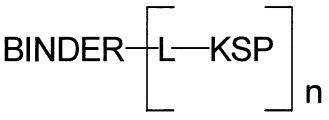
Claims

1. Conjugate of a binder or derivative thereof with one or more drug molecules or one or more prodrugs thereof, of the following formula:



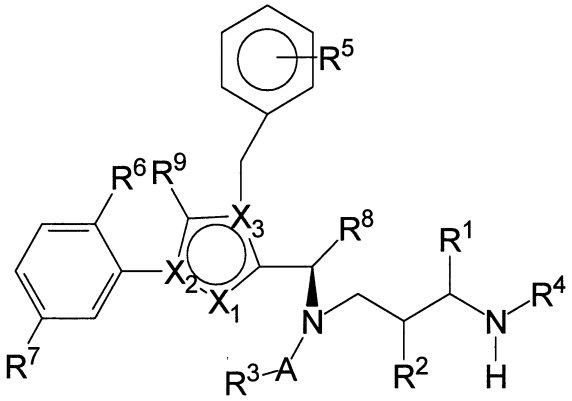
where

BINDER represents binder or a derivative thereof, preferably an antibody,

L represents a linker,

n represents a number from 1 to 50, preferably 1 to 20 and more preferably 2 to 8, and

KSP represents a kinesin spindle inhibitor or prodrug thereof, where -L-KSP has the following formula (IIa):



(IIa)

where

X_1 represents N, X_2 represents N and X_3 represents C; or

X_1 represents N, X_2 represents C and X_3 represents N; or

X_1 represents CH or CF, X_2 represents C and X_3 represents N; or

X_1 represents NH, X_2 represents C and X_3 represents C; or

X_1 represents CH, X_2 represents N and X_3 represents C;

(with X_1 representing CH, X_2 representing C and X_3 representing N being preferred);

R^1 represents -H, –L-#1, –MOD or $-(CH_2)_{0-3}Z$,

where Z represents -H, $-NHY^3$, $-OY^3$, $-SY^3$, halogen, $-C(=O)-NY^1Y^2$ or $-CO-OY^3$,

where Y^1 and Y^2 independently of one another represent -H, $-NH_2$, $-(CH_2CH2O)_{0-3}-(CH_2)_{0-3}Z'$ (e.g. $-(CH_2)_{0-3}Z'$) or $-CH(CH_2W)Z'$,

Y^3 represents -H or $-(CH_2)_{0-3}Z'$,

where Z' represents -H, NH_2, SO_3H, -COOH, $-NH-C(=O)-CH_2-CH_2-CH(NH_2)COOH$ or $-(C(=O)-NH-CHY^4)_{1-3}COOH$,

where W represents -H or -OH,

where Y^4 represents straight-chain or branched C_{1-6}-alkyl which is optionally substituted by $-NH-C(=O)-NH_2$, or represents aryl or benzyl which are optionally substituted by $-NH_2$;

R^2 represents –L-#1, -H, -MOD, $-C(=O)-CHY^4-NHY^5$ or $-(CH_2)_{0-3}Z$,

where Z represents -H, halogen, $-OY^3$, $-SY^3$, $-NHY^3$, $-C(=O)-NY^1Y^2$ or $-C(=O)-OY^3$,

where Y^1 and Y^2 independently of one another represent -H, $-NH_2$ or $-(CH_2)_{0-3}Z'$,

where Y^3 represents -H or $-(CH_2)_{0-3}Z'$,

where Z' represents -H, $-SO_3H$, $-NH_2$ or -COOH;

where Y^4 represents straight-chain or branched C_{1-6}-alkyl which is optionally substituted by $-NH-C(=O)-NH_2$, or represents aryl or benzyl which are optionally substituted by $-NH_2$,

where Y^5 represents -H or $-C(=O)-CHY^6-NH_2$,

where Y^6 represents straight-chain or branched C_{1-6}-alkyl;

R^4 represents –L-#1, -H, -C(=O)-CHY^4-NHY^5 or -$(CH_2)_{0-3}$Z,

where Z represents -H, halogen, -OY^3, -SY^3, -NHY^3, -C(=O)-NY^{1}Y^2 or –C(=O)-OY^3,

where Y^1 and Y^2 independently of one another represent -H, -NH_2 or -$(CH_2)_{0-3}$Z‘,

where Y^3 represents -H or -$(CH_2)_{0-3}$Z‘,

where Z‘ represents -H, -SO_3H, -NH_2 or -COOH;

where Y^4 represents straight-chain or branched C_{1-6}-alkyl which is optionally substituted by –NH-C(=O)-NH_2, or represents aryl or benzyl which are optionally substituted by –NH_2,

where Y^5 represents -H or –C(=O)-CHY^6-NH_2,

where Y^6 represents straight-chain or branched C_{1-6}-alkyl;

or

R^4 represents a group of the formula R^{21}-$(C(=O))_{(0-1)}$-$(P3)_{(0-2)}$-P2-NH-CH(CH_2C(=O)-NH_2)-C(=O)- or R^{21}-$(C(=O))_{(0-1)}$-$(P3)_{(0-2)}$-P2-NH-CH(CH_2COOH)-C(=O)- or the cathepsin-cleavable group of the formula R^{21}-$(C=O)_{(0-1)}$-$(P3)_{(1-2)}$-P2-,

where R^{21} represents a C_{1-10}-alkyl, C_5-aryl or C_{6-10}-aralkyl, C_{5-10}-heteroalkyl, C_{1-10}-alkyl-O-C_{6-10}-aryl, C_{5-10}-heterocycloalkyl, heteroaryl, heteroarylalkyl, C_{1-10}-alkoxy, C_{6-10}-aryloxy or C_{6-10}-aralkoxy, C_{5-10}-heteroalkoxy, C_{1-10}-alkyl-O-C_{6-10}-aryloxy, C_{5-10}-heterocycloalkoxy group which may be mono- or polysubstituted by - NH_2, -NH-alkyl, -N(alkyl)$_2$, NH-C(=O)-alkyl, -N(alkyl)-C(=O)-alkyl, -SO_3H, -S(=O)$_2NH_2$, -S(=O)$_2$-N(alkyl)$_2$, -COOH, -C(=O)NH_2, -C(=O)N(alkyl)$_2$, or –OH, -H or an –O_x-$(CH_2CH_2O)_y$-R^{22} group,

where x is 0 or 1

where v represents a number from 1 to 20, and

where R^{22} represents –H, –alkyl (preferably C_{1-12}-alkyl), $-CH_2-COOH$, $-CH_2-CH_2-COOH$, or $-CH_2-CH_2-NH_2$),

where P2 is an amino acid selected from Gly, Pro, Ala, Val, Nva, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg, citrulline and His;

where P3 is an amino acid selected from Gly, Pro, Ala, Val, Nva, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg, citrulline and His or the respective N-alkyl amino acids, preferably N-methyl amino acids;

or

R^2 and R^4 together represent (forming a pyrrolidine ring) $–CH_2-CHR^{10}-$ or $\#-CHR^{10}-CH_2-$,

where R^{10} represents -H, $-NH_2$, $-SO_3H$, -COOH, -SH, halogen (especially F or Cl), C_{1-4}-alkyl, C_{1-4}-haloalkyl, C_{1-4}-alkoxy, hydroxyl-substituted C_{1-4}-alkyl, $COO(C_{1-4}$-alkyl), -OH or R^{21}-C(=O)-P3-P2-NH-$CH(CH_2C(=O)-NH_2)$-C(=O)-SIG-,

where SIG represents a self-immolative group which, after cleavage of the C(=O)-SIG bond, releases the secondary amine;

A represents -C(=O)-, -S(=O)-, $-S(=O)_2-$, $-S(=O)_2NH-$ or -C(=N-NH2)-;

R^3 represents –L-#1, -MOD or an optionally substituted alkyl, cycloalkyl, aryl, heteroaryl, heteroalkyl, heterocycloalkyl group, preferably –L-#1 or a C_{1-10}-alkyl, C_{6-10}-aryl or C_{6-10}-aralkyl, C_{5-10}-heteroalkyl, C_{1-10}-alkyl-O-C_{6-10}-aryl or C_{5-10}-heterocycloalkyl group which may in each case be substituted by 1-3 –OH groups, 1-3 halogen atoms, 1-3 halogenated alkyl groups (each having 1-3 halogen atoms), 1-3 O-alkyl groups, 1-3 –SH groups, 1-3 -S-alkyl groups, 1-3 -O-C(=O)-alkyl groups, 1-3 -O-C(=O)-NH-alkyl groups,

1-3 -NH-C(=O)-alkyl groups, 1-3 -NH-C(=O)-NH-alkyl groups, 1-3 -$S(O)_n$-alkyl groups, 1-3 -$S(=O)_2$-NH-alkyl groups, 1-3 -NH-alkyl groups, 1-3 -$N(alkyl)_2$ groups, 1-3 -NH_2 groups or 1-3 -$(CH_2)_{0-3}Z$ groups,

where Z represents -H, halogen, -OY^3, -SY^3, -NHY^3, -C(=O)-NY^1Y^2 or -C(=O)-OY^3,

where n represents 0, 1 or 2,

where Y^1 and Y^2 independently of one another represent -H, -NH_2 or -$(CH_2)_{0-3}Z'$,

where Y^3 represents -H, -$(CH_2)_{0-3}$-$CH(NHCOCH_3)Z'$, -$(CH_2)_{0-3}$-$CH(NH_2)Z'$ or -$(CH_2)_{0-3}Z'$,

where Z' represents -H, -SO_3H, -NH_2 or -COOH, (where "alkyl" preferably represents C_{1-10}-alkyl);

R^5 represents -H, -NH_2, -NO_2, halogen (in particular -F, -Cl, -Br), -CN, -CF_3, -OCF_3, -CH_2F, -CH_2F, -SH or -$(CH_2)_{0-3}Z$,

where Z represents -H, -OY^3, -SY^3, halogen, -NHY^3,
-C(=O)-NY^1Y^2 or -C(=O)-OY^3,

where Y^1 and Y^2 independently of one another represent -H, -NH_2 or -$(CH_2)_{0-3}Z'$,

where Y^3 represents -H or -$(CH_2)_{0-3}Z'$,

where Z' represents -H, -SO_3H, -NH_2 or -COOH;

R^6 and R^7 independently of one another represent -H, cyano, C_{1-10}-alkyl, fluoro-C_{1-10}-alkyl, C_{2-10}-alkenyl, fluoro-C_{2-10}-alkenyl, C_{2-10}-alkynyl, fluoro-C_{2-10}-alkynyl, hydroxy, -NO_2, NH_2, -COOH or halogen (in particular -F, -Cl, -Br),

R^8 represents C_{1-10}-alkyl, fluoro-C_{1-10}-alkyl, C_{2-10}-alkenyl, fluoro-C_{2-10}-alkenyl, C_{2-10}-alkynyl, fluoro-C_{2-10}-alkynyl, C_{4-10}-cycloalkyl, fluoro-C_{4-10}-cycloalkyl, or –$(CH_2)_{0-2}$-(HZ^2),

where HZ^2 represents a 4- to 7-membered heterocycle having up to two heteroatoms selected from the group consisting of N, O and S,

where each of these groups may be substituted by –OH, -COOH or -NH_2 or –L-#1;

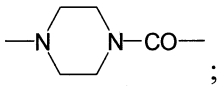
R^9 represents -H, -F, -CH_3, -CF_3, -CH_2F or -CHF_2;

where one of the substituents R^1, R^2, R^3, R^4 and R^8 represents or (in the case of R^8) contains –L-#1,

–L represents the linker and #1 represents the bond to the binder or derivative thereof,

where –MOD represents –$(NR^{10})_n$-$(G1)_o$-G2-G3,

where R^{10} represents -H or C_1-C_3-alkyl;

where G1 represents –NH-C(=O)- , -C(=O)NH- or ;

n is 0 or 1;

o is 0 or 1;

and

where G2 is a straight-chain and/or branched hydrocarbon group which has 1 to 10 carbon atoms and which may be interupted once or more than once by one or more of the groups -O-, -S-, -S(=O)-, $S(=O)_2$, -NR^y-, -$NR^yC(=O)$-, -C(=O)-NR^y-, -NR^yNR^y-, -$S(=O)_2NR^yNR^y$-, -C(=O)-NR^yNR^y-, -C(=O)-, -CR^x=N-O-,

where R^y represents -H, phenyl, C_1-C_{10}-alkyl, C_2-C_{10}-alkenyl or C_2-C_{10}-alkynyl, each of which may be substituted by -NH-C(=O)-NH_2, -COOH, -OH, -NH_2, -NH-CN-NH_2, sulphonamide, sulphone, sulphoxide or sulphonic acid

where Rx represents -H, C_1-C_3-alkyl or phenyl,

where the hydrocarbon chain including a C_1-C_{10}-alkyl group optionally substituted on the hydrocarbon group as side chain, if present, may be substituted by –NH-C(=O)-NH_2, -COOH, -OH, -NH_2, -NH-CN-NH_2, sulphonamide, sulphone, sulphoxide or sulphonic acid,

where G3 represents -H or -COOH;

where –MOD preferably has at least one –COOH group;

where one or more of the following conditions (i) to (iii) is fulfilled:

(i) –L-#1 comprises a group of the formula
-(C=O)$_{(0-1)}$-(P3)$_{(0-2)}$-P2-NH-CH(CH_2C(=O)-X)-C(=O)-,
where X represents –NH_2;
where P2 is an amino acid selected from Gly, Pro, Ala, Val, Nva, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg, citrulline and His;
where P3 is an amino acid selected from Gly, Pro, Ala, Val, Nva, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg, citrulline and His;

(ii) R^4 represents the group of the formula
R^{21}-(C=O)$_{(0-1)}$-(P3)$_{(0-2)}$-P2-NH-CH(CH_2C(=O)-NH_2)-C(=O)- or
R^{21}-(C=O)$_{(0-1)}$-(P3)$_{(0-2)}$-P2-NH-CH(CH_2COOH)-C(=O)- or the cathepsin-cleavable group of the formula R^{21}-(C=O)$_{(0-1)}$-(P3)$_{(1-2)}$-P2-;
where R^{21} represents a C_{1-10}-alkyl, C_{5-10}-aryl or C_{6-10}-aralkyl, C_{5-10}-heteroalkyl, C_{1-10}-alkyl-O-C_{6-10}-aryl, C_{5-10}-heterocycloalkyl, heteroaryl, heteroarylalkyl, C_{1-10}-alkoxy, C_{6-10}-aryloxy or C_{6-10}-aralkoxy, C_{5-10}-heteroalkoxy, C_{1-10}-alkyl-O-C_{6-10}-aryloxy, C_{5-10}-heterocycloalkoxy group which may be mono- or polysubstituted by -NH_2, -NH-alkyl, -N(alkyl)$_2$, -NH-C(=O)-alkyl, -N(alkyl)-C(=O)-alkyl, -SO_3H, -S(=O)$_2$-NH_2, -S(=O)$_2$-N(alkyl)$_2$, -COOH, -C(=O)-NH_2, -C(=O)-N(alkyl)$_2$

or -OH, -H or a $-O_x-(CH_2CH_2O)_y-R^{22}$ group,

where x is 0 or 1

where v represents a number from 1 to 20, and

where R^{22} represents –H, –alkyl (preferably C_{1-12}-alkyl), $-CH_2-COOH$, $-CH_2-CH_2-COOH$, or $-CH_2-CH_2-NH_2$),

where P2 is an amino acid selected from Gly, Pro, Ala, Val, Nva, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg, citrulline and His;

where P3 is an amino acid selected from Gly, Pro, Ala, Val, Nva, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg, citrulline and His or the respective N-alkyl amino acids, preferably N-methyl amino acids;

(iii) R^2 and R^4 together represent (forming a pyrrolidine ring) $-CH_2-CHR^{10}-$ or $-CHR^{10}-CH_2-$, where the secondary hydrogen atom of the secondary amine group of the pyrrolidine ring is replaced by $R^{21}-C(=O)-P3-P2-NH-CH(CH_2C(=O)-NH_2)-C(=O)-SIG-$,

where SIG represents a self-immolative group which, after cleavage of the C(=O)-SIG bond, releases the secondary amine and

where R^{21} represents a C_{1-10}-alkyl, C_{5-10}-aryl or C_{6-10}-aralkyl, C_{5-10}-heteroalkyl, C_{1-10}-alkyl-O-C_{6-10}-aryl, C_{5-10}-heterocycloalkyl, heteroaryl, heteroarylalkyl, C_{1-10}-alkoxy, C_{6-10}-aryloxy or C_{6-10}-aralkoxy, C_{5-10}-heteroalkoxy, C_{1-10}-alkyl-O-C_{6-10}-aryloxy, C_{5-10}-heterocycloalkoxy group which may be mono- or polysubstituted by $-NH_2$, -NH-

alkyl, -N(alkyl)$_2$, -NH-C(=O)-alkyl, -N(alkyl)-C(=O)-alkyl, -SO_3H, -S(=O)$_2$-NH_2, -S(=O)$_2$-N(alkyl)$_2$, -COOH, -C(=O)-NH_2, -C(=O)-N(alkyl)$_2$ or -OH, -H or a $-O_x-(CH_2CH_2O)_y-R^{22}$ group,

where x is 0 or 1

where v represents a number from 1 to 20, and

where R^{22} represents –H, –alkyl (preferably C_{1-12}-alkyl), -CH_2-COOH, -CH_2-CH_2-COOH, or -CH_2-CH_2-NH_2),

where P2 is an amino acid selected from Gly, Pro, Ala, Val, Nva, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg, citrulline and His;

where P3 is an amino acid selected from Gly, Pro, Ala, Val, Nva, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg, citrulline and His or the respective N-alkyl amino acids, preferably N-methyl amino acids;

and the salts, solvates, salts of the solvates and epimers thereof.

2. Conjugate according to Claim 1 where R^4 represents the group of the formula R^{21}-(C(=O))$_{(0-1)}$-(P3)$_{(0-2)}$-P2-NH-CH(CH_2C(=O)NH_2)-C(=O)-.

3. Conjugate according to Claim 1 or 2 where P2 is selected from Ala, Gly, Val, Leu, Ile, Pro, Ser, Thr and Asn.

4. Conjugate according to one or more of the preceding claims where P3 is selected from Pro, Ala, Val, Leu, Ile, Gly, Ser and Gln.

5. Conjugate according to one or more of the preceding claims where P2 is Ala.

6. Conjugate according to one or more of the preceding claims where P3 is Ala.

7. Conjugate according to one or more of the preceding claims

where R^{21} represents -H , a C_{1-5}-alkyl-, C_{5-10}-aralkyl-, C_{1-5}-alkoxy-, C_{6-10}-aryloxy group, C_{5-10}-heteroalkyl, C_{5-10}-heterocycloalkyl, heteroaryl, heteroarylalkyl, C_{5-10}-heteroalkoxy or a C_{5-10}-heterocycloalkoxy group, each of which may be substituted by -COOH, -C(=O)-Oalkyl, -C(=O)O-NH_2, -NH_2 or -N(alkyl)$_2$, or a $-O_x-(CH_2CH_2O)_y-R^{22}$ group,

where x is 0 or 1,

where v represents a number from 1 to 20, and

R^{22} is –H, –alkyl (preferably C1-12-alkyl), -CH2-COOH, -CH_2-CH_2-COOH, or -CH_2-CH_2-NH_2).

8. Conjugate according to one or more of the preceding claims

where R^4 represents –L-#1 and comprises the group of the formula

$-(C=O)_{(0-1)}-(P3)_{(0-2)}$-P2-NH-CH($CH_2$C(=O)-$NH_2$)-C(=O)-,

where P2 is an amino acid selected from Gly, Pro, Ala, Val, Nva, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg, citrulline and His and

where P3 is an amino acid selected from Gly, Pro, Ala, Val, Nva, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg, citrulline and His or the respective N-alkyl amino acids, preferably N-methyl amino acids.

9. Conjugate according to one or more of Claims 1 to 7 where the conjugate is a binder-prodrug conjugate,

where R^4 represents the group of the formula

$R^{21}-(C=O)_{(0-1)}-(P3)_{(0-2)}$-P2-NH-CH($CH_2$C(=O)-$NH_2$)-C(=O)-,

where R^{21} represents a C_{1-10}-alkyl, C_{5-10}-aryl or C_{6-10}-aralkyl, C_{5-10}-heteroalkyl, C_{1-10}-alkyl-O-C_{6-10}-aryl, C_{5-10}-heterocycloalkyl, heteroaryl, heteroarylalkyl, C_{1-10}-alkoxy, C_{6-10}-aryloxy or C_{6-10}-aralkoxy, C_{5-10}-heteroalkoxy, C_{1-10}-alkyl-O-C_{6-10}-aryloxy, C_{5-10}-heterocycloalkoxy group which may be mono- or polysubstituted by -NH_2, -NH-alkyl, -N(alkyl)$_2$, -NH-C(=O)-alkyl, -N(alkyl)-C(=O)-alkyl, -SO_3H, -S(=O)$_2$-NH_2, -S(=O)$_2$-N(alkyl)$_2$, -COOH, -

$C(=O)-NH_2$, $-C(=O)-N(alkyl)_2$ or –OH, or -H or a $–Ox-(CH_2CH_2O)v-R^{22}$ group,
where x is 0 or 1
where v represents a number from 1 to 20, and
where R^{22} represents –H, –alkyl (preferably C_{1-12}-alkyl),
$-CH_2-COOH$, $-CH_2-CH_2-COOH$, or
$-CH_2-CH_2-NH_2$),

where P2 is an amino acid selected from Gly, Pro, Ala, Val, Nva, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg, citrulline and His;

where P3 is an amino acid selected in each case independently from Gly, Pro, Ala, Val, Nva, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg, citrulline and His or the respective N-alkyl amino acids, preferably N-Methyl amino acids.

10. Conjugate according to one or more of the preceding claims where R^1 or R^3 represents –L-#1.

11. Conjugate according to one or more of the preceding claims where X_1 is CH, X_2 is C and X_3 is N.

12. Conjugate according to one or more of the preceding claims where R^6 and R^7 independently of one another represent -H, C_{1-3}-alkyl or halogen.

13. Conjugate according to Claim 12 where R^6 and R^7 represent –F.

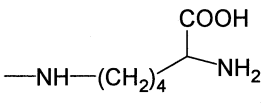
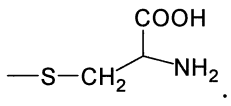
14. Conjugate according to one or more of the preceding claims where R^8 represents C_{1-4}-alkyl, preferably tert-butyl, or cyclohexyl.

15. Conjugate according to one or more of the preceding claims where R^9 represents H.

16. Conjugate according to one or more of the preceding claims where the binder or derivative thereof is a binder peptide or protein or a derivative of a binder peptide or protein.

17. Conjugate according to Claim 16 where each drug molecule is attached to different amino acids of the binder peptide or protein or derivative thereof via the linker.

18. Conjugate according to one or more of the preceding claims where the conjugate has on average 1.2 to 20 drug molecules or prodrugs per binder.

19. Conjugate according to one or more of Claims 16 to 18 where the binder peptide or protein represents an antibody or  or .

20. Conjugate according to one or more of the preceding claims where the binder binds to a cancer target molecule.

21. Conjugate according to Claim 20 where the binder binds to an extracellular target molecule.

22. Conjugate according to Claim 21 where the binder, after binding to the extracellular target molecule, is internalized and processed intracellularly (preferably lysosomally) by the cell expressing the target molecule.

23. Conjugate according to one or more of Claims 16 to 22 where the binder peptide or protein is a human, humanized or chimeric monoclonal antibody or an antigen-binding fragment thereof.

24. Conjugate according to Claim 23 where the binder peptide or protein is an anti-HER2 antibody, an anti-EGFR antibody, an anti-TWEAKR antibody or an antigen-binding fragment thereof.

25. Conjugate according to Claim 24 where the anti-TWEAKR antibody binds specifically to amino acid D in position 47 (D47) of TWEAKR (SEQ ID NO:169), preferably the anti-TWEAKR antibody TPP-2090.

26. Conjugate according to one or more of Claims 24 and 25 where the anti-TWEAKR antibody binds specifically to amino acid D in position 47 (D47) of TWEAKR (SEQ ID NO:169), preferably the anti-TWEAKR antibody TPP-2658.

27. Conjugate according to Claim 24 where the binder peptide or protein is an anti-EGFR antibody and R3 represents –L-#1.

28. Conjugate according to one or more of the preceding claims where the linker –L- has one of the basic structures (i) to (iv) below:

(i) -(C=O)$_m$–SG1-L1-L2-

(ii) -(C=O)$_m$ –L1-SG-L1-L2-

(iii) -(C=O)$_m$ –L1-L2-

(iv) -(C=O)$_m$ –L1-SG-L2-

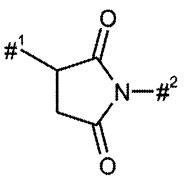
where m is 0 or 1, SG and SG1 represent *in vivo* cleavable groups, L1 independently of one another represent organic groups not cleavable *in vivo*, and L2 represents a coupling group to the binder.

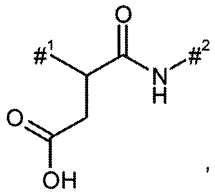
29. Conjugate according to Claim 28 where the *in vivo* cleavable group SG is a 2-8 oligopeptide group, preferably a dipeptide group or a disulphide, a hydrazone, an acetal or an aminal and SG1 is a 2-8 oligopeptide group, preferably a dipeptide group.

