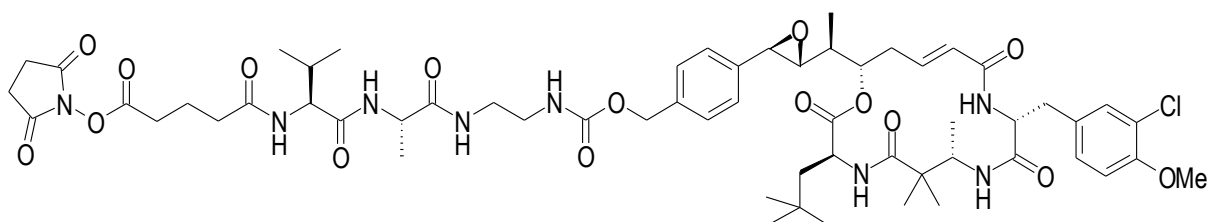
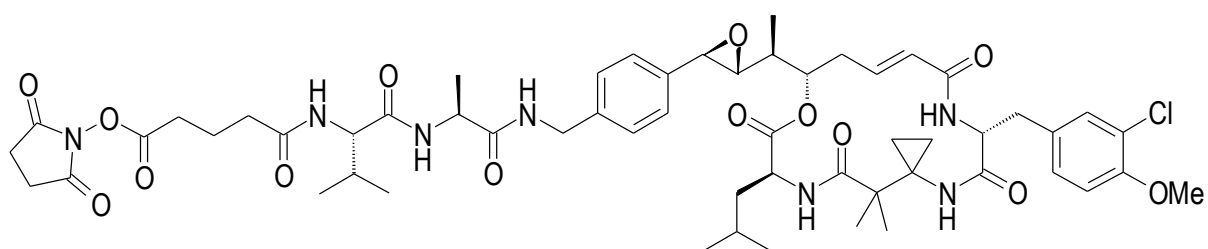
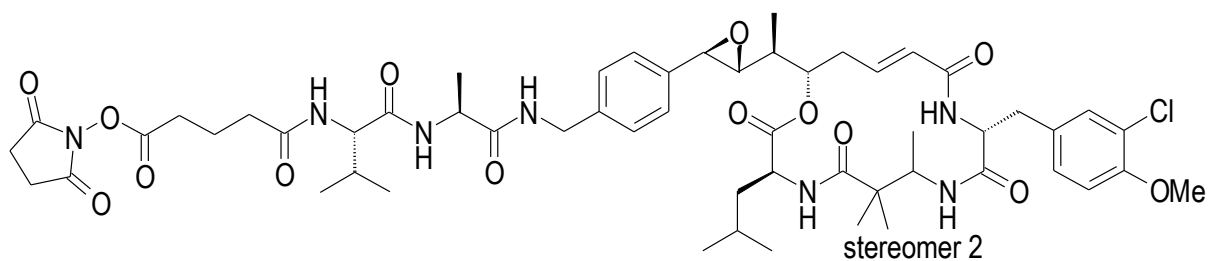
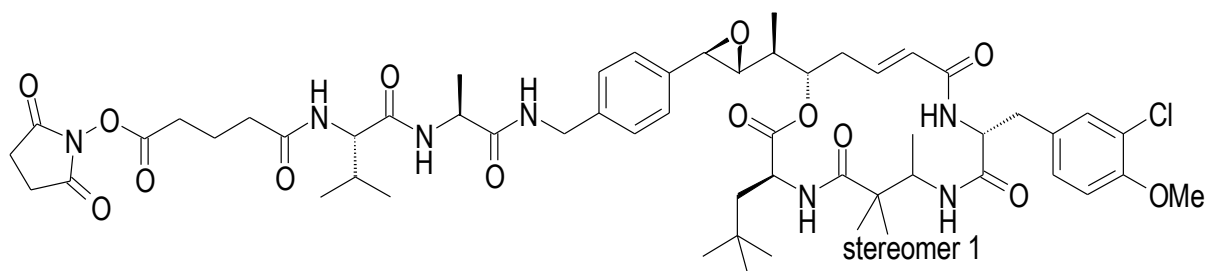
sequence (AA)_w has the formula:



