CLAIMS

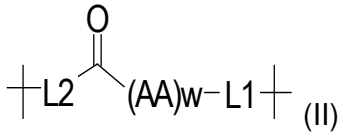
1. Compounds of formula (I):



(I)

wherein

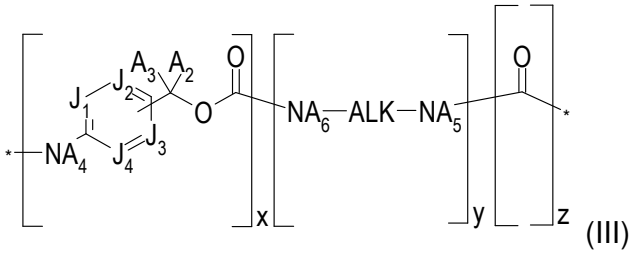
- **RCG1** represents a reactive chemical group that is reactive towards a chemical group present on a polypeptide such as an antibody;
- **P** represents a hydrogen atom, -OH or an activated O;
- **L** represents a linker of formula (II):



(II)

wherein:

- **L1** is of formula (III):



(III)

wherein:

- when P represents a hydrogen atom, then x = 0 or 1 and y = 1 and z = 0;
- when P represents -OH, then x = y = z = 0;
- when P represents an activated O, then x = 1 and y = z = 0, or x = y = z = 1;
- **J_1, J_2, J_3** and **J_4** are chosen, independently of each other, from CA_1 and N;
- **ALK** represents a (C_1-C_{12})alkylene group, for instance (C_1-C_6)alkylene, such as of the form -$(CH_2)_n$-, n being an integer ranging from 1 to 12 and for example ranging from 1 to 6;
- **A_1, A_2, A_3, A_4, A_5**, and **A_6** represent, independently of each other, a hydrogen atom or a (C_1-C_6)alkyl group, such as a

hydrogen atom or a methyl group.

- **(AA)w** represents a sequence of w substituted **AA_s** or non-substituted amino acids **AA_{ns}** connected together *via* peptide bonds;
- **w** represents an integer ranging from 2 to 12, for instance from 2 to 6, such as 2 or 3;

• if **(AA)w** contains at least one substituted amino acid **AA_s**, then **L2** represents a (C_1-C_6)alkyl group, a C(=O)-(C_1-C_6)alkyl group, a (C_1-C_6)alkyl-NA_7-(C_1-C_6)alkyl group, , or a C(=O)-(C_1-C_6)alkyl-NA_7-(C_1-C_6)alkyl group,;

• if (**AA)w** represents a sequence of w non-substituted amino acids **AA_{ns}**, then **L2** represents a (C_1-C_6)alkyl-NA_7-(C_1-C_6)alkyl group;

▪ **A_7** representing a straight or branched, saturated or unsaturated~~,~~ optionally substituted C_1-C_{160} hydrocarbon chain wherein ~~the C_1-C_{160} hydrocarbon is optionally substituted by 1 or more substituents independently selected from the group consisting of halogen, alkyl, NH_2, NH(alkyl), N(alkyl)$_2$, OH, and O(alkyl), and further wherein 1 or more~~optionally at least one methylene ~~units of the C_1-C_{160} hydrocarbon are optionally and~~ unit is independently replaced by ~~1 or more atoms or groups independently selected from the group consisting of~~ -NHC(=O)-, -N(alkyl)C(=O)-, -C(=O)NH-, -C(=O)N(alkyl)-, -OC(=O)-, -C(=O)O-, -OC(=O)O-, -CH(OH)-, -CH(SO_3H)- , -O-, -C(=O)-, -S(=O)-, -S(=O)$_2$-, -NHS(=O)$_2$-, -N(alkyl)S(=O)$_2$-, -S(=O)$_2$NH-, -S(=O)$_2$N(alkyl)-, -P(=O)(OH)-, -P(=O)(OH)O-, -O-P(=O)(OH)-, ~~and~~ -O-P(=O)(OH)-O-~~,~~- or a heterocycloalkyl group~~, wherein the heterocycloalkyl is~~ optionally substituted ~~by 1~~with at least one substituent, identical or ~~more substituents independently selected~~different, chosen from ~~the group consisting of~~ -OH, -Oalkyl, -alkyl, a halogen atom, -NH_2, -NHalkyl, and -N(alkyl)$_2$, being understood that each **A_7** comprising a SO_3H function can be under salt forms such as alkali metal salts, for instance sodium salts (SO_3^- $^+$Na);

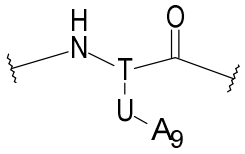
▪ **A_8** representing a hydrogen atom or a (C_1-C_6)alkyl group, for instance a hydrogen atom or a methyl group;

▪ **i** representing an integer ranging from 1 to 50, for instance ranging from 1 to 35;

- each (AA_{ns}) is a natural or non-natural amino acid independently selected from the group consisting of alanine, γ-aminobutyric acid, 2-amino-2-cyclohexylacetic acid, 2-amino-2-phenylacetic acid, arginine, asparagine, aspartic acid, citrulline, cysteine, α,α-dimethyl-γ-aminobutyric acid, 3,3-dimethyl-γ-aminobutyric acid, glutamine, glutamic acid, glycine, homocysteine, selenocysteine, homoselenocysteine, histidine, isoleucine, leucine, lysine, ε-

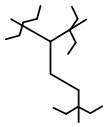
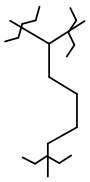
(acetyl)-lysine, methionine, ornithine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine

- each (**AA_s**) is independently of formula (VI):

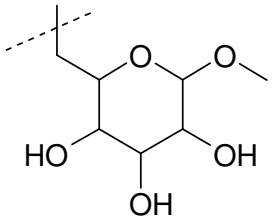


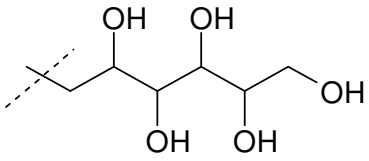
(VI)

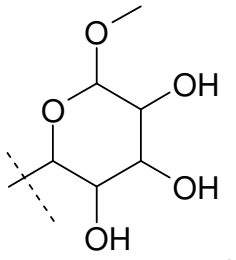
wherein:

- **T** represents a saturated or unsaturated, linear or branched, (C_1-C_8) trivalent alkyl group, preferably T is  , or  ;
- **U** group represents a single bond, -NHC(=O)-, -N(alkyl)C(=O)-, -C(=O)NH-, -C(=O)N(alkyl)-, -NHC(=O)NH-, -NHC(=NH)NH-, -OC(=O)-, -C(=O)O-, -OC(=O)O-, -S-, -Se-, -O-, -NH-, -N(alkyl)-, -C(=O)-, -OP(=O)-, -S(=O)-, -$S(=O)_2$-, -$NHS(=O)_2$-, -$N(alkyl)S(=O)_2$-, -$S(=O)_2NH$-, -$S(=O)_2N(alkyl)$-, -P(=O)(OH)-, -P(=O)(OH)O-, -O-P(=O)(OH)-, or -O-P(=O)(OH)-O, such as **U** group represents -NH-C(=O)-, or -C(=O)NH-;
- **A_9** represents a straight or branched, saturated or unsaturated, optionally substituted C_1-C_{160} hydrocarbon chain~~,~~ wherein ~~the C_1-C_{160} hydrocarbon is optionally substituted by 1 or more substituents independently selected from the group consisting of halogen, alkyl, NH_2, NH(alkyl), $N(alkyl)_2$, OH, and O(alkyl), and further wherein~~optionally at least one ~~or more~~ methylene unit ~~of the C_1-C_{160} hydrocarbon are optionally and~~ is independently replaced by~~ 1 or more atoms or groups independently selected from~~ -NH-C(=O)-, -N(alkyl)C(=O)-, -C(=O)NH-, -C(=O)N(alkyl)-, -NHC(=O)NH-, -NHC(=NH)NH-, -OC(=O)-, -C(=O)O-, -OC(=O)O-, -CH(OH)-, -$CH(SO_3H)$-, -CH(Oalkyl)-, -CHF-, -CF_2-, -S-, -Se-, -O-, -NH-, -N(alkyl)-, -$N^+H(alkyl)$-, -$N^+(alkyl)_2$-, -C(=O)-, -OP(=O)-, -S(=O)-, -$S(=O)_2$-, -$NHS(=O)_2$-, -$N(alkyl)S(=O)_2$-, -$S(=O)_2NH$-, -$S(=O)_2N(alkyl)$-, -P(=O)(OH)-, -P(=O)(OH)O-, -O-P(=O)(OH)-, ~~and~~ -O-P(=O)(OH)-O~~,~~ or a heterocycloalkyl group~~, wherein the heterocycloalkyl is~~ optionally substituted ~~by~~with at least one substituent, identical or ~~more substituents independently selected~~different, chosen

from ~~the group consisting of~~ -OH, -Oalkyl, -alkyl, a halogen atom, $-NH_2$, -NHalkyl, and $-N(alkyl)_2$, for instance **A_9** is $–[(CH_2)_2-O]_4-CH_3$, $-[(CH_2)_2-O]_{24}-CH_3$,



,


,


,

or $-[(CH_2)_2-O)]_4-(CH_2)_2-C(=O)-NH-(CH_2)_2-SO_3H$;

being understood that each **A_9** comprising a SO_3H function can be under salt forms such as alkali metal salts, for instance sodium salts ($SO_3^- {}^+Na$),

wherein **(AA)w** contains at least one substituted amino acid **AA_s** and/or w non-substituted amino acid **AA_{ns}** and if **L2** comprises a **A_7** then **A_7** represents :

a $-C(=O)-[(CH_2)_2-O]_4-CH_3$ group; a $-C(=O)-[(CH_2)_2-O]_7-CH_3$ group; a $-C(=O)-[(CH_2)_2-O]_{24}-CH_3$ group; a $-C(=O)-(CH_2)_2-C(=O)-NH-(CH_2)_2-SO_3H$ group; a $-C(=O)-(CH_2)_2-C(=O)-NH-[(CH_2)_2-O]_4-(CH_2)_2-C(=O)-NH-(CH_2)_2-SO_3H$ group; being understood that each **A_7** comprising a SO_3H function can be under salt forms such as alkali metal salts, for instance sodium salts ($SO_3^- {}^+Na$),

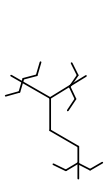
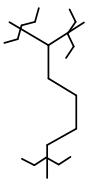
with the proviso that:

the substituted amino acid, $(AA)_s$, of formula (VI) is not selected from the group consisting of alanine, γ-aminobutyric acid, 2-amino-2-cyclohexylacetic acid, 2-amino-2-phenylacetic acid, arginine, asparagine, aspartic acid, citrulline, cysteine, α,α-dimethyl-γ-aminobutyric acid, 3,3-dimethyl-γ-aminobutyric acid, glutamine, glutamic acid, glycine, homocysteine, selenocysteine, homoselenocysteine, histidine, isoleucine, leucine, lysine, ε-(acetyl)-lysine, methionine, ornithine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine.

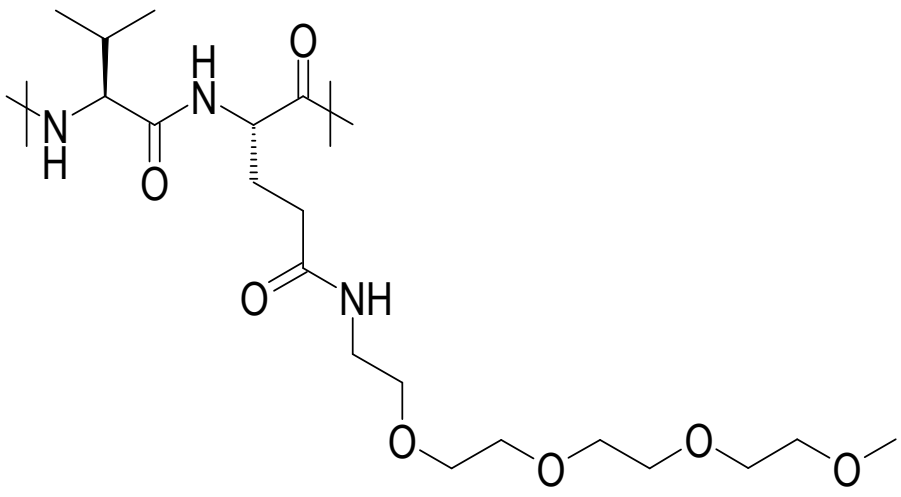
2. Compounds of formula (I) according to claim 1, wherein said sequence **(AA)w** of non-substituted amino acids **AA_{ns}** is selected from the following list: Gly-Gly, Phe-Lys, Val-Lys, Val-AcLys, Val-Cit, Phe-Phe-Lys, D-Phe-Phe-Lys, Gly-Phe-Lys, Ala-Lys, Val-Ala, Phe-Cit, Phe-Gly, Leu-Cit, Ile-Cit, Trp-Cit, Phe-Ala, Ala-Phe, Gly-Gly-Gly, Gly-Ala-

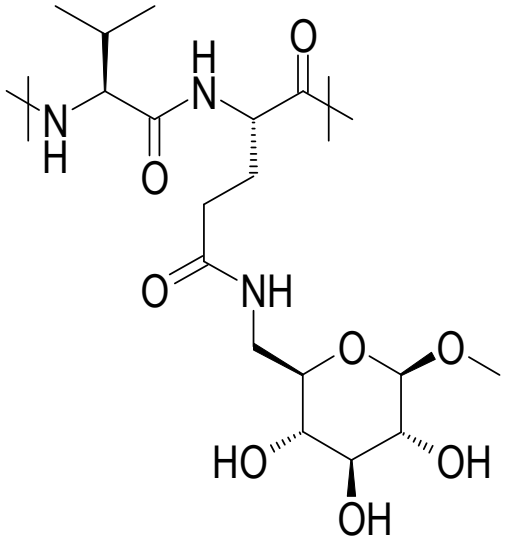
Phe, Gly-Phe-Gly, Gly-Val-Cit, Gly-Phe-Leu-Cit, Gly-Phe-Leu-Gly, and Ala-Leu-Ala-Leu, such as Val-Ala and Val-Cit, for instance Val-Ala.

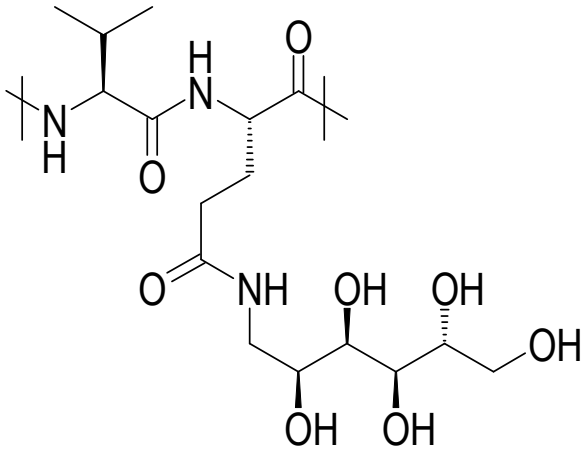
3. Compounds of formula (I) according to claim 1, wherein the substituted amino acids **AA_s** have the formula (VI) as defined in claim 1 in which;

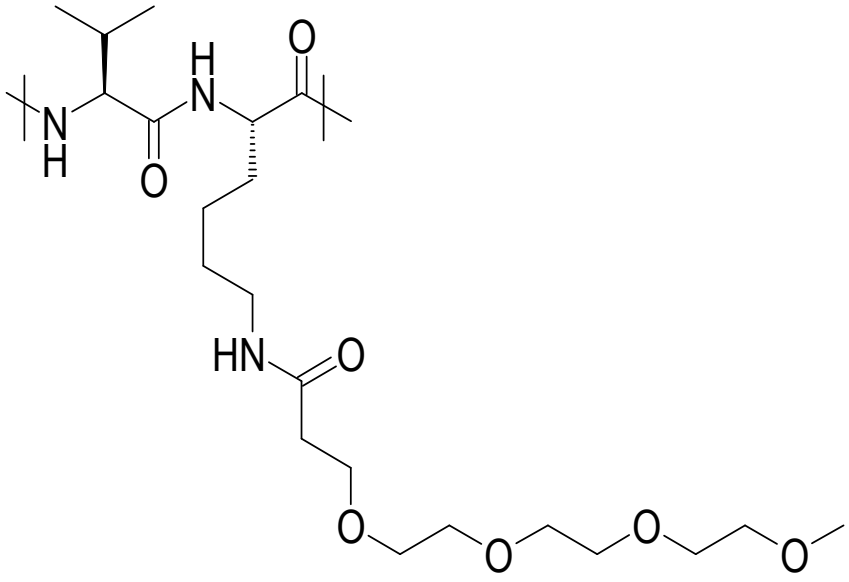
- **T** represents  , or  ;
- **U** group represents -NH-C(=O)-, or -C(=O)NH-;
- **A_9** represents $–[(CH_2)_2-O]_b-CH_3$ wherein b represents an integer ranging from 1 to 50, for instance ranging from 1 to 24, such as 4, 7 and 24, for instance 4 and 24.