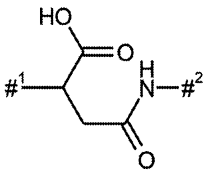
30. Conjugate according to one or more of the preceding claims
where the linker is attached to a cysteine side chain or a cysteine residue and has the following formula:

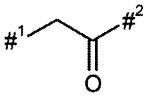
§-(C=O)m-L1-L2-§§

where
m is 0 or 1;
§ represents the bond to the drug molecule and
§§ represents the bond to the binder peptide or protein, and
-L2- represents



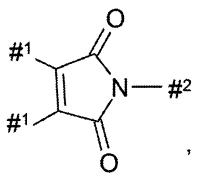
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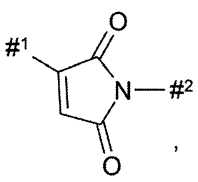
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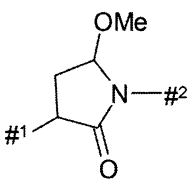
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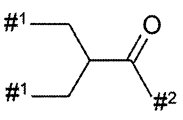
,


,



,


,


or


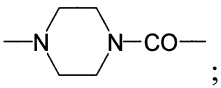
where

$\#^1$ denotes the point of attachment to the sulphur atom of the binder,

$\#^2$ denotes the point of attachment to the group L1,

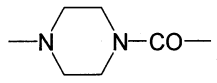
L1 represents $-(NR^{10})_n$-(G1)o-G2-,
where

R^{10} represents -H, $-NH_2$ or C_1-C_3-alkyl;

G1 represents –NH-C(=O)- or ;

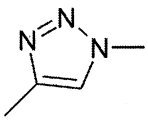
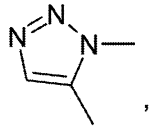
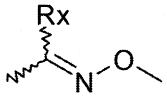
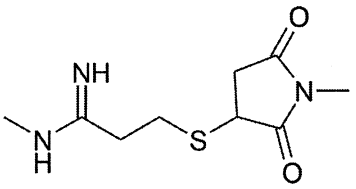
n is 0 or 1;

o is 0 or 1; and

G2 represents a straight-chain or branched hydrocarbon chain having 1 to 100 carbon atoms from arylene groups and/or straight-chain and/or branched and/or cyclic alkylene groups and which may be interrupted once or more than once by one or more of the groups -O-, -S-, -SO-, $-S(=O)_2$-, -NH-, -C(=O)-, -NMe-, -NHNH-, $-S(=O)_2$-NHNH-, -NH-C(=O)-, -C(=O)-NH-, -C(=O)-NHNH- and a 5- to 10-membered aromatic or non-aromatic heterocycle having up to 4 heteroatoms selected from the group consisting of N, O and S, -S(=O)- or $-S(=O)_2$- (preferably ), where the side chains, if present, may be substituted by –NH-C(=O)-NH_2, -COOH, -OH, $-NH_2$, -NH-CN-NH_2, sulphonamide, sulphone, sulphoxide or sulphonic acid,

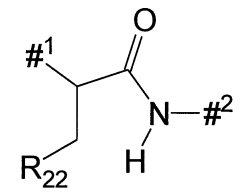
or

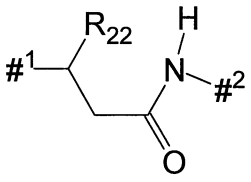
or represents one of the following groups:

, ,  or 

where Rx represents -H, $-C_1$-C_3-alkyl or phenyl.

31. Conjugate according to Claim 30 where L2 is represented by one or both of the formulae below:





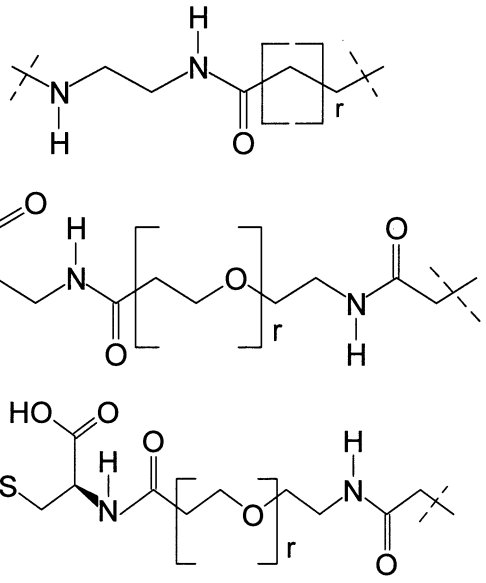
where

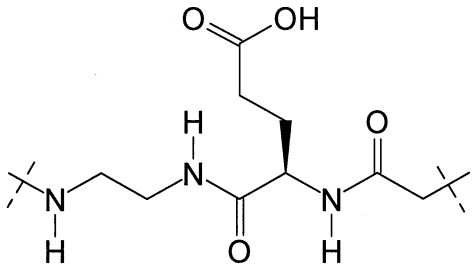
$\#^1$ denotes the point of attachment to the sulphur atom of the binder,

$\#^2$ denotes the point of attachment to group L^1,

R^{22} represents -COOH, and the bonds to the sulphur atom of the binder are present in one of these two structures to an extent of more than 80% (based on the total number of bonds in the linker to the binder).

32. Conjugate according to one or more of Claims 30 or 31 where L^1 has the following formulae:

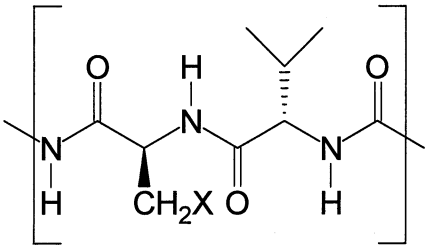


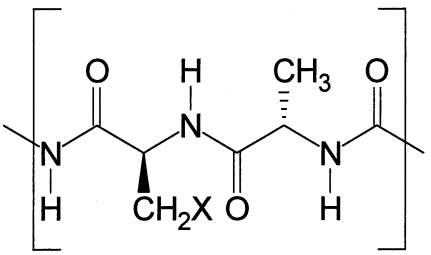


in which

r is a number from 0 to 8.

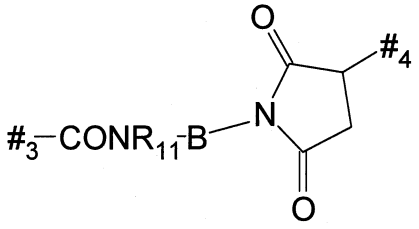
33. Conjugate according to one or more of Claims 30 to 32 where the hydrocarbon chain is interrupted by one of the groups below:





where X represents -H or a C_{1-10}-alkyl group which may optionally be substituted by –NH-C(=O)-NH_2, -COOH, -OH, -NH_2, -NH-CN-NH_2, sulphone, sulphoxide or sulphonic acid.

34. Conjugate according to Claim 30 where the linker has the formula below:



where

#3 represents the bond to the drug molecule,

#4 represents the bond to the binder peptide or protein,

R^{11} represents $-NH_2$;

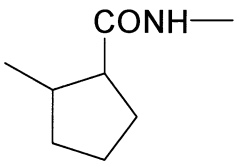
B represents $-[(CH_2)_x-(X^4)_y]_w-(CH_2)_z-$,

w is 0 to 20;

x is 0 to 5;

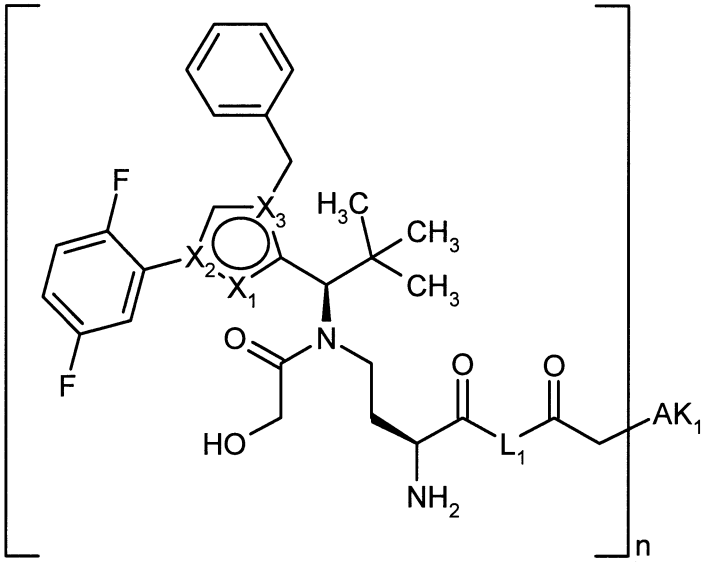
y is 0 or 1;

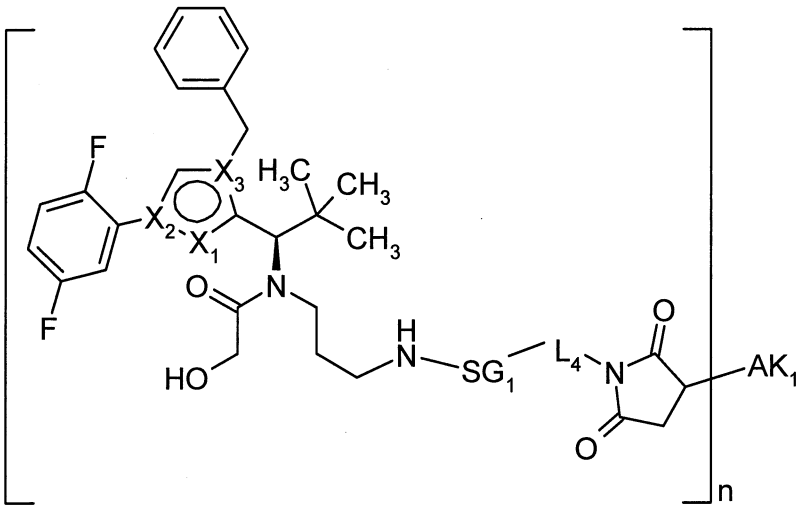
z is 0 to 5; and

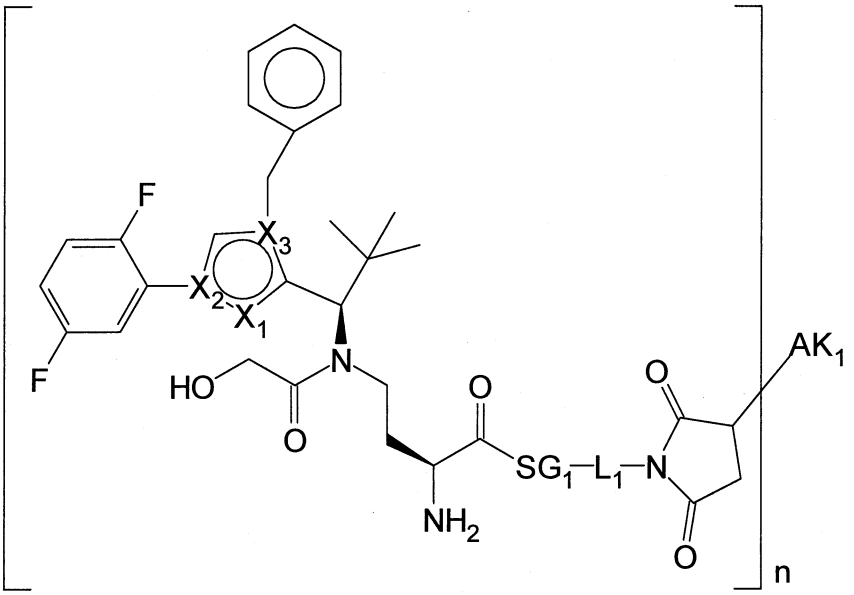
X^4 represents –O-, -C(=O)-NH- or –NH-C(=O)- 

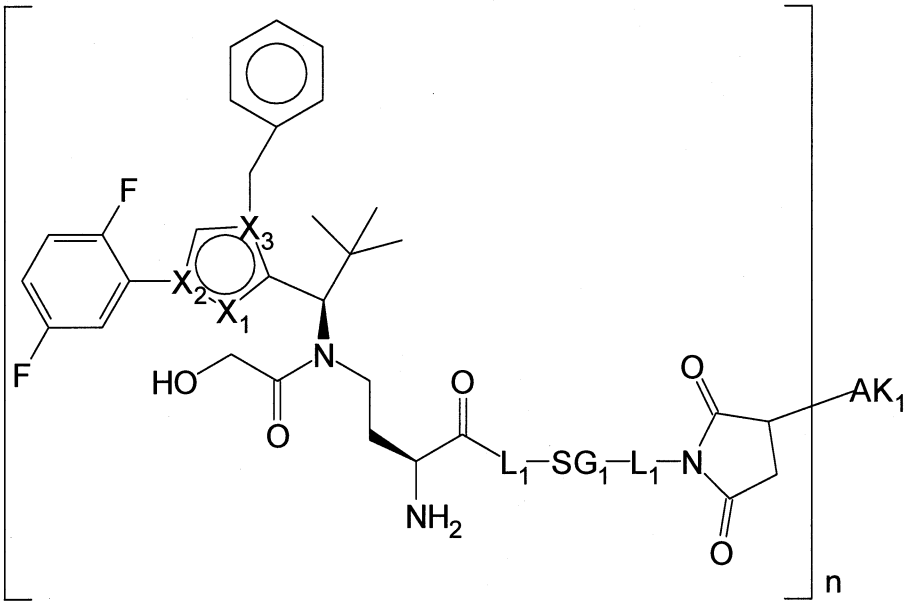
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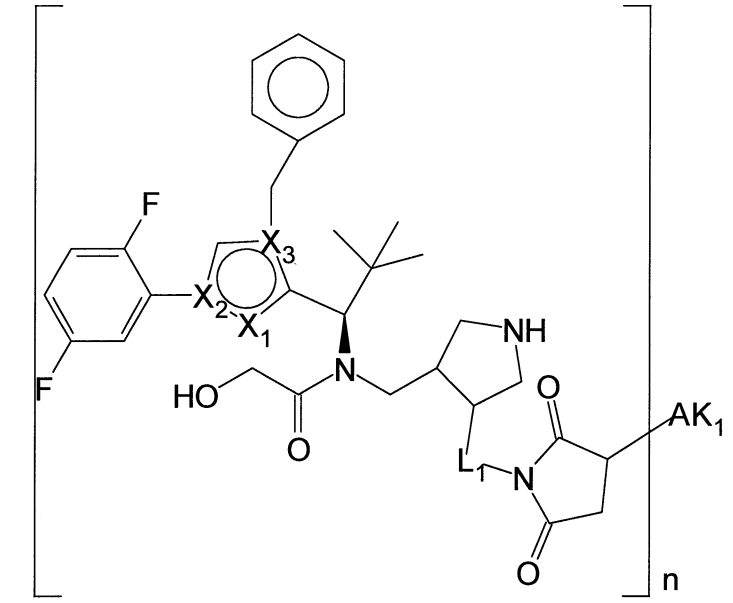
35. Conjugate according to one or more of Claims 26 to 30 where the conjugate satisfies one of the following formulae:

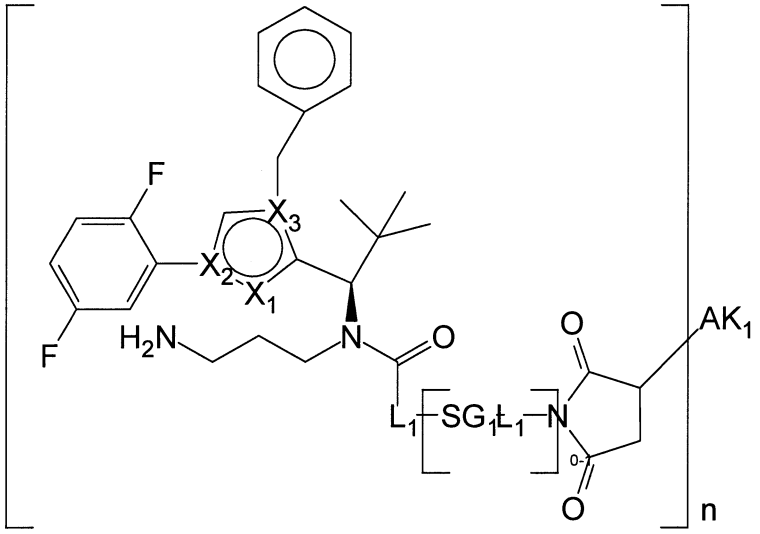


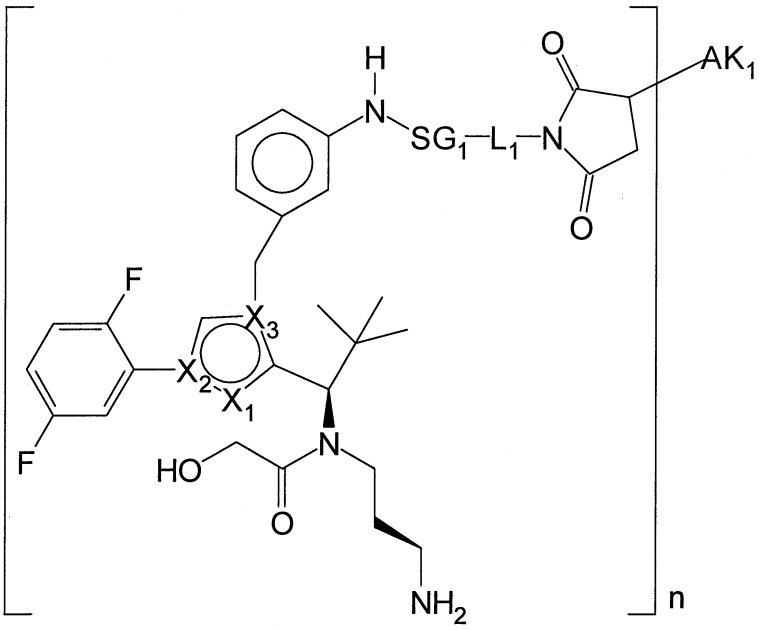







F
X3
X2
X1
F
HO
N
O
NH
O
AK1
L1
N
O
n


F
X3
X2
X1
F
H2N
N
O
L1
SG1
L1
N
0-1
O
O
AK1
n



where

X_1, X_2 and X_3 have the same meaning as in Claim 1,

AK_1 represents a binder peptide or protein bound via a sulphur atom of the binder;

n represents a number from 1 to 20; and

L_1 is an optionally branched hydrocarbyl group which has 1 to 70 carbon atoms, or is a straight-chain or branched hydrocarbyl chain having 1 to 100 carbon atoms composed of arylene groups and/or straight-chain and/or branched and/or cyclic alkylene groups, which may be singly or multiply interrupted by one or more of the groups –O-, -S-, -SO-, -SO_2-, -NH-, -C(=O)-, -C(=O)-NH-, -NH-C(=O)-, -NMe-, -NHNH-, -S(=O)$_2$-NHNH-, -C(=O)-NHNH- and a 5- to 10-membered aromatic or nonaromatic heterocycle having up to 4 heteroatoms selected from N, O and S, -S(=O)- or –S(=O)$_2$-, where the side chains, if present, may be substituted by –NH-

$C(=O)$-NH_2, -COOH, -OH, $-NH_2$, -NH-CN-NH_2, sulphonamide, sulphone, sulphoxide or sulphonic acid,

and

SG1 is a 2-8 oligopeptide, preferably a dipeptide;

L4 represents a single bond or a group $-(C=O)_y$-G4-,

where y represents 0 or 1, and

where G4 is a straight-chain or branched hydrocarbyl chain having 1 to 100 carbon atoms composed of arylene groups and/or straight-chain and/or branched and/or cyclic alkylene groups, which may be singly or multiply interrupted by one or more of the groups -O-, -S-, $-S(=O)$-, $-S(=O)_2$-, -NH-, $-C(=O)$-, -NH-$C(=O)$-, $-C(=O)NH$-, -Nme-, -NHNH-, $-S(=O)_2$-NHNH-, $-C(=O)$-NHNH- and a 5- to 10-membered aromatic or nonaromatic heterocycle having up to 4 heteroatoms selected from N, O and S, $-S(=O)$- or $-S(=O)_2$-, where the side chains, if present, may be substituted by $-NH-C(=O)-NH_2$, -COOH, -OH, $-NH_2$, -NH-CN-NH_2, sulphonamide, sulphone, sulphoxide or sulphonic acid; where the hydrogen atom in position R^4 of formula IIa (i.e. in the $-NH_2$ group) is replaced by legumain-cleavable group of the formula

R^{21}-$(C=O)_{(0-1)}$-$(P3)_{(0-2)}$-P2-NH-$CH(CH_2C(=O)-NH_2)$-$C(=O)$-,

where

R^{21} represents a C_{1-10}-alkyl, C_{5-10}-aryl or C_{6-10}-aralkyl, C_{5-10}-heteroalkyl, C_{1-10}-alkyl-O-C_{6-10}-aryl, C_{5-10}-heterocycloalkyl, heteroaryl, heteroarylalkyl, C_{1-10}-alkoxy, C_{6-10}-aryloxy or C_{6-10}-aralkoxy, C_{5-10}-heteroalkoxy, C_{1-10}-alkyl-O-C_{6-10}-aryloxy, C_{5-10}-heterocycloalkoxy group which may be mono- or

polysubstituted by - NH_2, -NH-alkyl, -$N(alkyl)_2$, -NH-C(=O)-alkyl, -N(alkyl)-C(=O)-alkyl, -SO_3H, -$S(=O)_2NH_2$, -$S(=O)_2$-$N(alkyl)_2$, -COOH, -C(=O)-NH_2, -C(=O)-$N(alkyl)_2$, or –OH, -H or an $–O_x-(CH_2CH_2O)_v-R^{22}$ group,

where x is 0 or 1,

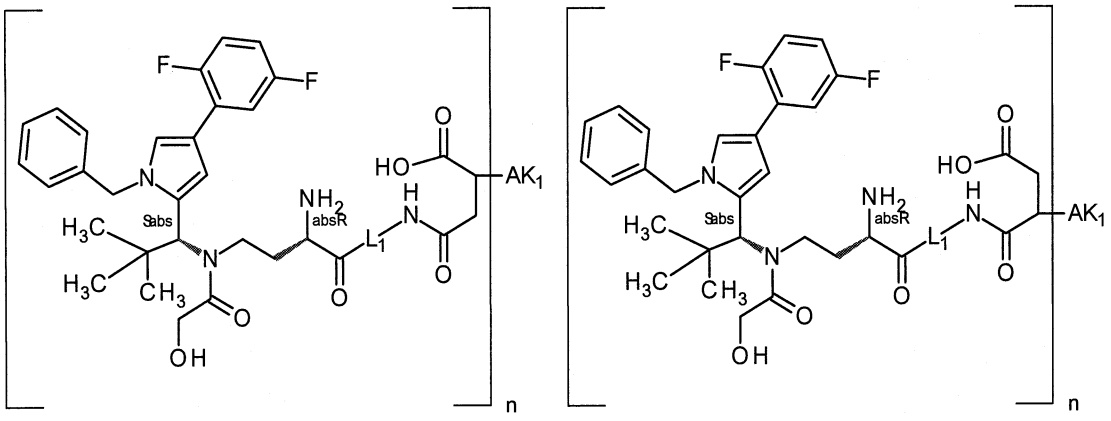
where v represents a number from 1 to 20, and

R^{22} represents –H, –alkyl (preferably C1-12-alkyl), -CH2-COOH, -CH2-CH2-COOH, or -CH_2-CH_2-NH_2;

P2 is an amino acid selected from Gly, Pro, Ala, Val, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg and His;

P3 is an amino acid selected from Gly, Pro, Ala, Val, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg and His or one of the respective N-alkyl amino acids, preferably N-methyl amino acids.

36. Conjugate of a binder or derivative thereof with one or more drug molecules where the conjugate has one or both of the following formulae:



where

AK_1 or AK_{1A} represents a binder peptide or protein bound via a sulphur atom of the binder;

n represents a number from 1 to 20; and

L_1 is a straight-chain or branched hydrocarbyl chain having 1 to 100 carbon atoms composed of arylene groups and/or straight-chain and/or branched and/or cyclic alkylene groups, which may be singly or multiply interrupted by one or more of the groups –O-, -S-, -S(=O)-, -S(=O)$_2$-, -NH-, -C(=O)-, -C(=O)-NH-, -NH-C(=O)-, -NMe-, -NHNH-, -S(=O)$_2$-NHNH-, -C(=O)-NHNH- and a 5- to 10-membered aromatic or nonaromatic heterocycle having up to 4 heteroatoms selected from N, O and S, -S(=O)- or –S(=O)$_2$-, where the side chains, if present, may be substituted by –NH-C(=O)-NH$_2$, -COOH, -OH, -NH$_2$, -NH-CN-NH$_2$, sulphonamide, sulphone, sulphoxide or sulphonic acid,

where the hydrogen atom in position R^4 of formula IIa (i.e. in the –NH$_2$ group) is replaced by a legumain-cleavable group of the formula R^{21}-(C=O)$_{(0-1)}$-(P3)$_{(0-2)}$-P2-NH-CH(CH$_2$-C(=O)-NH$_2$)-C(=O)-,

where

R^{21} represents a C_{1-10}-alkyl, C_{5-10}-aryl or C_{6-10}-aralkyl, C_{5-10}-heteroalkyl, C_{1-10}-alkyl-O-C_{6-10}-aryl, C_{5-10}-heterocycloalkyl, heteroaryl, heteroarylalkyl, C_{1-10}-alkoxy, C_{6-10}-aryloxy or C_{6-10}-aralkoxy, C_{5-10}-heteroalkoxy, C_{1-10}-alkyl-O-C_{6-10}-aryloxy, C_{5-10}-heterocycloalkoxy group which may be mono- or polysubstituted by -NH$_2$, -NH-alkyl, -N(alkyl)$_2$, -NH-C(=O)-alkyl, -N(alkyl)-C(=O)-alkyl, -SO$_3$H, -S(=O)$_2$-NH$_2$, -S(=O)$_2$-N(alkyl)$_2$, -COOH, -C(=O)-NH$_2$, -C(=O)-N(alkyl)$_2$, or –OH, -H or an –O$_x$-(CH$_2$CH$_2$O)$_v$-R^{22} group,

where x is 0 or 1,

where v represents a number from 1 to 20, and

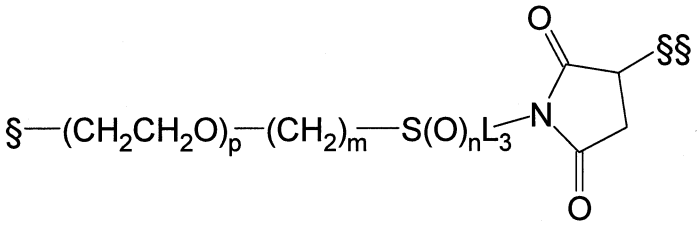
R^{22} is –H, –alkyl (preferably

C_{1-12}-alkyl),
$-CH_2-COOH$,
$-CH_2-CH_2-COOH$ or
$-CH_2-CH_2-NH_2$);

P2 is an amino acid selected from Gly, Pro, Ala, Val, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg and His;

P3 is an amino acid selected from Gly, Pro, Ala, Val, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg and His or one of the respective N-alkyl amino acids, preferably N-methyl amino acids.