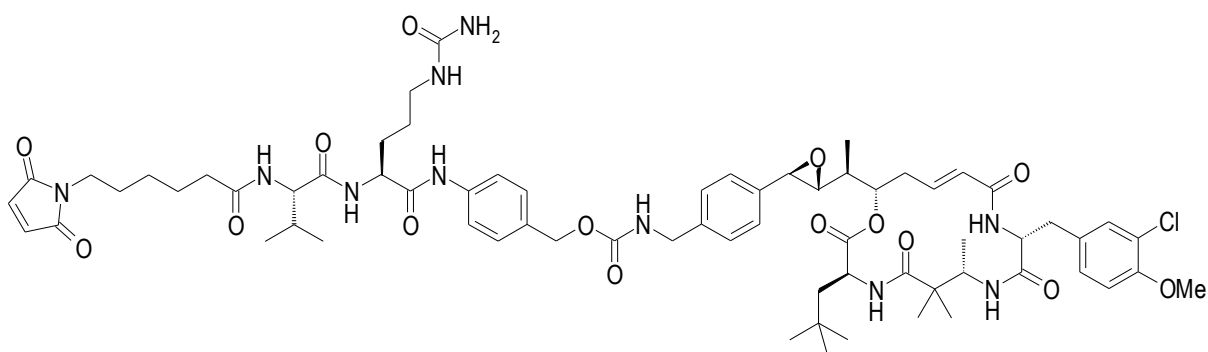
in which **R**₂₃ represents the side chain of AA and ALK represents a (C₁-C₁₂) alkylene group.

- 5 18. Cryptophycin payload of formula (II) according to any one of claim 14 or 15, characterized in that the sequence AA represents alanine (Ala), citrulline (Cit), glutamine (Gln), glycine (Gly), ε-acetyl-lysine (AcLys), valine (Val).
- 10 19. Cryptophycin payload of formula (II) according to claim 14, characterized in that L2 represents a (C1-C6)alkyl group or a (C1-C6)alkyl-(OCH₂CH₂)_i group or a CH(SO₃H)-(C1-C6)alkyl group
20. Cryptophycin payloads of formula (II) according to claim 14, which are selected from the following list:





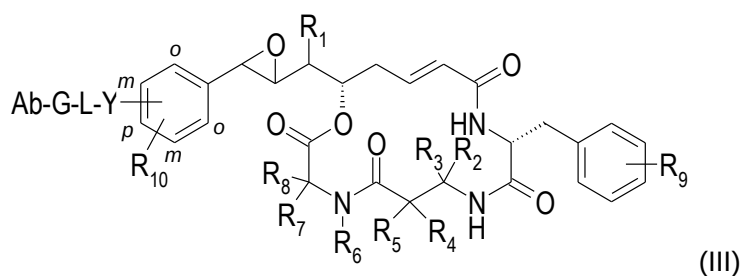
5



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15

21. Conjugate of formula (III):

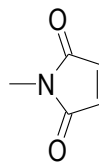


wherein

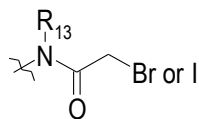
- **R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₉ and R₁₀** are as defined in claim 1 to 11;
- **Y** and **L** are as defined in claims 14 to 16;
- **G** represents the product of reaction between **RCG1**, a reactive group present at the end of the linker and **RCG2**, an orthogonal reactive group present on Ab;
- **Ab** represents an antibody;

RCG1 being chosen from:

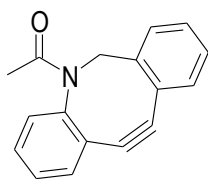
- **-C(=O)-Z_aR_a** group for which
 - Z_a represents a single bond, O or NH, and
 - R_a represents H or a (C₁-C₆)alkyl, (C₃-C₇)cycloalkyl, (C₅-C₁₀)aryl, (C₅-C₁₀)heteroaryl or (C₃-C₇)heterocycloalkyl group or a succinimidyl group;



- one of the following reactive groups: the maleimido group; the haloacetamido



- group with R₁₃ representing a hydrogen atom or a (C₁-C₆)alkyl group; -Cl; -N₃; -OH; -SH; -NH₂;