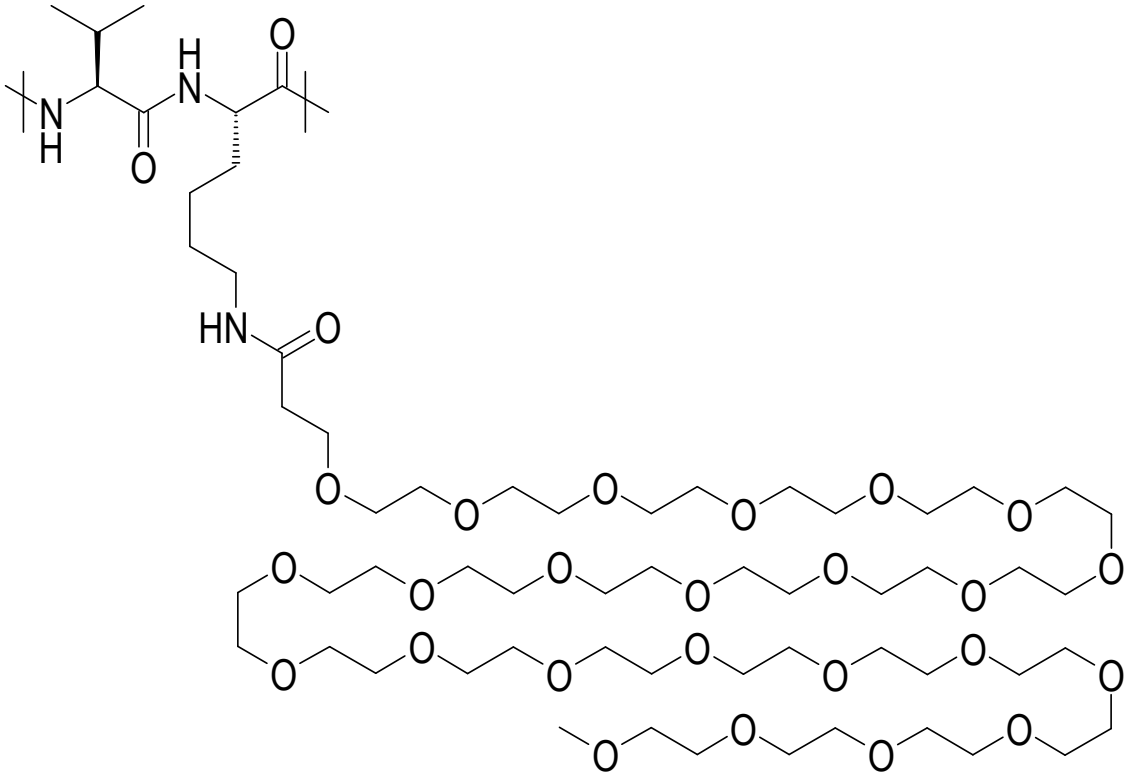
4. Compounds of formula (I) according to claim 1, wherein the sequence **$(AA_s)w$** containing at least one substituted amino acid **AA_s**, is selected from the list:

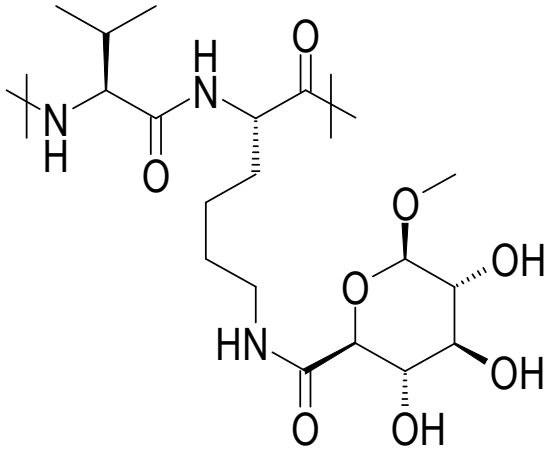



H
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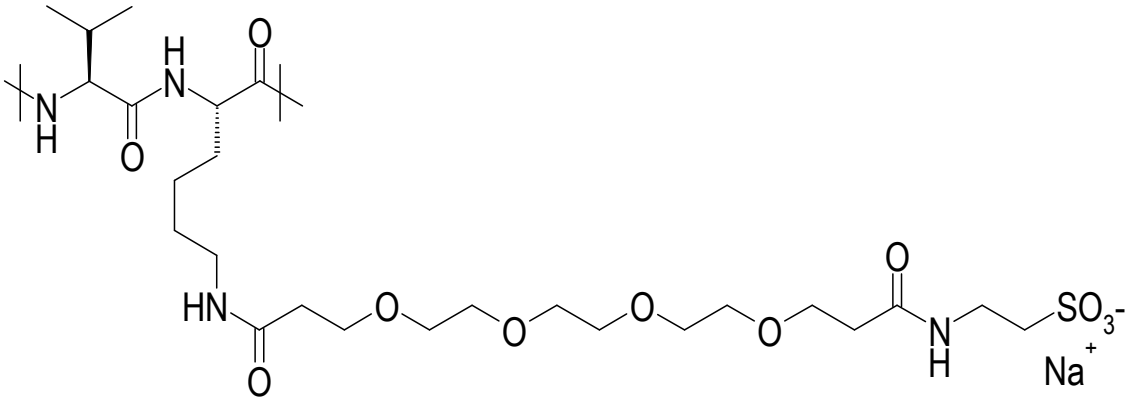

H
N
O
N
H
O
O
NH
OH
OH
OH
OH
OH







or



5. Compounds of formula (I) according to claim 1, wherein **(AA)w** contains at least one substituted amino acid **AA_s** and **L2** represents:

- a -(C_1-C_6)alkyl- group, such as a –$(CH_2)_3$- group;
- a -C(=O)-(C_1-C_6)alkyl- group, such as a -C(=O)-$(CH_2)_3$- group; or
- a -(C_1-C_6)alkyl-NA_7-(C_1-C_6)alkyl- group, such as a -$(CH_2)_2$-NA_7-$(CH_2)_2$- group in which **A_7** is a -C(=O)-$(CH_2)_2$-C(=O)-NH-$(CH_2)_2$-SO_3H group;

being understood that each **A_7** comprising a SO_3H function can be under salt forms such as alkali metal salts, for instance sodium salts (SO_3^- $^+$Na).

6. Compounds of formula (I) according to claim 1, wherein **(AA)w** contains w non-substituted amino acid **AA_{ns}** and **L2** represents :

a -(C_1-C_6)alkyl-NA_7-(C_1-C_6)alkyl- group, such as a -$(CH_2)_2$-NA_7-$(CH_2)_2$- group in which **A_7** represents:

- a –C(=O)-$[(CH_2)_2$-$O]_a$-CH_3 group wherein **"a"** represents an integer ranging

from 1 to 50, such as ranging from 1 to 24, for instance 4, 7 and 24, such as **A_7** is a -C(=O)-$[(CH_2)_2$-O$]_4$-CH_3 group, a -C(=O)-$[(CH_2)_2$-O$]_7$-CH_3 group, or a -C(=O)-$[(CH_2)_2$-O$]_{24}$-CH_3 group;

-a -C(=O)-$(CH_2)_2$-C(=O)-NH-$(CH_2)_2$-SO_3H group; or

-a -C(=O)-$(CH_2)_2$-C(=O)-NH-$[(CH_2)_2$-O$]_a$-$(CH_2)_2$-C(=O)-NH-$(CH_2)_2$-SO_3H group

wherein **"a"** represents an integer ranging from 1 to 50, such as ranging from 1 to 24, for instance 4, such as **A_7** is -C(=O)-$(CH_2)_2$-C(=O)-NH-$[(CH_2)_2$-O$]_4$-$(CH_2)_2$-C(=O)-NH-$(CH_2)_2$-SO_3H group;

being understood that each **A_7** comprising a SO_3H function can be under salt forms such as alkali metal salts, for instance sodium salts (SO_3^- $^+$Na).

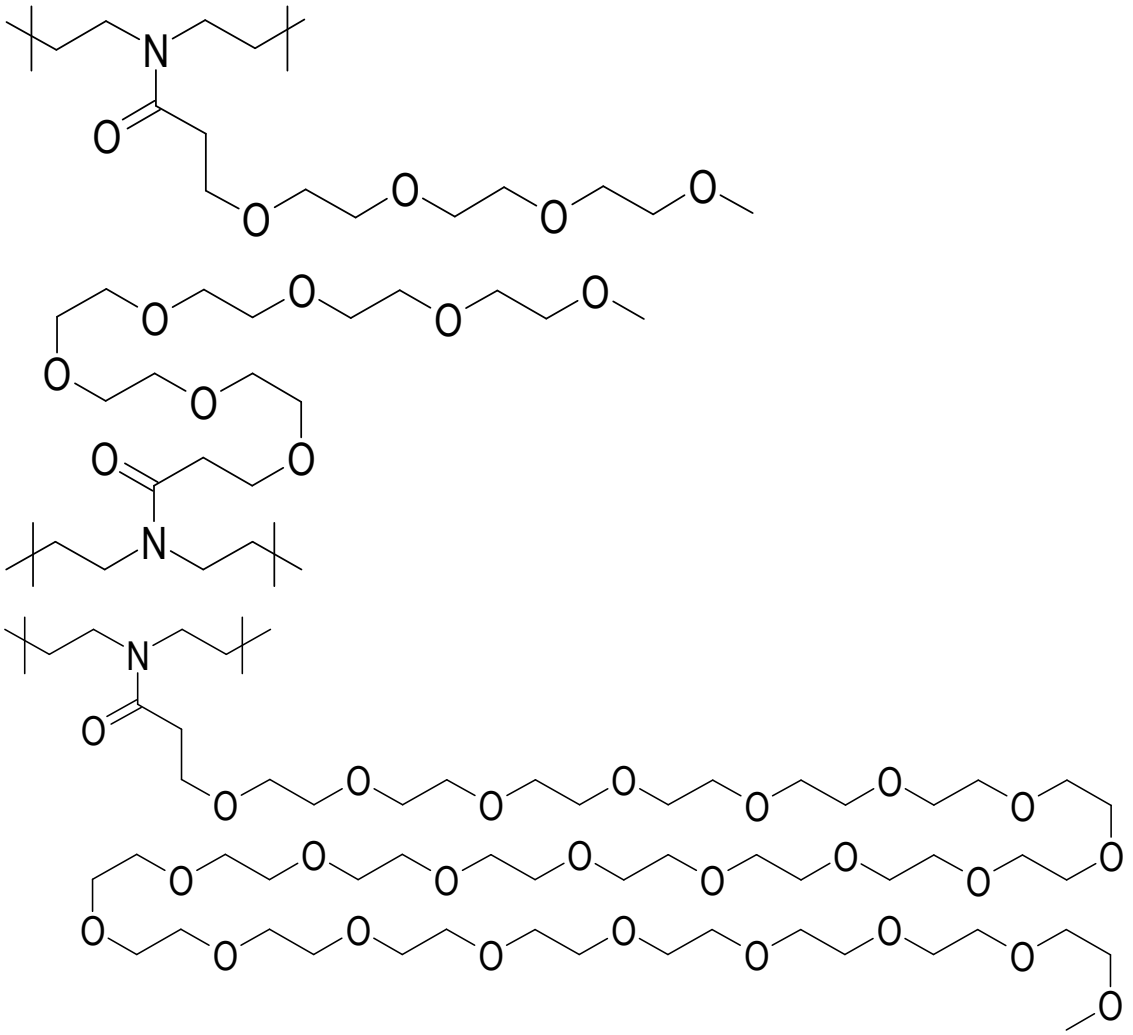
7. Compounds of formula (I) according to claim 1, wherein ~~**A_7**~~**(AA)w** contains at least one substituted amino acid **AA_s** and/or w non-substituted amino acid **AA_{ns}** and **L2** represents:

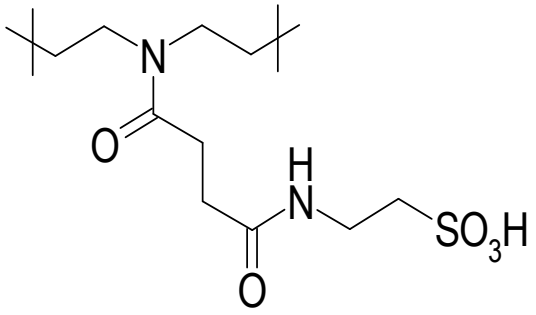
, a ~~-C(=O)-$[(CH_2)_2$-O$]_4$-CH_3~~$(C_1$-$C_6)$alkyl-NA_7-$(C_1$-$C_6)$alkyl group~~;~~, or a ~~-C(=O)-$[(CH_2)_2$-O$]_7$-CH_3~~C(=O)-$(C_1$-$C_6)$alkyl-NA_7-$(C_1$-$C_6)$alkyl group~~,~~ ~~a -C(=O)-$[(CH_2)_2$-O$]_{24}$-CH_3 group; a -C(=O)-$(CH_2)_2$-C(=O)-NH-$(CH_2)_2$-SO_3H group; a C(=O)-$(CH_2)_2$-C(=O)-NH-$[(CH_2)_2$-O-$]_4$-$(CH_2)_2$-C(=O)-NH-$(CH_2)_2$-SO_3H group;~~ .. ~~being understood that each **A_7** comprising a SO_3H function can be under salt forms such as alkali metal salts, for instance sodium salts (SO_3^--$^+$Na).~~

8. Compounds of formula (I) according to claim 1, wherein **(AA)w** contains at least one substituted amino acid **AA_s** and/or w non-substituted amino acid **AA_{ns}** and **L2** represents~~:~~

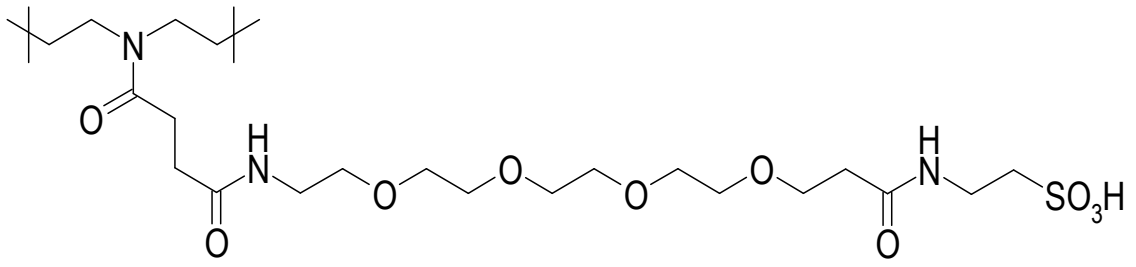
~~, a $(C_1$-$C_6)$alkyl-NA_7-$(C_1$-$C_6)$alkyl group, or a C(=O)-$(C_1$-$C_6)$alkyl-NA_7-$(C_1$-$C_6)$alkyl group,.~~

~~**9.** Compounds of formula (I) according to claim 1, wherein **(AA)w** contains at least one substituted amino acid **AA_s** and/or w non-substituted amino acid **AA_{ns}** and **L2** represents~~ :





or

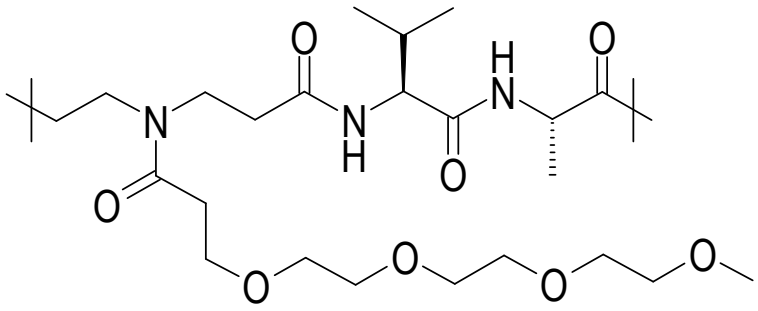


~~**10.** Compounds of formula (I) according to claim 1, wherein **(AA)w** contains at least one substituted amino acid **AA_s** and/or w non substituted amino acid **AA_{ns}** and **L2** comprises a **A_7** representing :~~

