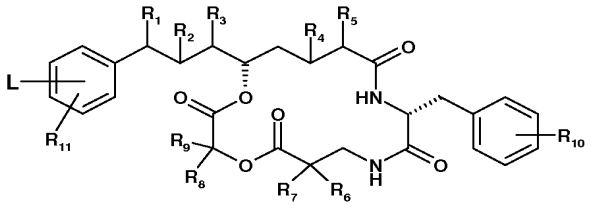
1. A compound of formula (II):



(II)

in which:

- **R_1** represents a halogen atom and **R_2** represents an –OH, an acyl group derived from an amino acid **AA**, or a (C_1-C_4)alkanoyloxy group
  or alternatively **R_1** and **R_2** form an epoxide unit;
- **AA** denotes a natural or unnatural amino acid;
- **R_3** represents a (C_1-C_6)alkyl group;
- **R_4** and **R_5** both represent H or together form a double bond CH=CH between C13 and C14;
- **R_6** and **R_7** represent, independently of each other, H or a (C_1-C_6)alkyl group;
- **R_8** and **R_9** represent, independently of each other, H or a (C_1-C_6)alkyl group;
- **R_{10}** represents at least one substituent of the phenyl nucleus chosen from: H, an OH, (C_1-C_4)alkoxy, a halogen atom, -NH_2, -NH(C_1-C_6)alkyl or -N(C_1-C_6)alkyl$_2$;
- **R_{11}** represents at least one substituent of the phenyl nucleus chosen from H and a (C_1-C_4)alkyl group;
- **L** represents a linker in the ortho (o), meta (m) or para (p) position of the phenyl nucleus bearing the unit RCG_1 chosen from:

-G' X $(CR_{13}R_{14})_t(OCH_2CH_2)_y(CR_{15}R_{16})_u$ Q RCG_1;

-G' X $(CR_{13}R_{14})_t(OCH_2CH_2)_y$-Y'-$(CR_{15}R_{16})_u$ Q RCG_1;

-G' X $(CR_{13}R_{14})_t(CR_{17}=CR_{18})(CR_{15}R_{16})_u(OCH_2CH_2)_y$ Q RCG_1;

-G' X $(CR_{13}R_{14})_t(OCH_2CH_2)_y(CR_{17}=CR_{18})(CR_{15}R_{16})_u$ Q RCG_1;

-G' X $(CR_{13}R_{14})_t$-phenyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G' X $(CR_{13}R_{14})_t$-furyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G' X $(CR_{13}R_{14})_t$-oxazolyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G' X $(CR_{13}R_{14})_t$-thiazolyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G' X $(CR_{13}R_{14})_t$-thienyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G' X $(CR_{13}R_{14})_t$-imidazolyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G' X $(CR_{13}R_{14})_t$-piperazinyl-$CO(CR_{15}R_{16})_u$ Y' Q RCG_1; -G' X $(CR_{13}R_{14})_t$-piperidyl-methyl-NR_{12}-$CO(CR_{15}R_{16})_u$ Y' Q RCG_1; -G' X $(CR_{13}R_{14})_t$-piperidyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G' X $(CR_{13}R_{14})_t$-piperidyl-NR_{12}-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G' X $(CR_{13}R_{14})_t$-triazolyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G' X $(CR_{13}R_{14})_t$-triazolyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1;
-G' X $(CR_{13}R_{14})_t$-phenyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G' X $(CR_{13}R_{14})_t$-furyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G' X $(CR_{13}R_{14})_t$-oxazolyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G' X $(CR_{13}R_{14})_t$-thiazolyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G' X $(CR_{13}R_{14})_t$-thienyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G' X $(CR_{13}R_{14})_t$-imidazolyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G' X $(CR_{13}R_{14})_t$-piperazinyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G' X $(CR_{13}R_{14})_t$-piperidyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G' X $(CR_{13}R_{14})_t$-piperidyl-methyl-NR_{12}-$(CR_{15}R_{16})_u$ Q RCG_1; -G' X $(CR_{13}R_{14})_t$-piperidyl-NR_{12}-$(CR_{15}R_{16})_u$ Q RCG_1; -G' X $(CR_{13}R_{14})_t$-triazolyl-$(CR_{15}R_{16})_u$ Q RCG_1;
-G" Y $(CR_{13}R_{14})_t(OCH_2CH_2)_y(CR_{15}R_{16})_u$ Q RCG_1;
-G" Y $(CR_{13}R_{14})_t(OCH_2CH_2)_y$-Y'-$(CR_{15}R_{16})_u$ Q RCG_1;
-G" Y $(CR_{13}R_{14})_t(CR_{17}=CR_{18})(CR_{15}R_{16})_u(OCH_2CH_2)_y$ Q RCG_1;
-G" Y $(CR_{13}R_{14})_t(OCH_2CH_2)_y(CR_{17}=CR_{18})(CR_{15}R_{16})_u$ Q RCG_1;
-G" Y $(CR_{13}R_{14})_t$-phenyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-furyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-oxazolyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-thiazolyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-thienyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-imidazolyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-piperazinyl-$CO(CR_{15}R_{16})_u$ Y' Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-piperidyl-methyl-NR_{12}-$CO(CR_{15}R_{16})_u$ Y' Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-piperidyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-piperidyl-NR_{12}-$(CR_{15}R_{16})_u$ Y' Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-triazolyl-$(CR_{15}R_{16})_u$ Y' Q RCG_1;
-G" Y $(CR_{13}R_{14})_t$-phenyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-furyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-oxazolyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-thiazolyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-thienyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-imidazolyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-piperazinyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-piperazinyl-$(CR_{15}R_{16})_u$ Q CCR_1; G" Y $(CR_{13}R_{14})_t$-piperidyl-$(CR_{15}R_{16})_u$ Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-piperidyl-methyl-NR_{12}-$(CR_{15}R_{16})_u$ Q RCG_1; -G" Y $(CR_{13}R_{14})_t$-piperidyl-NR_{12}-$(CR_{15}R_{16})_u$ Q RCG_1; or -G" Y $(CR_{13}R_{14})_t$-triazolyl-$(CR_{15}R_{16})_u$ Q RCG_1;
in which formulae:

G' represents a -CH=CH- or $-(CH_2)_n-$ group;

G" represents a $-(CH_2)_n-$ group;

n represents an integer ranging from 1 to 6;

X represents a single bond or a -CO-, -COO- or -$CONR_{12}$-, wherein the CO is attached to **G'**;