- C≡CH, a group or a O-(C₁-C₆)alkyl hydroxylamine group,

RCG2 being selected from:

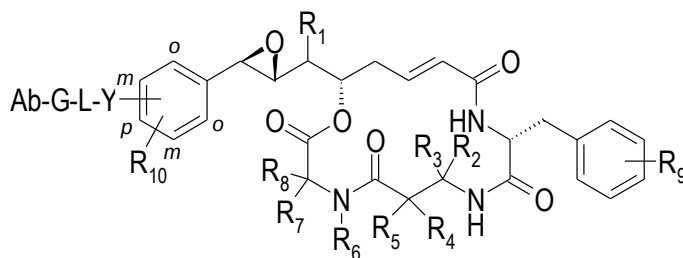
- ε-amino groups of lysines borne by the side chains of the lysine residues that are present at the surface of an antibody;
- α-amino groups of N-terminal amino acids of antibody heavy and light chains;
- saccharide groups of the hinge region;
- thiols of cysteines generated by reducing intra-chain disulfide bonds or the thiols of engineered cysteines;

- amide groups borne by the side chains of some glutamine residues that are present at the surface of an antibody;
- aldehyde groups introduced using formylglycine generating enzyme,

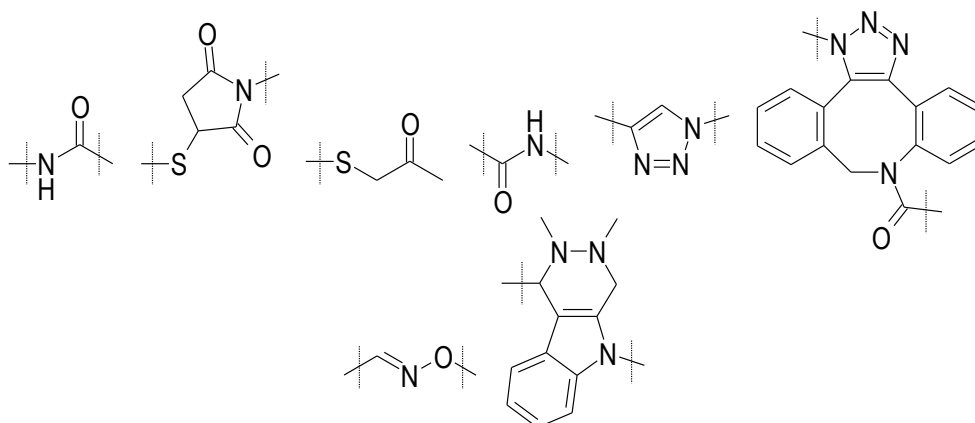
and wherein

- 5 • when **RCG1** represents a N-hydroxysuccinimidyl ester, **RCG2** represents a $-NH_2$ group;
- when **RCG1** represents a maleimido or haloacetamido function or a $-Cl$ group, **RCG2** represents a $-SH$ group;
- when **RCG1** represents a $-N_3$ group, **RCG2** represents a $-C\equiv CH$ group or an activated $C\equiv C$;
- 10 • when **RCG1** represents a $-OH$ or $-NH_2$ group, **RCG2** represents a carboxylic acid or amide function;
- when **RCG1** represents a $-SH$ group, **RCG2** represents a maleimido or haloacetamido function;
- when **RCG1** represents a $-C\equiv CH$ function or an activated $C\equiv C$, **RCG2** represents a $-N_3$ group;
- 15 • when **RCG1** represents a O-alkyl hydroxylamine function or a Pictet-Spengler reaction substrate, **RCG2** represents an aldehyde or ketone function.