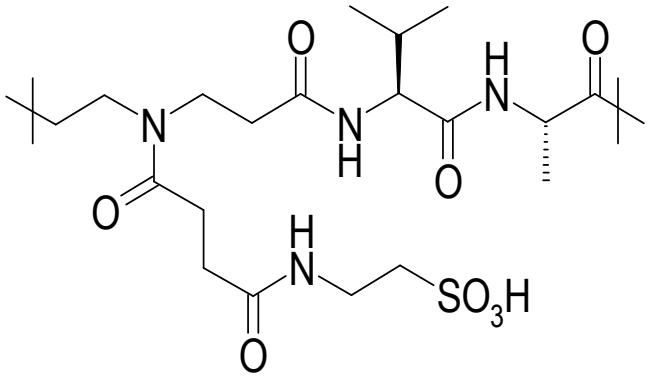
~~a -C(=O)-$[(CH_2)_2$-O$]_4$-CH_3 group; a -C(=O)-$[(CH_2)_2$-O$]_7$-CH_3 group; a -C(=O)-$[(CH_2)_2$-O$]_{24}$-CH_3 group; a -C(=O)-$(CH_2)_2$-C(=O)-NH-$(CH_2)_2$-SO_3H group; a -C(=O)-$(CH_2)_2$-C(=O)-NH-$[(CH_2)_2$-O$]_4$-$(CH_2)_2$-C(=O)-NH-$(CH_2)_2$-SO_3H group; being understood that each **A_7** comprising a SO_3H function can be under salt forms such as alkali metal salts, for instance sodium salts (SO_3^--$^+$Na).~~

~~**11**~~

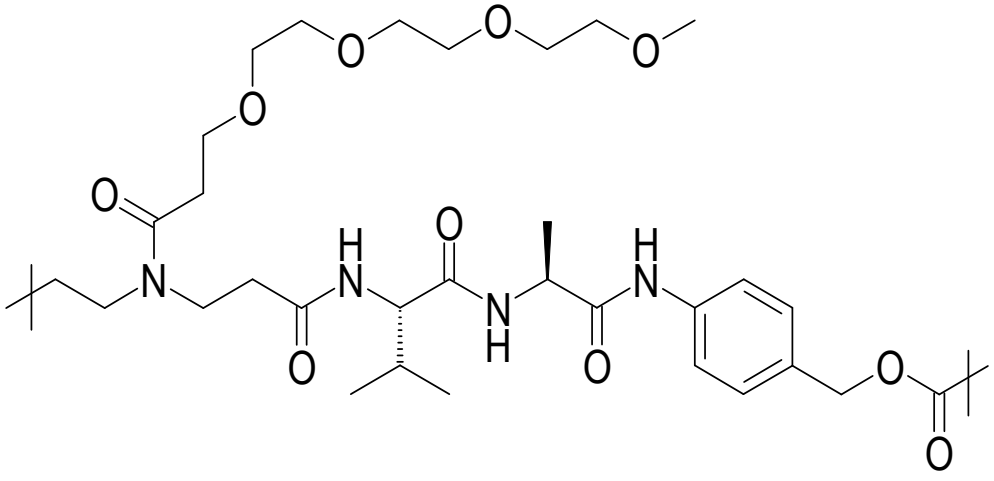
9. Compounds of formula (I) according to anyone of claims 1 to ~~10~~8, wherein said linker **L** is selected from the following list:

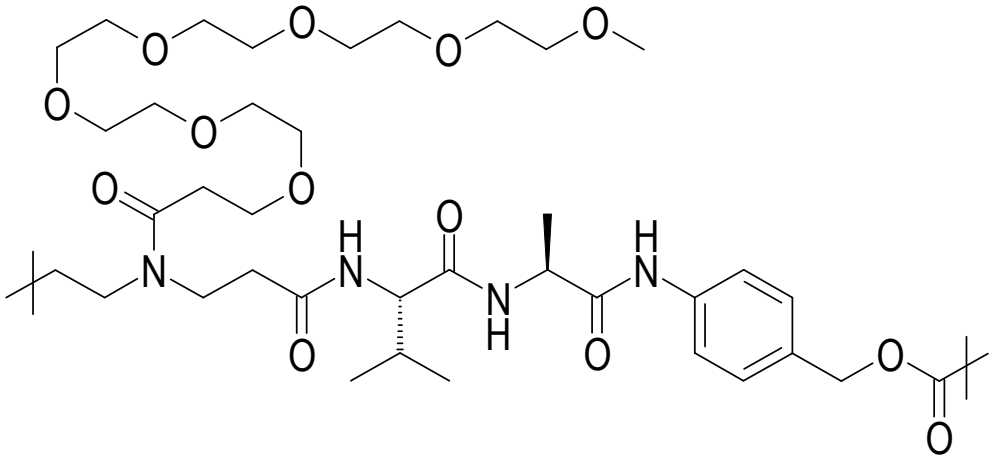


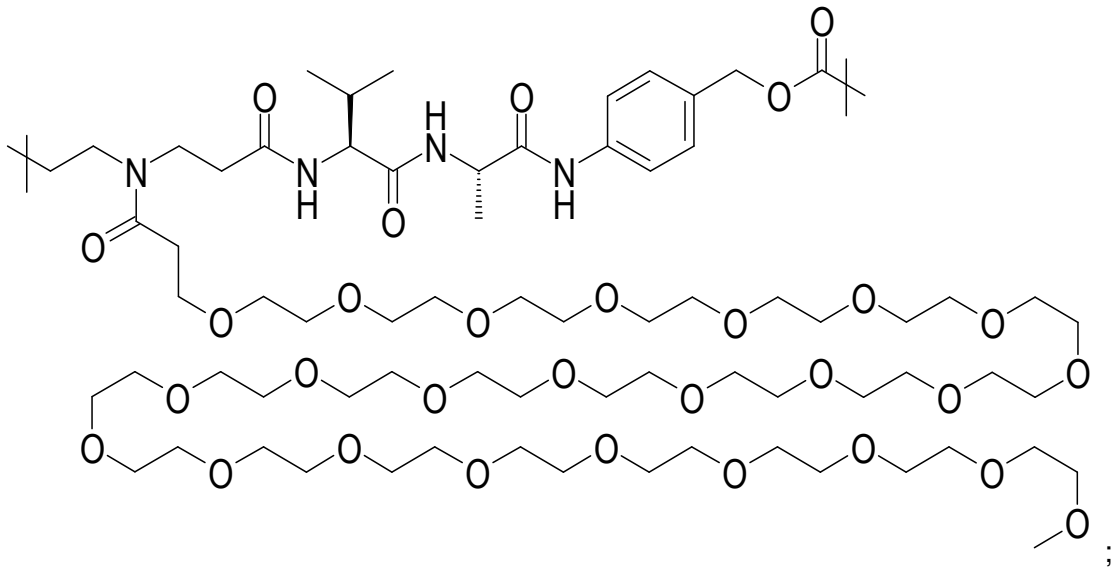
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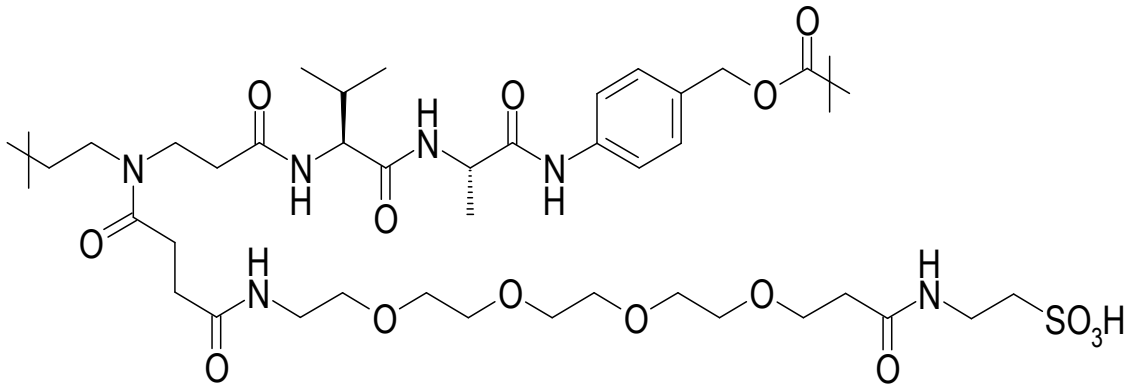


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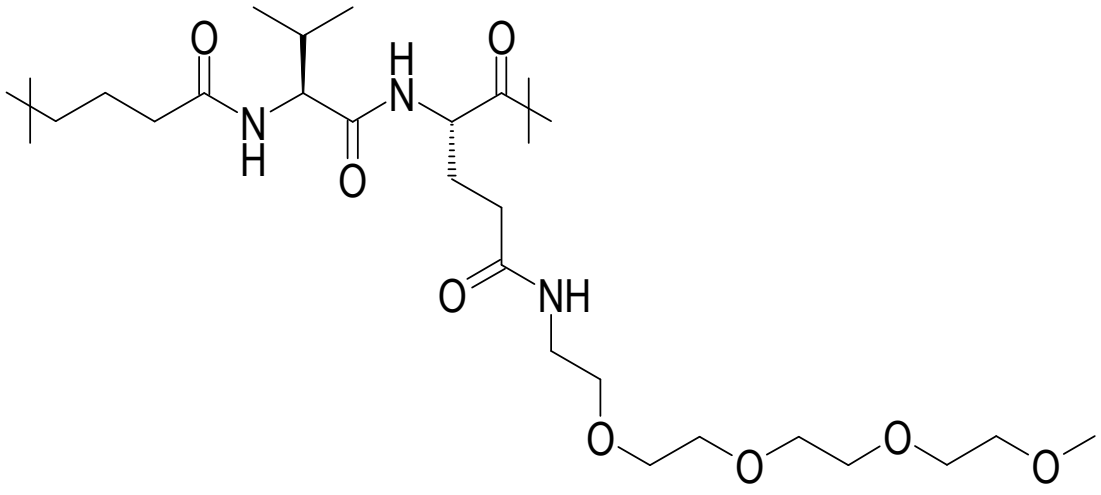

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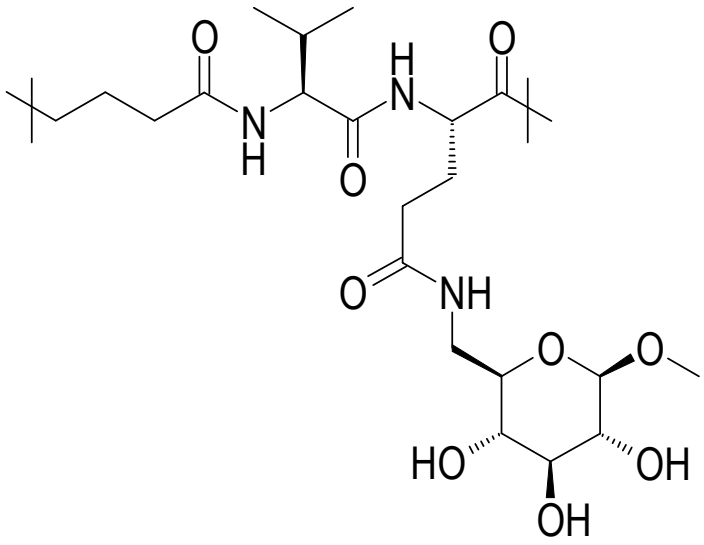