Y represents a -O-, -OCO-, -OCOO-, -$OCONR_{12}$-, -NR_{12}-, -$NR_{12}CO$-, -$NR_{12}CONR'_{12}$-, -$NR_{12}COO$- or -$S(O)_q$-, wherein the O and the NR_{12} are attached to G'';

q represents an integer that may be 0, 1 or 2;

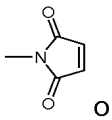
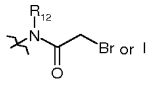
Y' represents a -O-, -OCO-, -OCOO-, -$OCONR_{12}$-, -NR_{12}-, -$NR_{12}CO$-, -$NR_{12}CONR'_{12}$-, -$NR_{12}COO$-, -$S(O)_q$-, -CO-, -COO-, or -$CONR_{12}$-;

R_{12}, R'_{12}, R_{13}, R_{14}, R_{15}, R_{16}, R_{17} and **R_{18}** represent, independently of each other, H or a (C_1-C_6)alkyl group;

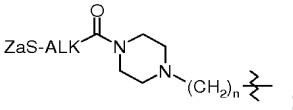
t, **u** and **y** represent integers that may range from 0 to 20 and such that t+u+y is greater than or equal to 1;

in the case of the linker of formula –G"Y$(CR_{13}R_{14})_t(OCH_2CH_2)_Y$-Y'-$(CR_{15}R_{16})_u$ Q RCG_1, if y is 0 and Q represents a single bond, then u cannot be 0;

Q represents a single bond, a (C_1-C_{10})alkylene group or a $(OCH_2CH_2)_I$ group, wherein i is an integer ranging from 1 to 20;

RCG1 represents –SZ_a, -C(=O)-Z_bR_b,  or  with R_{12} representing H or (C_1-C_6)alkyl;

or **L** is chosen from: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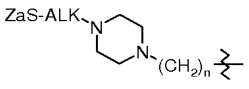
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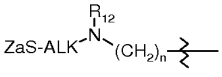
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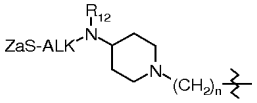
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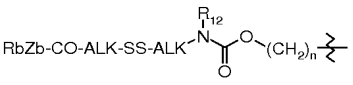
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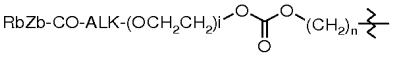
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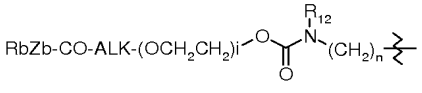
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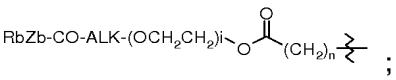
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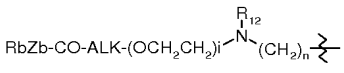
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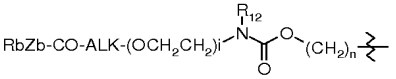
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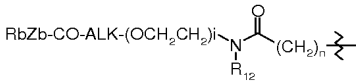
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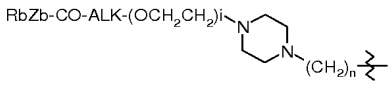

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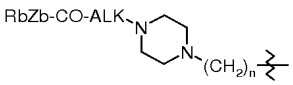

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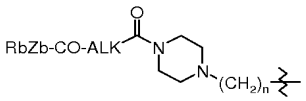

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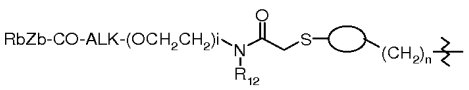

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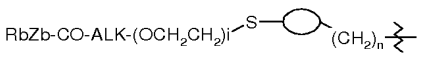

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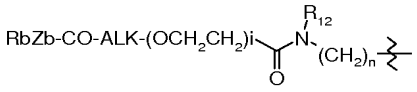

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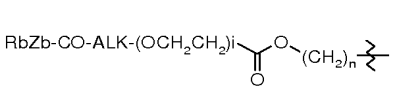

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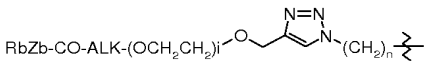

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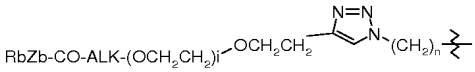

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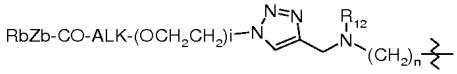

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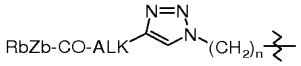

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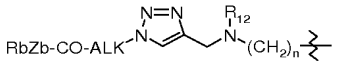

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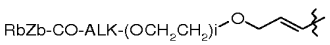

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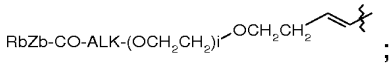

;RbZb-CO-ALK

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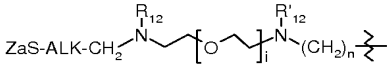

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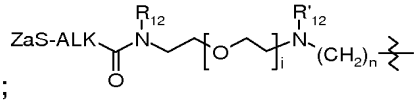

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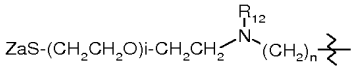

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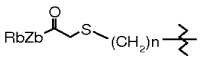

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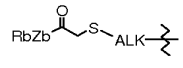
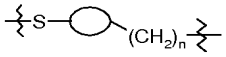


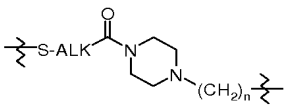
; -ALK-SZ_a; or

-$(CH_2)_n$-SZ_a;

in which formulae:



represents one of the following 9 groups:



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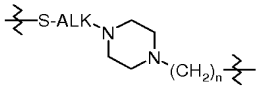

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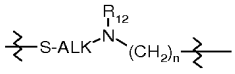

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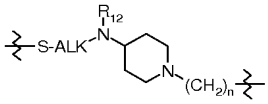

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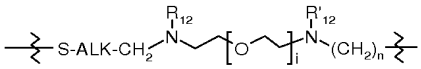

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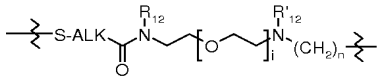

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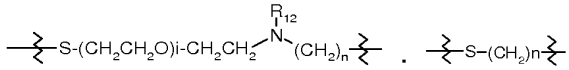

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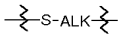
or 

;