37. Conjugate according to one or more of the preceding claims where the linker –L- is attached to a cysteine side chain or a cysteine residue and has the formula below:



where

§ represents the bond to the drug molecule and

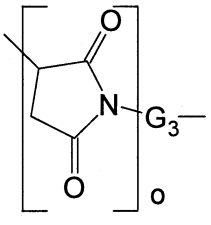
§§ represents the bond to the binder peptide or protein,

m is 0, 1, 2, or 3;

n is 0, 1 or 2;

p is 0 to 20; and

L3 represents the group



;

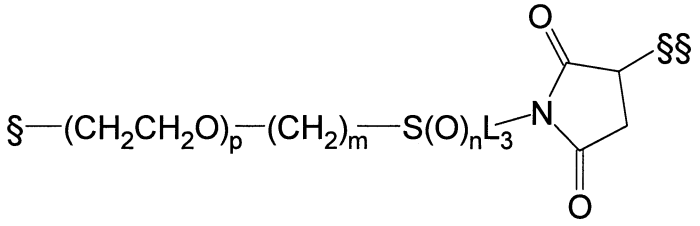
where

o is 0 or 1;

and

G3 is a straight-chain or branched hydrocarbyl chain having 1 to 100 carbon atoms composed of aryl groups and/or straight-chain and/or branched and/or cyclic alkyl groups, which may be singly or multiply interrupted by one or more of the groups –O-, -S-, -S(=O)-, -S(=O)$_2$-, -NH-, -C(=O)-, -NH-C(=O)-, -C(=O)-NH- and a 5- to 10-membered aromatic or nonaromatic heterocycle having up to 4 heteroatoms selected from N, O and S, --NMe-, -NHNH-, -S(=O)$_2$-NHNH-, -C(=O)-NHNH-, -S(=O)- and –S(=O)$_2$-, where the side chains, if present, may be substituted by –NH-C(=O)-NH$_2$, -COOH, -OH, -sulphone, sulphoxide or sulphonic acid.

38. Conjugate according to Claim 37 where the linker –L- is attached to a cysteine side chain or a cysteine residue and has the formula below:



where

§ represents the bond to the drug molecule and

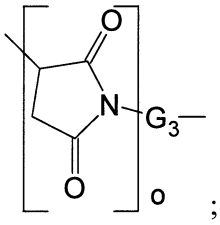
§§ represents the bond to the binder peptide or protein,

m is 1;

p is 0;

n is 0; and

L3 represents the group



;

where

o	is 0 or 1; and
G3	represents -$(CH_2CH_2O)_s(CH_2)_t(CONH)_u$ $CH_2CH_2O)_v(CH_2)_w$-, where
s, t, v and w	each independently of one another is from 0 to 20 and
u	is 0 or 1.

39. Conjugate according to one of the preceding claims where R^2 or R^3 represents –L-#1.

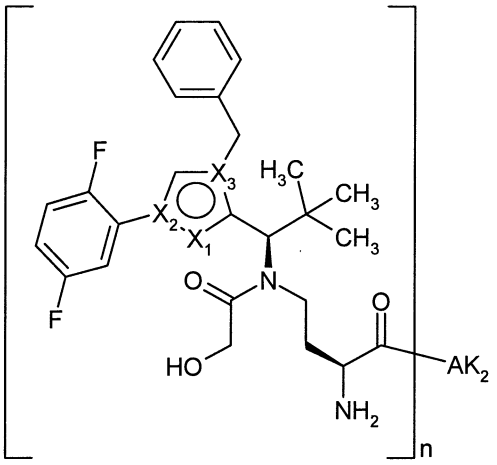
40. Conjugate according to one or more of Claims 1 to 32 where the linker –L- is attached to a lysine side chain and has the formula below:

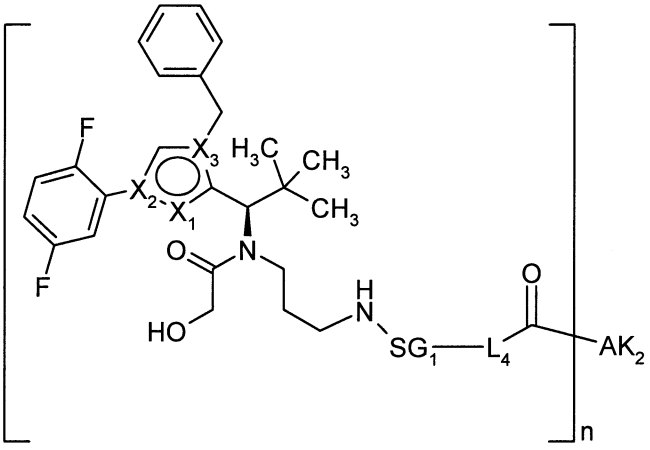
-§-$(SG)_x$-L4-CO-§§

where

§	represents the bond to the drug molecule and
§§	represents the bond to the binder peptide or protein,
x	represents 0 or 1;
SG	represents a cleavable group, preferably a 2-8 oligopeptide, particularly preferably a dipeptide, and
L4	represents a single bond or a group –$(C=O)_y$-G4-, where
y	represents 0 or 1, and
G4	is a straight-chain or branched hydrocarbyl chain having 1 to 100 carbon atoms composed of aryl groups and/or straight-chain and/or branched and/or cyclic alkyl groups, which may be singly or multiply interrupted by one or more of the groups –O-, -S-, -S(=O)-, -$S(=O)_2$-, -NH-, -C(=O)-, -NH-C(=O)-, -C(=O)-NH-, -Nme-, -NHNH-, -$S(=O)_2$-NHNH-, -C(=O)-NHNH- and a 5- to 10-membered aromatic or nonaromatic heterocycle having up to 4 heteroatoms selected from N, O and S, or –S(=O)-, where the side chains, if present, may be substituted by –NH-C(=O)-NH_2, -COOH, -OH, -NH_2, -NH-CN-NH_2, sulphonamide, sulphone, sulphoxide or sulphonic acid.

41. Conjugate of a binder peptide or protein according to Claim 40 where the conjugate has one of the formulae below:





where

X_1, X_2 and X_3	have the same meaning as in Claim 1,
AK_2	represents a lysine-bonded antibody;
n	is a number from 1 to 20;
L4	is an optionally straight-chain or branched hydrocarbyl chain having 1 to 100 carbon atoms composed of aryl groups and/or straight-chain and/or branched and/or cyclic alkyl groups, which may be singly or multiply interrupted by one or more of the groups –O-, -S-, -S(=O)-, -S(=O)$_2$-, -NH-, -C(=O)-, -Nme-, -NHNH-, -S(=O)$_2$-NHNH-, -NH-C(=O)-, -C(=O)-NH-, -C(=O)-NHNH- and a 5- to 10-membered aromatic or nonaromatic heterocycle having up to 4 heteroatoms selected from N, O and S, -S(=O)- or

$-S(=O)_2-$, where the side chains, if present, may be substituted by $-NH-C(=O)-NH_2$, -COOH, -OH, $-NH_2$, $-NH-CN-NH_2$, sulphonamide, sulphone, sulphoxide or sulphonic acid,

and where the conjugate satisfies one of the following formulae, where n is a number from 1 to 20, and the hydrogen atom in position R^4 of formula IIa (i.e. in the $-NH_2$ group) is replaced by legumain-cleavable group of the formula $R^{21}-(C=O)_{(0-1)}-(P3)_{(0-2)}-P2-NH-CH(CH_2C(=O)-NH_2)-C(=O)-$,

where R^{21} represents a C_{1-10}-alkyl, C_{510}-aryl or C_{6-10}-aralkyl, C_{5-10}-heteroalkyl, C_{1-10}-alkyl-O-C_{6-10}-aryl, C_{5-10}-heterocycloalkyl, heteroaryl, heteroarylalkyl, C_{1-10}-alkoxy, C_{6-10}-aryloxy or C_{6-10}-aralkoxy, C_{5-10}-heteroalkoxy, C_{1-10}-alkyl-O-C_{6-10}-aryloxy, C_{5-10}-heterocycloalkoxy group which may be mono- or polysubstituted by - NH_2, -NH-alkyl, $-N(alkyl)_2$, NH-C(=O)-alkyl, -N(alkyl)-C(=O)-alkyl, $-SO_3H$, $-S(=O)_2-NH_2$, $-S(=O)_2-N(alkyl)_2$, -COOH, $-C(=O)-NH_2$, $-C(=O)-N(alkyl)_2$, or –OH, or -H or an $-O_x-(CH_2CH_2O)_v-R^{22}$ group,

where x is 0 or 1,

where v represents a number from 1 to 20, and

R^{22} represents –H, –alkyl (preferably C_{1-12}-alkyl), $-CH_2-COOH$, $-CH_2-CH_2-COOH$, or $-CH_2-CH_2-NH_2$);

where P2 is an amino acid selected from Gly, Pro, Ala, Val, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg and His;

where P3 is an amino acid selected from Gly, Pro, Ala, Val, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg and His or one of the respective N-alkyl amino acids, preferably N-methyl amino acids; and

SG1 represents a cleavable group, preferably a 2-8 oligopeptide, particularly preferably a dipeptide.

42. Conjugate according to one or more of Claims 23 to 41 where the anti-TWEAKR antibody is an agonistic antibody.

43. Conjugate according to one or more of Claims 23 to 42 where the anti-TWEAKR antibody or the antigen-binding fragment thereof comprises:

a variable heavy chain comprising:

a. a CDR1 of the heavy chain encoded by an amino acid sequence comprising the formula PYPMX (SEQ ID NO: 171), where X is I or M;

b. a CDR2 of the heavy chain encoded by an amino acid sequence comprising the formula YISPSGGXTHYADSVKG (SEQ ID NO: 172), where X is S or K; and

c. a CDR3 of the heavy chain encoded by an amino acid sequence comprising the formula GGDTYFDYFDY (SEQ ID NO: 173);

and a variable light chain comprising:

d. a CDR1 of the light chain encoded by an amino acid sequence comprising the formula RASQSISXYLN (SEQ ID NO: 174), where X is G or S;

e. a CDR2 of the light chain encoded by an amino acid sequence comprising the formula XASSLQS (SEQ ID NO: 175), where X is Q, A or N; and

f. a CDR3 of the light chain encoded by an amino acid sequence comprising the formula QQSYXXPXIT (SEQ ID NO: 176), where X at position 5 is T or S, X at position 6 is T or S and X at position 8 is G or F.

44. Conjugate according to one or more of Claims 23 to 43 where the anti-TWEAKR antibody or the antigen-binding fragment thereof comprises:

a. a variable sequence of the heavy chain, as shown in SEQ ID NO:10, and also a variable sequence of the light chain, as shown in SEQ ID NO:9, or

b. a variable sequence of the heavy chain, as shown in SEQ ID NO:20, and also a variable sequence of the light chain, as shown in SEQ ID NO:19, or

c. a variable sequence of the heavy chain, as shown in SEQ ID NO:30, and also a variable sequence of the light chain, as shown in SEQ ID NO:29, or

d. a variable sequence of the heavy chain, as shown in SEQ ID NO:40, and also a variable sequence of the light chain, as shown in SEQ ID NO:39, or

e. a variable sequence of the heavy chain, as shown in SEQ ID NO:50, and also a variable sequence of the light chain, as shown in SEQ ID NO:49, or

f. a variable sequence of the heavy chain, as shown in SEQ ID NO:60, and also a variable sequence of the light chain, as shown in SEQ ID NO:59, or

g. a variable sequence of the heavy chain, as shown in SEQ ID NO:70, and also a variable sequence of the light chain, as shown in SEQ ID NO:69, or

h. a variable sequence of the heavy chain, as shown in SEQ ID NO:80, and also a variable sequence of the light chain, as shown in SEQ ID NO:79, or

i. a variable sequence of the heavy chain, as shown in SEQ ID NO:90, and also a variable sequence of the light chain, as shown in SEQ ID NO:89, or

j. a variable sequence of the heavy chain, as shown in SEQ ID NO:100, and also a variable sequence of the light chain, as shown in SEQ ID NO:99, or

k. a variable sequence of the heavy chain, as shown in SEQ ID NO:110, and also a variable sequence of the light chain, as shown in SEQ ID NO:109, or

l. a variable sequence of the heavy chain, as shown in SEQ ID NO:120, and also a variable sequence of the light chain, as shown in SEQ ID NO:119.

45. Conjugate according to one or more of Claims 18 to 44 where the antibody is an IgG antibody.

46. Conjugate according to one or more of Claims 20 to 45 where the anti-TWEAKR antibody comprises:

a. a sequence of the heavy chain as shown in SEQ ID NO:2,

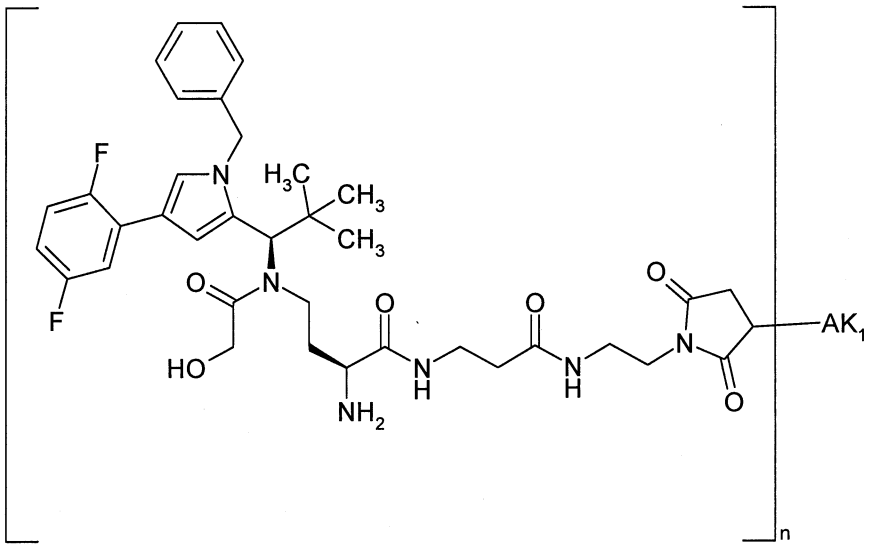
and a sequence of the light chain as shown in SEQ ID NO:1 or

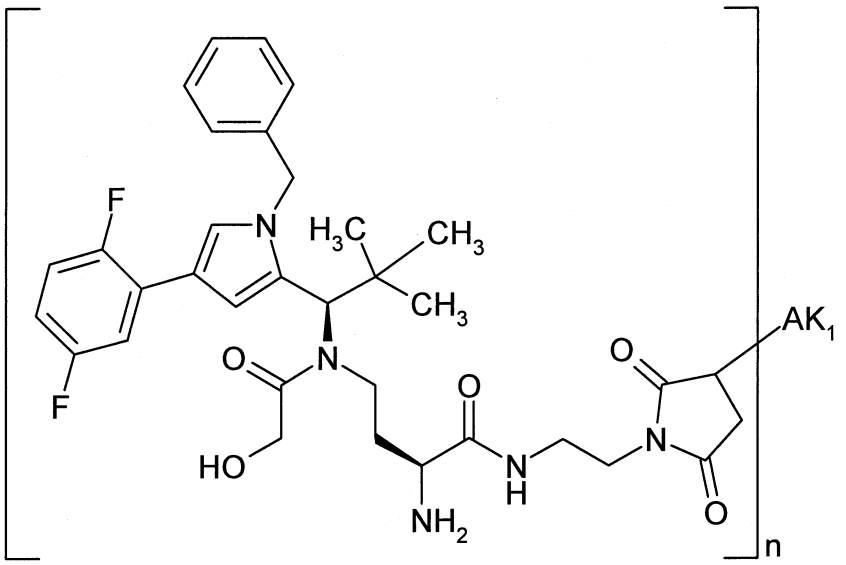
b. a sequence of the heavy chain as shown in SEQ ID NO:12, and a sequence of the light chain as shown in SEQ ID NO:11 or
c. a sequence of the heavy chain as shown in SEQ ID NO:22, and a sequence of the light chain as shown in SEQ ID NO:21 or
d. a sequence of the heavy chain as shown in SEQ ID NO:32, and a sequence of the light chain as shown in SEQ ID NO:31 or
e. a sequence of the heavy chain as shown in SEQ ID NO:42, and a sequence of the light chain as shown in SEQ ID NO:41 or
f. a sequence of the heavy chain as shown in SEQ ID NO:52, and a sequence of the light chain as shown in SEQ ID NO:51 or
g. a sequence of the heavy chain as shown in SEQ ID NO:62, and a sequence of the light chain as shown in SEQ ID NO:61 or
h. a sequence of the heavy chain as shown in SEQ ID NO:72, and a sequence of the light chain as shown in SEQ ID NO:71 or
i. a sequence of the heavy chain as shown in SEQ ID NO:82, and a sequence of the light chain as shown in SEQ ID NO:81 or
j. a sequence of the heavy chain as shown in SEQ ID NO:92, and a sequence of the light chain as shown in SEQ ID NO:91 or
k. a sequence of the heavy chain as shown in SEQ ID NO:102, and a sequence of the light chain as shown in SEQ ID NO:101 or
l. a sequence of the heavy chain as shown in SEQ ID NO:112,

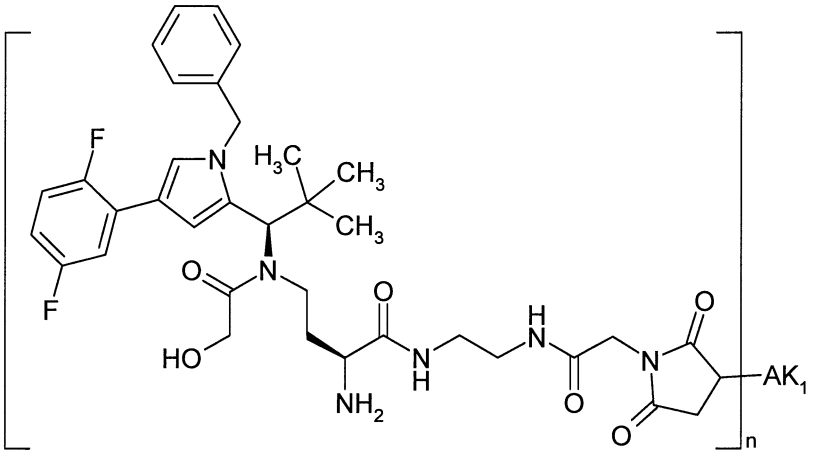
and a sequence of the light chain as shown in SEQ ID NO:111.

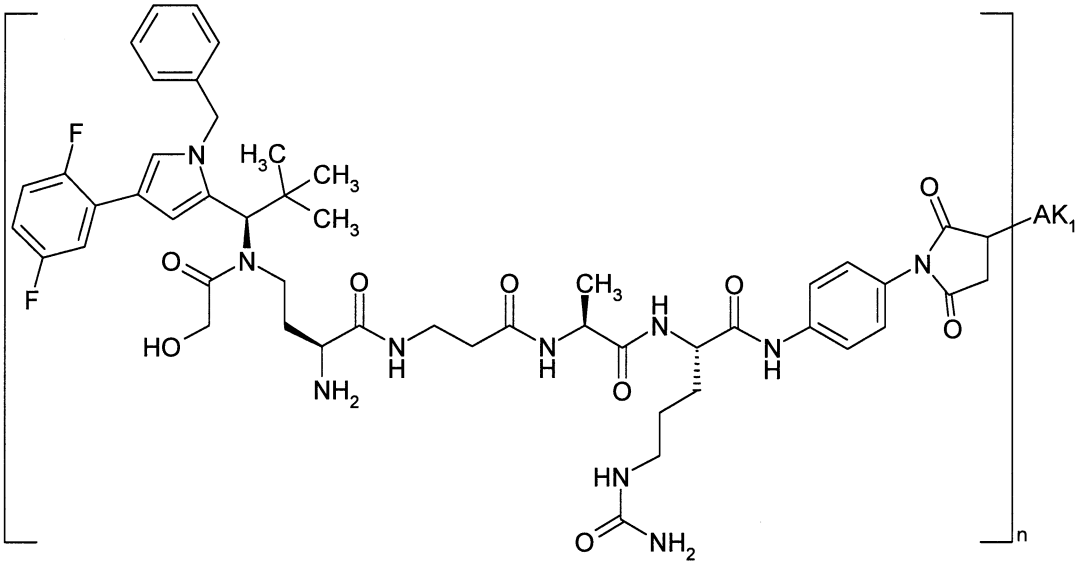
47. Conjugate according to one or more of the preceding claims where the conjugate has 1 to 10, preferably 2 to 8, drug molecules or prodrug molecules per binder peptide or protein.