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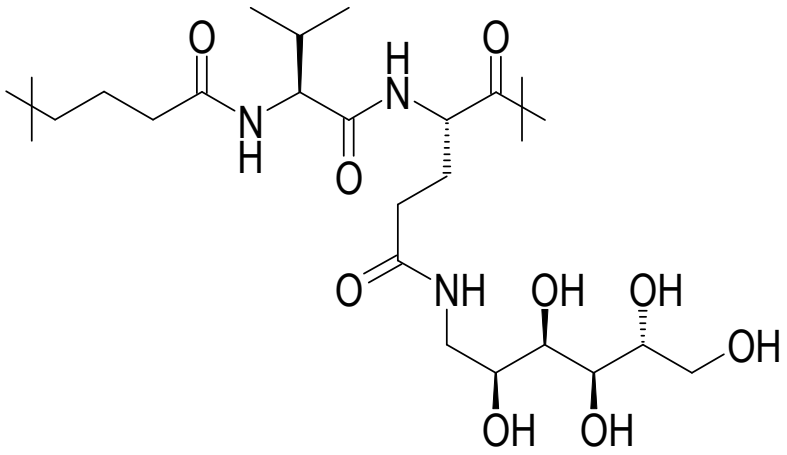
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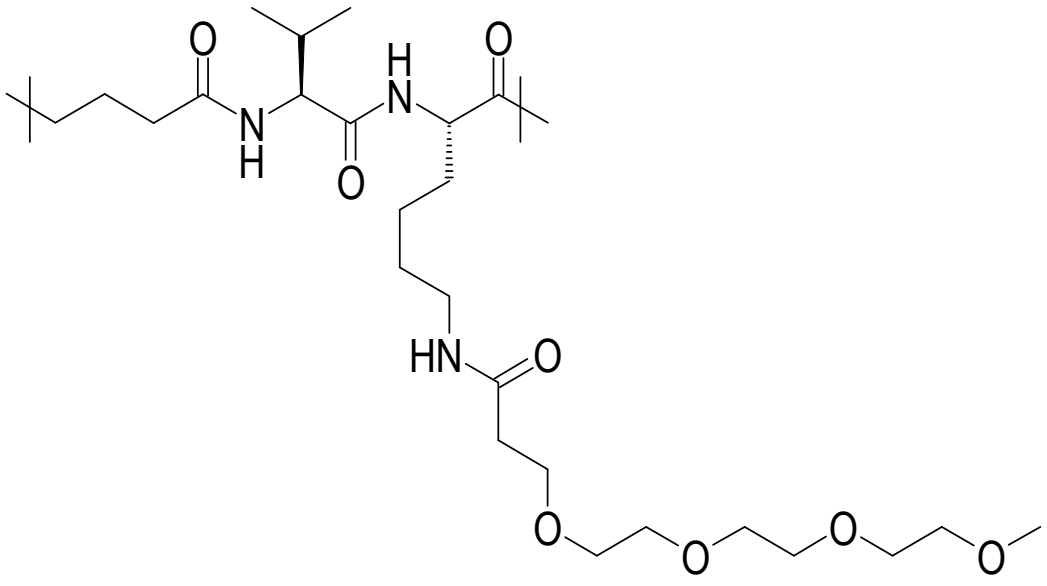
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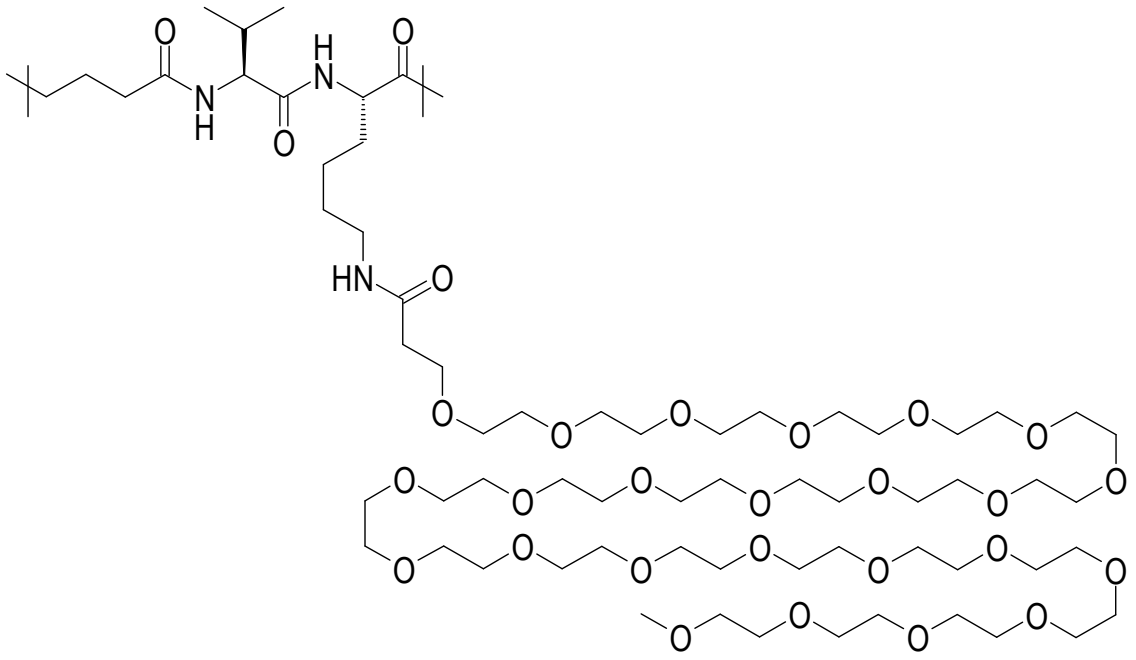
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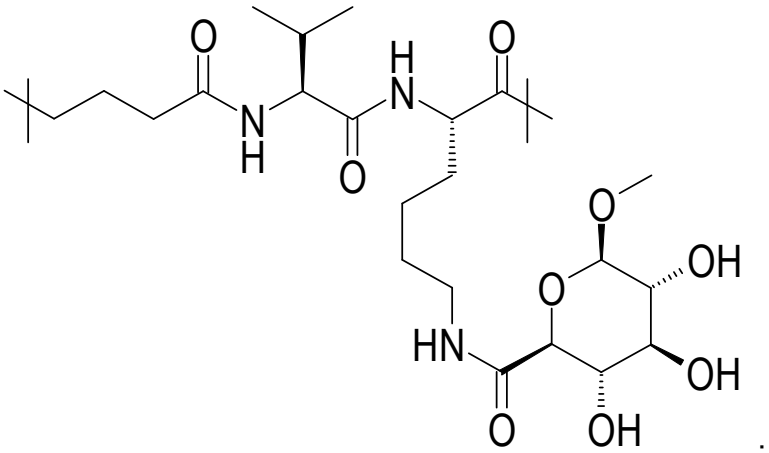
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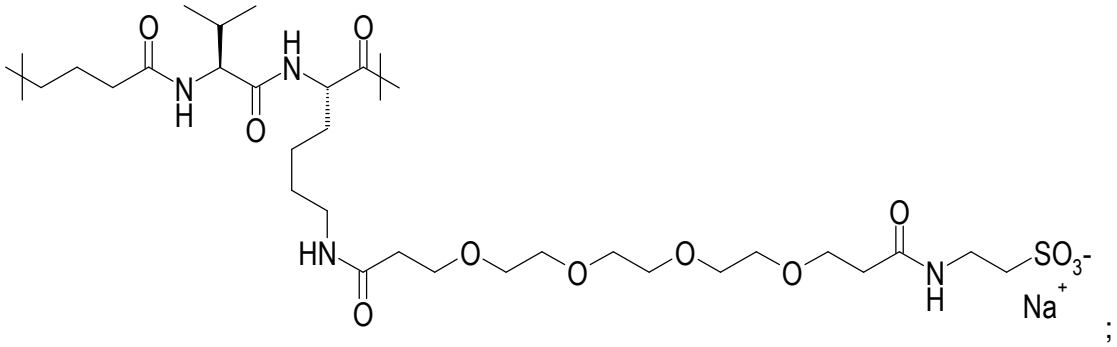
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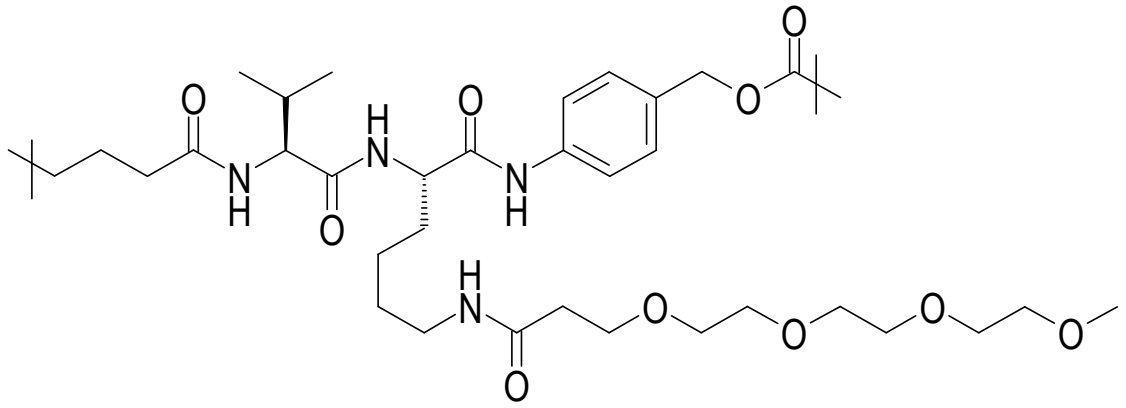
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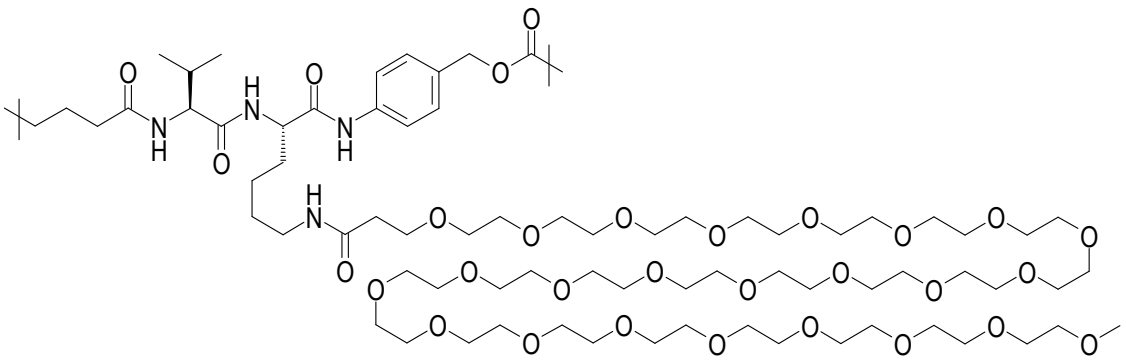
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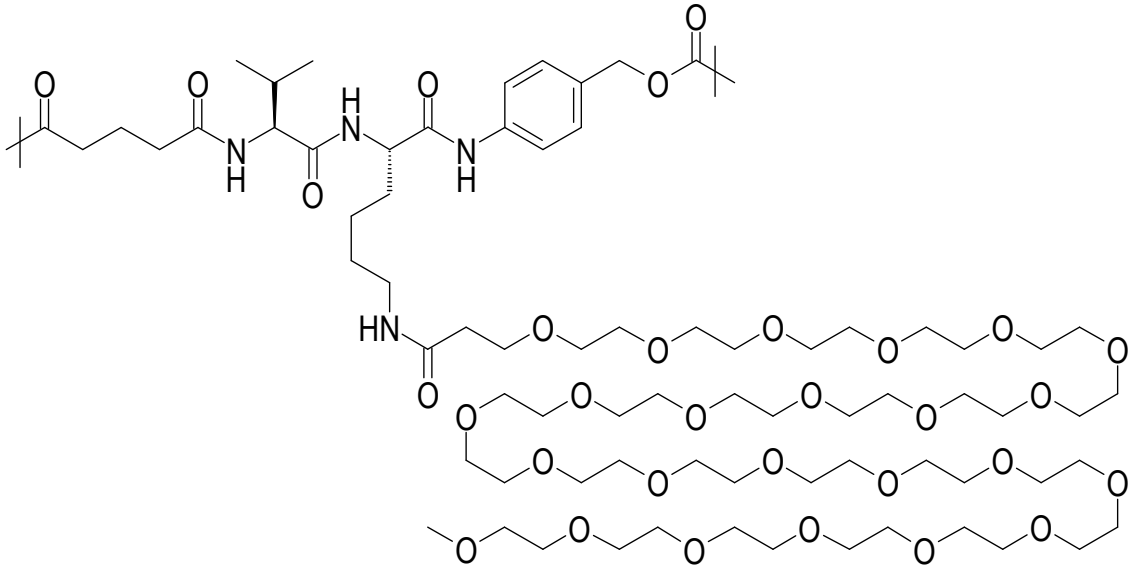
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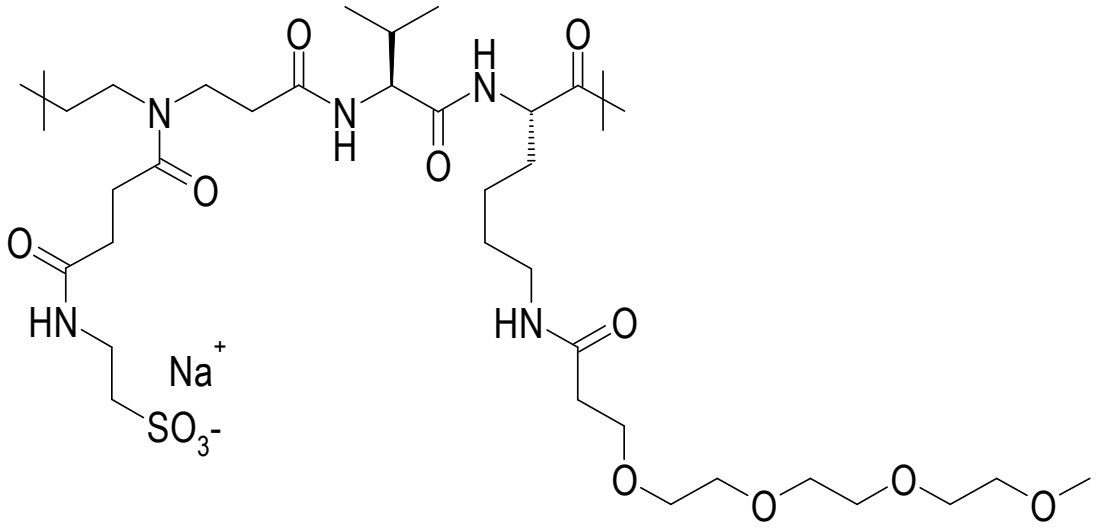
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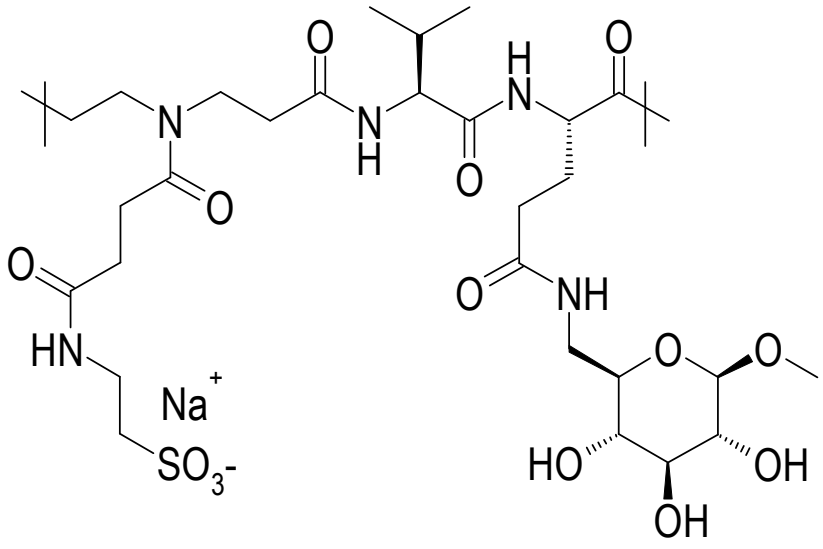
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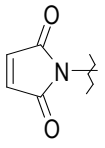
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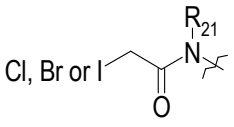


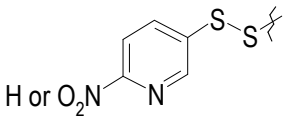
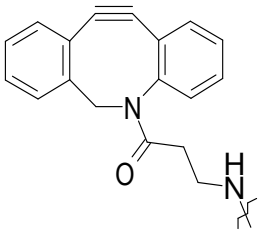
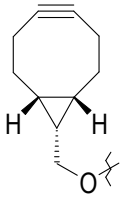
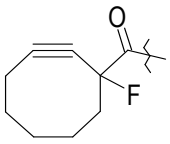
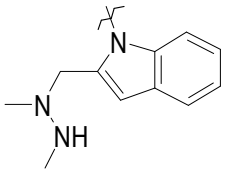
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~~12~~**10.** Compounds of formula (I) according to anyone of claims 1 to ~~11~~9, wherein **RCG1** is selected from the following list:

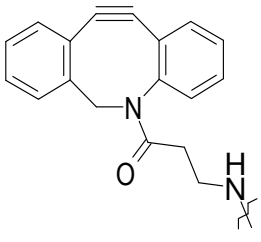
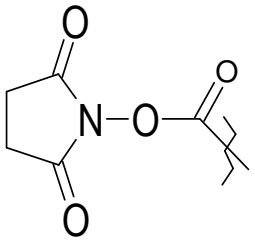
(i) a R_aZ_a-C(=O) reactive group for which $\mathbf{Z_a}$ represents a single bond, -O- or -NH-, for instance -O-, and $\mathbf{R}_a$ represents a hydrogen atom, a (C_1-C_6)alkyl group, a (C_3-C_7)cycloalkyl group, an alkenyl group, an aryl group, a heteroaryl group or a (C_3-C_7)heterocycloalkyl group, the aryl group, the heteroaryl group and/or the (C_3-C_7)heterocycloalkyl group being optionally substituted by 1 to 5 atoms/groups chosen from a halogen atom, for instance a fluorine atom, an alkyl group, an alkoxy group, a hydroxyl group, an oxo group, a nitro group and a cyano group;

(ii) one of the following reactive groups: a maleimido  group; a haloacetamido

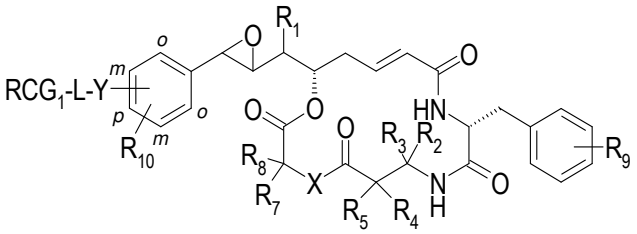
 group with **R_{21}** representing a hydrogen atom or a (C_1-C_6)alkyl group, such as Me; Cl-; N_3-; HO-; HS-; an activated disulfide such as

 ; H_2N-; HC≡C- group or an activated C≡C group such as a cyclooctyne moiety for instance a DBCO-amine  or BCN  or MFCO  ; an O-alkyl hydroxylamine or a Pictet-Spengler reaction substrate such as  ;

for instance **RCG1** is selected from the following list:

 -COOH, and  .

~~13~~11. Cryptophycin payloads of formula (IV):



(IV)

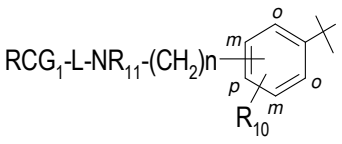
wherein:

- **R_1** represents a (C_1-C_6)alkyl group;
- **R_2** and **R_3** represent, independently of each other, a hydrogen atom or a (C_1-C_6)alkyl group;

  or alternatively **R_2** and **R_3** form together with the carbon atom to which they are attached a (C_3-C_6)cycloalkyl or a (C_3-C_6)heterocycloalkyl group;
- **R_4** and **R_5** represent, independently of each other, a hydrogen atom or a (C_1-C_6)alkyl group or a (C_1-C_6)alkyl-NH(R_{12}) group or a (C_1-C_6)alkyl-OH group or a (C_1-C_6)alkyl-SH group or a (C_1-C_6)alkyl-CO_2H group;

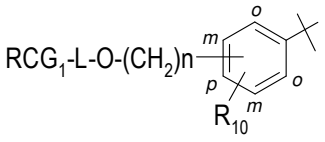
  or alternatively **R_4** and **R_5** form together with the carbon atom to which they are attached a (C_3-C_6)cycloalkyl or a (C_3-C_6)heterocycloalkyl group;
- **X** represents O or N(R_6);
- **R_6** represents a hydrogen atom or a (C_1-C_6)alkyl group;
- **R_7** and **R_8** represent, independently of each other, a hydrogen atom or a (C_1-C_6)alkyl group or a (C_1-C_6)alkyl-CO_2H group or a (C_1-C_6)alkyl-N(C_1-C_6)alkyl$_2$ group;

  or alternatively **R_7** and **R_8** form together with the carbon atom to which they are attached a (C_3-C_6)cycloalkyl group or a (C_3-C_6)heterocycloalkyl group;
- **R_9** represents at least one substituent of the phenyl nucleus chosen, independently of each other, from: a hydrogen atom, -OH, (C_1-C_4)alkoxy, a halogen atom, -NH_2, -NH(C_1-C_6)alkyl or -N(C_1-C_6)alkyl$_2$ or -NH(C_1-C_6)cycloalkyl or (C_3-C_6)heterocycloalkyl group;
- **R_{10}** represents at least one substituent of the phenyl nucleus chosen from a hydrogen atom and a (C_1-C_4)alkyl group;
- **Y** represents
  - -NR_{11}-(C_1-C_6)alkyl-, such as -NR_{11}-(CH_2)$_n$- like

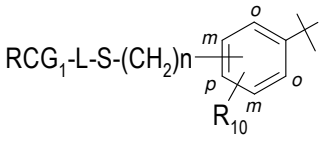
    ;

- -O-(C_1-C_6)alkyl-, such as -O-(CH_2)$_n$- like



;

- -S-(C_1-C_6)alkyl-, such as -S-(CH_2)$_n$- like

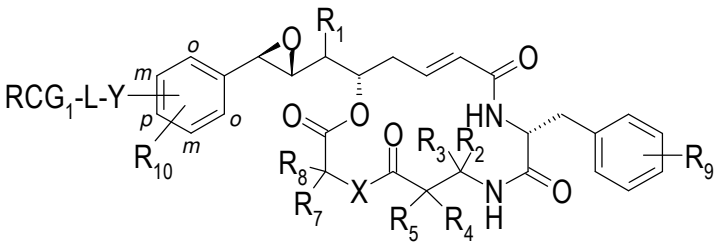


;

Y being positioned in an *ortho* (*o*), *meta* (*m*) or *para* (*p*) position of the phenyl nucleus;

- **R_{11}** and **R_{12}** represent, independently of each other, a hydrogen atom or (C_1-C_6)alkyl, such as a hydrogen atom or a methyl group;
- **n** represents an integer ranging from 1 to ~~5;~~6;
- **L** is defined as in formula (I) according to claim 1 and represents a linker of formula (II) as defined in any one of claims 1 to ~~11~~9;
- **RCG1** represents a reactive chemical group present at the end of the linker **L**, **RCG1** being reactive towards a chemical group present on a polypeptide such as an antibody.