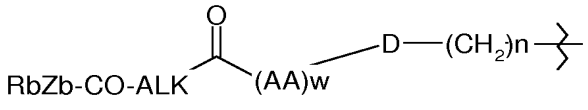
n represents an integer ranging from 1 to 6;

ALK represents a group $(C_1\text{-}C_{12})$alkylene;

$\mathbf{R_{12}}$ and $\mathbf{R'_{12}}$ represent, independently of each other, H or a group $(C_1\text{-}C_6)$alkyl;

i represents an integer ranging from 1 to 20;

or alternatively **L** is a linker of formula (IV):



(IV)

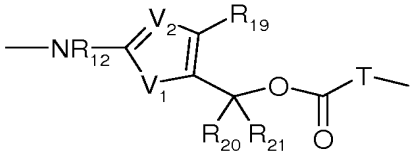
in which:

$\mathbf{(AA)_w}$ represents a sequence of **w** amino acids **AA** connected together via peptide bonds;

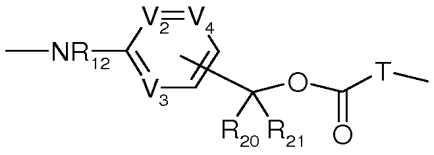
w represents an integer ranging from 1 to 12;

n represents an integer ranging from 1 to 6;

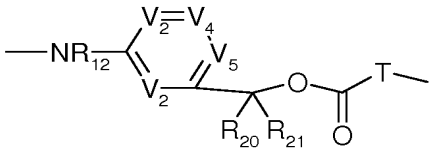
D represents one of the following units:



(D1)



(D2)



(D3)

for which:

$\mathbf{R_{12}}$ represents H or a $(C_1\text{-}C_6)$alkyl group;

$\mathbf{R_{19}}$, $\mathbf{R_{20}}$, $\mathbf{R_{21}}$ and $\mathbf{R_{22}}$ represent, independently of each other, H, a halogen atom, -OH,

-CN or a $(C_1\text{-}C_4)$alkyl group;

T attached to $(CH_2)_n$ represents NR_{12} or O;

$\mathbf{V_1}$ represents O, S or NR_{12};

$\mathbf{V_2}$ represents CR_{22} or N;

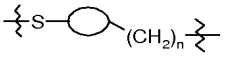
$\mathbf{V_3}$, $\mathbf{V_4}$ and $\mathbf{V_5}$ are chosen, independently of each other, from CR_{22} and N;

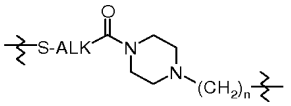
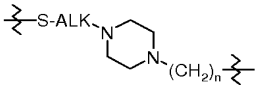
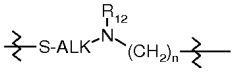
- $\mathbf{Z_a}$ represents H or the group $-SR_a$, wherein $\mathbf{R_a}$ represents a $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_7)$cycloalkyl, aryl, heteroaryl or $(C_3\text{-}C_7)$heterocycloalkyl;

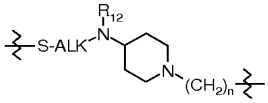
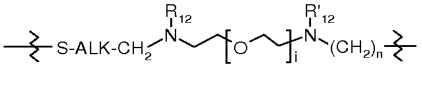
- $\mathbf{Z_b}$ represents a single bond, -O- or -NH-, wherein $\mathbf{R_b}$ represents H, (C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, aryl, heteroaryl or (C_3-C_7)heterocycloalkyl.

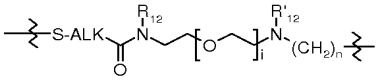
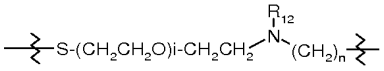
2. The compound according to Claim 1, in which $\mathbf{R_{10}}$ represents at least one substituent on the phenyl nucleus chosen from: H, an OH, (C_1-C_4)alkoxy, or a halogen atom.

3. The compound according to Claim 1, in which RCG1 represents $-SZ_a$ or -C(=O)-Z_bR_b.

4. The compound according to Claim 1, in which  represents one of the following 7 groups:

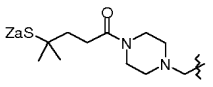
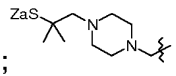
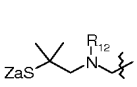
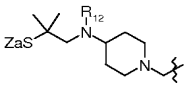
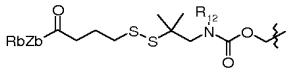
 ;  ;  ;

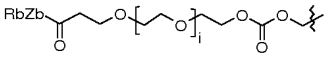
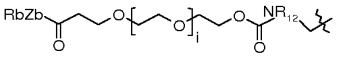
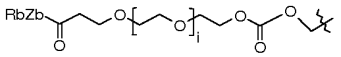
 ;  ;

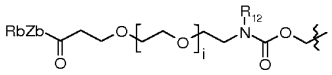
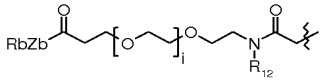
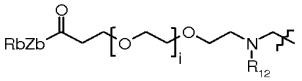
 ; or  .

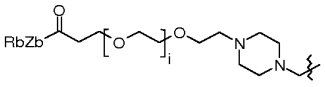
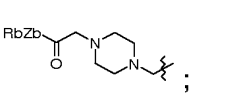
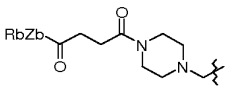
5. The compound according to Claim 1, in which n is 1.

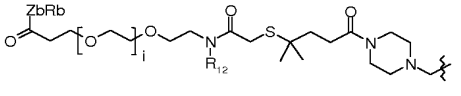
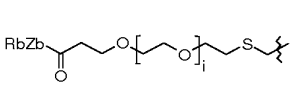
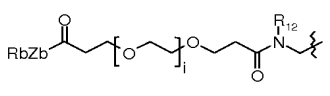
6. The compound according to Claim 1, in which L is chosen from:

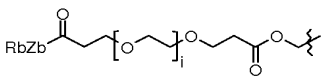
 ;  ;  ;  ;  ;

 ;  ;  ;

 ;  ;  ;

 ;  ;  ;