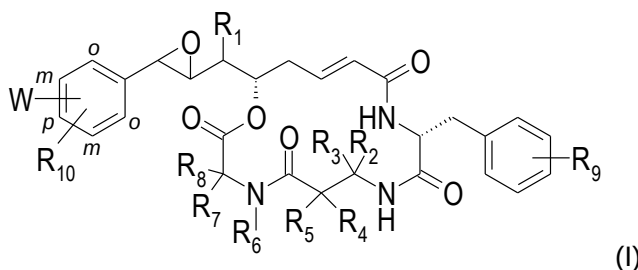
22. Conjugate of formula (III) according to claim 21 having the following structure:



23. Conjugate of formula (III) according to any one of claims 21 to 22, characterized in that **G** is selected from:



24. Process for preparing the cryptophycin compound of formula (I)



wherein:

- **R₁** represents a (C₁-C₆)alkyl group;
- **R₂** and **R₃** represent, independently of each other, a hydrogen atom or a (C₁-C₆)alkyl group;
 or alternatively **R₂** and **R₃** form together with the carbon atom to which they are attached a (C₃-C₆)cycloalkyl or a (C₃-C₆)heterocycloalkyl group;
- **R₄** and **R₅** represent, independently of each other, a hydrogen atom or a (C₁-C₆)alkyl group or a (C₁-C₆)alkyl-NH(R₁₂) group or a (C₁-C₆)alkyl-OH group or a (C₁-C₆)alkyl-SH group or a (C₁-C₆)alkyl-CO₂H group;
 or alternatively **R₄** and **R₅** form together with the carbon atom to which they are attached a (C₃-C₆)cycloalkyl or a (C₃-C₆)heterocycloalkyl group;
- **R₆** represents a hydrogen atom or a (C₁-C₆)alkyl group;
- **R₇** and **R₈** represent, independently of each other, a hydrogen atom or a (C₁-C₆)alkyl group or a (C₁-C₆)alkyl-CO₂H group or a (C₁-C₆)alkyl-N(C₁-C₆)alkyl₂ group;
 or alternatively **R₇** and **R₈** form together with the carbon atom to which they are attached a (C₃-C₆)cycloalkyl group or a (C₃-C₆)heterocycloalkyl group;
- **R₉** represents one or more substituents of the phenyl nucleus chosen, independently of each other, from: a hydrogen atom, -OH, (C₁-C₄)alkoxy, a halogen atom, -NH₂, -NH(C₁-C₆)alkyl or -N(C₁-C₆)alkyl₂ or -NH(C₁-C₆)cycloalkyl or (C₃-C₆)heterocycloalkyl;
- **R₁₀** represents at least one substituent of the phenyl nucleus chosen from a hydrogen atom