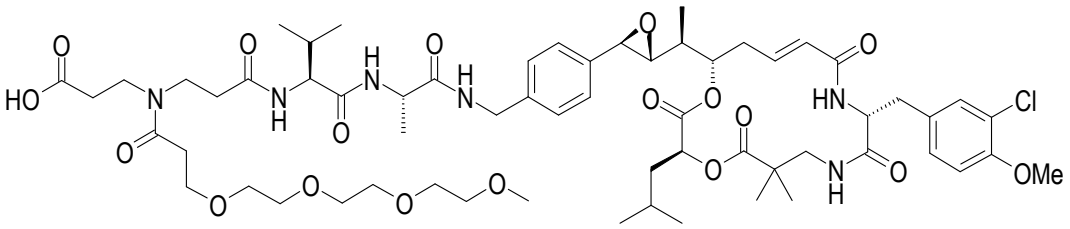
~~14~~12. Cryptophycin payloads of formula (IV) according to claim ~~13~~11, having the following structure:



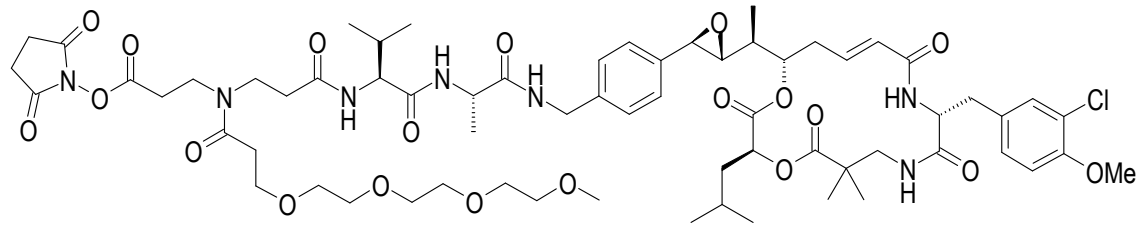
wherein:

- **R_1**, **R_2**, **R_3**, **R_4**, **R_5**, **R_6**, **R_7**, **R_8**, **R_9**, **R_{10}**, **R_{11}**, **R_{12}**, **n**, **RCG_1**, **X, Y** and **L** are as defined in formula (IV) according to claim ~~14~~11.

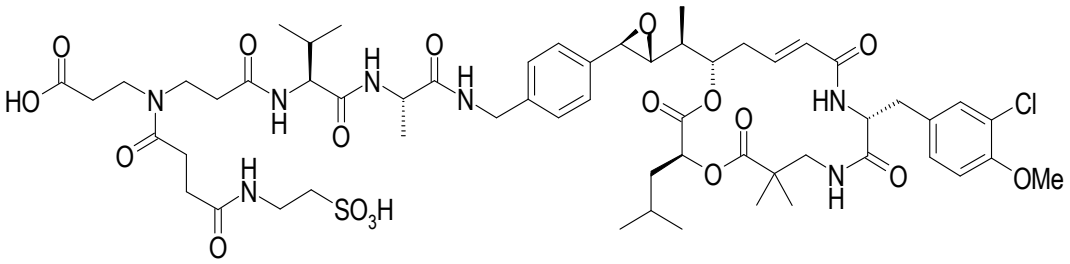
~~15~~13. Cryptophycin payloads of formula (IV) according to claim ~~13~~11 which are selected from the following list:



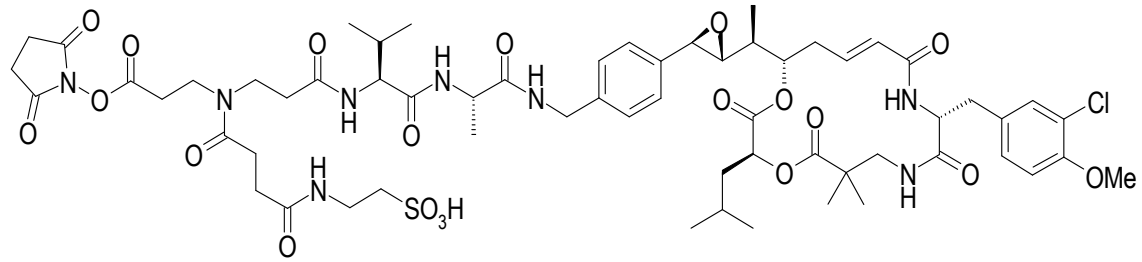
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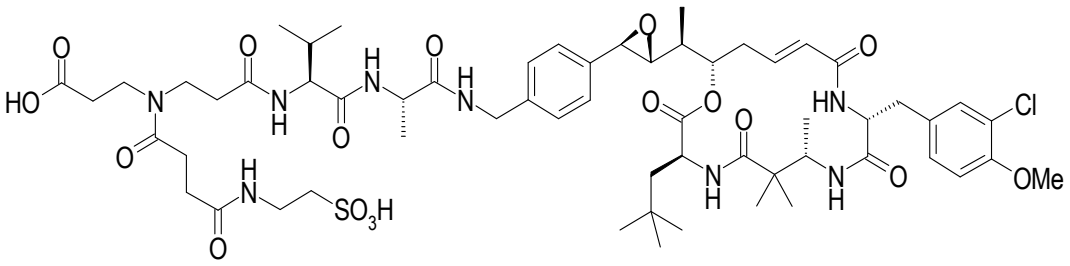
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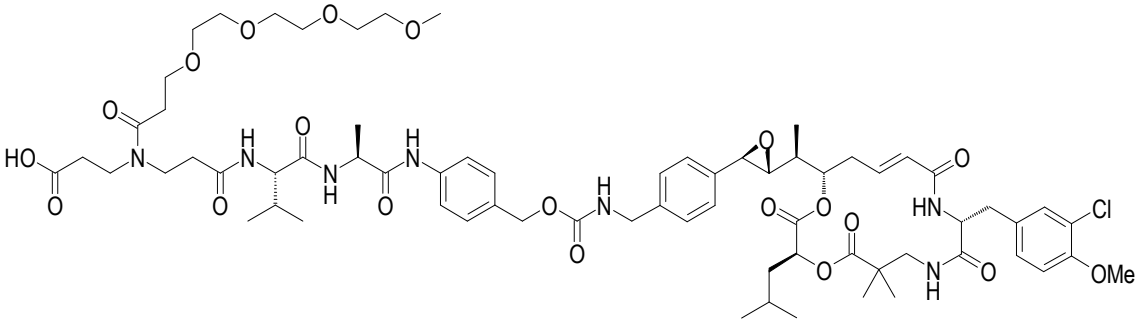
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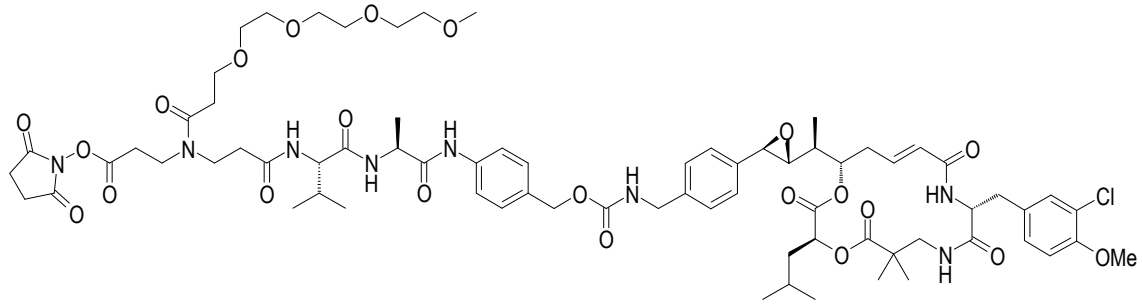
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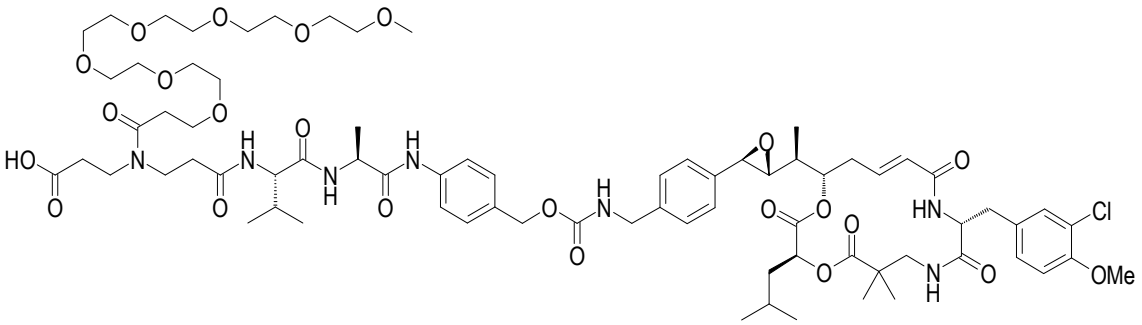
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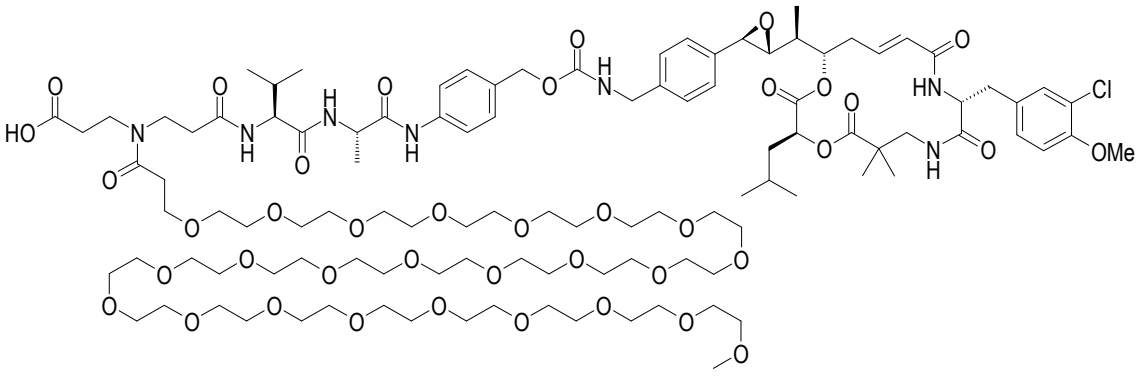
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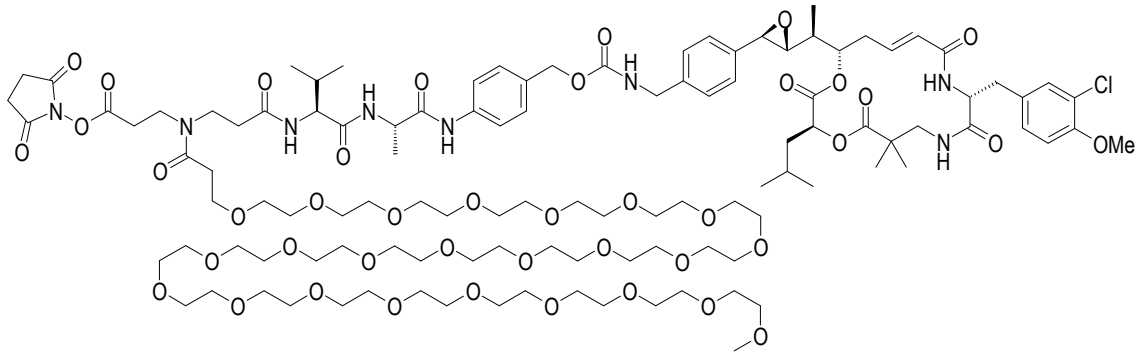
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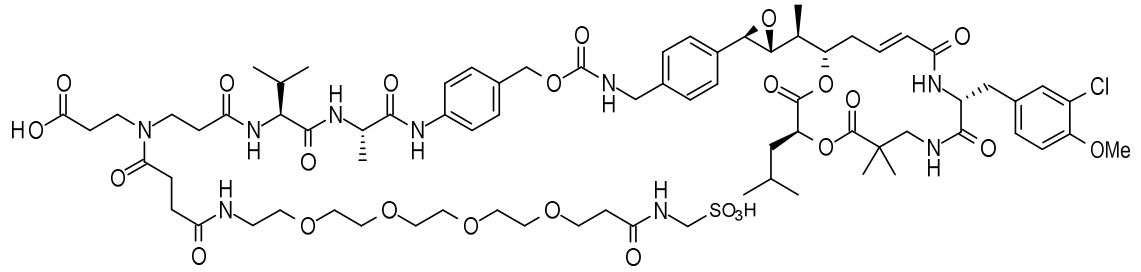
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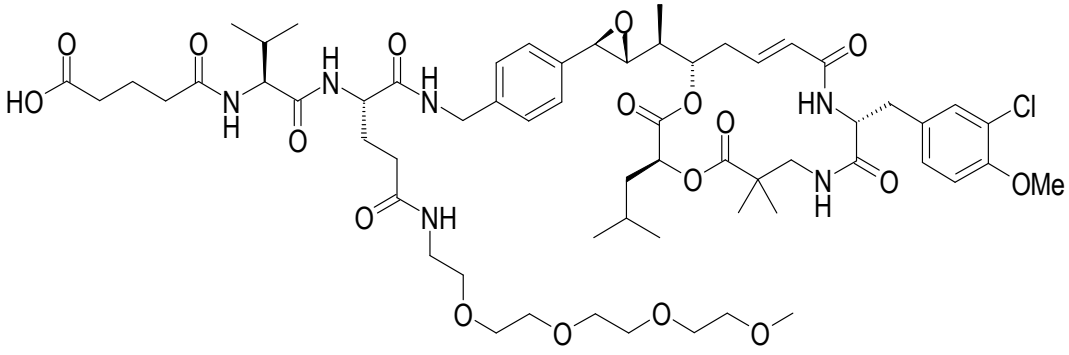
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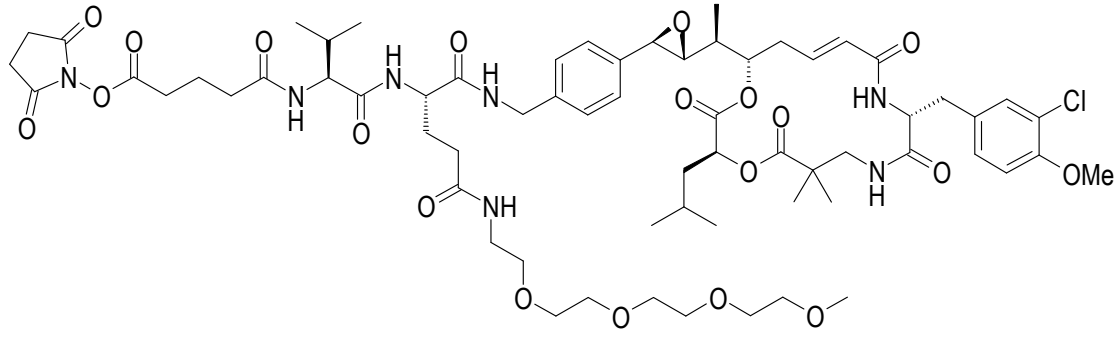
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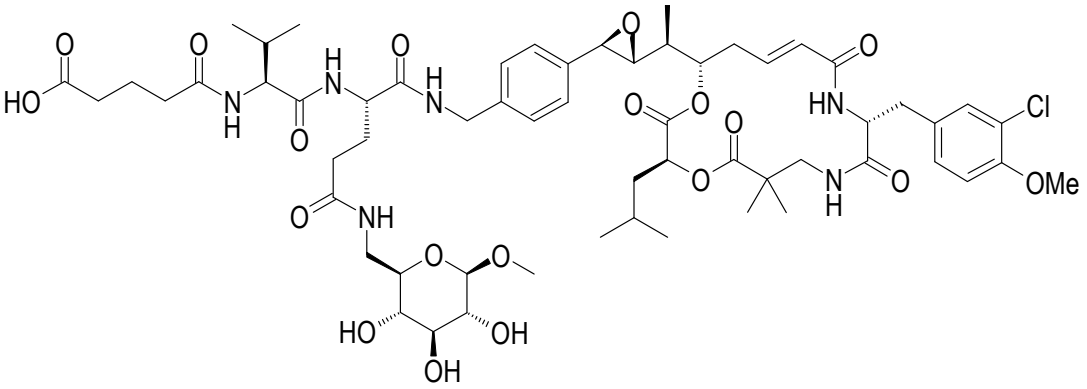
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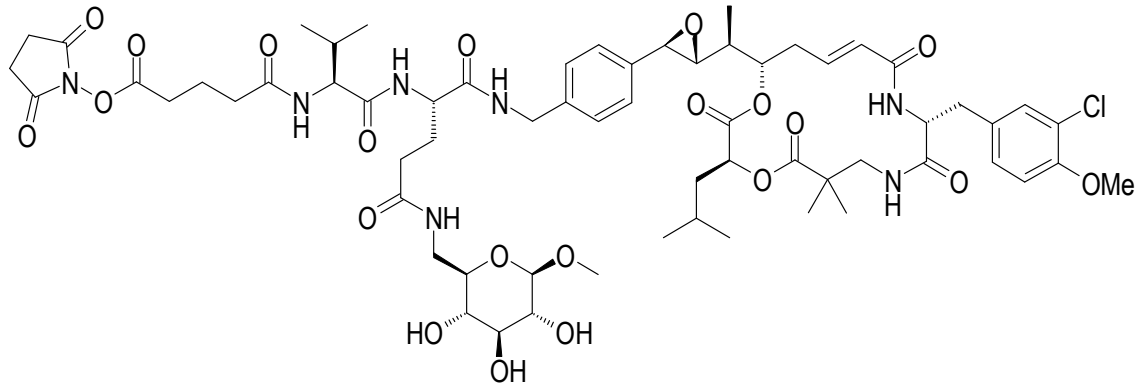
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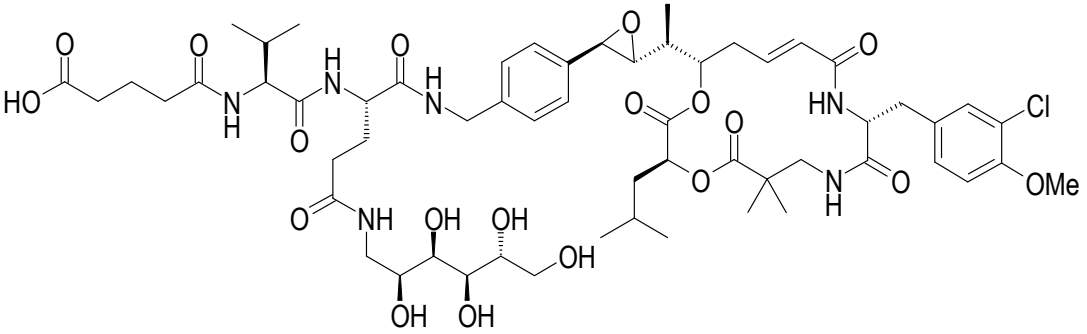
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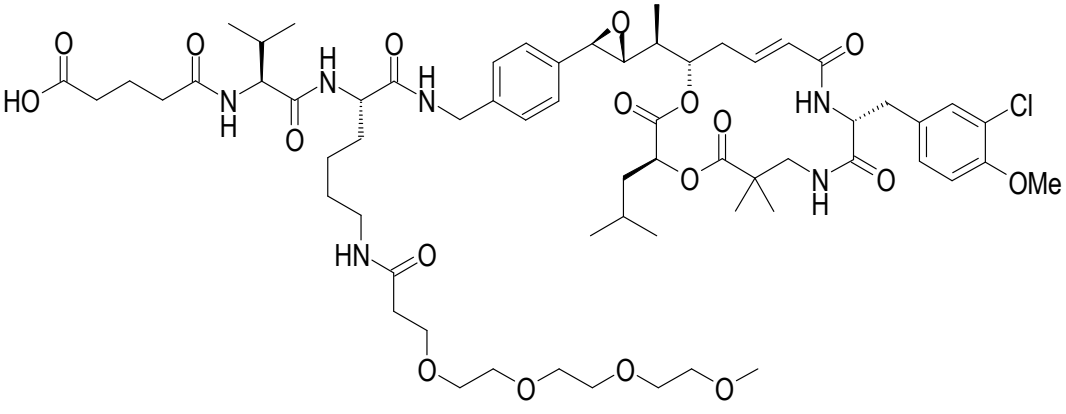
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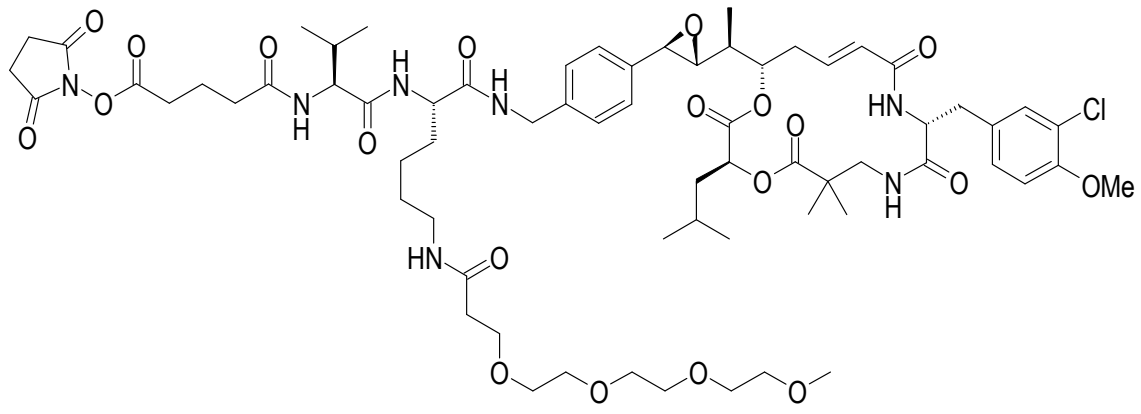
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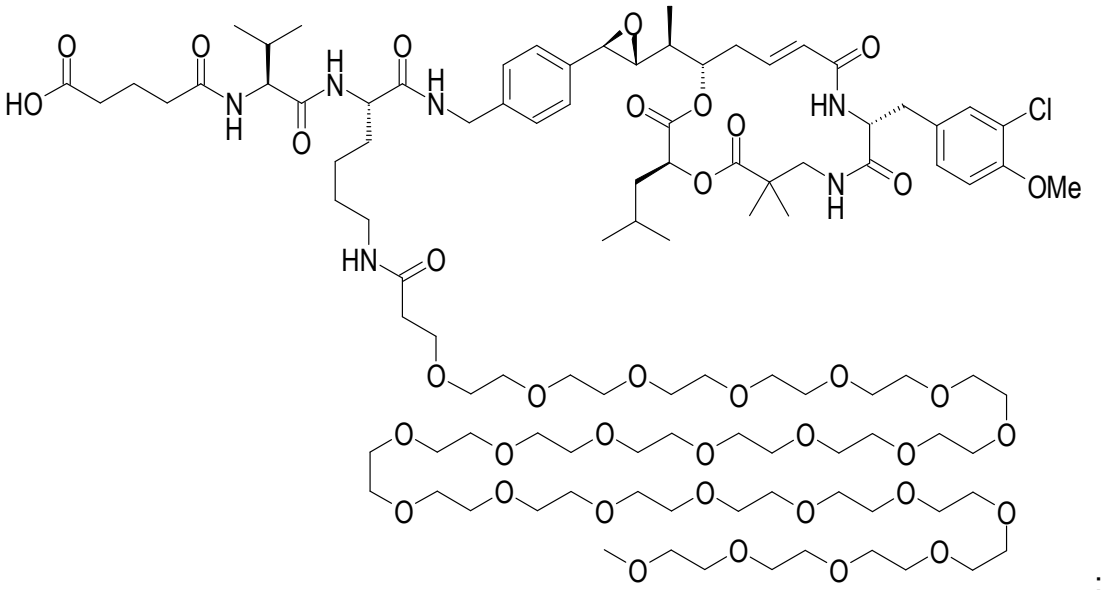
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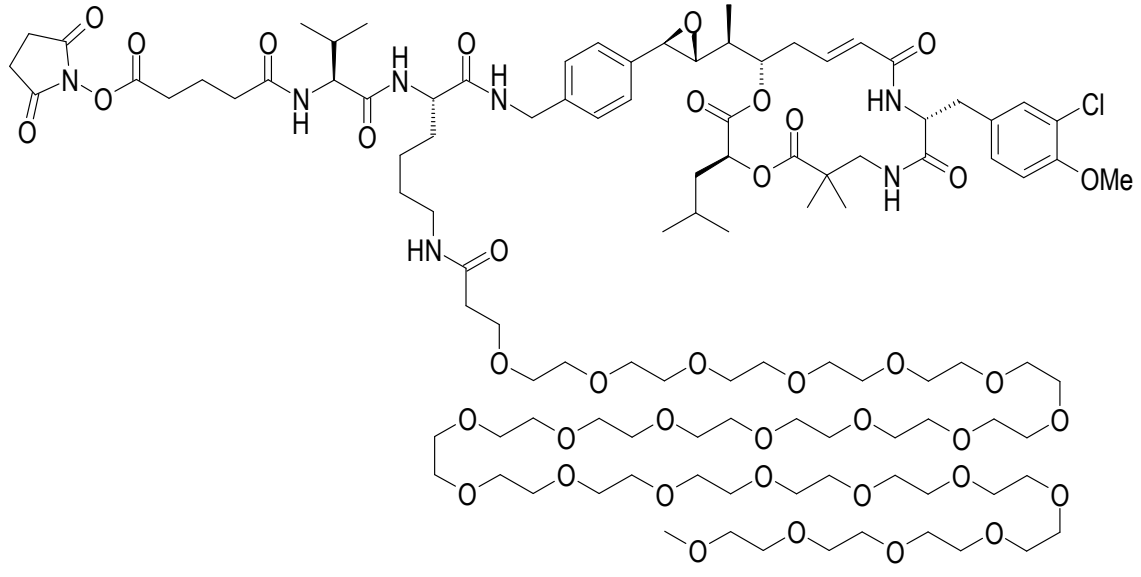
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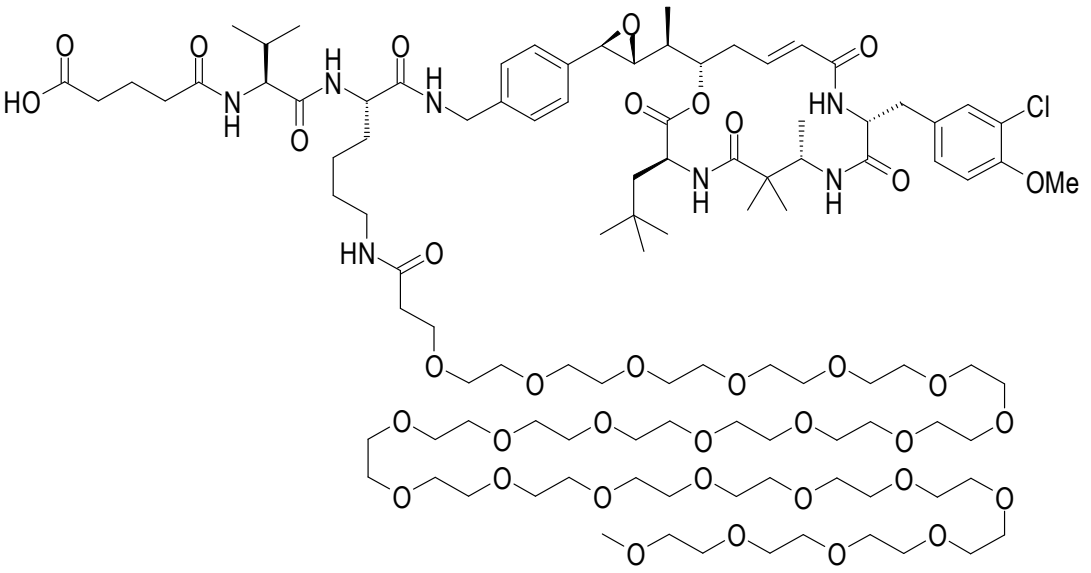
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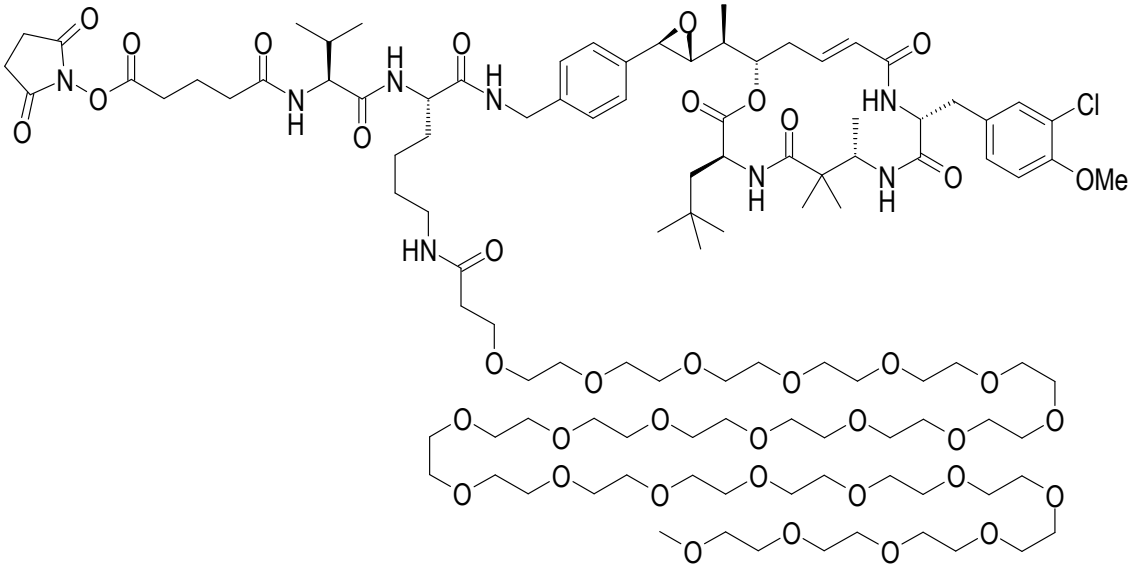
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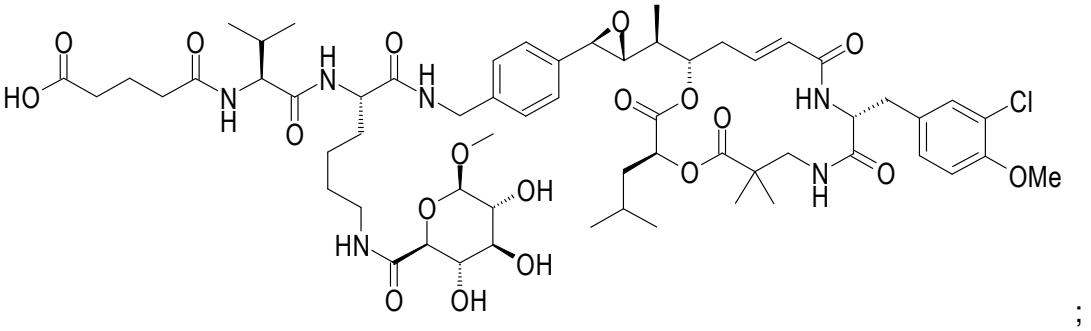
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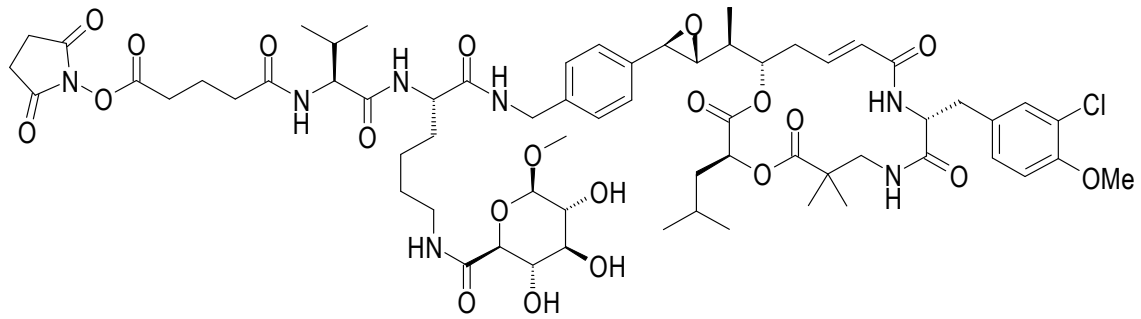
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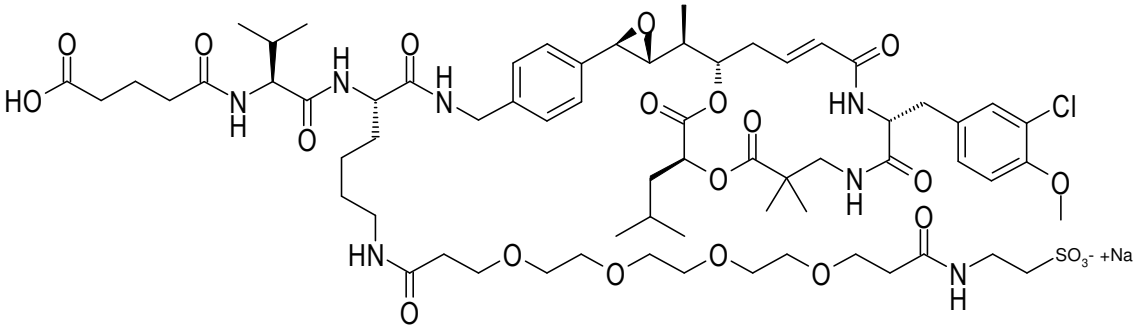
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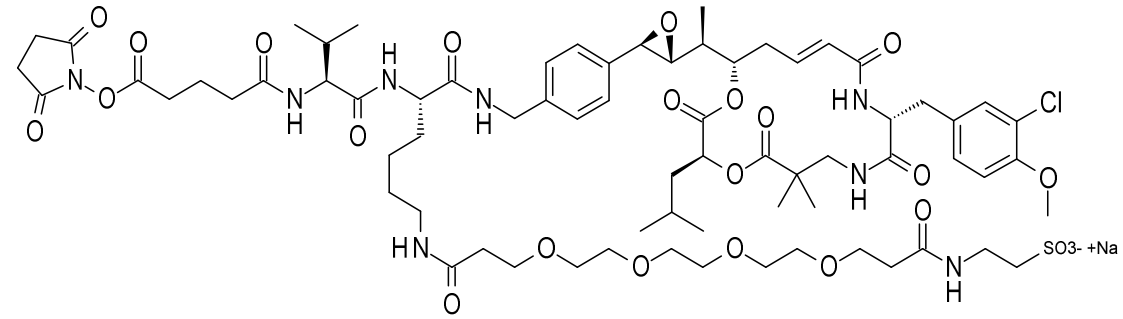
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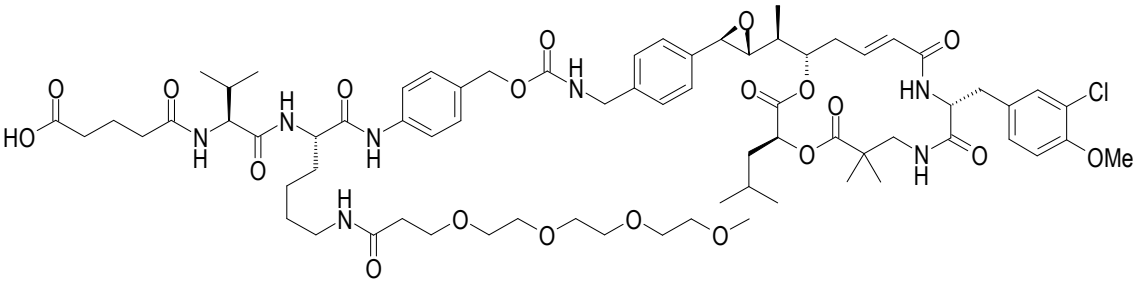
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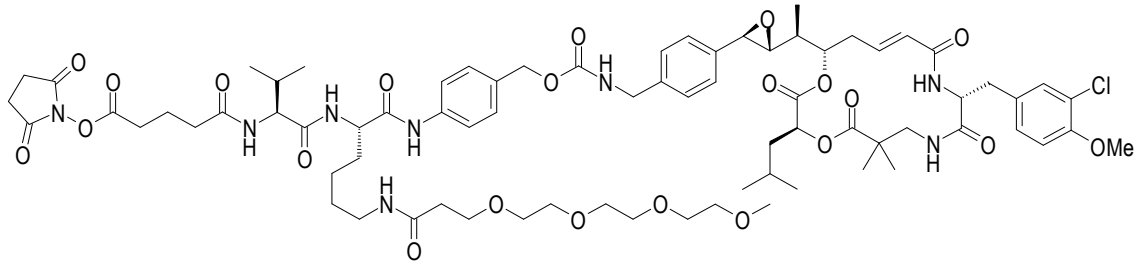
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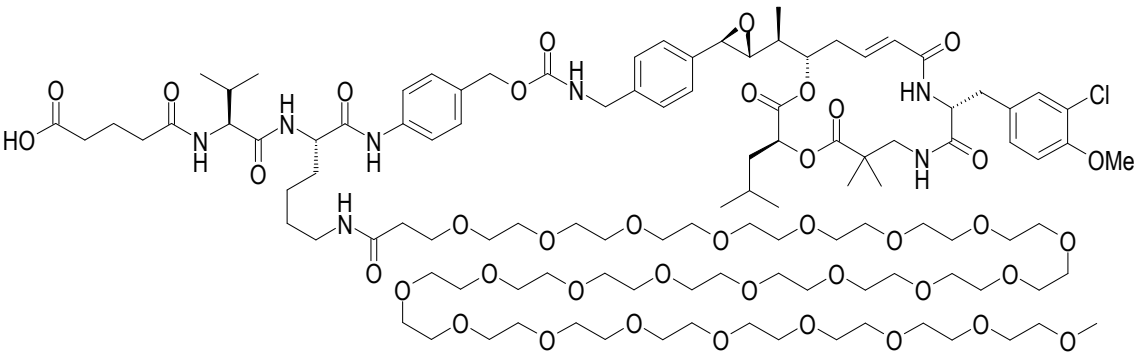
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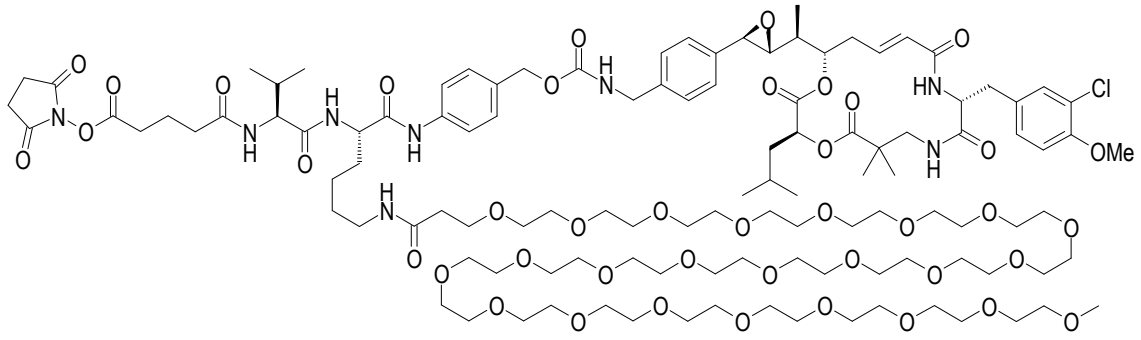
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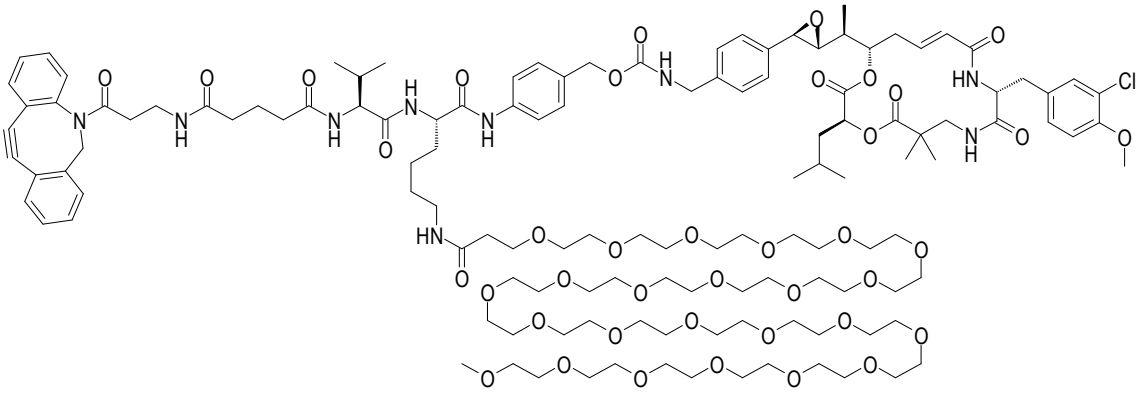
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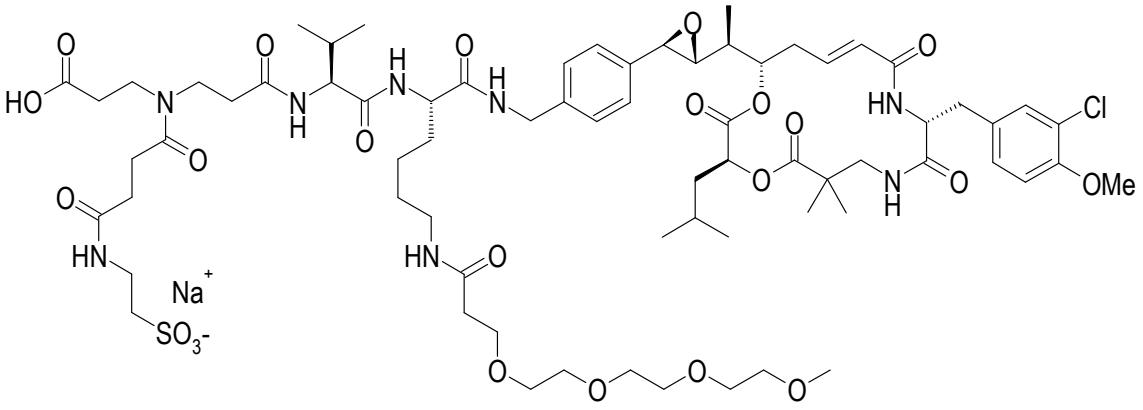
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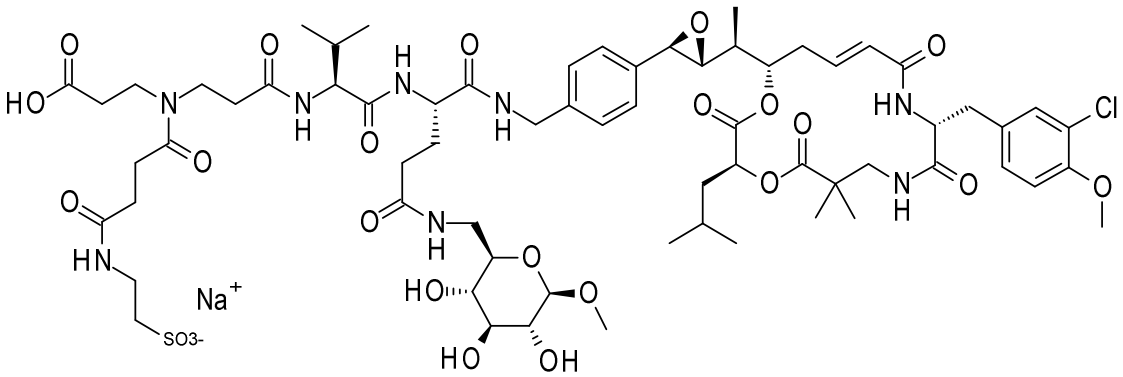
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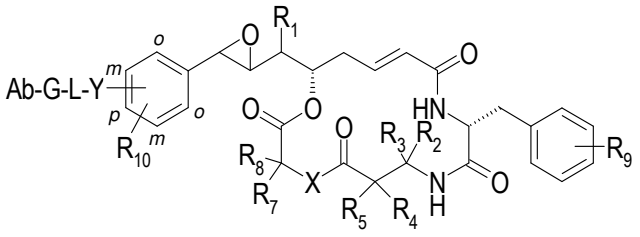
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and