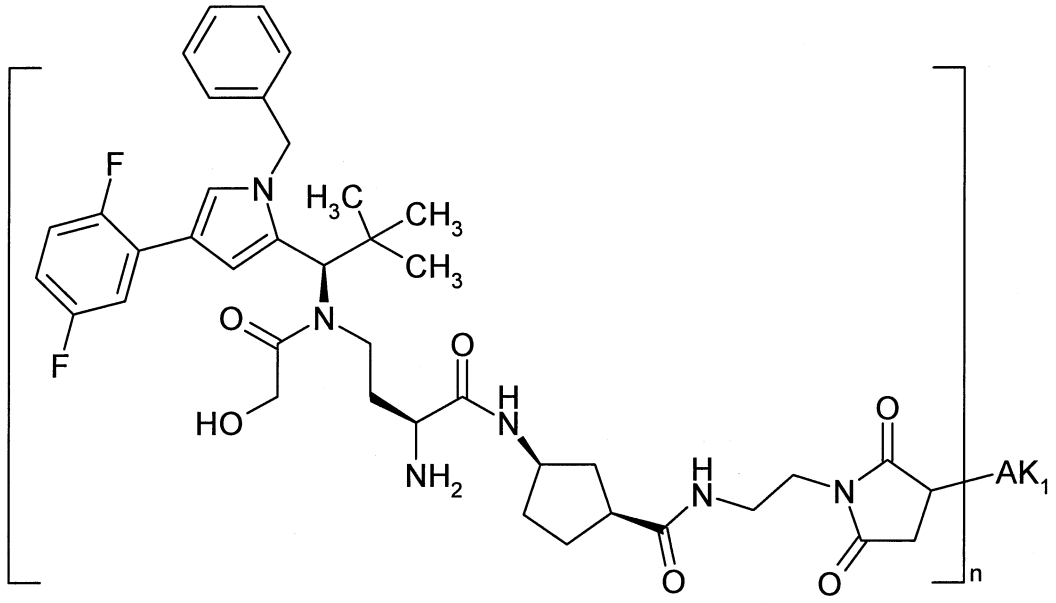
48. Antibody-prodrug conjugate according to one or more of the preceding claims where the antibody-prodrug conjugate satisfies one of the following formulae:

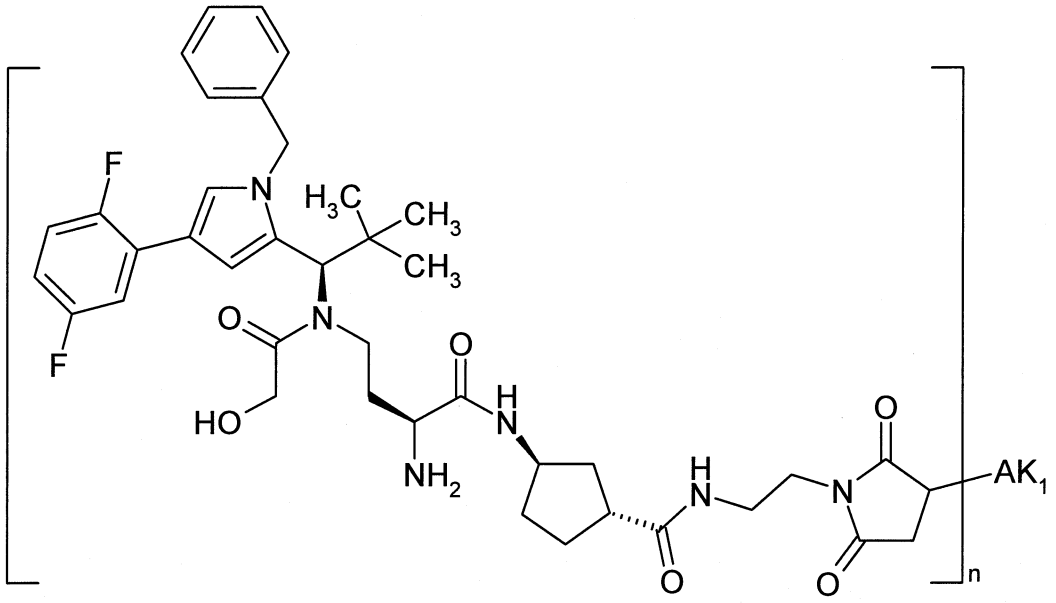

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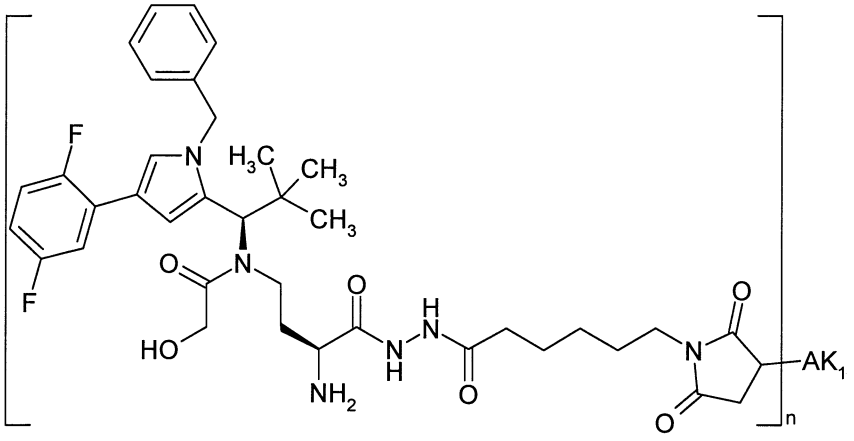

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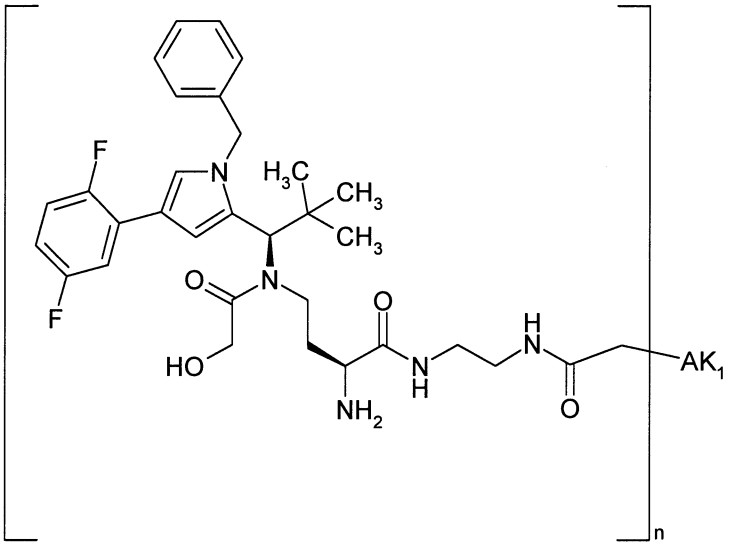


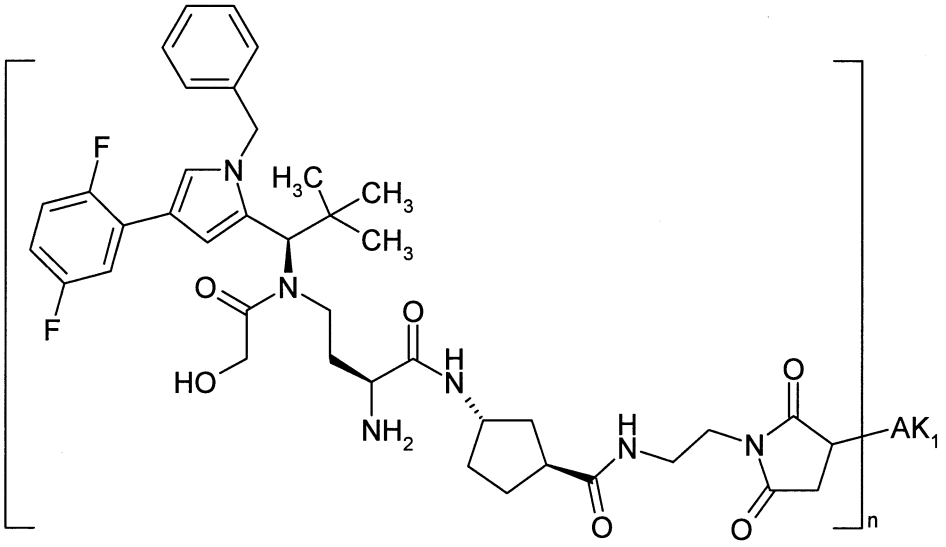


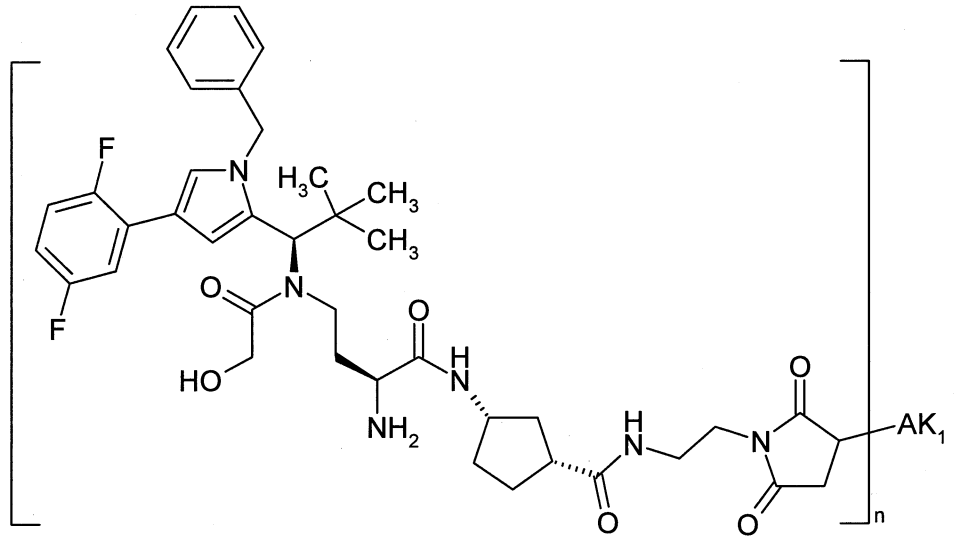

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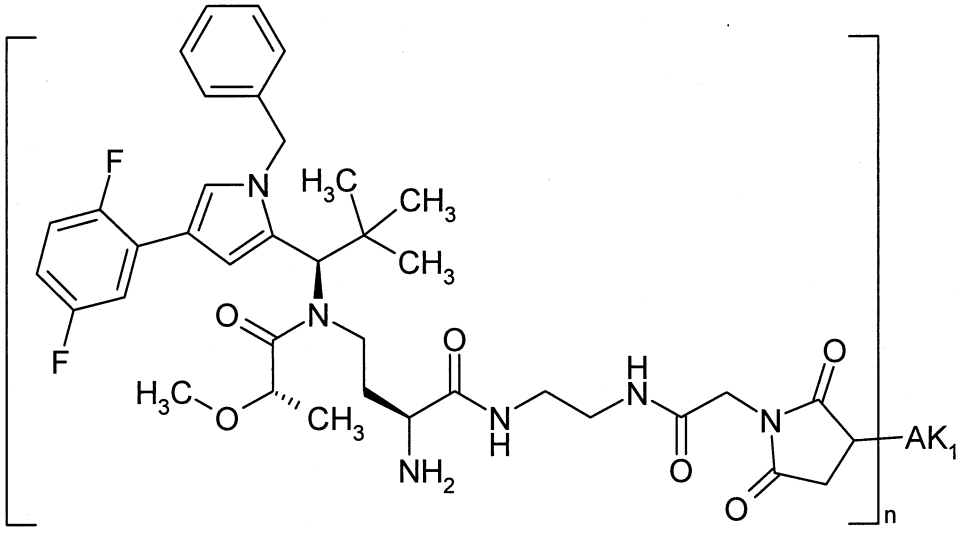

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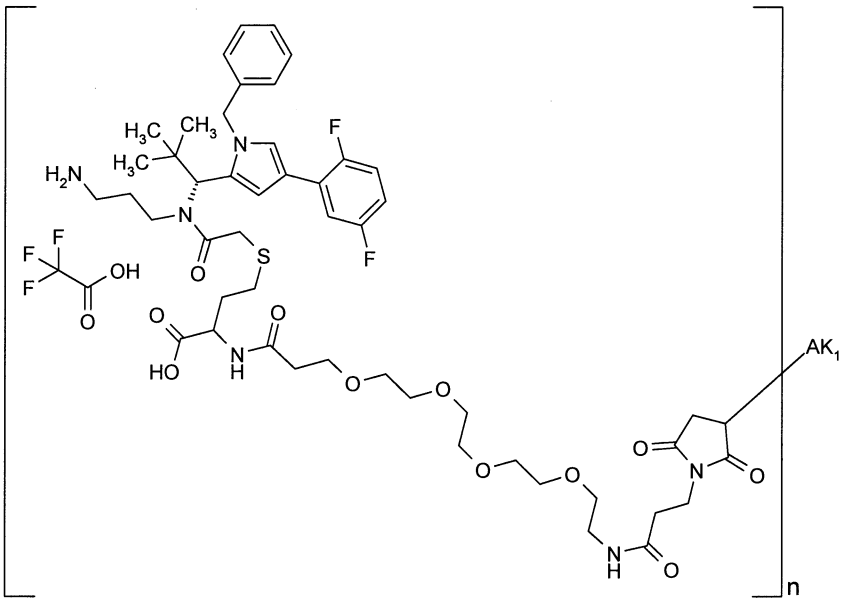