 ;  ;  ;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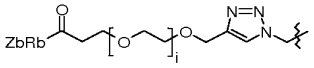
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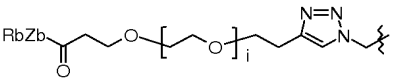
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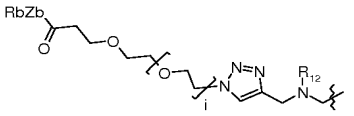
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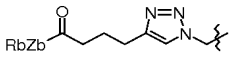
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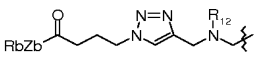
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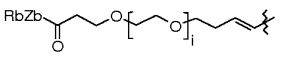
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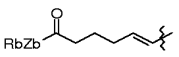
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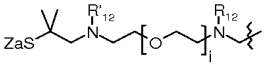
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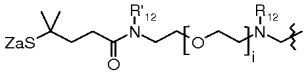
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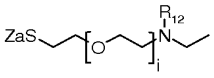
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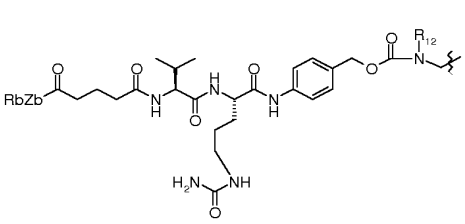
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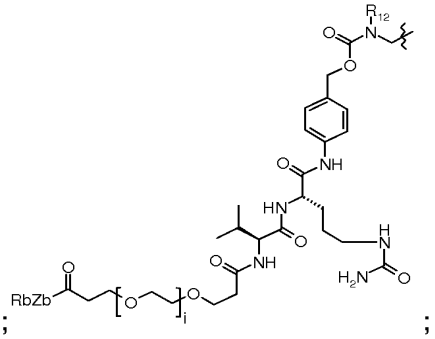
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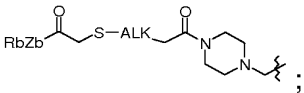
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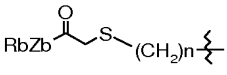
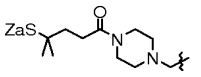

; -CH_2SZ_a ; or -ALK-SZ_a.

7. The compound according to Claim 1, in which L is chosen from: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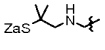
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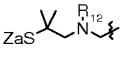
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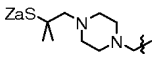
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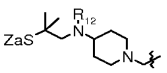
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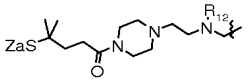
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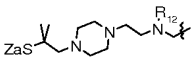
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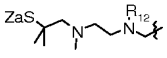