~~16~~14. Conjugate of formula (V):

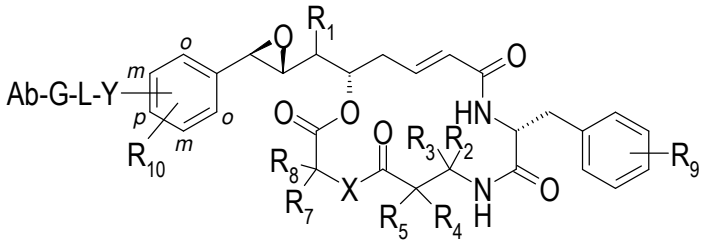


(V)

wherein:

- **R_1**, **R_2**, **R_3**, **R_4**, **R_5**, **R_6**, **R_7**, **R_8**, **R_9** ,**R_{10}**, **R_{11}**, **R_{12}**, **n, X, Y** and **L** are as defined in formula (IV) according to claims ~~13~~11 or ~~14~~12;
- **G** represents the product of reaction between **RCG1** as defined in claim ~~12~~10, a reactive chemical group present at the end of the linker **L** of formula (II) as defined in claim any one of claims 1 to ~~11~~9, and **RCG2**, an orthogonal reactive chemical group present on a polypeptide such as the antibody (Ab); and
- **Ab** represents an antibody.

~~17~~**15.** Conjugates of formula (V) according to claim ~~16~~14, having the following structure:



wherein:

- **R_1**, **R_2**, **R_3**, **R_4**, **R_5**, **R_6**, **R_7**, **R_8**, **R_9** ,**R_{10}**, **R_{11}**, **R_{12}**, **n, X, Y, L**, **G, RCG1, RCG2** and **Ab** are as in formula (V) according to claim ~~16~~14.

~~18~~**16.** Conjugates of formula (V) according to claim ~~16~~14 or ~~17~~15, wherein **RCG2** is selected from:

(i) ε-amino groups borne by the side chains of lysine residues that are present at the surface of the antibody;

(ii) α-amino groups of N-terminal amino acids of heavy and light chains of the antibody;

(iii) the saccharide groups of the hinge region of the antibody;

(iv) the thiols of cysteines generated by reducing intra-chain disulfide bonds of the antibody or the thiols of engineered cysteines of the antibody;

(v) amide groups borne by side chains of glutamine residues that are present at the surface of the antibody; and

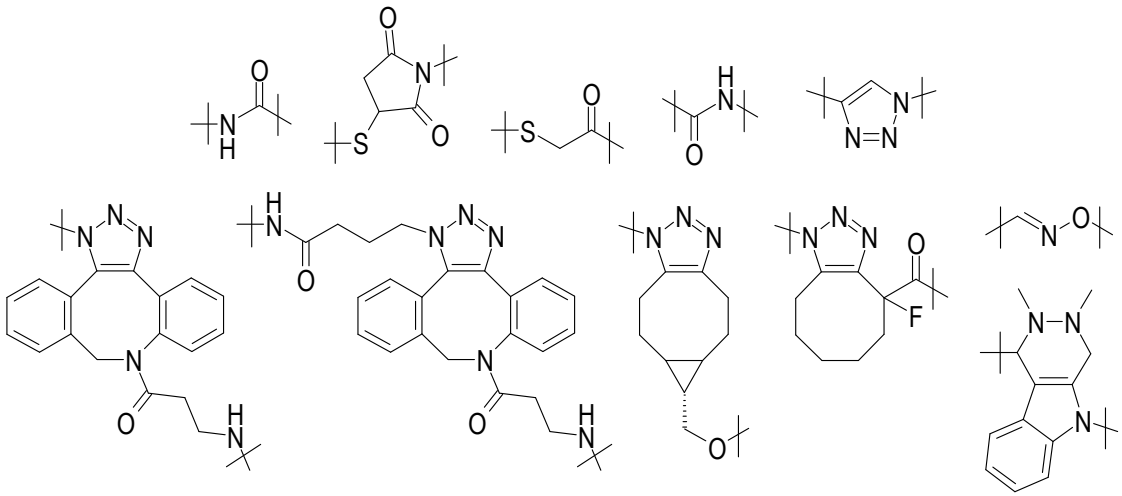
(vi) aldehyde groups introduced into the antibody using a formylglycine generating enzyme.