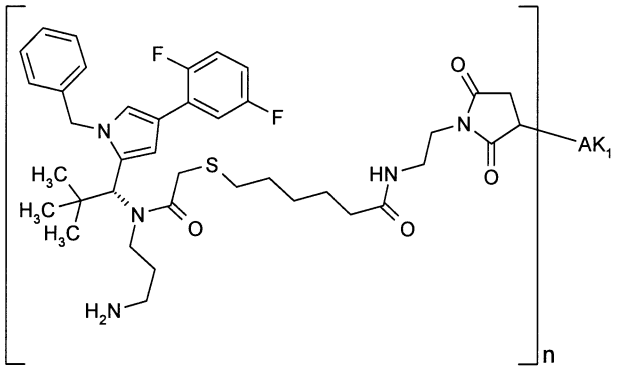


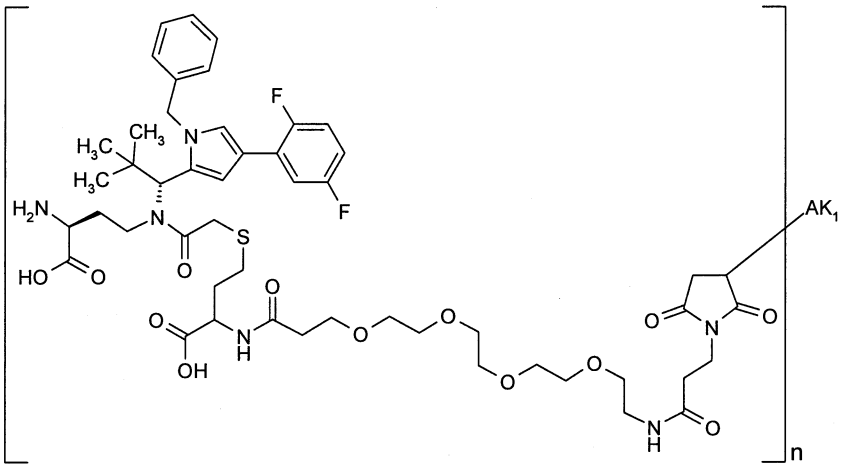


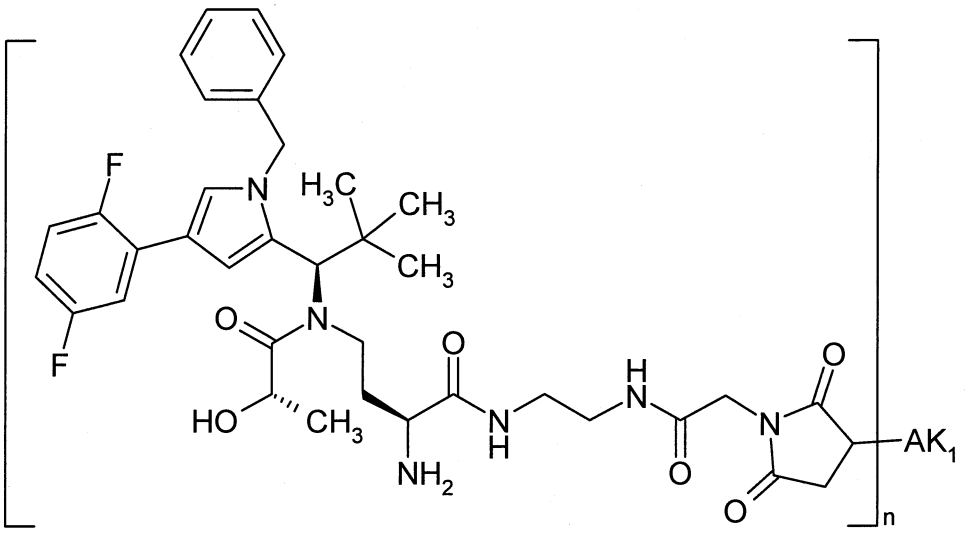


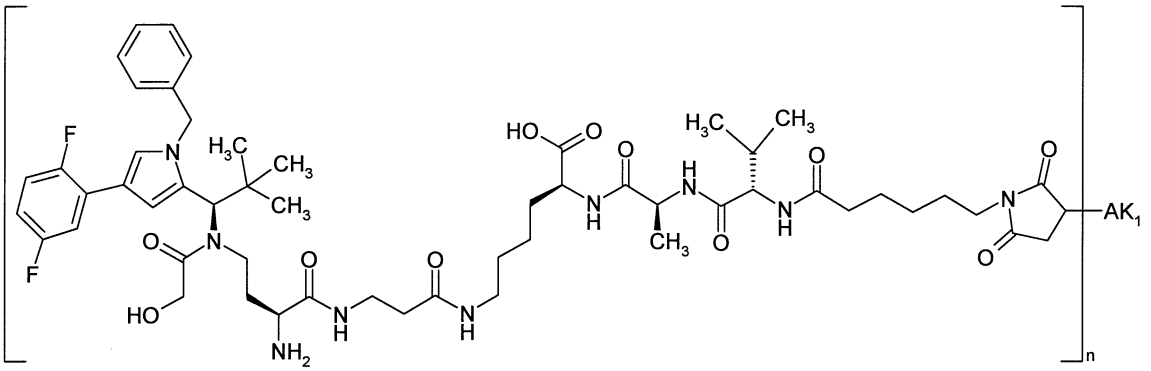


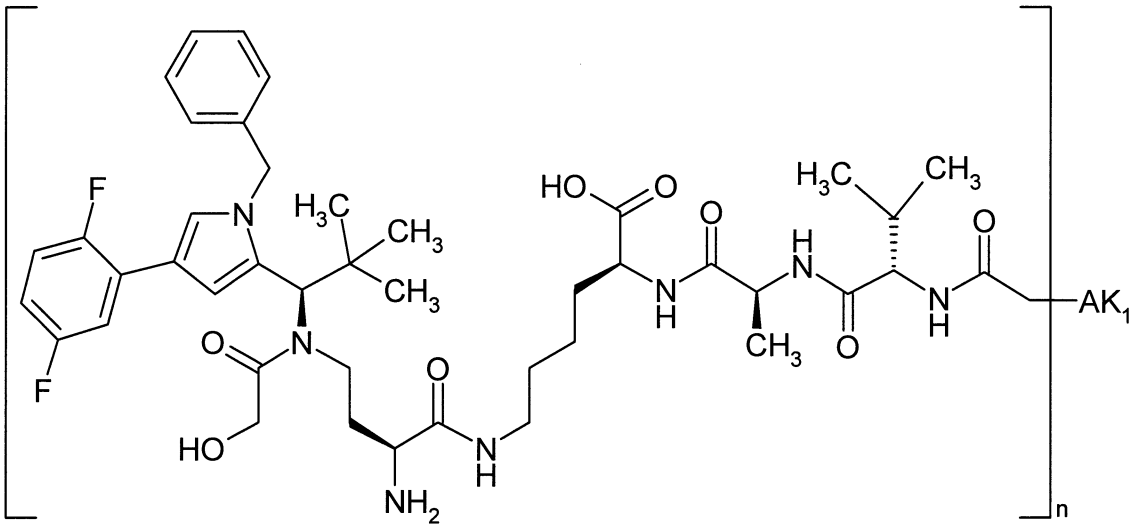


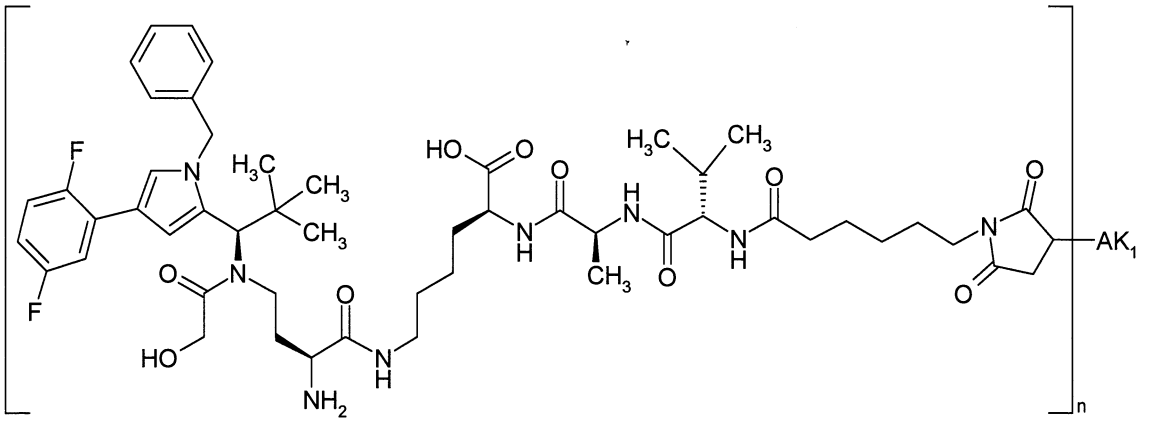


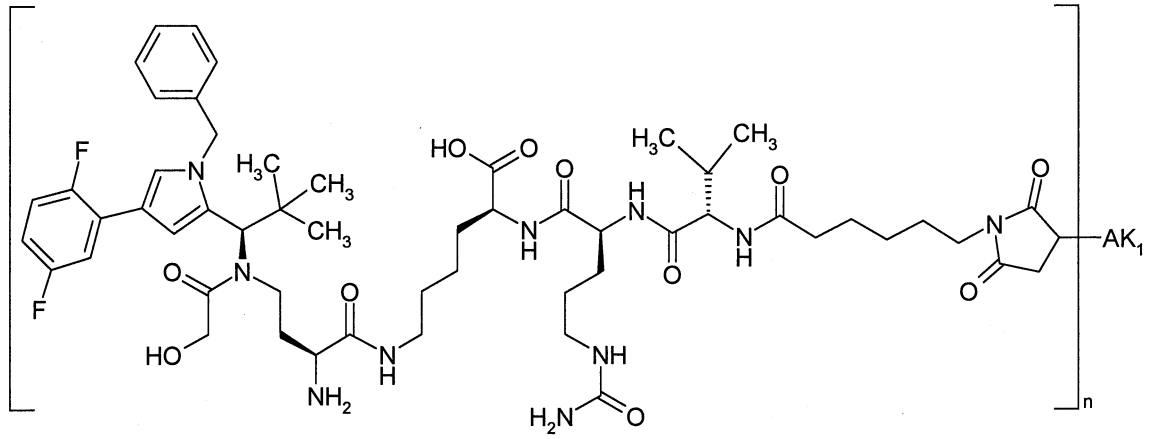


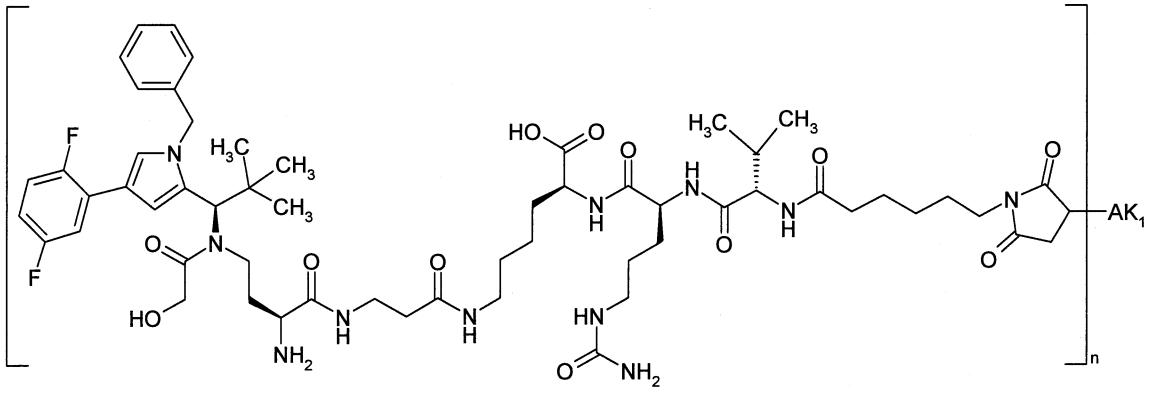


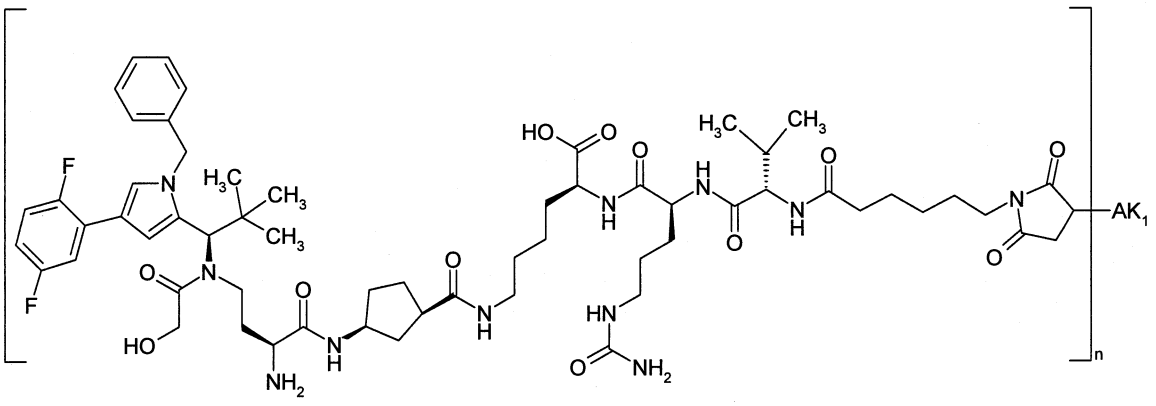


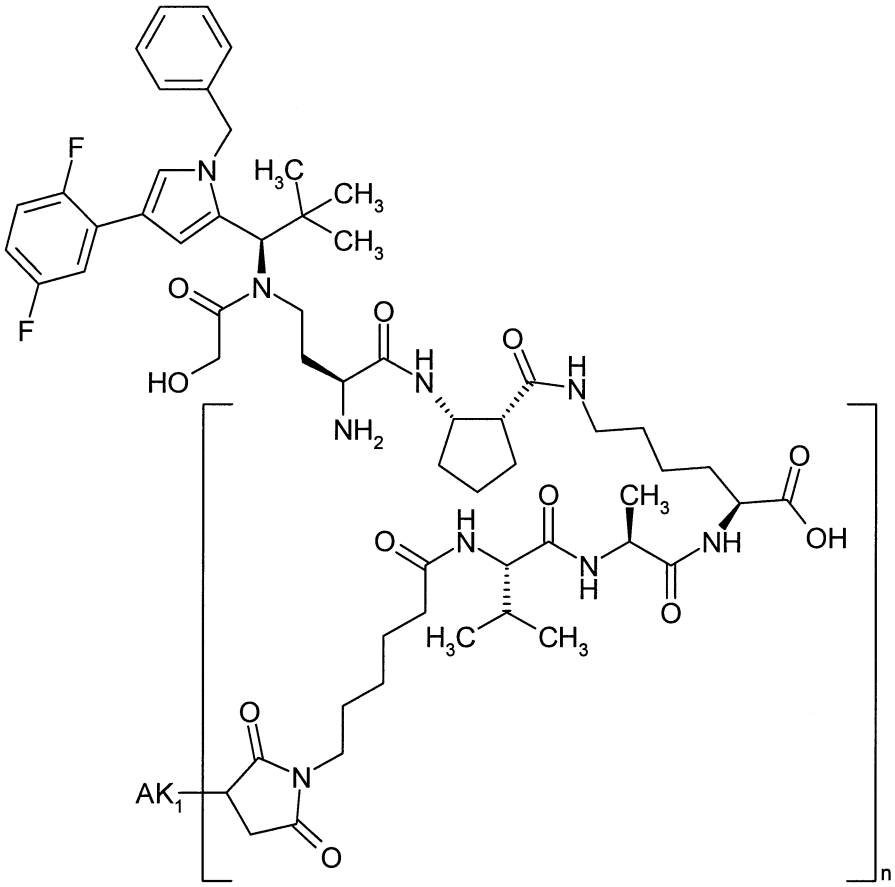


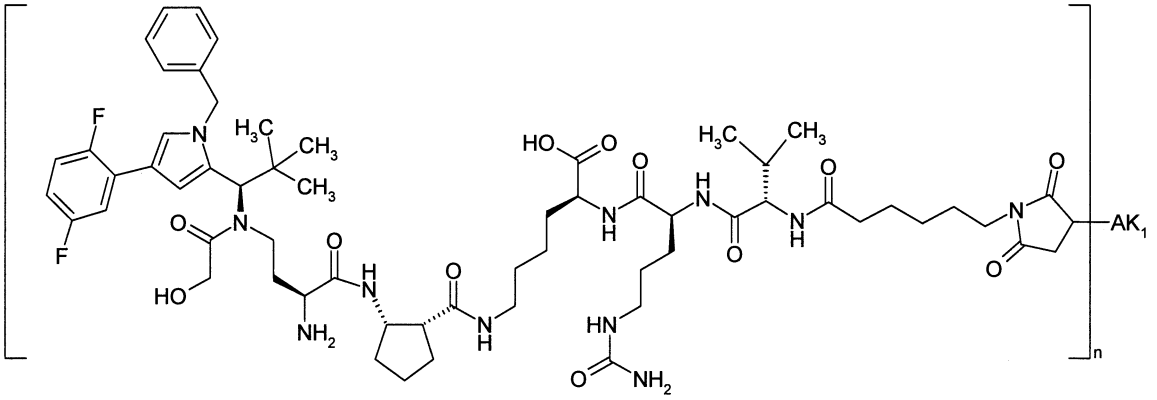


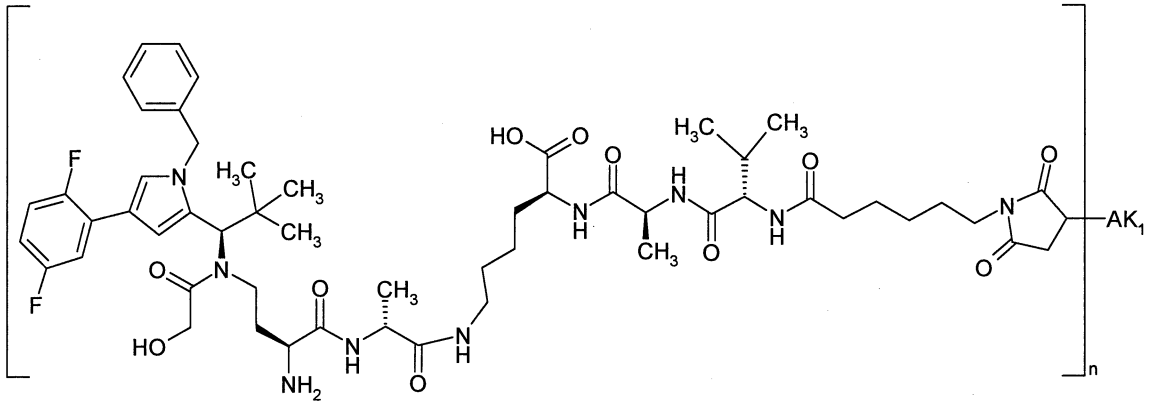


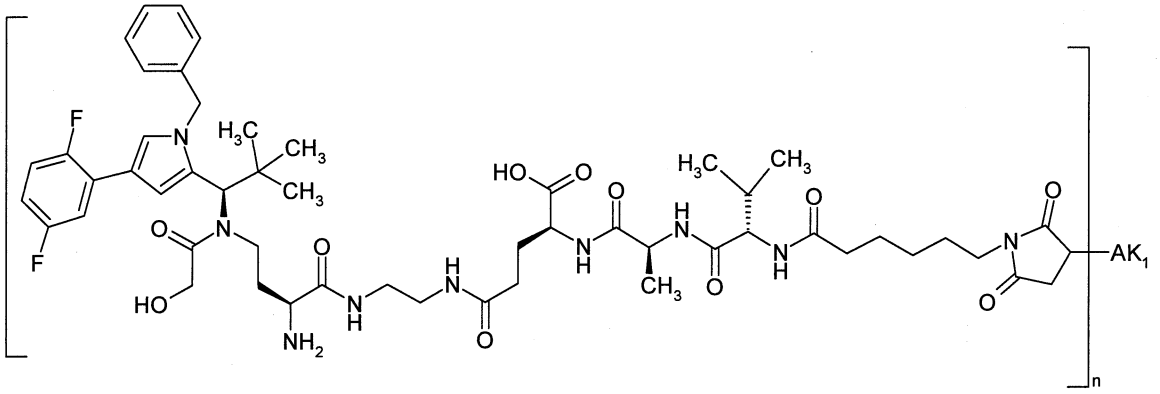


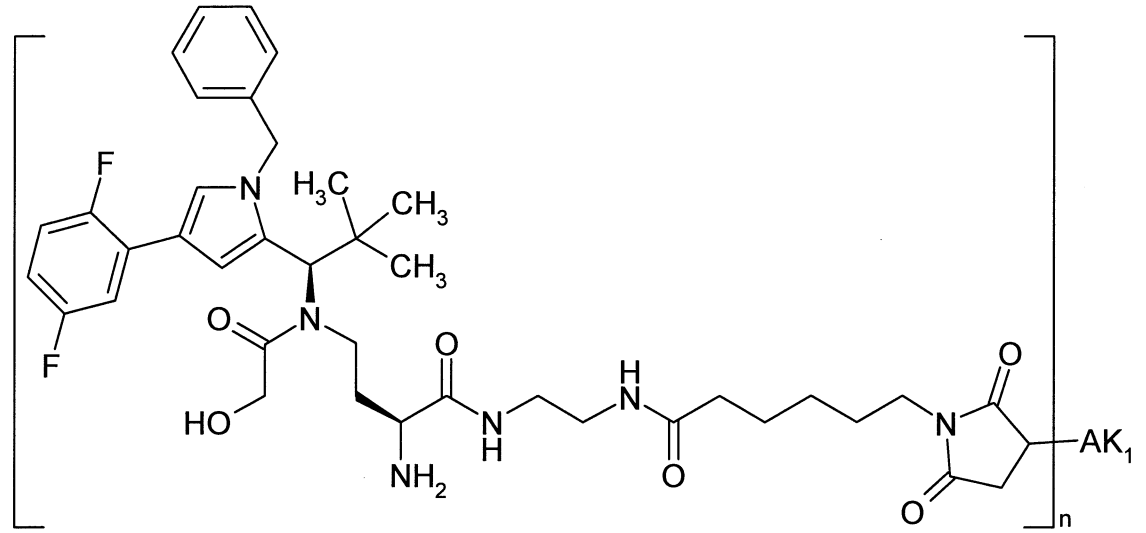


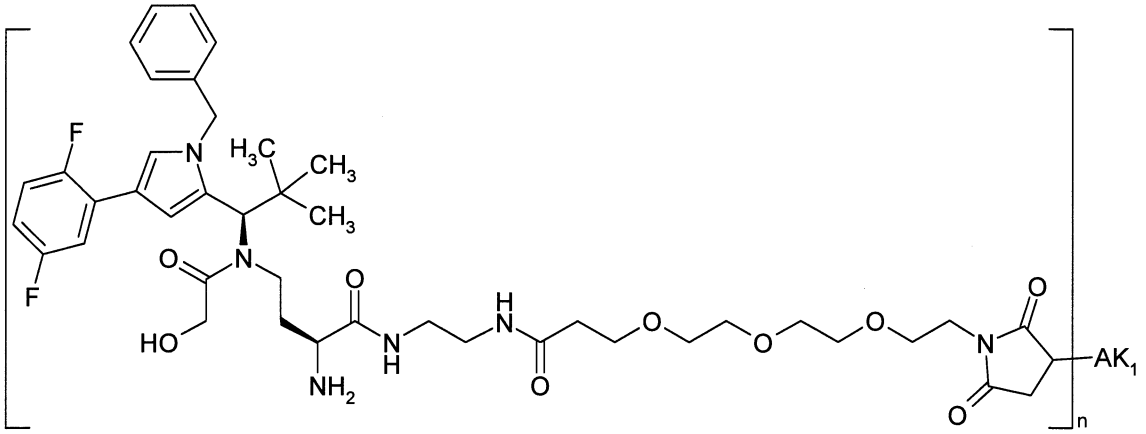


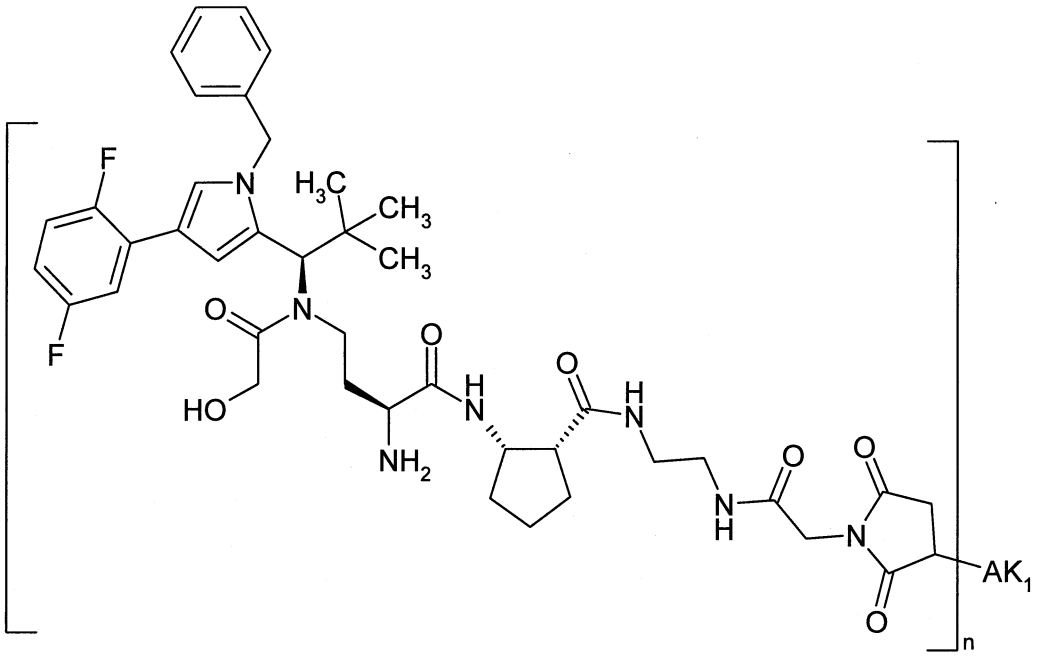


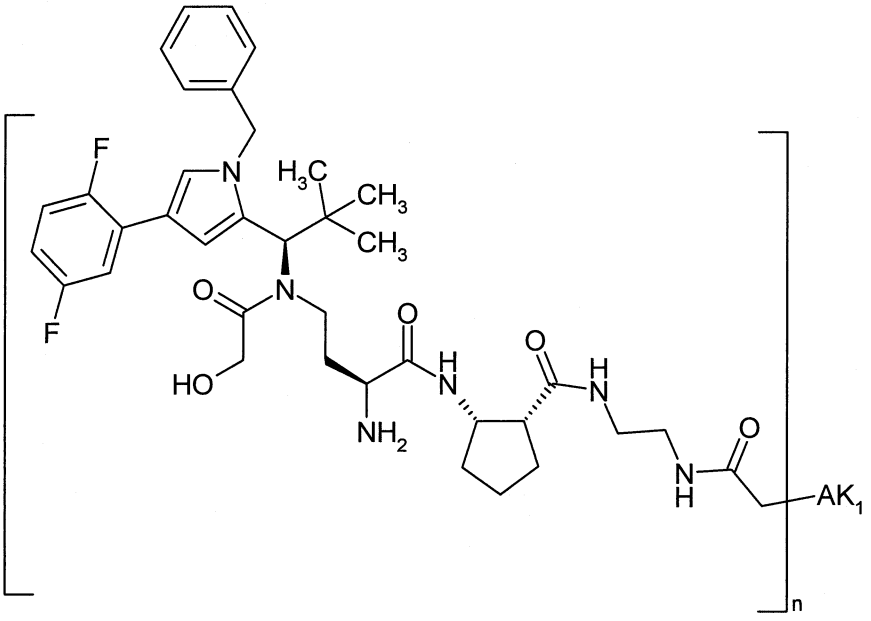


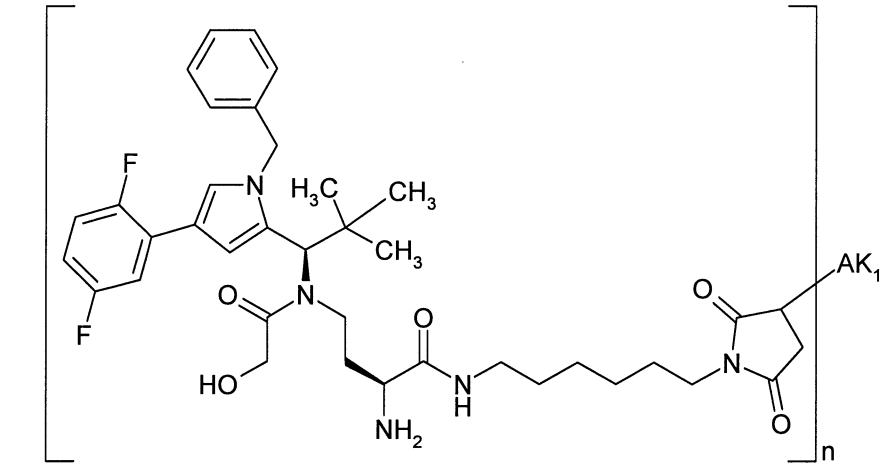


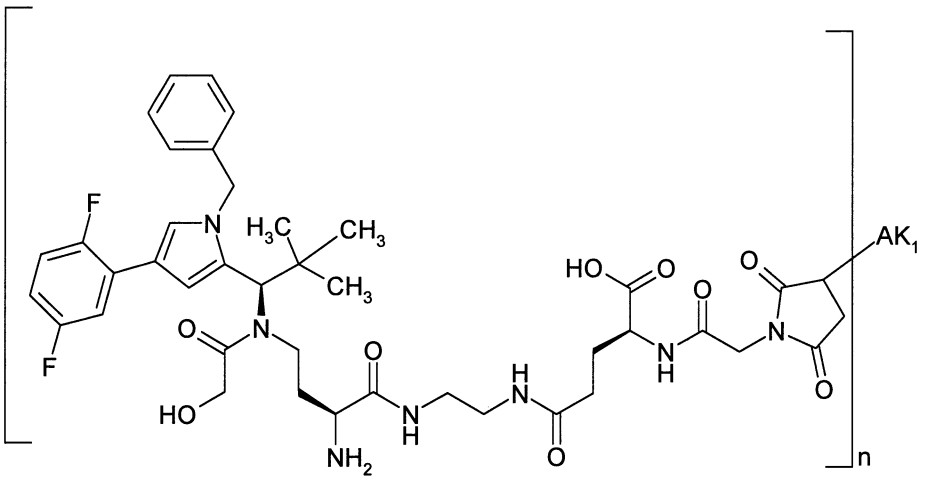


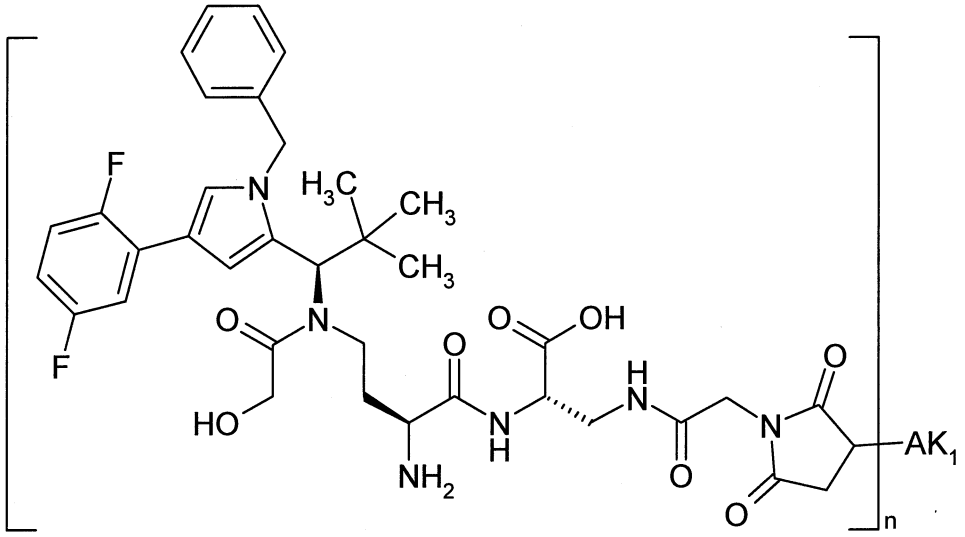


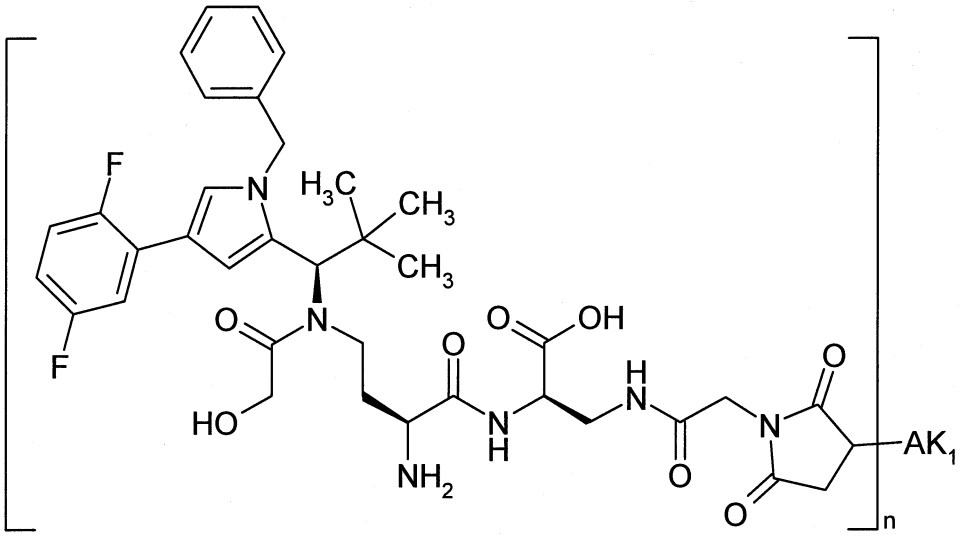

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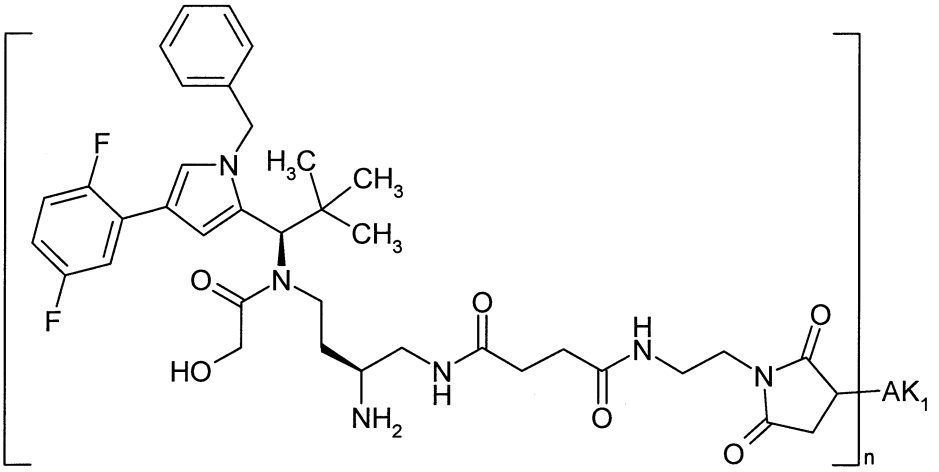

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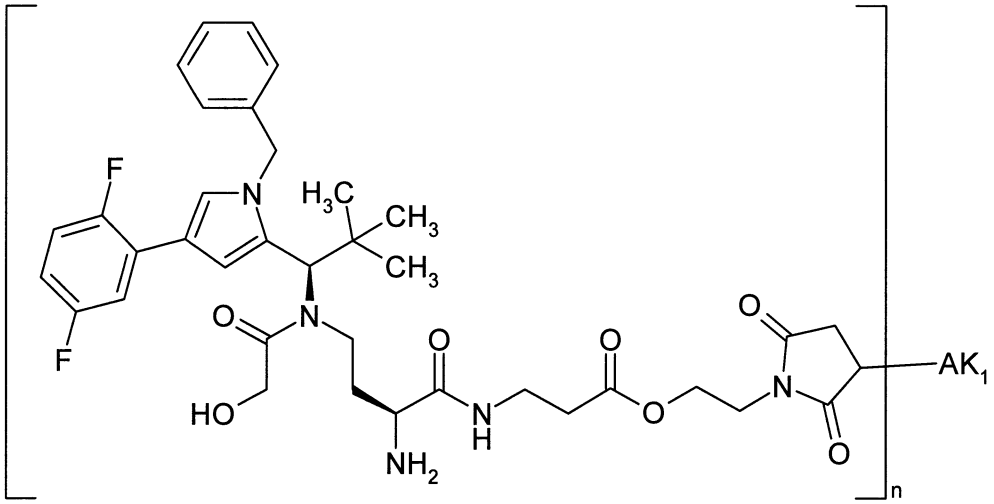

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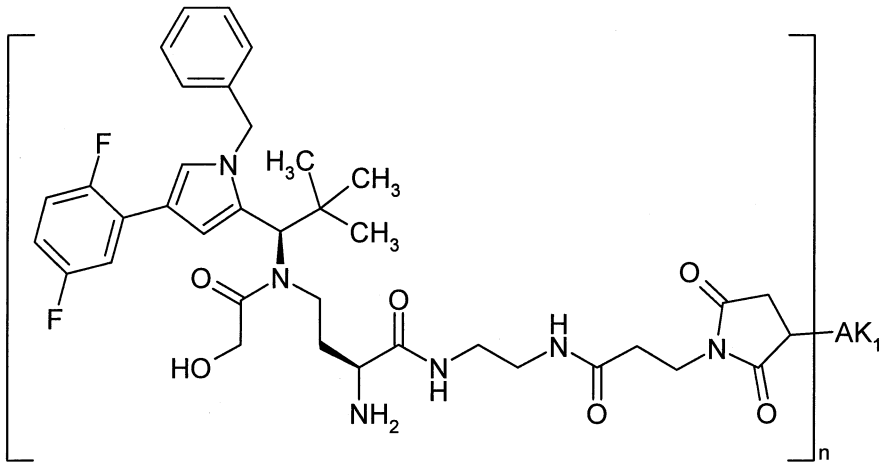

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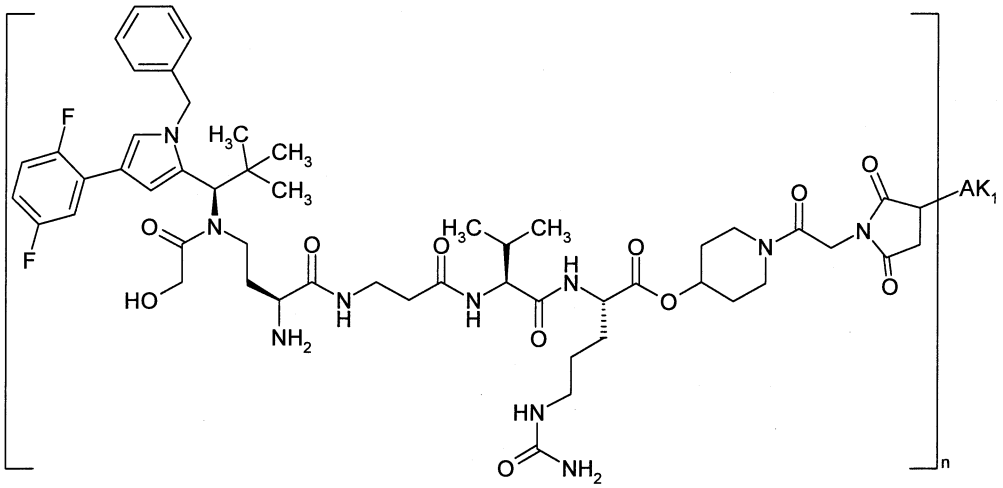