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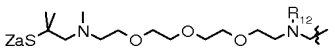
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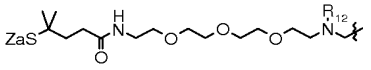
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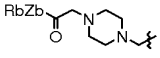
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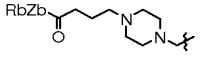
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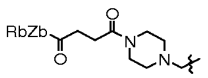
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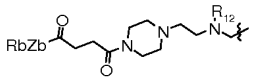
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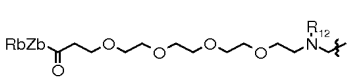
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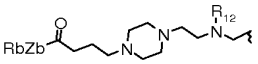
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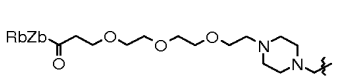
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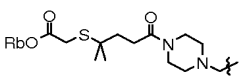
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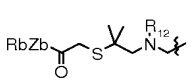
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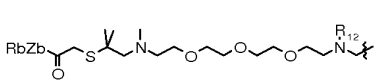
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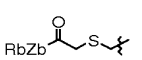
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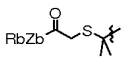
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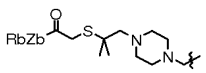
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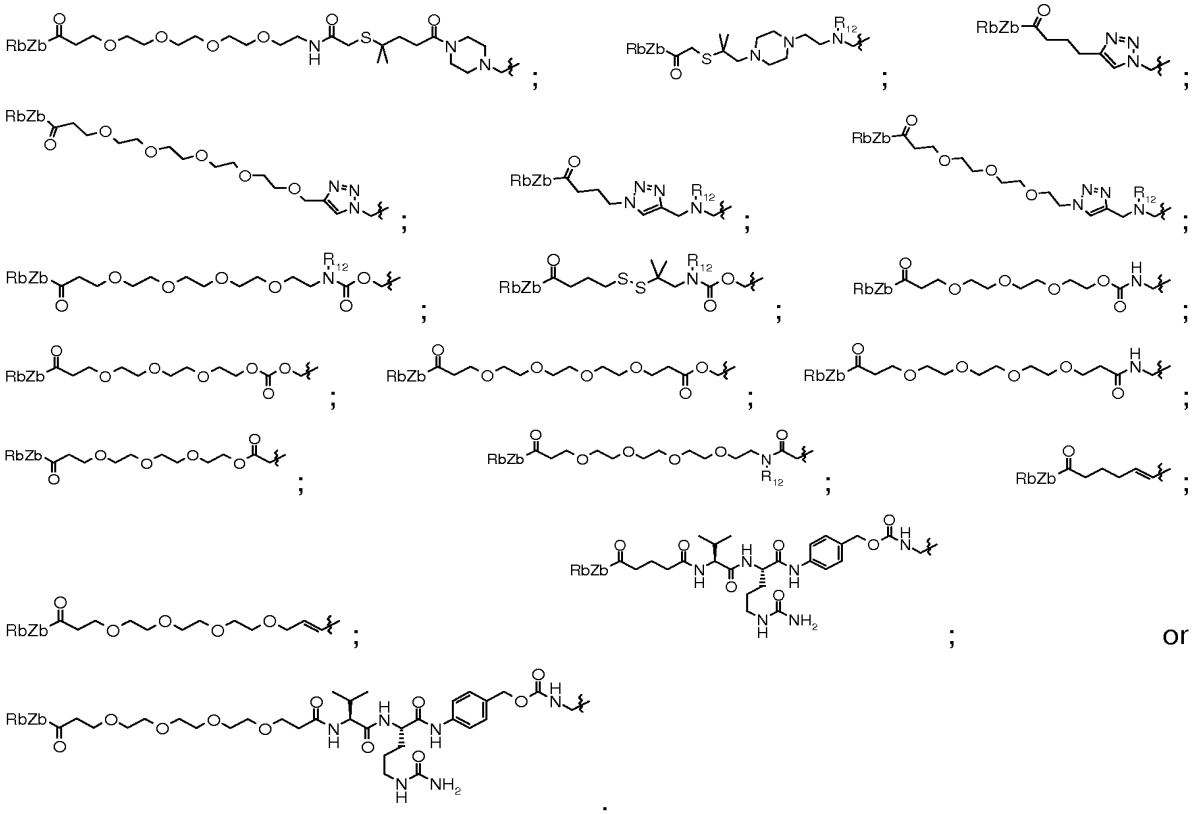
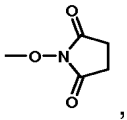
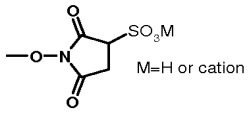
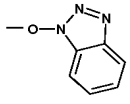
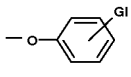
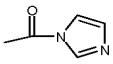
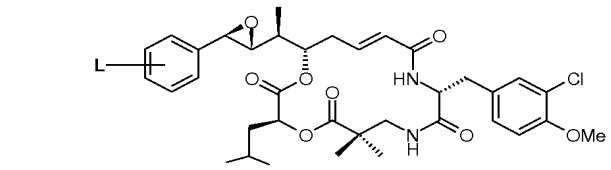
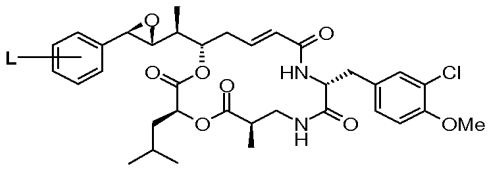
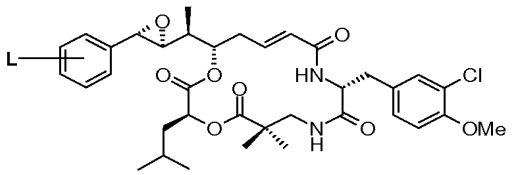
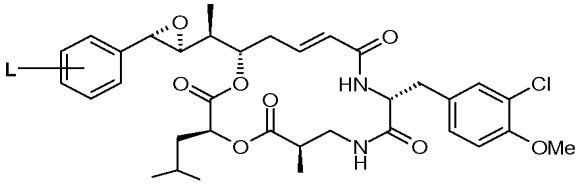
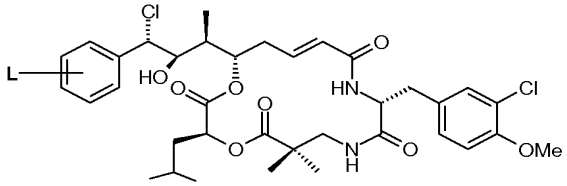
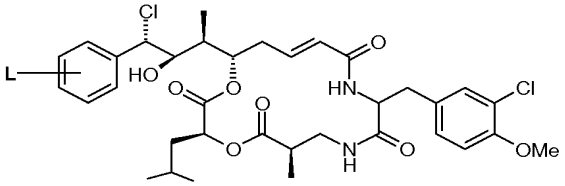
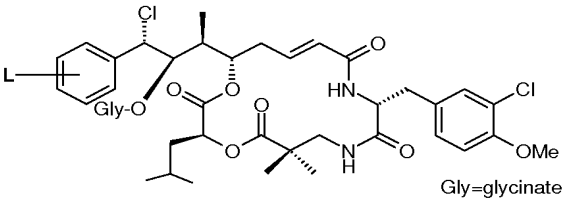
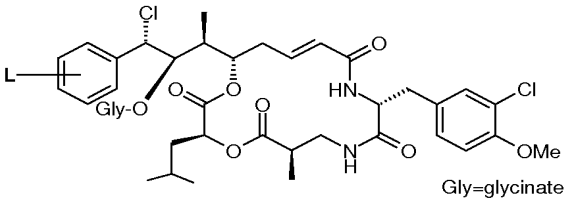