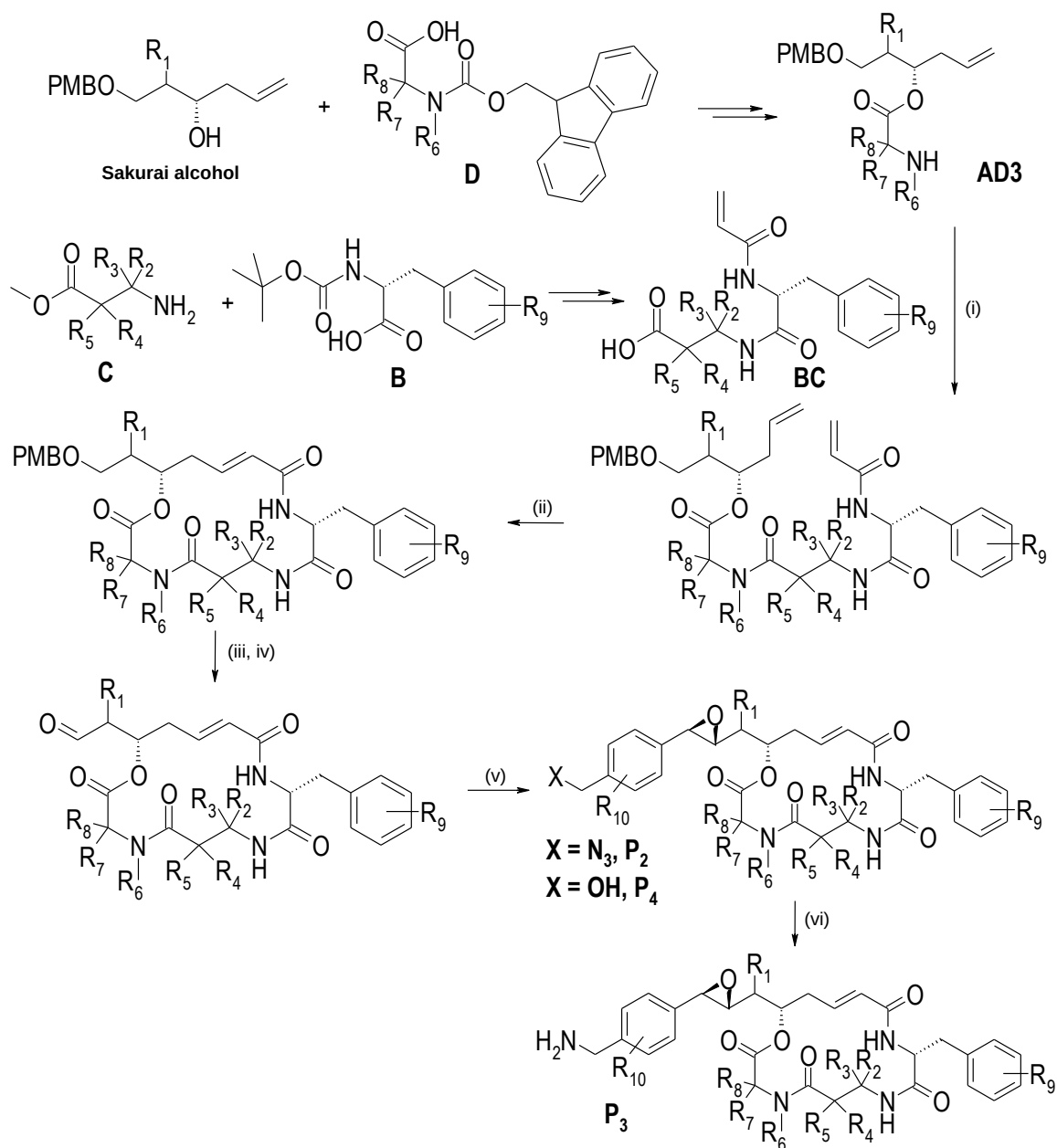
and (C₁-C₄)alkyl;

▪ **W** represents

- (C₁-C₆)alkyl-NH(R₁₁),
- (C₁-C₆)alkyl-OH,
- 5 • (C₁-C₆)alkyl-SH,
- CO₂H or C(=O)NH₂;
- (C₁-C₆)alkyl-CO₂H or (C₁-C₆)alkyl-C(=O)NH₂; or
- (C₁-C₆)alkyl-N₃.

▪ **R₁₁** and **R₁₂** represent, independently of each other, a hydrogen atom or a (C₁-C₆)alkyl group,

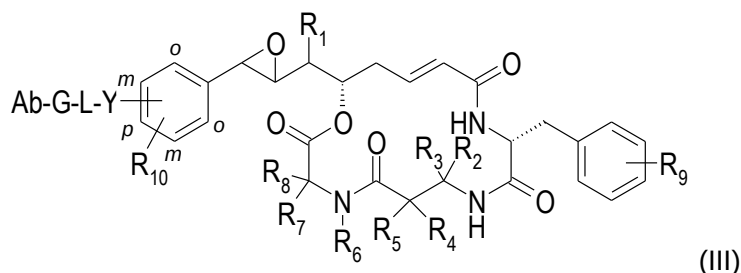
10 said process comprising the step:



wherein:

- Step (i) is a peptidic coupling between fragments AD3 and alternative BC in the presence of coupling reagents;
- Step (ii) is a macrocyclization by ring closing metathesis in the presence of a catalyst;
- Step (iii) is a deprotection of the *p*-methoxybenzyl ether in acidic conditions;
- 5 - Step (iv) is an oxidation of the alcohol using an oxidizing agent;
- Step (v) is an introduction of the epoxide by asymmetric Corey-Chaykovsky reaction using appropriately substituted isothiocineole-derived chiral sulfonium in the presence of a base;
- Step (vi) is a reduction of the azido group.