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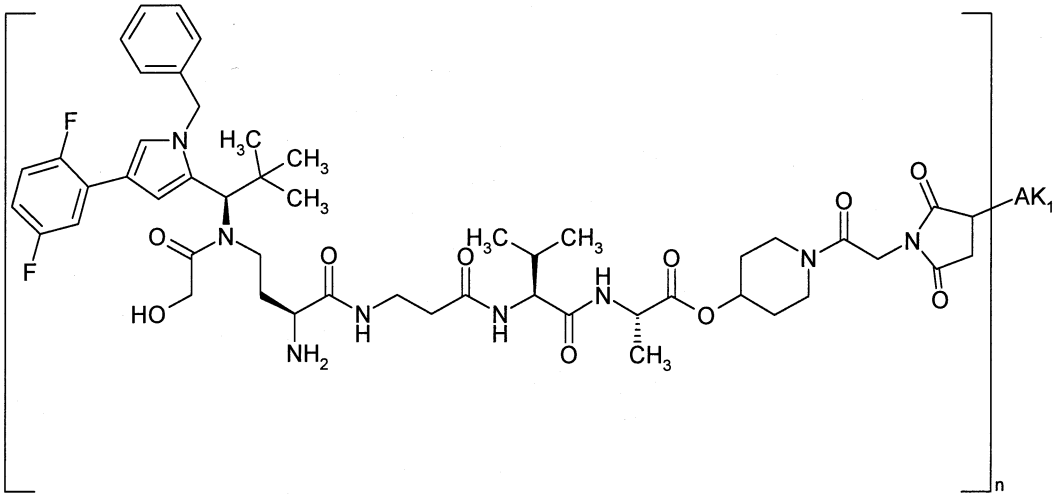

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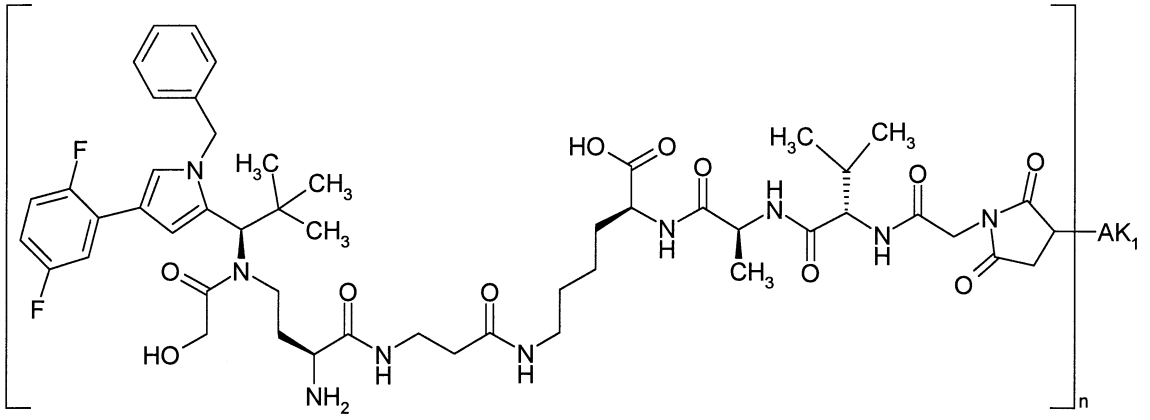

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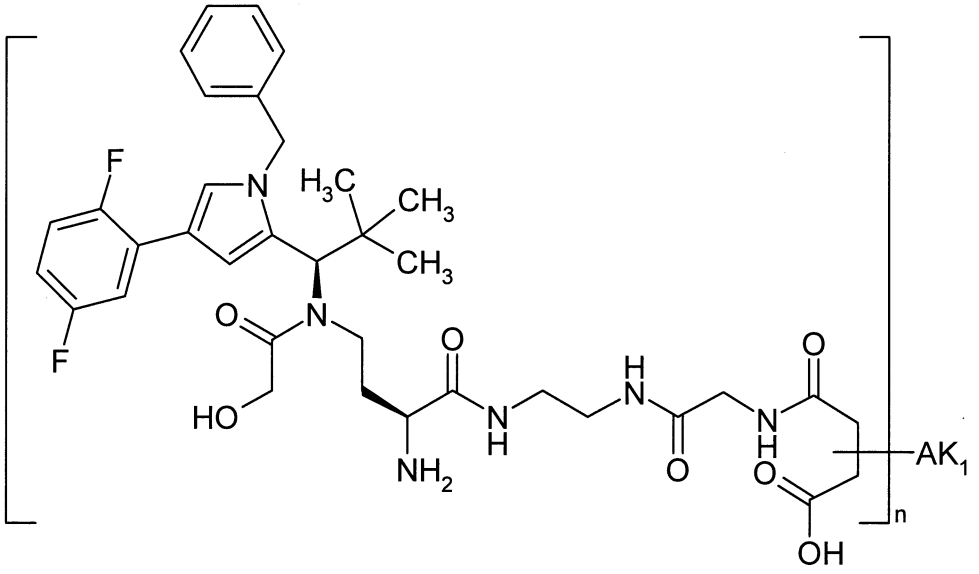

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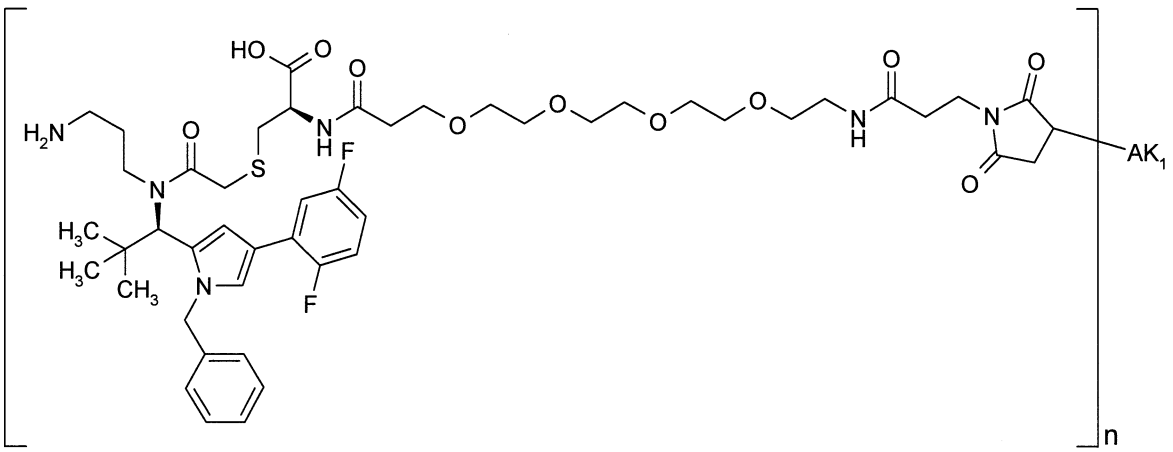