8. The compound according to Claim 7, in which R_{12} represents H.

9. The compound according to Claim 7, in which R_{12} represents (C_1-C_6)alkyl.

10. The compound according to Claim 1, in which $\mathbf{Z_a}$ represents H, –S(C_1-C_6)alkyl, or –S-heteroaryl; or $\mathbf{Z_bR_b}$ represents –O(C_1-C_6)alkyl, -OH, -OCH_3, -$OCH_2CH{=}CH_2$,  ,  ,  or the group  in which **Gl** represents at least one electroinductive group; or alternatively in which –C(=O)Z_bR_b represents  .

11. The compound according to Claim 1 defined according to one of the following formulae:








Gly=glycinate or

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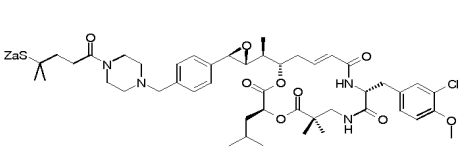
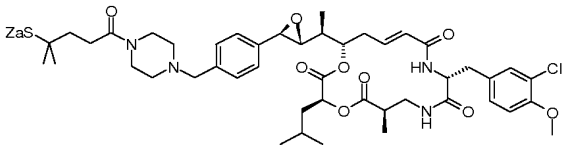
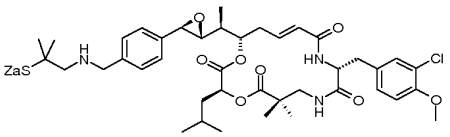
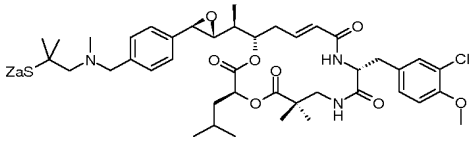
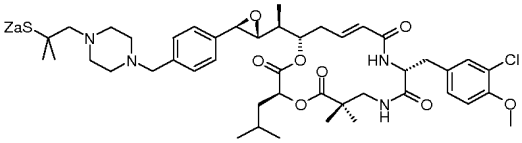
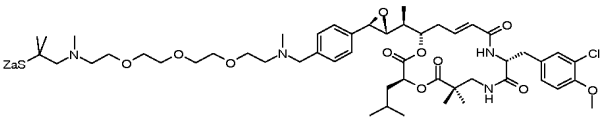
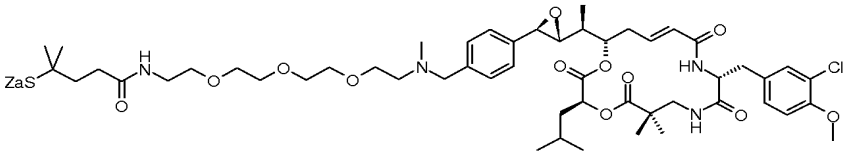
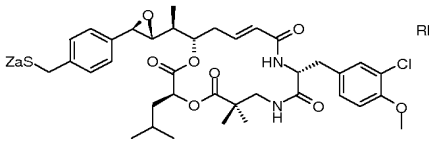
12. The compound according to Claim 1, chosen from: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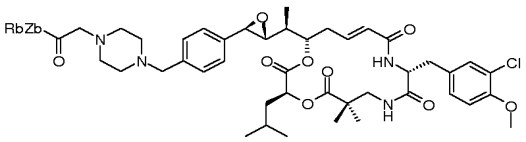
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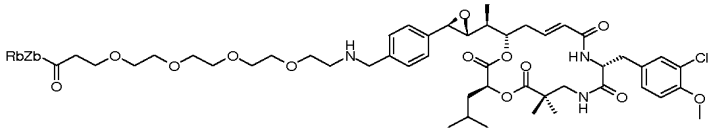
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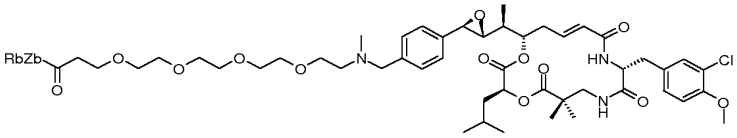
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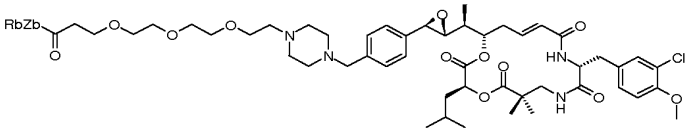
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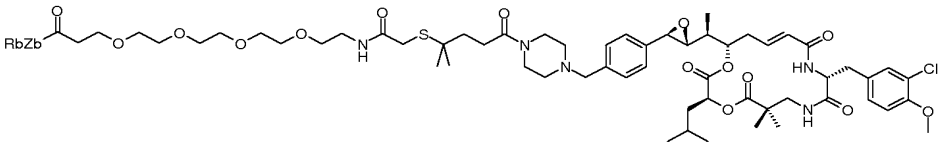
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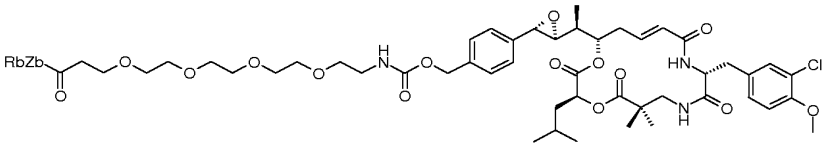
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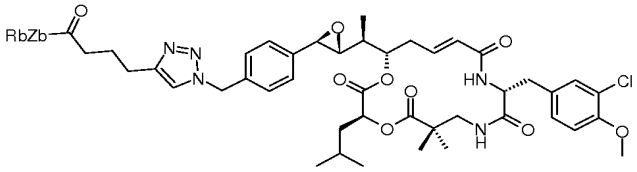
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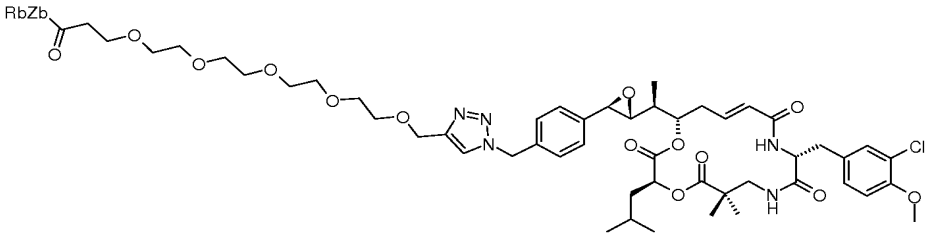
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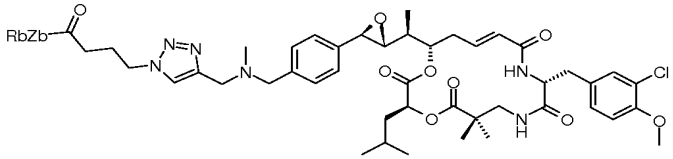
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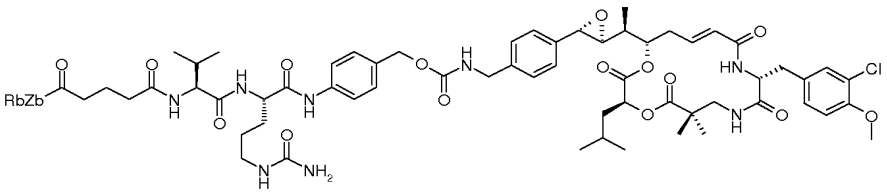
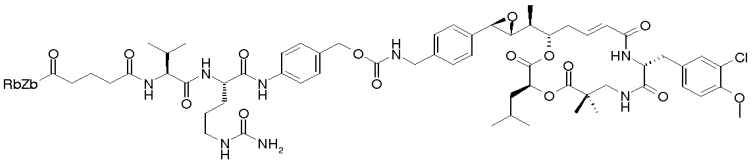
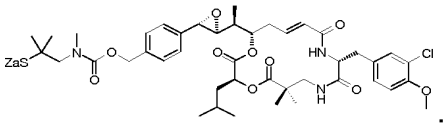
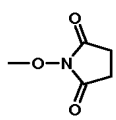
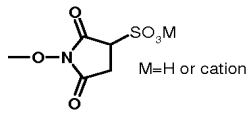
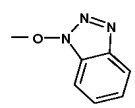
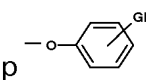
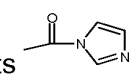
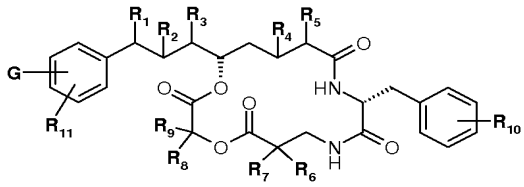




or  .

13. The compound according to Claim 12, in which $\mathbf{Z_a}$ represents H, –S(C_1-C_6)alkyl, or –S-heteroaryl; or $\mathbf{Z_bR_b}$ represents –O(C_1-C_6)alkyl, -OH, -OCH_3, -$OCH_2CH{=}CH_2$,  ,  ,  or the group  in which **Gl** represents at least one electroinductive group; or alternatively in which –C(=O)Z_bR_b represents  .