10 25. Process for preparing a conjugate of formula (III)



wherein

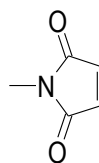
- **R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₉ and R₁₀** are as defined in claim 1 to 11;
- **Y** and **L** are as defined in claims 14 to 16;

- 15
- **G** represents the product of reaction between **RCG1**, a reactive group present at the end of the linker and **RCG2**, an orthogonal reactive group present on Ab;
 - **Ab** represents an antibody;

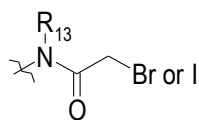
RCG1 being chosen from:

- **-C(=O)-Z_aR_a** group for which

- 20
- **Z_a** represents a single bond, O or NH, and
 - **R_a** represents H or a (C₁-C₆)alkyl, (C₃-C₇)cycloalkyl, (C₅-C₁₀)aryl, (C₅-C₁₀)heteroaryl or (C₃-C₇)heterocycloalkyl group or a succinimidyl group;

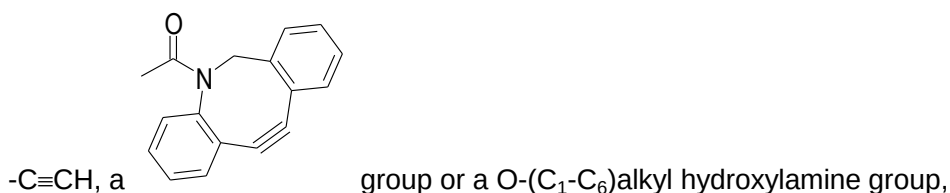


- one of the following reactive groups: the maleimido group; the haloacetamido



group with **R₁₃** representing a hydrogen atom or a (C₁-C₆)alkyl group; -Cl; -N₃; -

25 OH; -SH; -NH₂;



RCG2 being selected from:

- ε-amino groups of lysines borne by the side chains of the lysine residues that are present at the surface of an antibody;
- α-amino groups of N-terminal amino acids of antibody heavy and light chains;
- saccharide groups of the hinge region;
- thiols of cysteines generated by reducing intra-chain disulfide bonds or the thiols of engineered cysteines;
- amide groups borne by the side chains of some glutamine residues that are present at the surface of an antibody;
- aldehyde groups introduced using formylglycine generating enzyme,

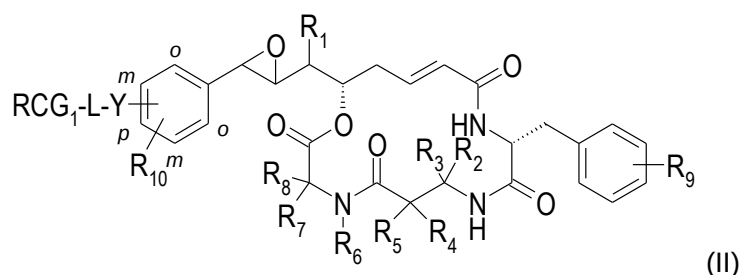
and wherein

- when **RCG1** represents a N-hydroxysuccinimidyl ester, **RCG2** represents a -NH₂ group;
- when **RCG1** represents a maleimido or haloacetamido function or a -Cl group, **RCG2** represents a -SH group;
- when **RCG1** represents a -N₃ group, **RCG2** represents a -C≡CH group or an activated C=C;
- when **RCG1** represents a -OH or -NH₂ group, **RCG2** represents a carboxylic acid or amide function;
- when **RCG1** represents a -SH group, **RCG2** represents a maleimido or haloacetamido function;
- when **RCG1** represents a -C≡CH function or an activated C=C, **RCG2** represents a -N₃ group;
- when **RCG1** represents a O-alkyl hydroxylamine function or a Pictet-Spengler reaction substrate, **RCG2** represents an aldehyde or ketone function,

said process comprising the steps of:

(i) placing in contact and leaving to react:

- an optionally buffered aqueous solution of an antibody, optionally modified by means of a modifying agent,
- and
- a solution of a cryptophycin payload of formula (II) as defined in one of claims 14 to 20

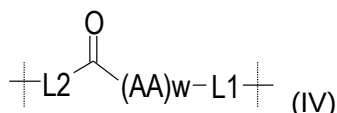


wherein

R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₉ and R₁₀ are as defined in claim 1 to 11, and