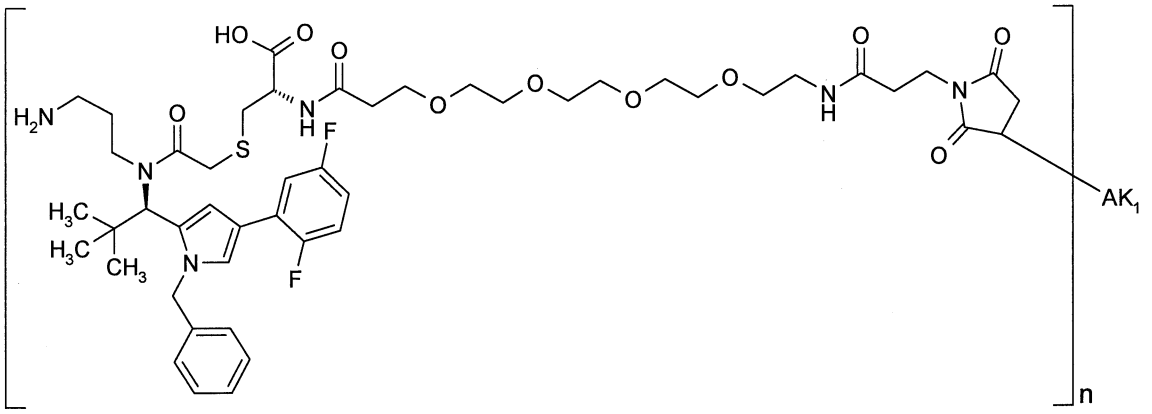


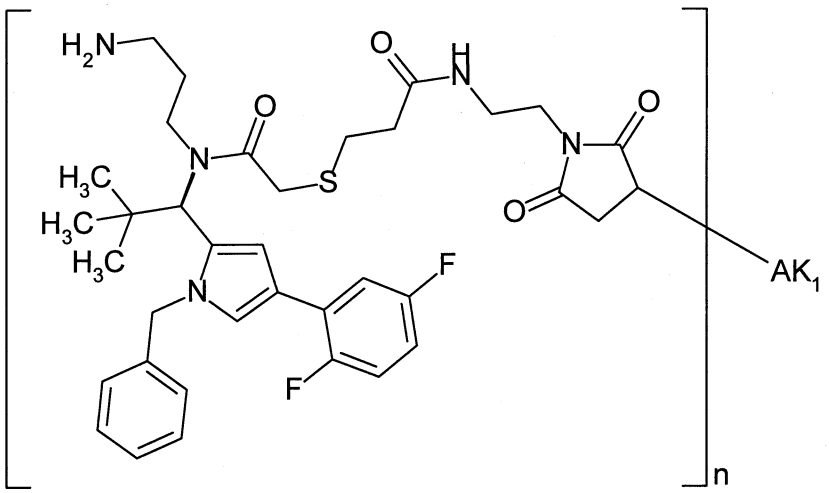


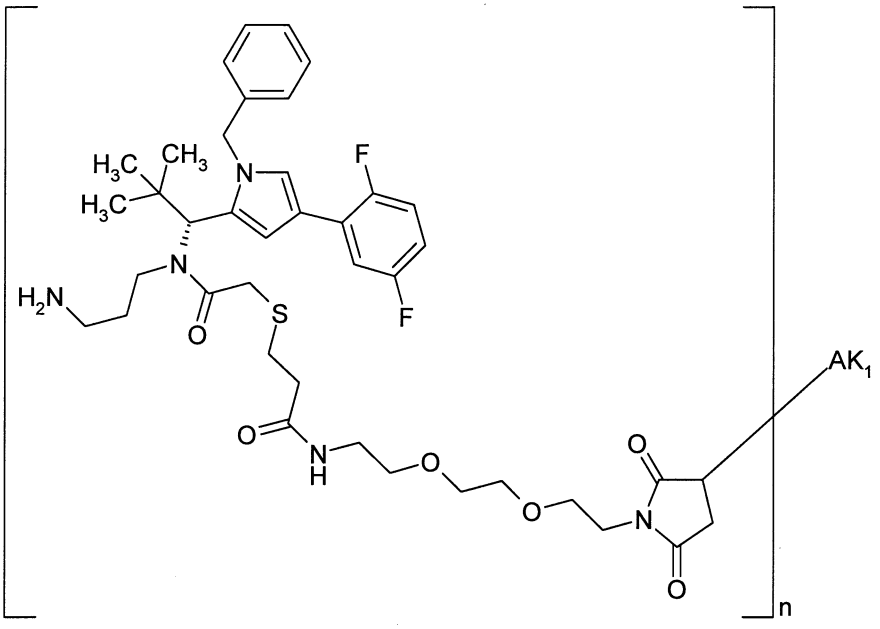


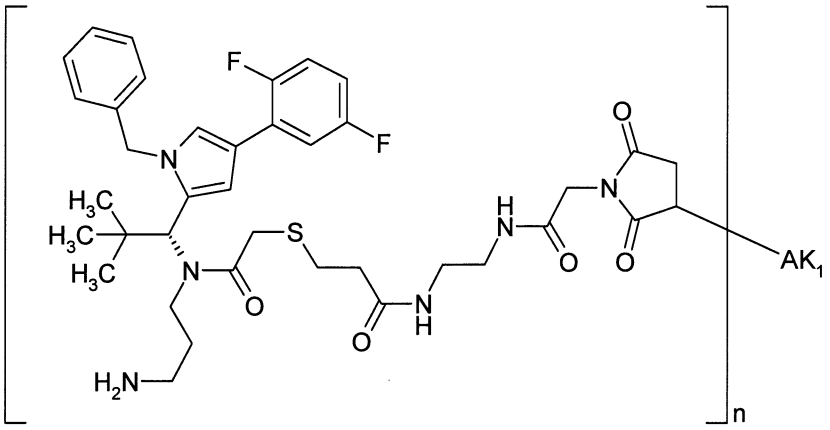


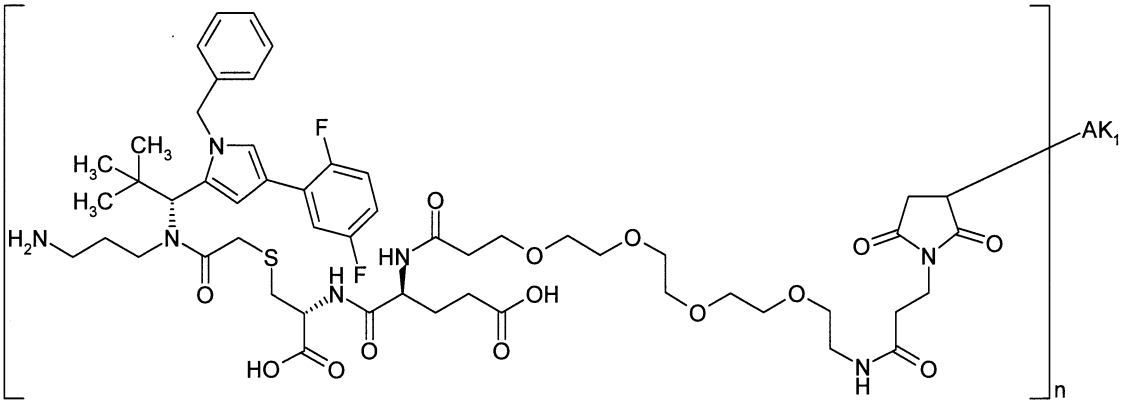


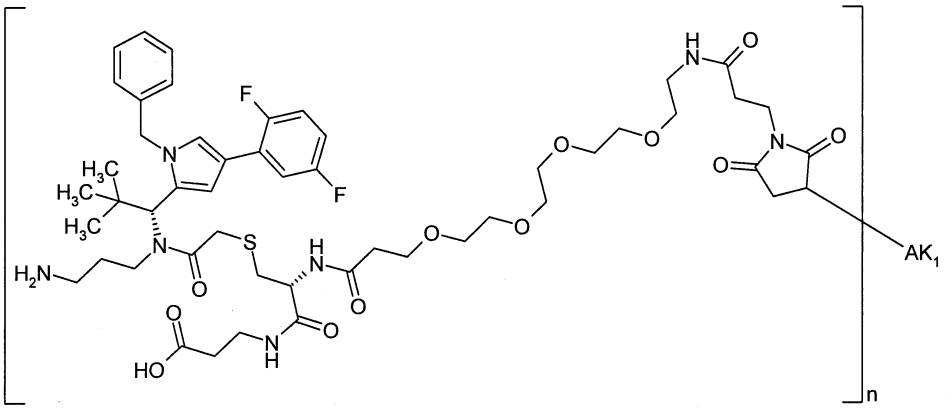


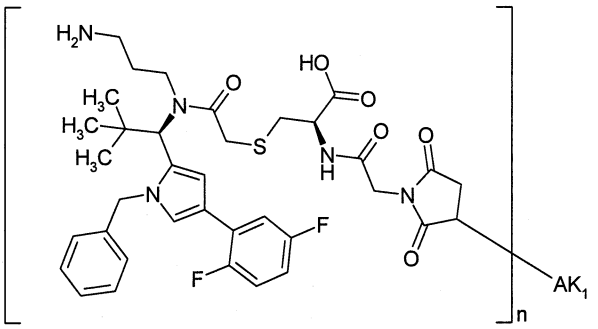


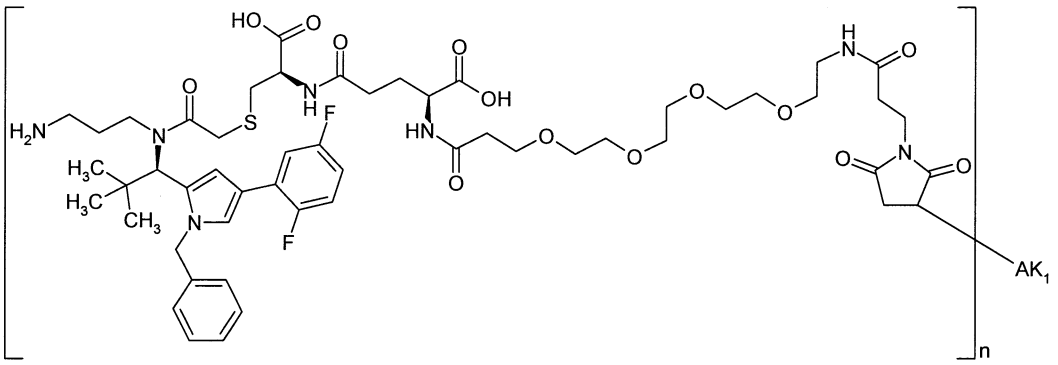


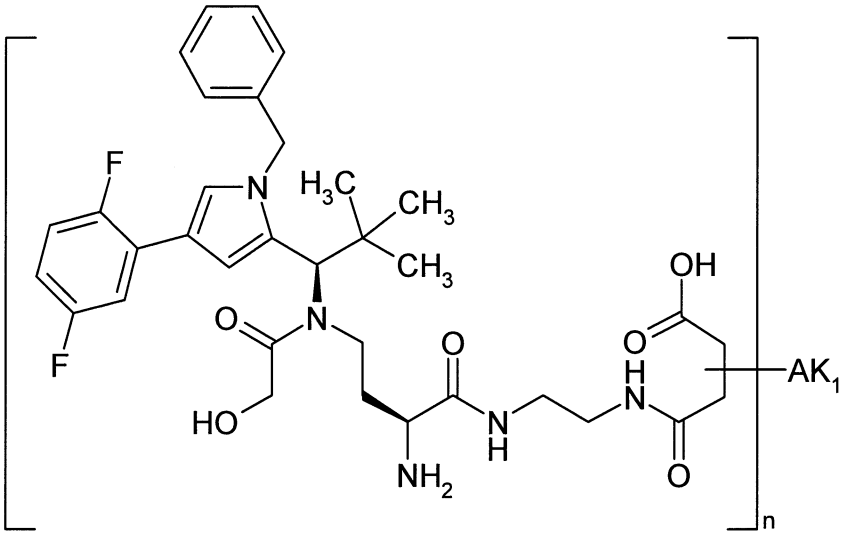


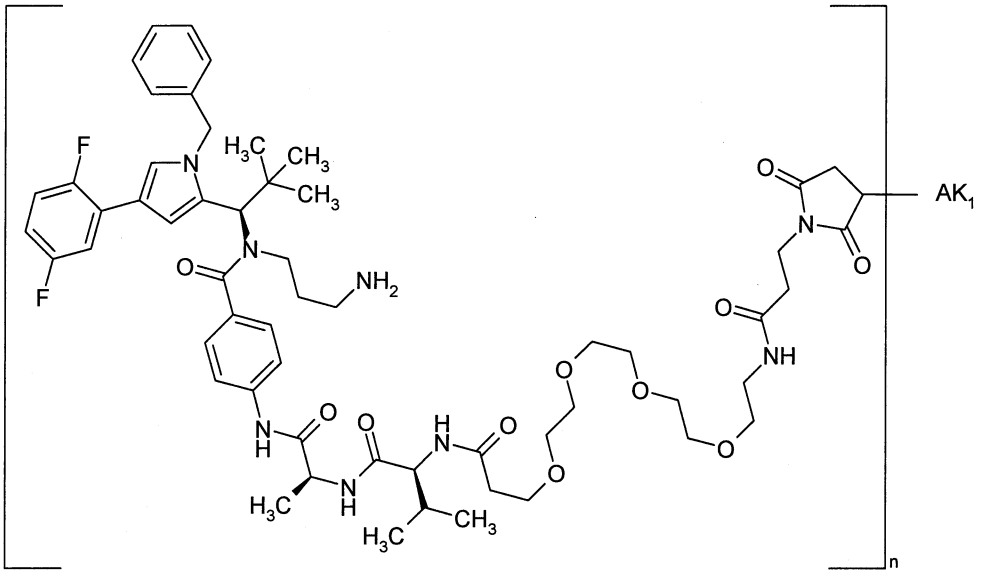


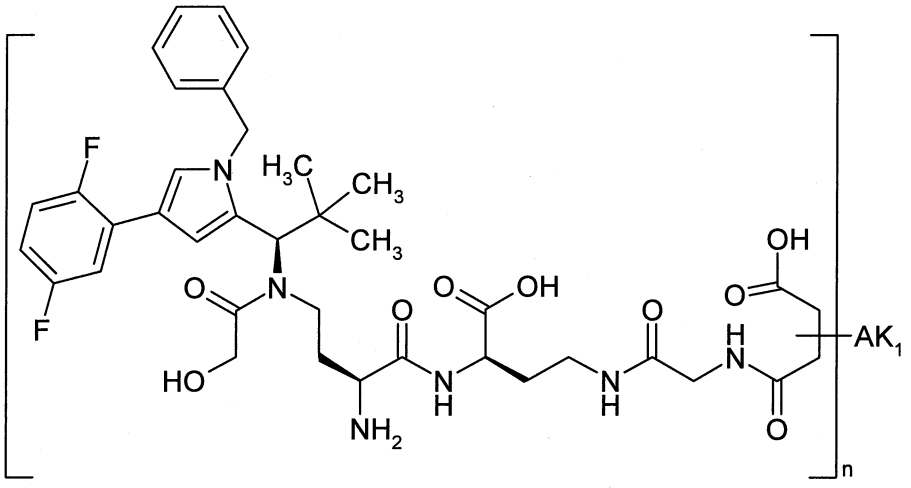


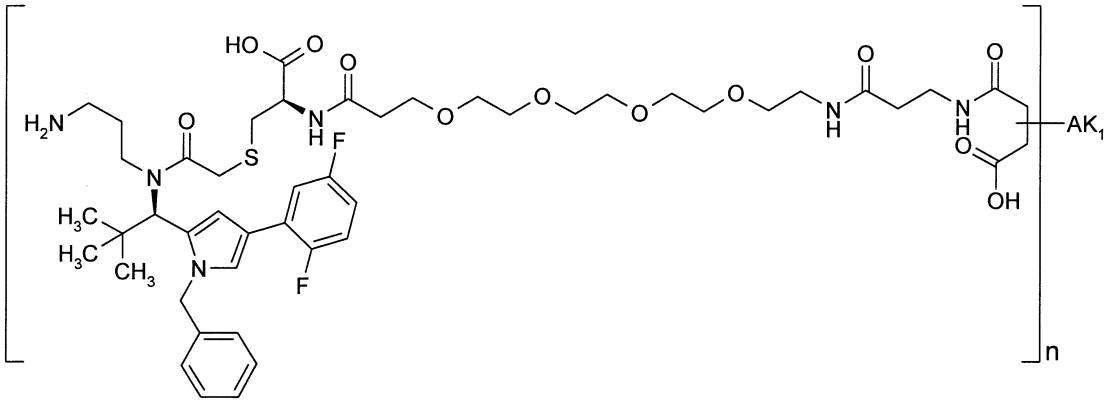


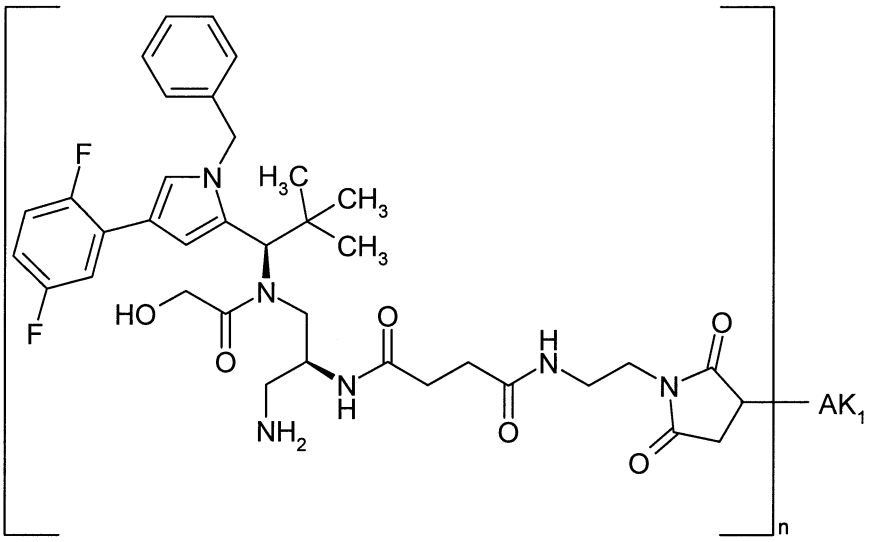


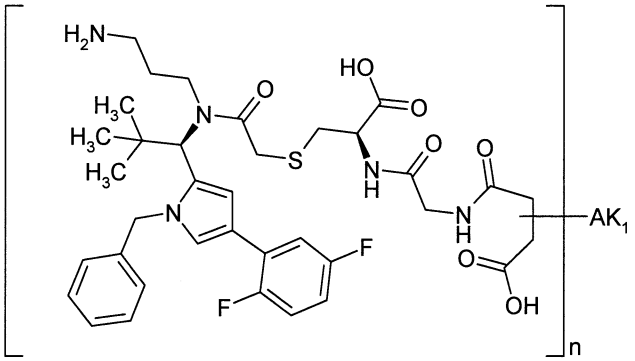


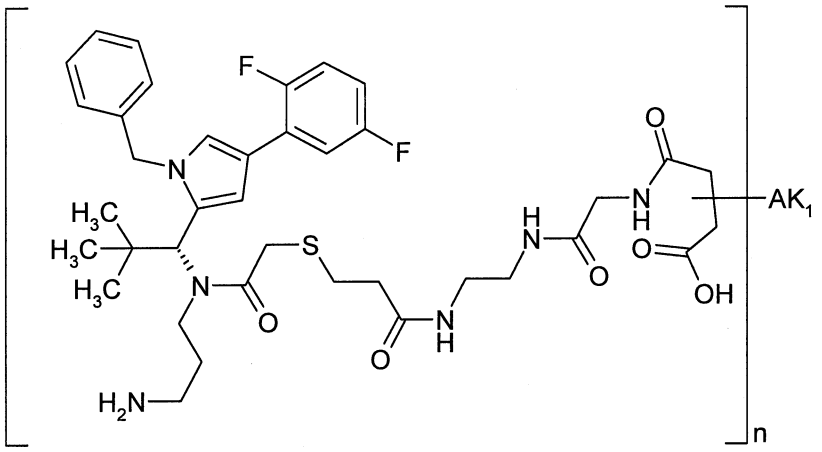


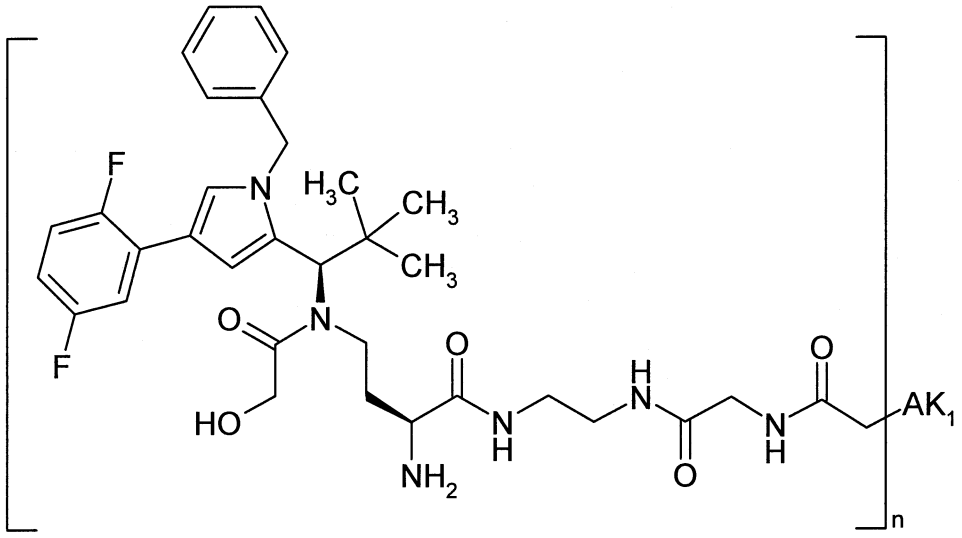


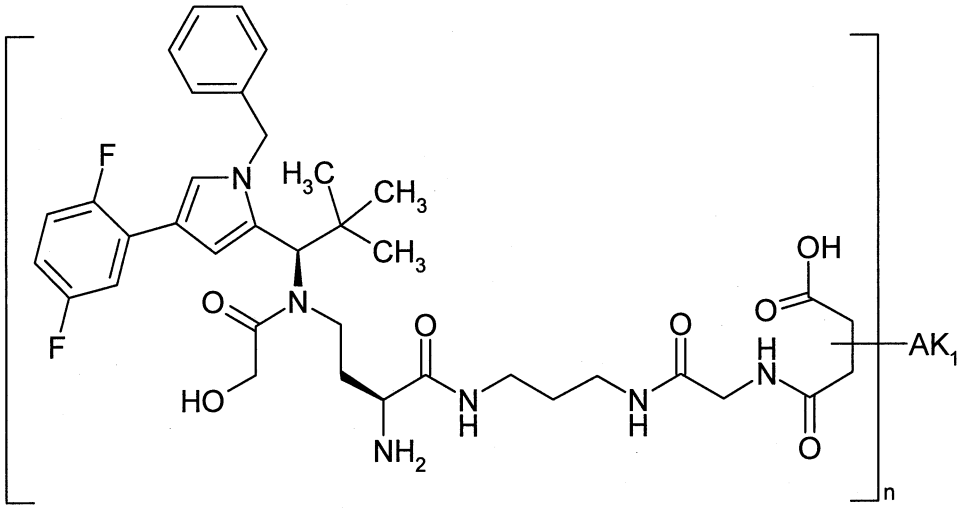


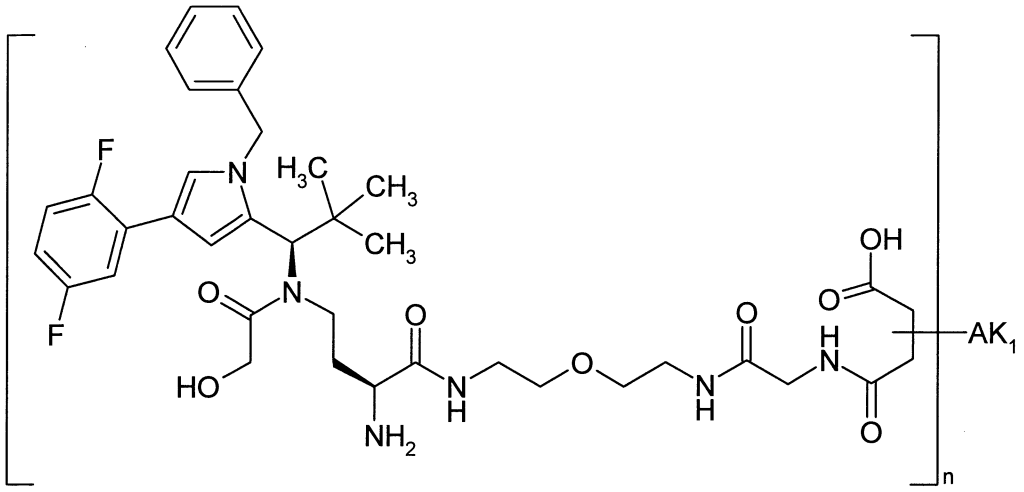


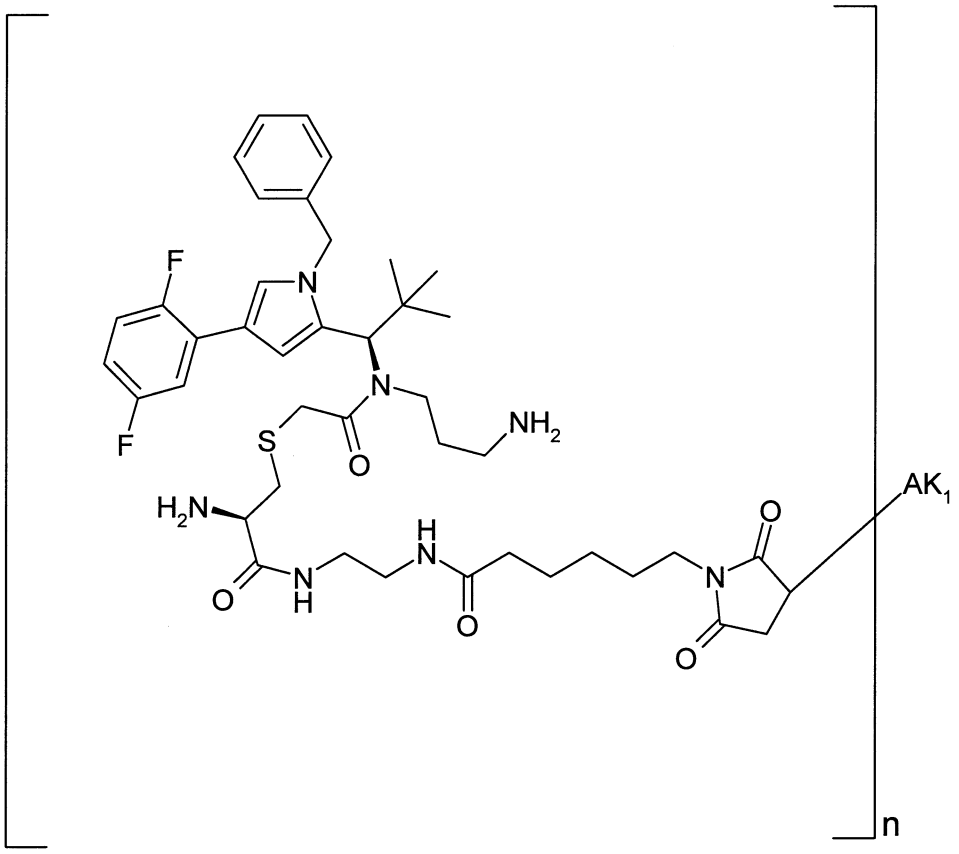


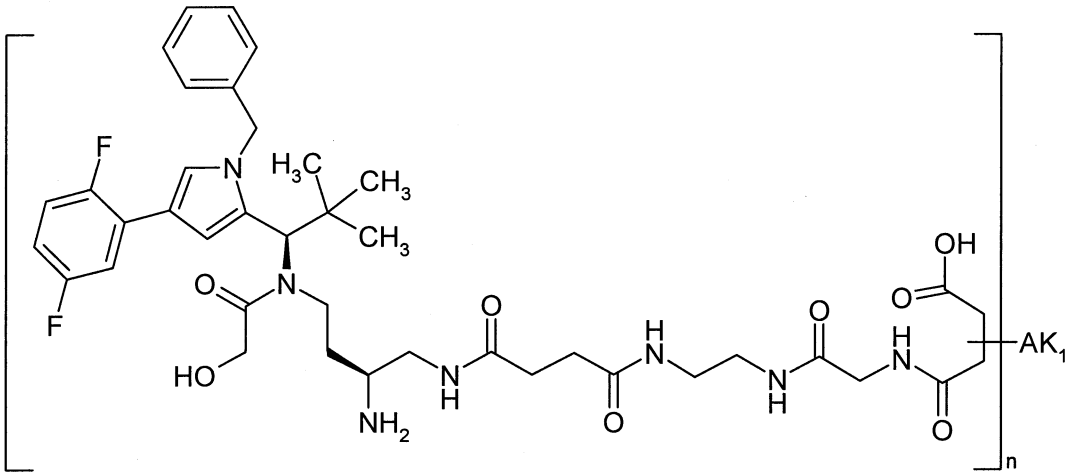


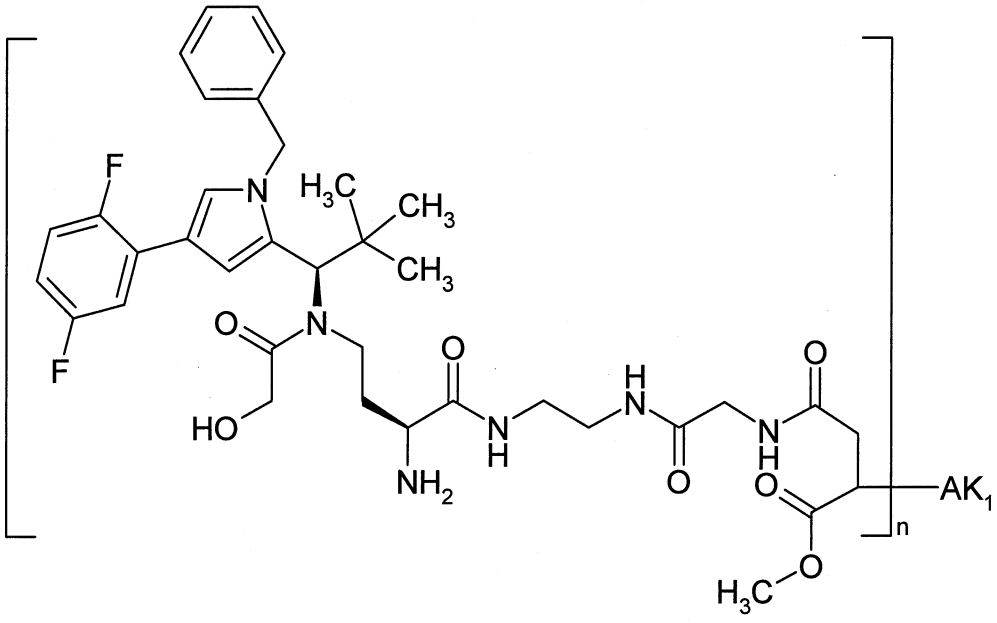


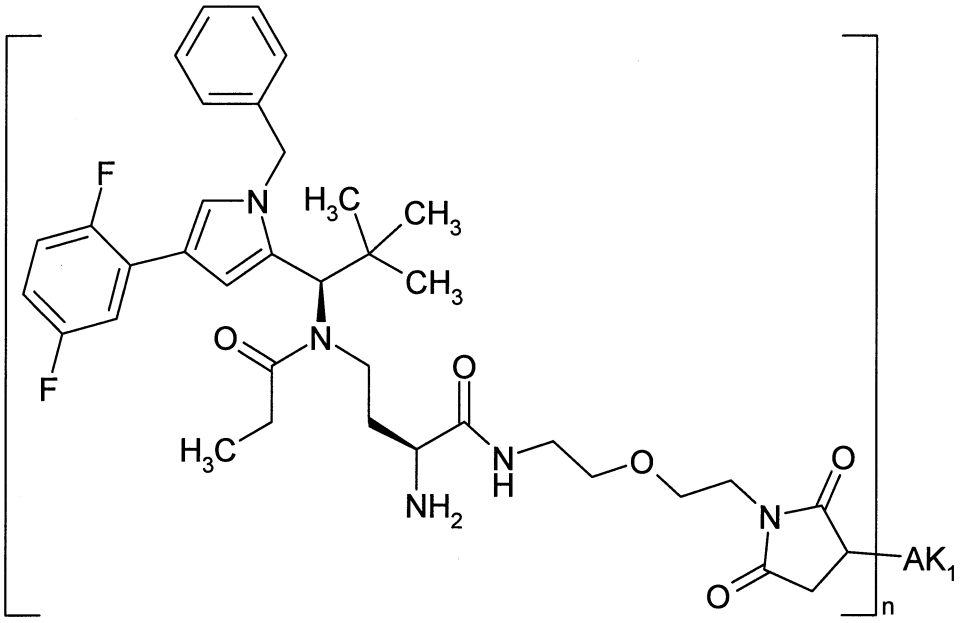


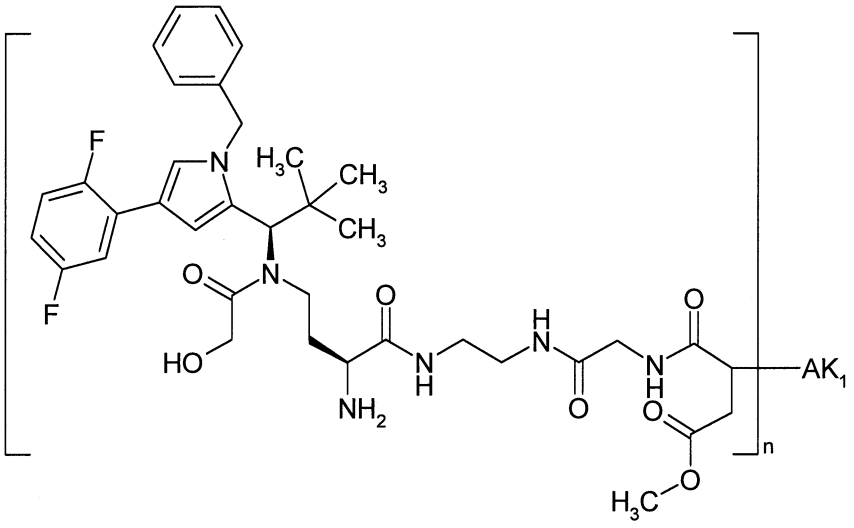


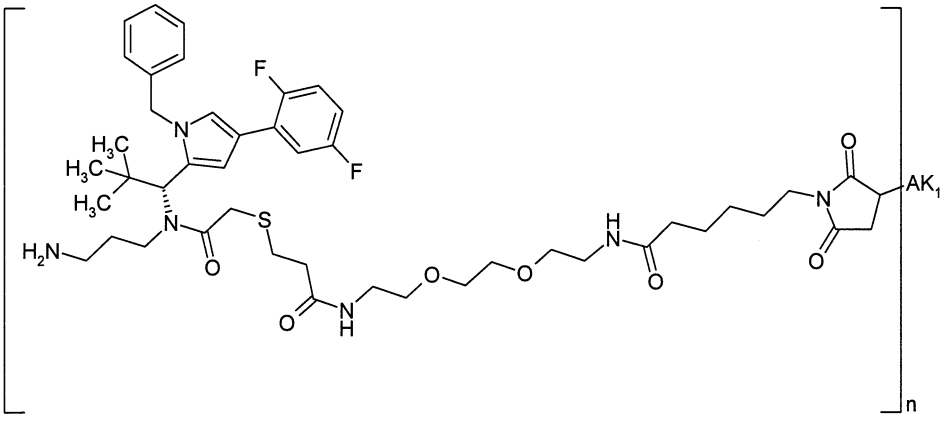