14. A compound of formula (III):



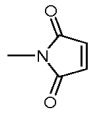
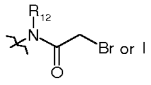
in which:

- $\mathbf{R_1}$ represents a halogen atom and $\mathbf{R_2}$ represents an –OH, an acyl group derived from an amino acid **AA**, or a (C_1-C_4)alkanoyloxy group;

or alternatively $\mathbf{R_1}$ and $\mathbf{R_2}$ form an epoxide unit;

- **AA** denotes a natural or unnatural amino acid;
- $\mathbf{R_3}$ represents a (C_1-C_6)alkyl group;
- $\mathbf{R_4}$ and $\mathbf{R_5}$ both represent H or together form a double bond CH=CH between C13 and C14;
- $\mathbf{R_6}$ and $\mathbf{R_7}$ represent, independently of each other, H or a (C_1-C_6)alkyl group;

- **R_8** and **R_9** represent, independently of each other, H or a (C_1-C_6)alkyl group;
- **R_{10}** represents at least one substituent of the phenyl nucleus chosen from: H, an OH, (C_1-C_4)alkoxy, a halogen atom, -NH_2, -NH(C_1-C_6)alkyl or -N(C_1-C_6)alkyl$_2$;
- **R_{11}** represents at least one substituent of the phenyl nucleus chosen from H and a (C_1-C_4)alkyl group; and
- **G** represents a group -$(CH_2)_n$Y, which is in an ortho (o), meta (m) or para (p) position on the phenyl nucleus bearing the unit CR_1,

n is an integer ranging from 1 to 6, and Y denoting Cl, -N_3, OH, NH_2, -NR_{12}-CH_2-C≡CH in which **R_{12}** represents H; (C_1-C_6)alkyl; -OMs; -OC(=O)-O-(4-nitrophenyl);  ; or 

, wherein R_{12} represents H or (C_1-C_6)alkyl.

15. The compound according to Claim 14, in which Y represents -N_3; -NR_{12}-CH_2-C≡CH, in which R_{12} represents H; (C_1-C_6)alkyl; -OMs or -OC(=O)-O-(4-nitrophenyl).

16. The compound according to Claim 14, wherein G is -$(CH_2)_n$Y with Y is -Cl, -N_3, -OH, -NH_2, maleimido or haloacetamido.

17. The compound according to claim 1 wherein said compound is conjugated to a binding agent.

18. The compound according to claim 14 wherein said compound is conjugated to a binding agent.

19. The compound according to Claim 17, in which the binding agent is a ligand, a protein, an antibody, a protein , or antibody fragment, a peptide, an oligonucleotide, or an oligosaccharide.

20. The compound according to Claim 18, in which the binding agent is a ligand, a protein, an antibody, a protein or antibody fragment, a peptide, an oligonucleotide, or an oligosaccharide.

21. A process for preparing a cryptophycin conjugate, said process comprising:

(i) placing in contact and leaving to react an aqueous solution of an optionally buffered binding agent and a solution of a compound of claim 1;

(ii) and then optionally separating the conjugate formed in step (i) from the cryptophycin derivative or the unreacted binding agent or any aggregates formed, or any combination thereof.

22. The process according to Claim 21, wherein

- when the compound comprises a reactive chemical group RCG1 of the type $–SZ_a$, the binding agent comprises:
  - disulfide chemical groups in the case where RCG1 represents –SH;
  - thiol chemical groups in the case where RCG1 represents $-SZ_a$ with $Z_a \neq H$; or
  - maleimido or iodoacetamido chemical groups in the case where RCG1 represents –SH;
- when the compound comprises a reactive chemical group RCG1 of the type $–C(=O)-Z_bR_b$, the compound is reacted with the amino functions of the binding agent; or
- when the compound comprises a reactive chemical group RCG1 of maleimido or haloacetamido type, the binding agent comprises thiol chemical groups.

23. A process for preparing a cryptophycin conjugate, said process comprising:

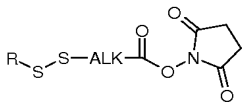
(i) placing in contact and leaving to react an aqueous solution of an optionally buffered binding agent and a solution of a compound of claim 14;

(ii) and then optionally separating the conjugate formed in step (i) from the cryptophycin derivative or the unreacted binding agent or any aggregates formed, or any combination thereof.

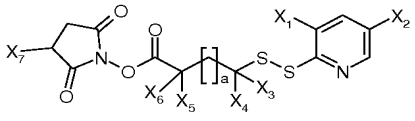
24. The process according to Claim 23, wherein when G is $-(CH_2)_nY$, the binding agent comprises –SH when Y is -Cl or -maleimido, $-C\equiv CH$ when Y is $-N_3$, or carboxylic acid groups when Y is -OH or $-NH_2$.

25. The process according to Claim 21, in which:

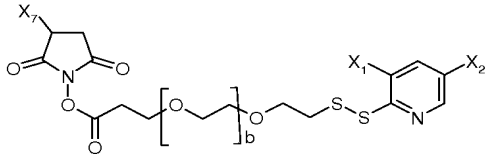
- when the compound comprises a reactive chemical group RCG1 of the type $-SZ_a$, the binding agent is modified with a modifying agent chosen from a compound of formula:



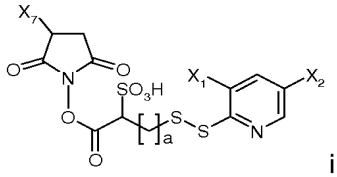
in which R represents a (C_1-C_6)alkyl, aryl, heteroaryl, (C_3-C_7)cycloalkyl, or (C_3-C_7)heterocycloalkyl, wherein ALK represents a (C_1-C_6)alkylene;



; a pegylated analogue of formula:

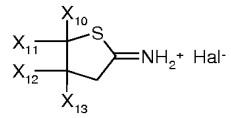


; or a sulfonic analogue of formula



in which:

- X_3, X_4, X_5 and X_6 represent H or a (C_1-C_6)alkyl; X_1 and X_2 represent -H, -$CONX_8X_9$, or -NO_2; X_8 and X_9 representing H or a (C_1-C_6)alkyl, X_7 represents -$SO_3^-M^+$, H, or a quaternary ammonium group; a denotes an integer ranging from 0 to 4; and b denotes an integer ranging from 0 to 2000; and



in which:

- Hal represents a halogen atom;

- each of the X_{11}, X_{12} and X_{13} independently represents a hydrogen atom or may represent X_3;