~~19~~**17.** Conjugates of formula (V) according to claim ~~16~~14 or ~~17~~15, wherein:

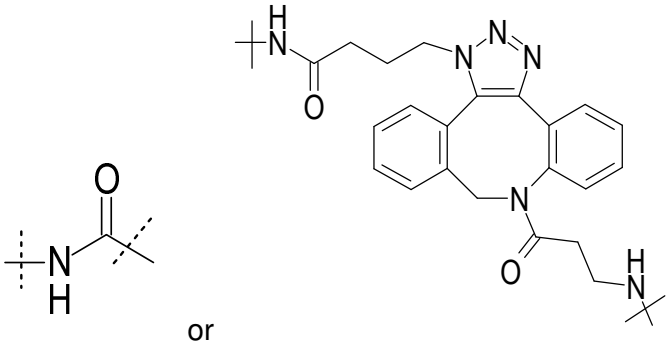
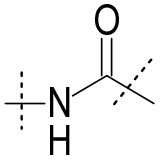
- when **RCG1** represents a N-hydroxysuccinimidyl ester, **RCG2** represents a NH_2 group;
- when **RCG1** represents a maleimido function, a haloacetamido function, a chlorine atom or an activated disulfide, **RCG2** represents a -SH group;
- when **RCG1** represents a N_3 group, **RCG2** represents a C≡CH group or an activated C≡C group such as a cyclooctyne moiety;
- 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 function, a haloacetamido function or an activated disulfide function;
- when **RCG1** represents a C≡CH group or an activated C≡C group, **RCG2** represents a N_3 group;
- when **RCG1** represents a O-alkyl hydroxylamine function or a Pictet-Spengler reaction substrate, **RCG2** represents an aldehyde or ketone function.

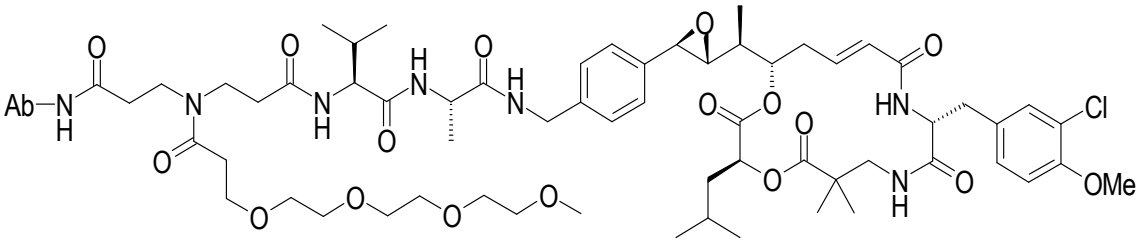
~~20~~18. Conjugates of formula (V) according to any one of claims ~~16~~14 to ~~19~~17, wherein **G** is selected from:



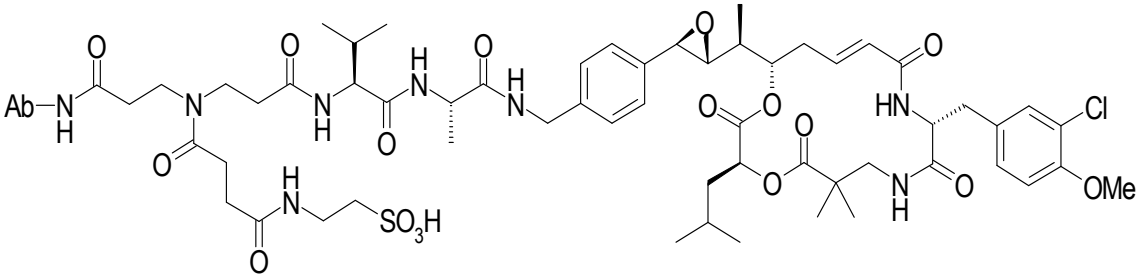
; for instance, G represents the following groups:

 or , such as .

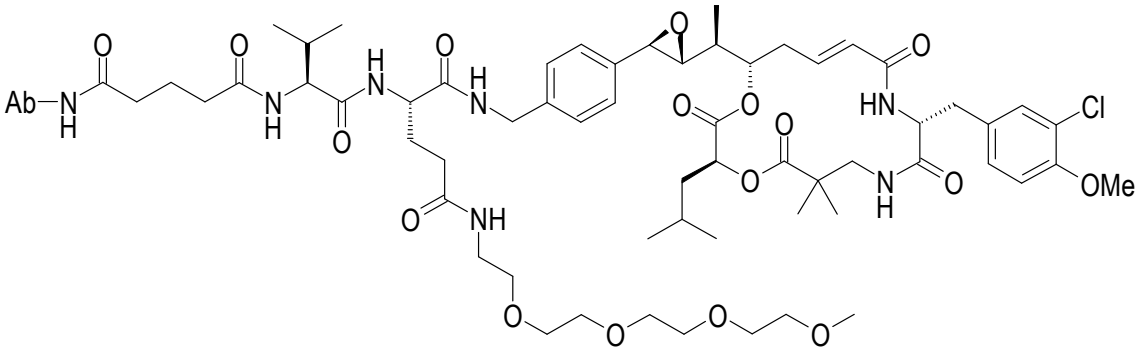
~~21~~19. Conjugates of formula (V) according to claim ~~16~~14, which is selected from the following list:



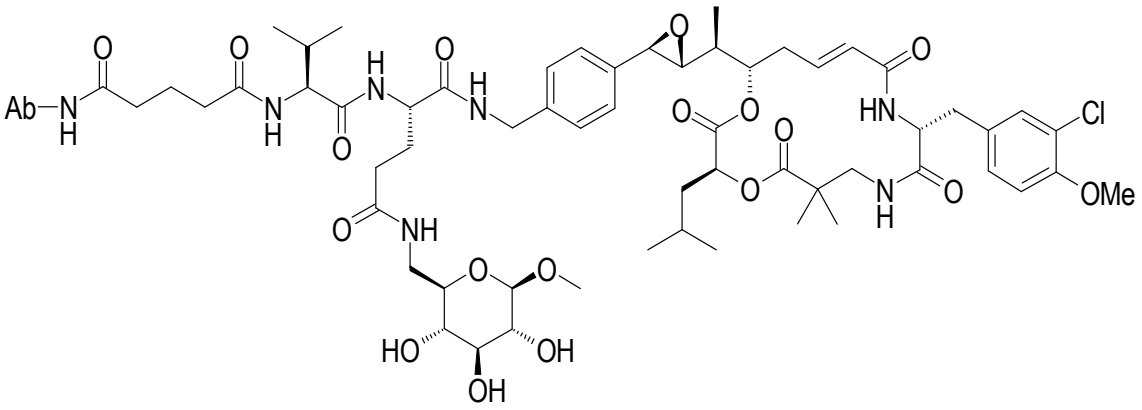
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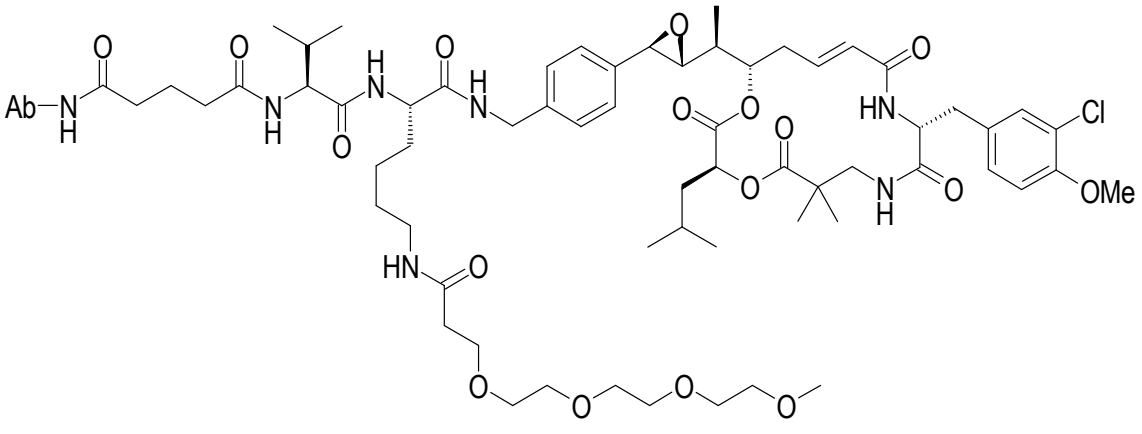
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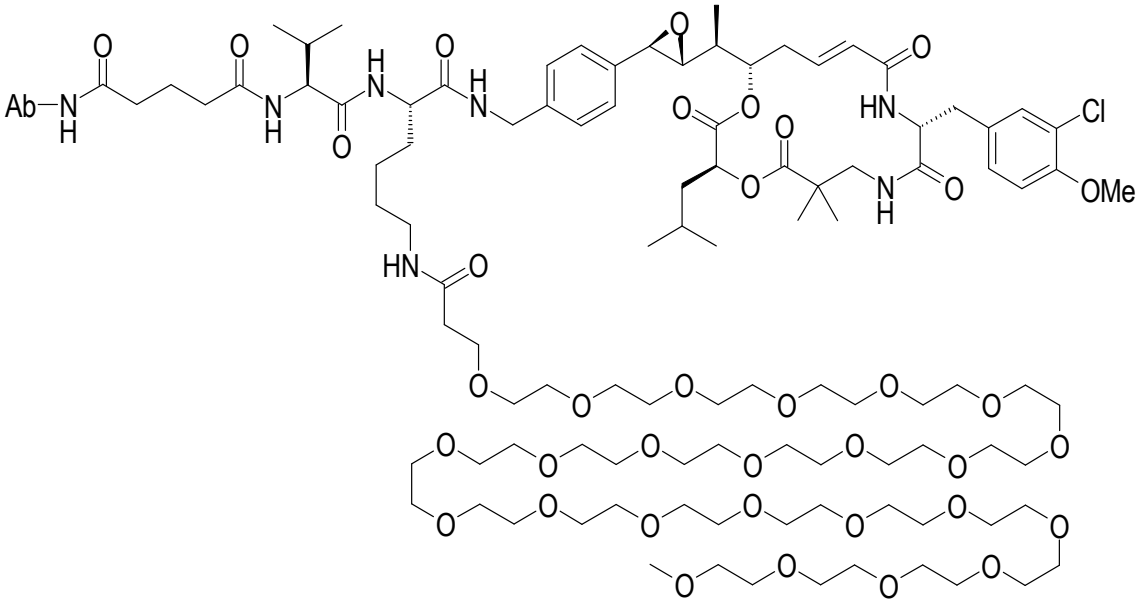
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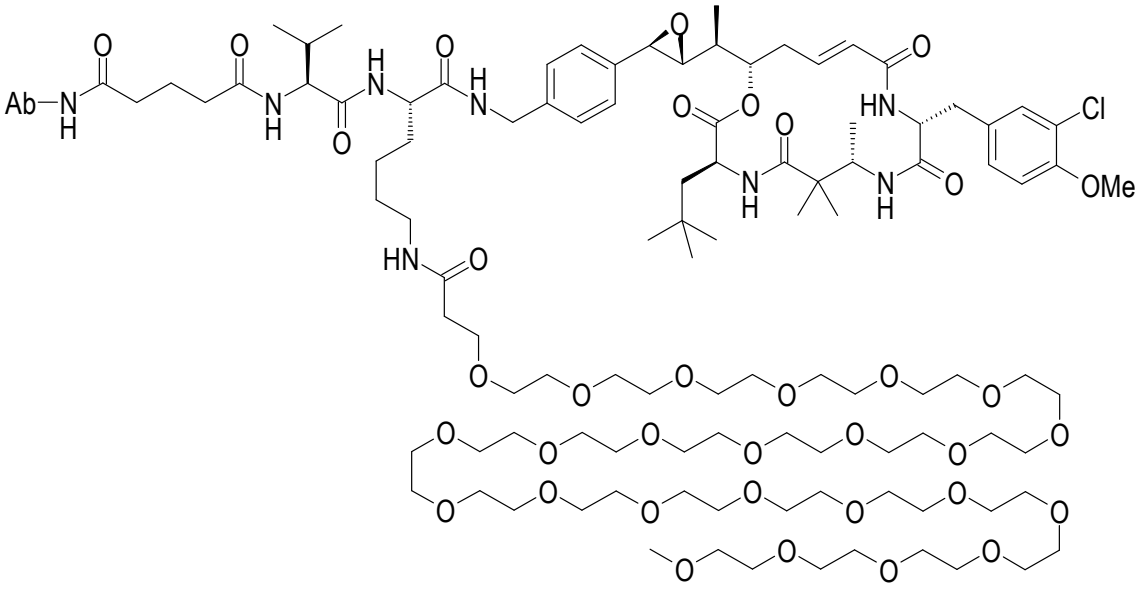
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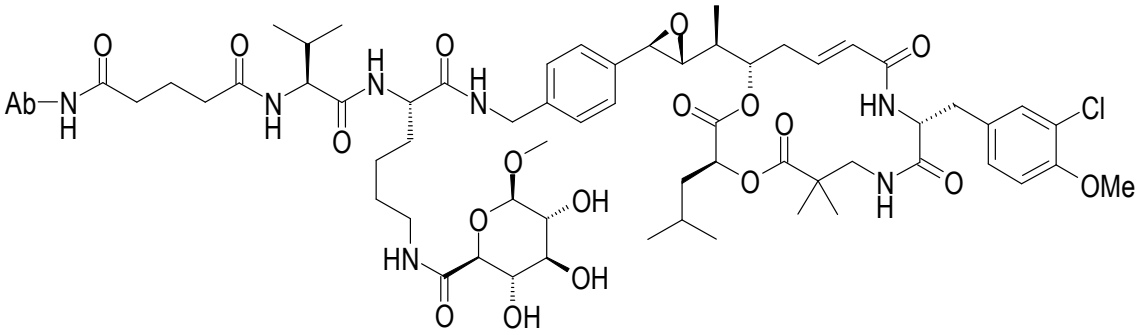
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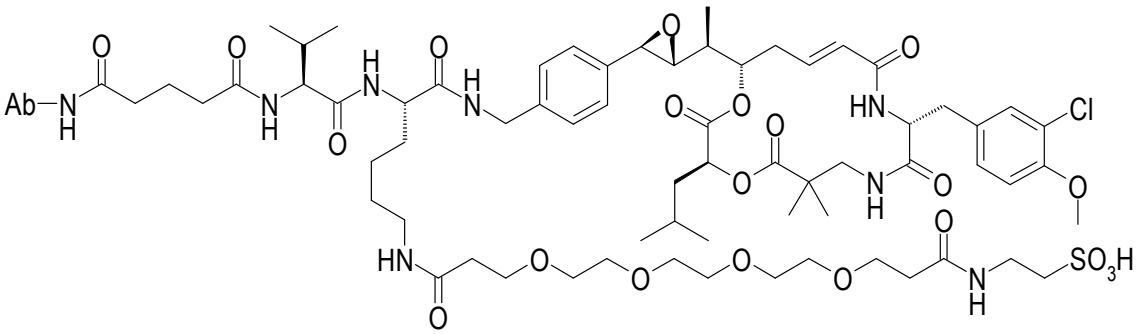
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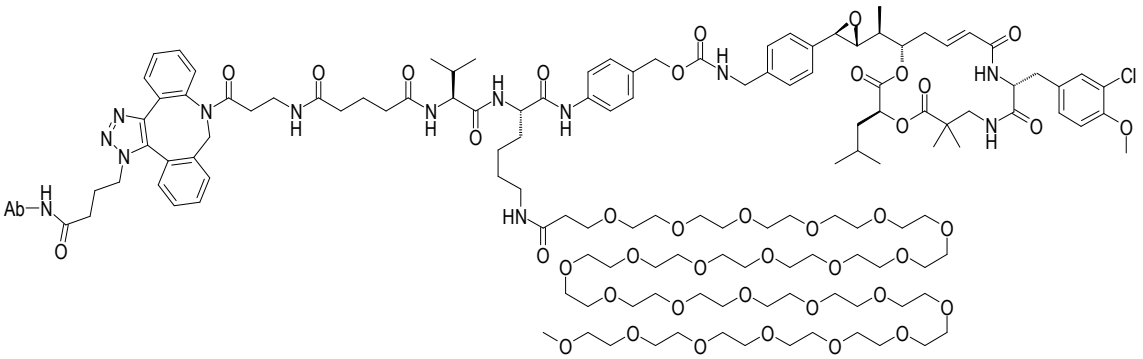
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;



and



wherein Ab represents an antibody.

~~22~~**20.** Process for preparing a conjugate of formula (V) as defined in any one of claims ~~16~~14 to ~~21~~19 comprising at least the steps of~~-~~:

(i) placing in contact and leaving to react:

- an optionally buffered aqueous solution of an antibody, ~~optionnally~~optionally modified by means of a modifying agent,

and

- a solution of a cryptophycin payload of formula (IV) as defined in any one of claims ~~13~~11 to ~~15~~13,

the chemical group **RCG1** of the cryptophycin payload of formula (IV) being reactive towards the chemical groups **RCG2** present on the polypeptide such as ~~-~~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 (IV) 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 (IV) and/or from the unreacted antibody and/or from any aggregates that may have formed.

~~23~~**21.** Medicament, wherein it comprises at least one conjugate of formula (V) according to any one of claims ~~16~~14 to ~~21~~19.

~~24~~**22.** Pharmaceutical composition, wherein it comprises at least one conjugate of formula (V) according to any one of claims ~~16~~14 to ~~21~~19, and also at least one pharmaceutically acceptable excipient.

~~25~~**23.** Conjugates of formula (V) according to any one of claims ~~16~~14 to ~~21~~19 for use in the treatment of cancer.