- **Y** is selected from (C₁-C₆)alkyl-NR₁₁, (C₁-C₆)alkyl-O, (C₁-C₆)alkyl-S, C(=O)O, C(=O)NH, (C₁-C₆)alkyl-C(=O)O, (C₁-C₆)alkyl-C(=O)NH or (C₁-C₆)alkyl-triazole group;
- **R₁₁** represents a hydrogen atom or a (C₁-C₆)alkyl group;
- **L** represents a linker;
- **RCG1** represents a reactive chemical group present at the end of the linker,

L being of formula (IV):



in which:

- **L1** represents
 - a single bond or a NR₁₆(hetero)aryl-CR₁₅R₁₄-O-C(=O) group if Y = (C₁-C₆)alkyl-N(R₁₁);
 - a NR₁₈-(C₂-C₆)alkyl-NR₁₇-C(=O) group or a NR₁₆(hetero)aryl-CR₁₅R₁₄-O-C(=O)-NR₁₈-(C₂-C₆)alkyl-NR₁₇-C(=O) group if Y = (C₁-C₆)alkyl-O or (C₁-C₆)alkyl-S;
 - a NR₁₆(hetero)aryl-CR₁₅R₁₄- group if Y = C(=O)O, C(=O)NH, (C₁-C₆)alkyl-C(=O)O or (C₁-C₆)alkyl-C(=O)NH;
- **R₁₁, R₁₄, R₁₅, R₁₆, R₁₇ and R₁₈** represent, independently of each other, a hydrogen atom or a (C₁-C₆)alkyl group;
- **(AA)_w** represents a sequence of **w** amino acids **AA** connected together *via* peptide bonds;
- **w** represents an integer ranging from 1 to 12;
- **L2** represents a single bond or a (C₁-C₆)alkyl group or a (C₁-C₆)alkyl-(OCH₂CH₂)_i group or a (C₁-C₆)alkyl-(OCH₂CH₂)_i-O(C₁-C₆)alkyl group or a (CH₂CH₂O)_i(C₁-C₆)alkyl group or a CH(SO₃H)-(C₁-C₆)alkyl group or a (C₁-C₆)alkyl-CH(SO₃H) group or a (C₁-C₆)alkyl-cyclohexyl group or a NR₁₉-(C₁-C₆)alkyl group or a NR₂₀-(CH₂CH₂O)_i(C₁-C₆)alkyl group or a NR₂₁-aryl group or a NR₂₁-heteroaryl group or a (C₁-C₆)alkyl-NR₂₂C(=O)-(C₁-C₆)alkyl group or a (C₁-C₆)alkyl-NR₂₂C(=O)-(C₁-C₆)alkyl-(OCH₂CH₂)_i group;
- **R₁₉, R₂₀, R₂₁ and R₂₂** represent, independently of each other, a hydrogen atom or a (C₁-C₆)alkyl group;
- **i** represents an integer between 1 and 50 ;

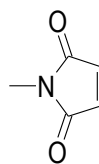
AA denotes a natural or unnatural amino acid, of configuration D or L, chosen from: alanine

(Ala), β -alanine, γ -aminobutyric acid, 2-amino-2-cyclohexylacetic acid, 2-amino-2-phenylacetic acid, arginine (Arg), asparagine (Asn), aspartic acid (Asp), citrulline (Cit), cysteine (Cys), α,α -dimethyl- γ -aminobutyric acid, β,β -dimethyl- γ -aminobutyric acid, glutamine (Gln), glutamic acid (Glu), glycine (Gly), histidine (His), isoleucine (Ile), leucine (Leu), lysine (Lys), ϵ -acetyl-lysine (AcLys), methionine (Met), ornithine (Orn), phenylalanine (Phe), proline (Pro), serine (Ser), threonine (Thr), tryptophan (Trp), tyrosine (Tyr), valine (Val);

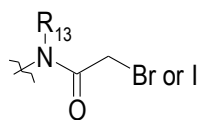
RCG1 being chosen from:

-C(=O)-Z_aR_a group for which

- Z_a represents a single bond, O or NH, and
- R_a represents H or a (C₁-C₆)alkyl, (C₃-C₇)cycloalkyl, (C₅-C₁₀)aryl, (C₅-C₁₀)heteroaryl or (C₃-C₇)heterocycloalkyl group or a succinimidyl group;

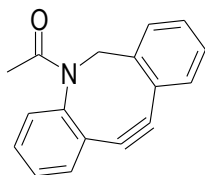


- one of the following reactive groups: the maleimido group; the haloacetamido



group with R₁₃ representing a hydrogen atom or a (C₁-C₆)alkyl group; -Cl; -N₃; -

OH; -SH; -NH₂;



-C≡CH, a group or a O-(C₁-C₆)alkyl hydroxylamine group,

the chemical group **RCG1** of the cryptophycin payload of formula (II) being reactive towards the chemical groups **RCG2** present on the antibody especially towards the amino groups present on antibodies, the said chemical groups **RCG2** having been introduced, where appropriate, by the modifying agent,

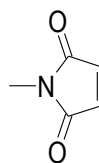
so as to attach the cryptophycin payload of formula (II) to the antibody by formation of a covalent bond;

(ii) and then optionally to separate the conjugate formed in step (i) from the cryptophycin payload of formula (II) and/or from the unreacted antibody and/or from any aggregates that may have formed,

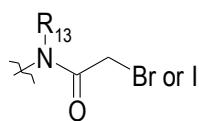
RCG1 being chosen from:

-C(=O)-Z_aR_a group for which

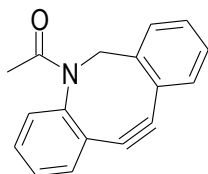
- Z_a represents a single bond, O or NH, and
- R_a represents H or a (C₁-C₆)alkyl, (C₃-C₇)cycloalkyl, (C₅-C₁₀)aryl, (C₅-C₁₀)heteroaryl or (C₃-C₇)heterocycloalkyl group or a succinimidyl group;



- one of the following reactive groups: the maleimido group; the haloacetamido



group with R_{13} representing a hydrogen atom or a (C_1-C_6) alkyl group; -Cl; -N₃; -OH; -SH; -NH₂;



-C≡CH, a group or a O-(C₁-C₆)alkyl hydroxylamine group,

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RCG2 being selected from:

- ε-amino groups of lysines borne by the side chains of the lysine residues that are present at the surface of an antibody;
- α-amino groups of N-terminal amino acids of antibody heavy and light chains;
- saccharide groups of the hinge region;
- thiols of cysteines generated by reducing intra-chain disulfide bonds or the thiols of engineered cysteines;
- amide groups borne by the side chains of some glutamine residues that are present at the surface of an antibody;
- aldehyde groups introduced using formylglycine generating enzyme,

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and characterized in that

- when **RCG1** represents a N-hydroxysuccinimidyl ester, **RCG2** represents a -NH₂ group;
- when **RCG1** represents a maleimido or haloacetamido function or a -Cl group, **RCG2** represents a -SH group;
- when **RCG1** represents a -N₃ group, **RCG2** represents a -C≡CH group or an activated C≡C;
- when **RCG1** represents a -OH or -NH₂ group, **RCG2** represents a carboxylic acid or amide function;
- when **RCG1** represents a -SH group, **RCG2** represents a maleimido or haloacetamido function;
- when **RCG1** represents a -C≡CH function or an activated C≡C, **RCG2** represents a -N₃ group;
- when **RCG1** represents a O-alkyl hydroxylamine function or a Pictet-Spengler reaction substrate, **RCG2** represents an aldehyde or ketone function.

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26. Medicament, characterized in that it comprises a conjugate of formula (III) according to any one of claims 21 to 23.

5 27. Pharmaceutical composition, characterized in that it comprises a conjugate of formula (III) according to any one of claims 21 to 23, and also at least one pharmaceutically acceptable excipient.

10 28. Cryptophycin compound of formula (I) according to any one of claims 1 to 13 for use in the treatment of cancer.

29. Conjugate of formula (III) according to any one of claims 21 to 23 for use in the treatment of cancer.