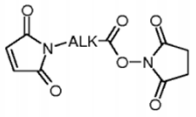
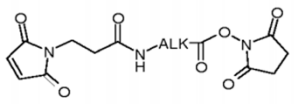
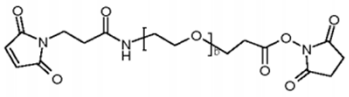
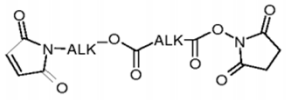
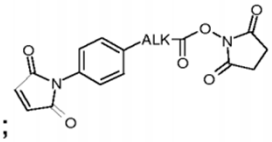
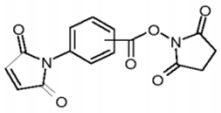
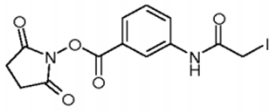
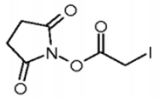
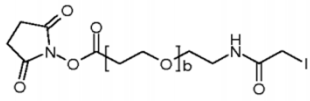
- X_{10} represents a halogen atom, $COOX_{14}$, nitro, unsubstituted or halogenated (C_1-C_8)alkyl, unsubstituted or halogenated (C_1-C_8)alkoxy, unsubstituted or halogenated (C_2-C_8)alkenyl, unsubstituted or halogenated (C_2-C_8)alkynyl, unsubstituted (C_3-C_8)cycloalkyl, aryl that is unsubstituted or substituted with one to three substituents selected from amino, halogen atom, unsubstituted or halogenated (C_1-C_8)alkyl group, or unsubstituted or halogenated (C_1-C_8)alkoxy;

or X_{10} and X_{11} together form a ring (C_2-C_5)alkylene, which is unsubstituted or substituted with one to five (C_1-C_4)alkyl groups;

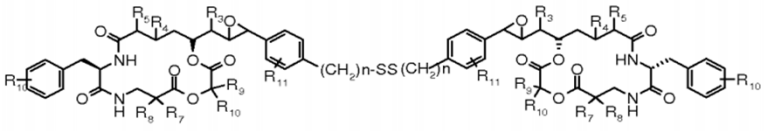
or X_{10} and X_{11} form, together with X_{12}, a (C_1-C_5)alkylene ring, which is

unsubstituted or substituted with one to five (C_1-C_4) alkyl groups; and

- X_{14} is –H or a (C_1-C_8)alkyl group; or

➢ when the compound comprises a reactive chemical group RCG1 of the type -SH, the binding agent is modified with a modifying agent chosen from succinimidyl-4-(N-maleimidomethyl)cyclohexane-1-carboxylate; sulfosuccinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate;  ;  ;  ;  ;  ; or  , wherein ALK represents a (C_1-C_{12})alkylene group and b is an integer between 0 and 2000;  ;  ; succinimidyl-N-bromoacetate; succinimidyl-3-(N-bromoacetamido)propionate; and  , wherein b is an integer between 0 and 2000.

26. A compound of formula:



in which:

- **R_1** represents a halogen atom and **R_2** represents an –OH, an acyl group derived from an amino acid **AA**, or a group (C_1-C_4)alkanoyloxy;

or alternatively **R_1** and **R_2** form an epoxide unit;

- **AA** denotes a natural or unnatural amino acid;
- **R_3** represents a (C_1-C_6)alkyl group;
- **R_4** and **R_5** both represent H or together form a double bond CH=CH between C13 and C14;
- **R_6** and **R_7** represent, independently of each other, H or a (C_1-C_6)alkyl group;
- **R_8** and **R_9** represent, independently of each other, H or a (C_1-C_6)alkyl group;
- **R_{10}** represents at least one substituent of the phenyl nucleus chosen from: H, an OH, (C_1-C_4)alkoxy, a halogen atom, -NH_2, -NH(C_1-C_6)alkyl or -N(C_1-C_6)alkyl$_2$;

- **R_{11}** represents at least one substituent of the phenyl nucleus chosen from H and a (C_1-C_4)alkyl group; and
- n is an integer ranging from 1 to 6.

27. The compound according to Claim 1, in which **L** represents a linker in the para position, of the phenyl nucleus bearing the unit RCG_1.

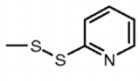
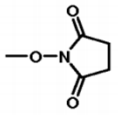
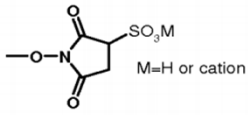
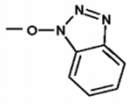
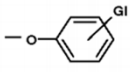
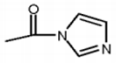
28. The compound according to Claim 1, in which i is an integer ranging from 1 to 6.

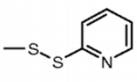
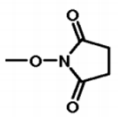
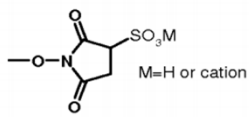
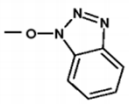
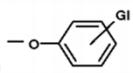
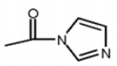
29. The compound according to Claim 28, in which i is an integer ranging from 2 to 5.

30. The compound according to Claim 1, in which **R_{12}** and **R'_{12}** represent, independently of each other, H or a methyl group.

31. The compound according to Claim 1, in which **w** represents an integer ranging from 1 to 6.

32. The compound according to Claim 9, in which **R_{12}** represents a methyl group.

33. The compound according to Claim 1, in which **Z_a** represents H, —SMe, or  ; or **Z_bR_b** represents –O(C_1-C_6)alkyl, -OH, $-OCH_3$, $-OCH_2CH{=}CH_2$,  ,  M=H or cation ,  or the group  in which **GI** represents at least one electroinductive group; or alternatively in which –C(=O)Z_bR_b represents  .

34. The compound according to Claim 12, in which **Z_a** represents H,—SMe, or  ; or **Z_bR_b** represents –O(C_1-C_6)alkyl, -OH, $-OCH_3$, $-OCH_2CH{=}CH_2$,  ,  M=H or cation ,  or the group  in which **GI** represents at least one electroinductive group; or alternatively in which –C(=O)Z_bR_b represents  .

35. The compound according to Claim 11 wherein **L** is in the para position.

36. The compound according to Claim 14, wherein **G** represents a group $-(CH_2)_nY$, which is para (p) position on the phenyl nucleus bearing the unit CR_1 .

37. The compound according to Claim 14, wherein R_{12} is a methyl group.

38. The compound according to Claim 19, wherein the antibody is a monoclonal antibody.

39. The compound according to Claim 20, wherein the antibody is a monoclonal antibody.

40. The compound according to any one of claims 1-20 or 26-39 for use in therapy.

41. Use of the compound according to any one of claims 1-20 or 26-39 in the manufacture of a medicament for the treatment of cancer.