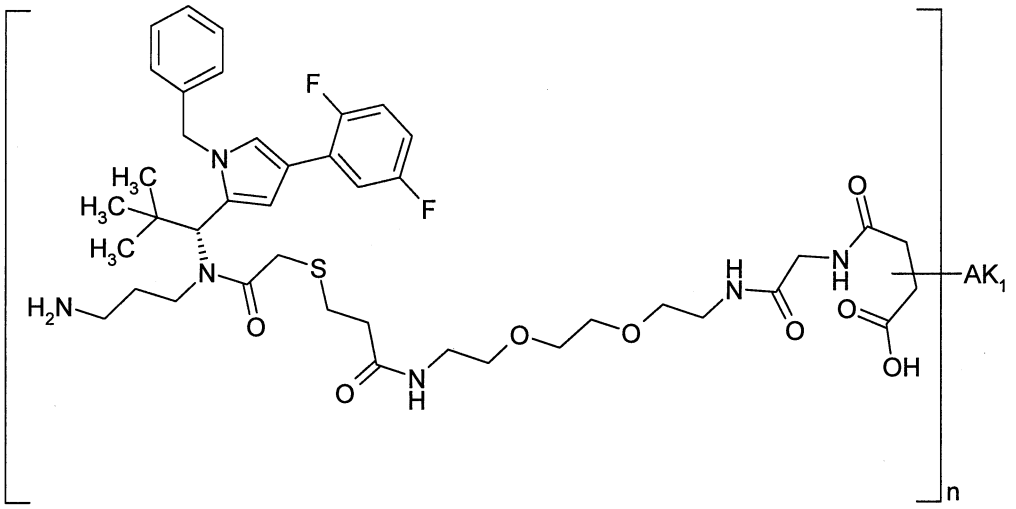


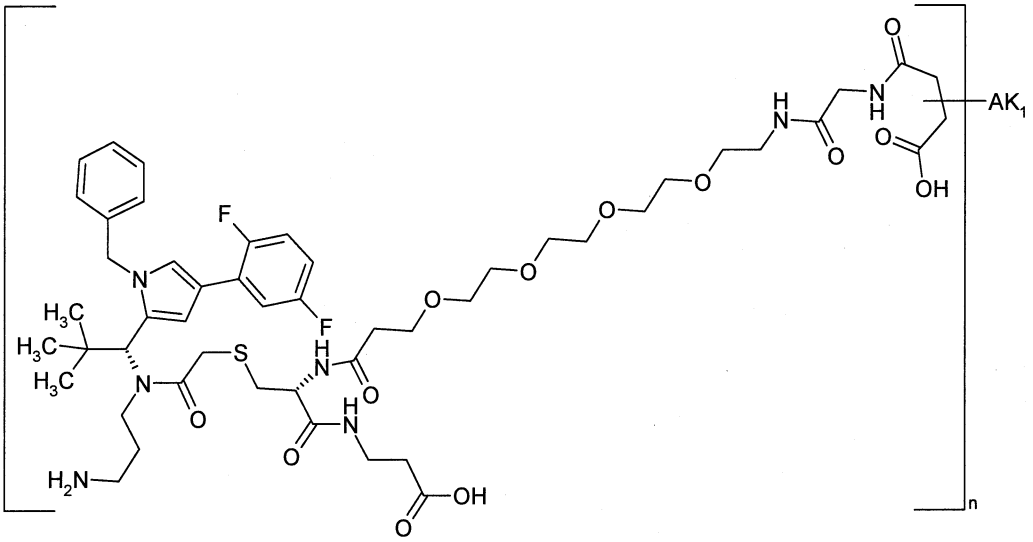


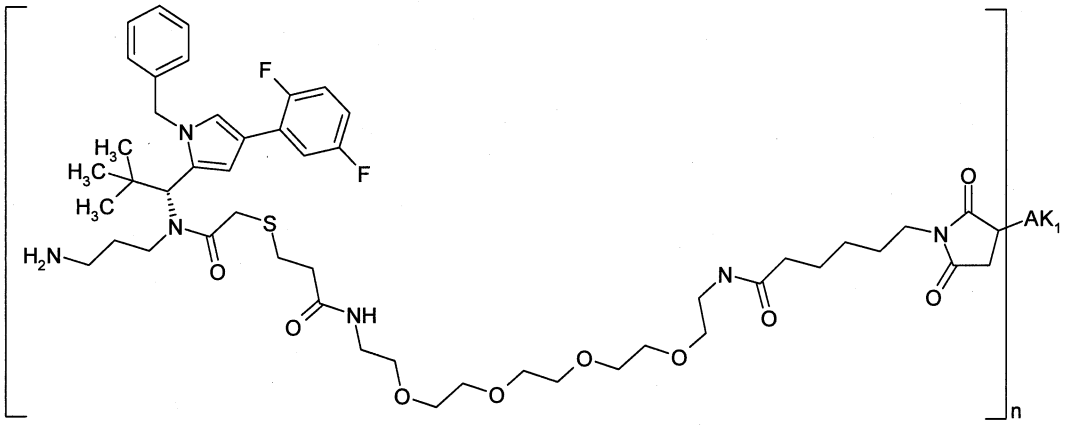


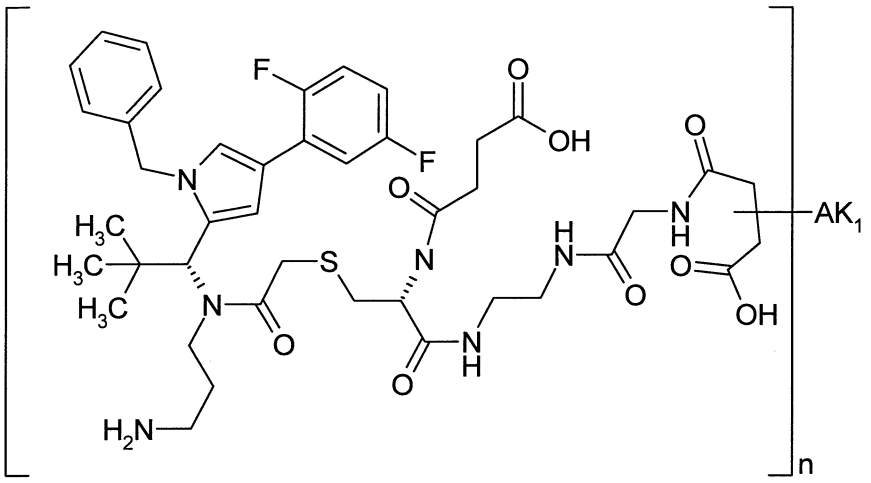


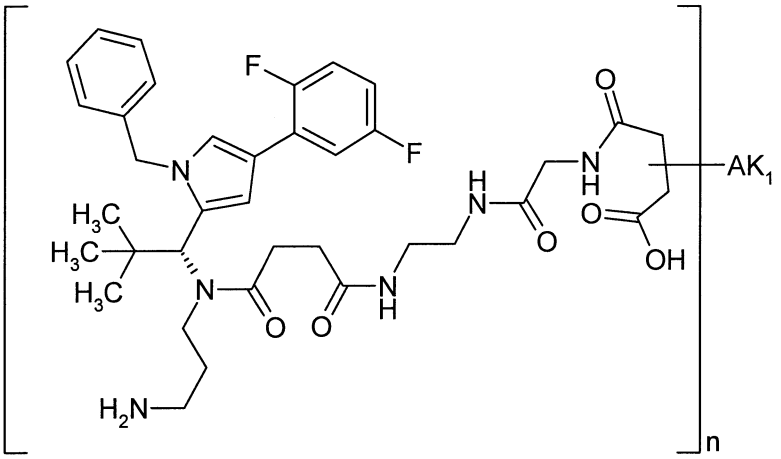


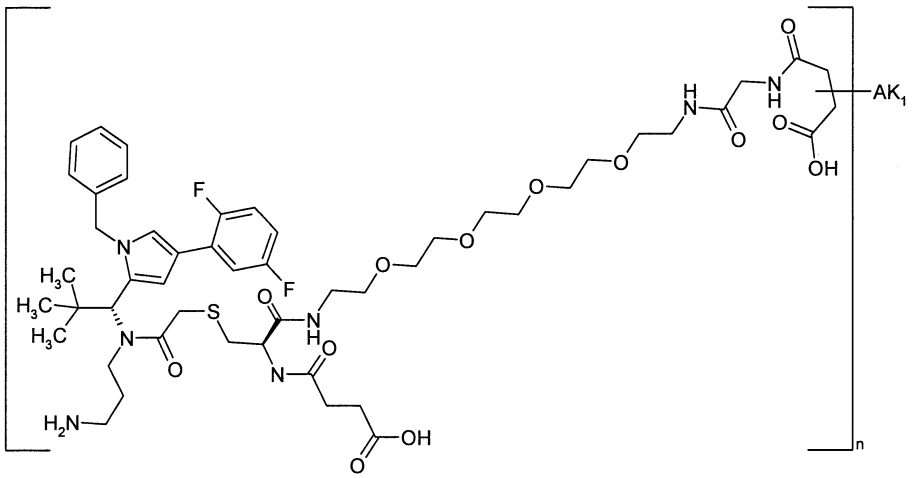


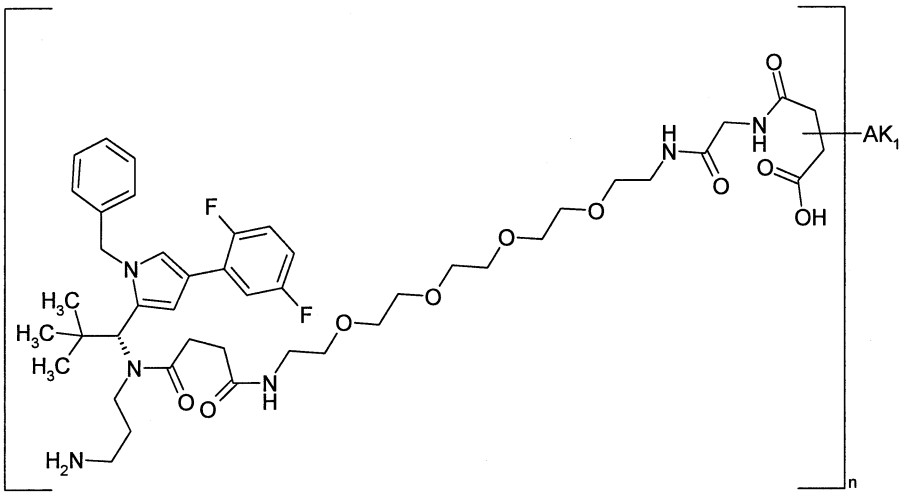


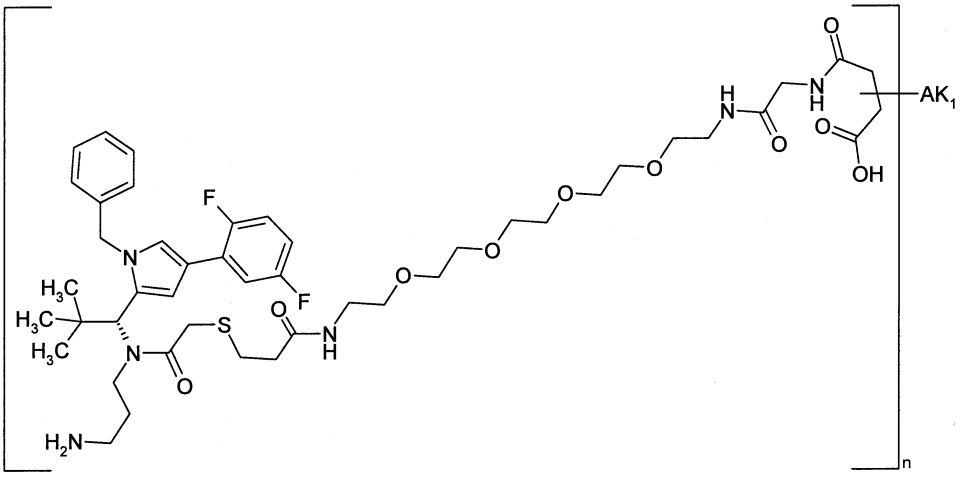


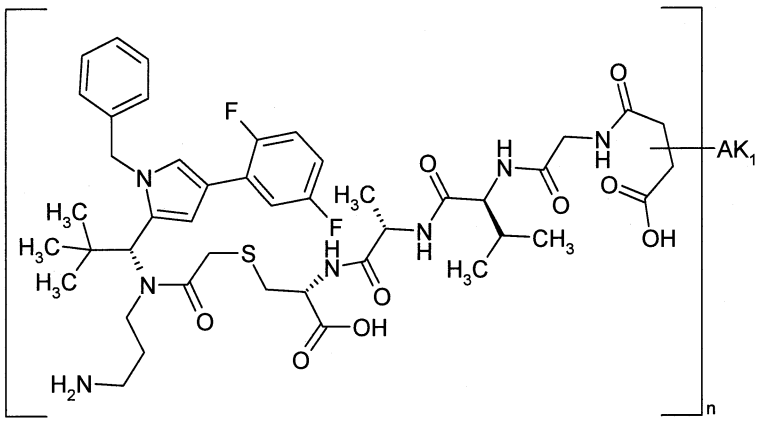


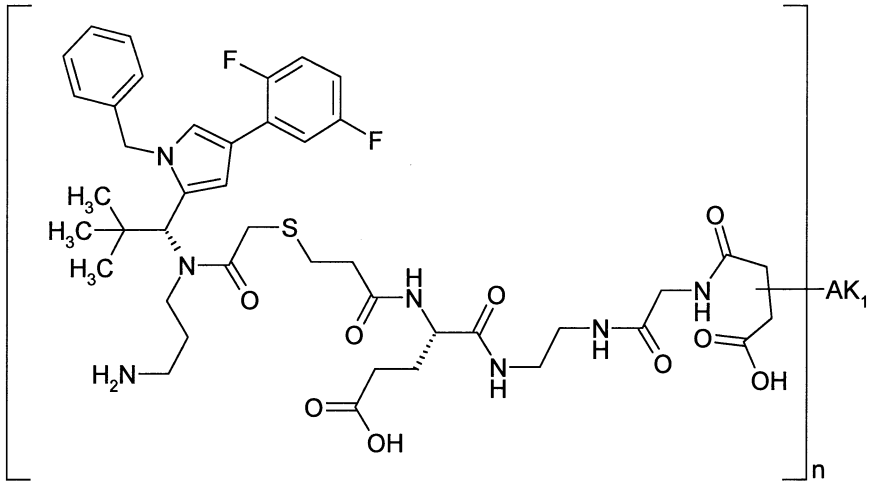


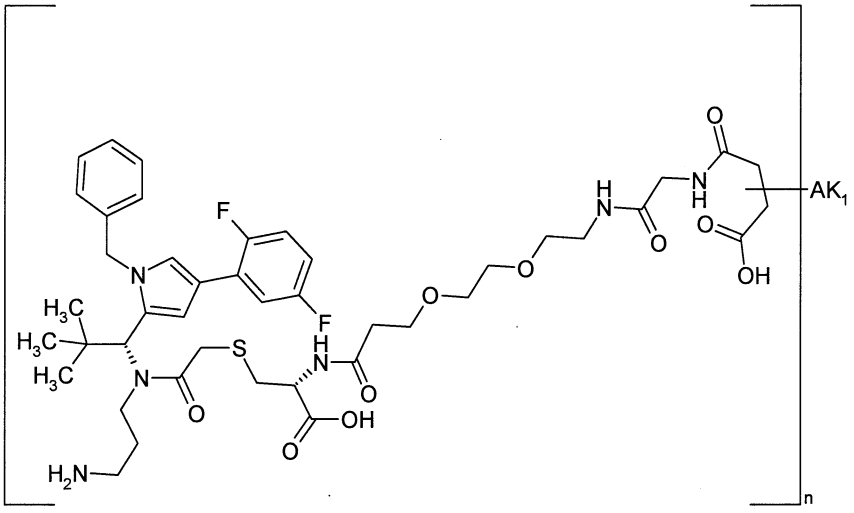


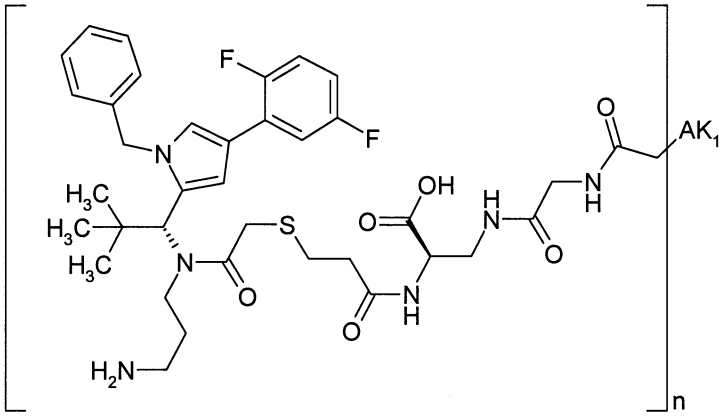


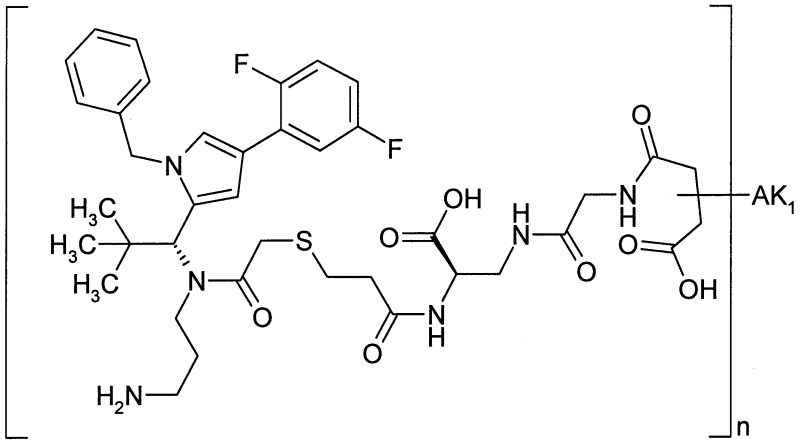


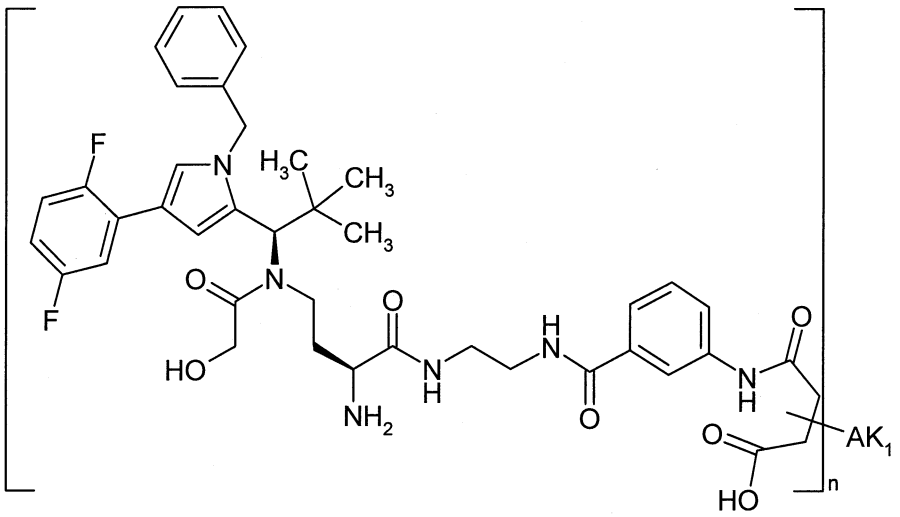


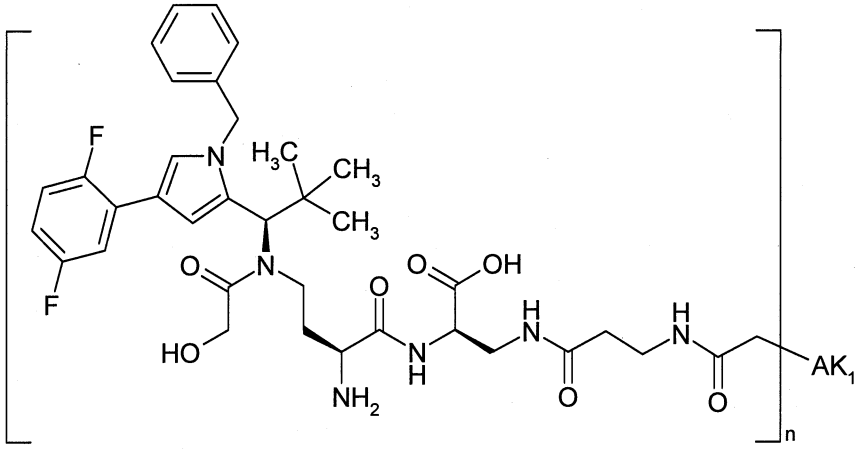


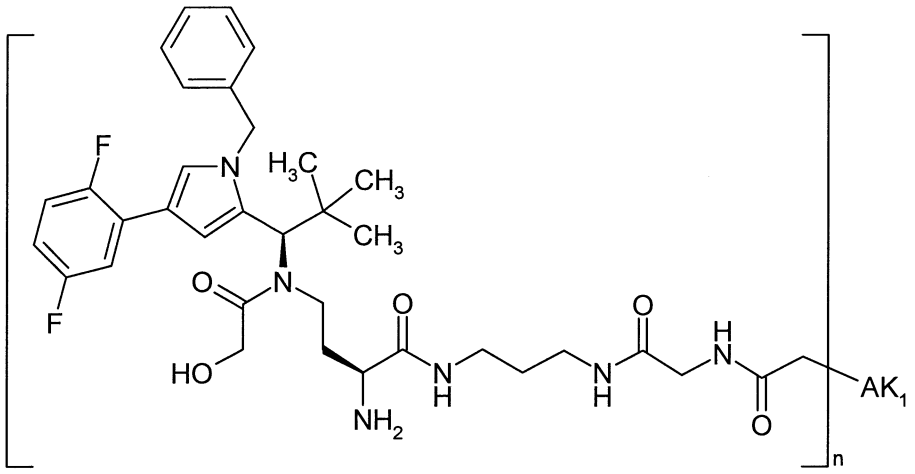


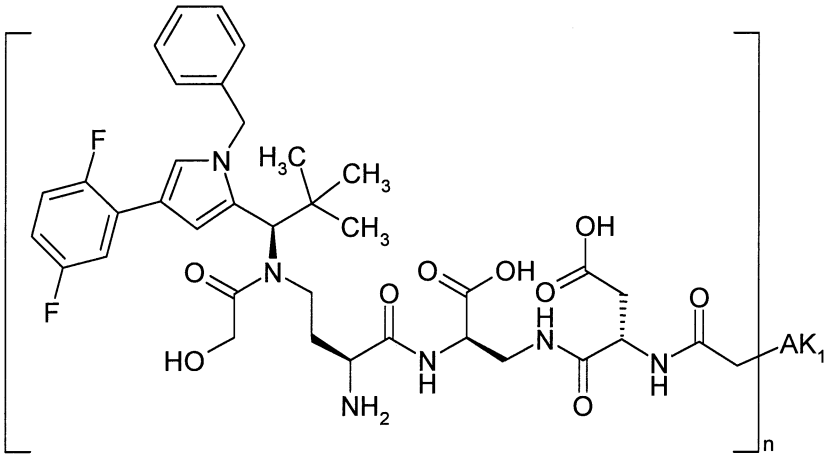


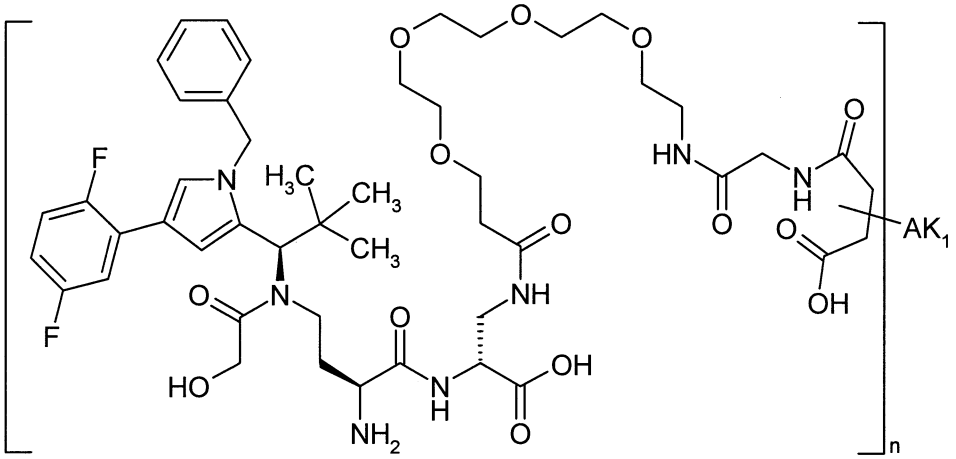


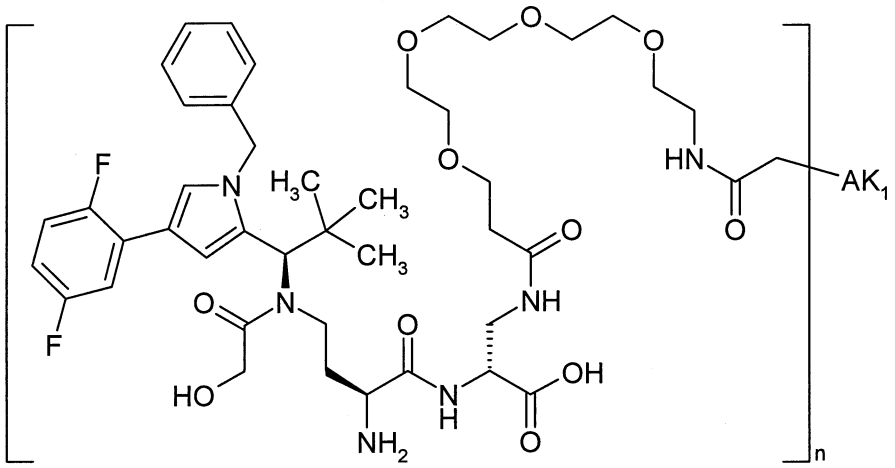


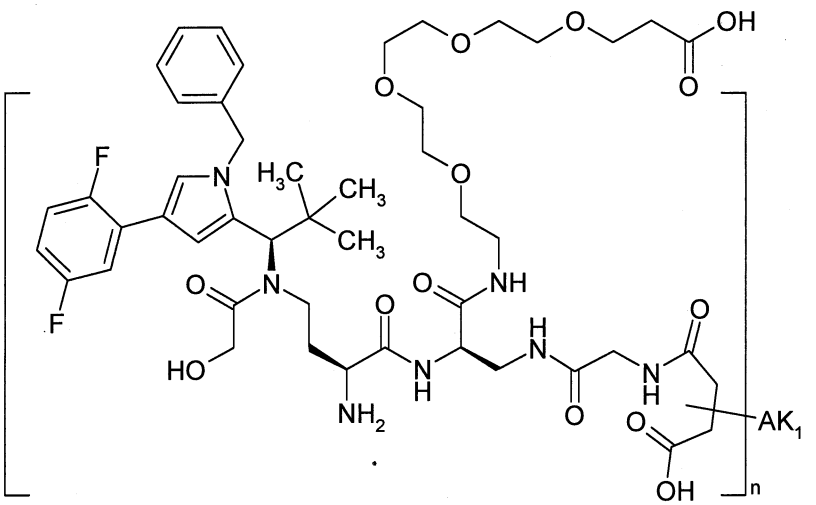


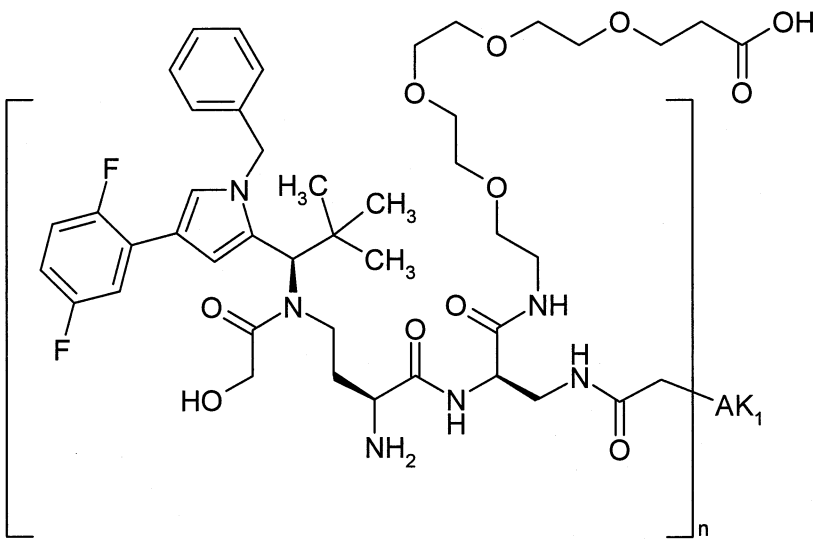


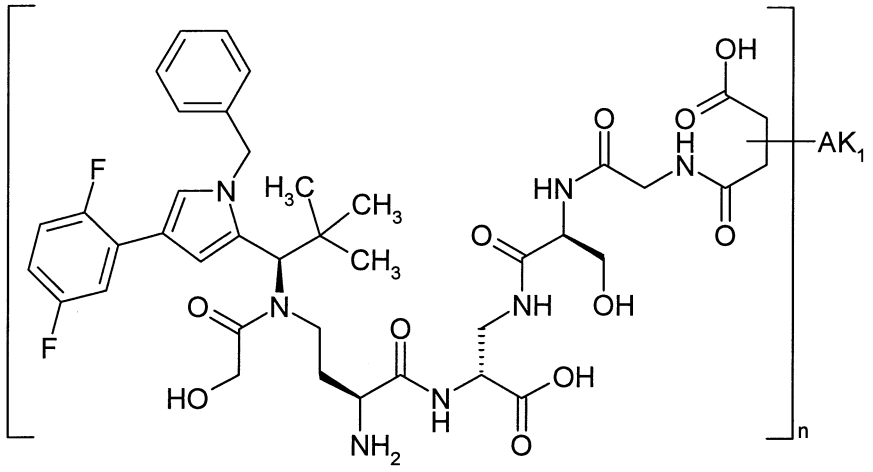


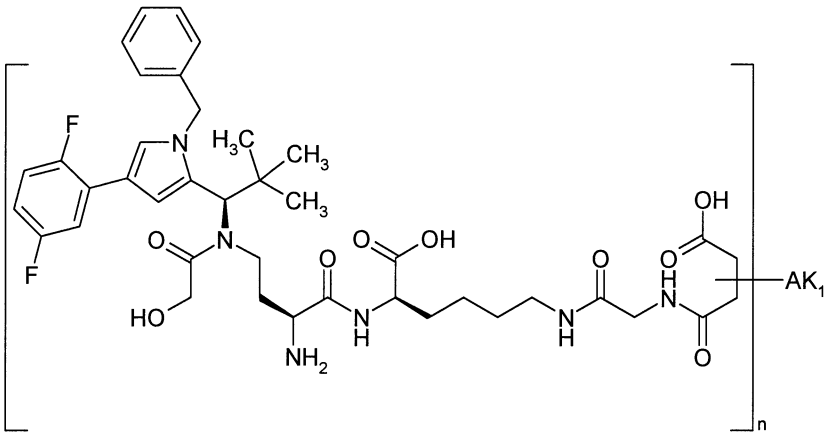


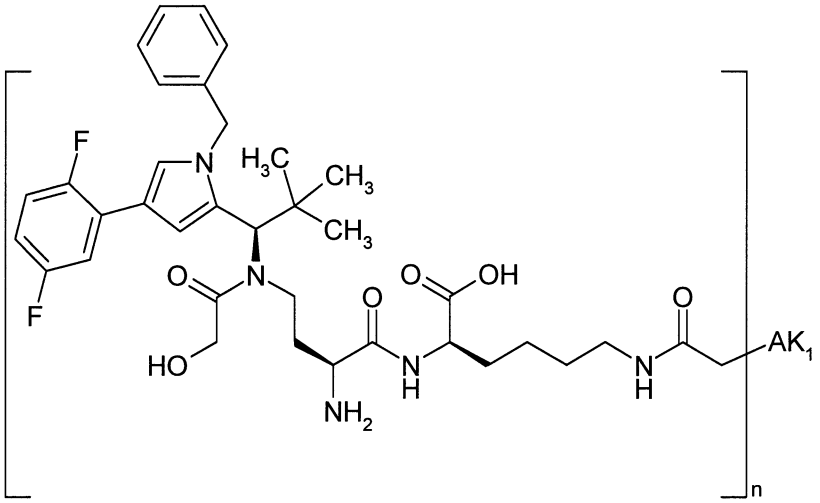


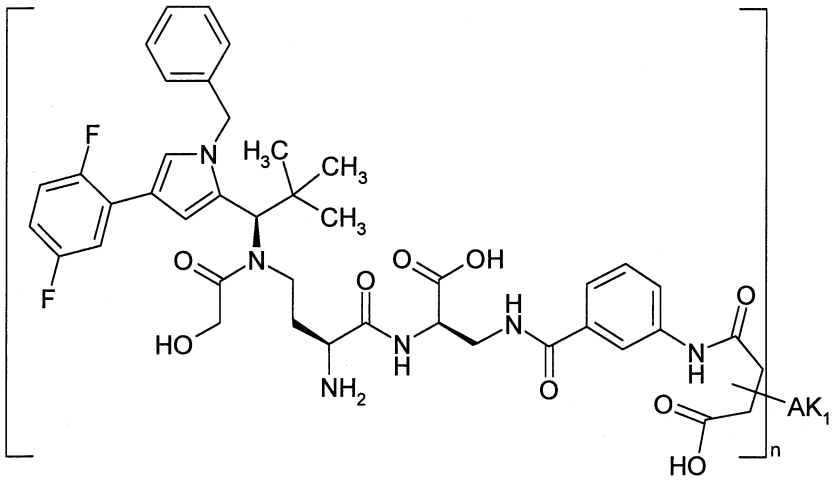


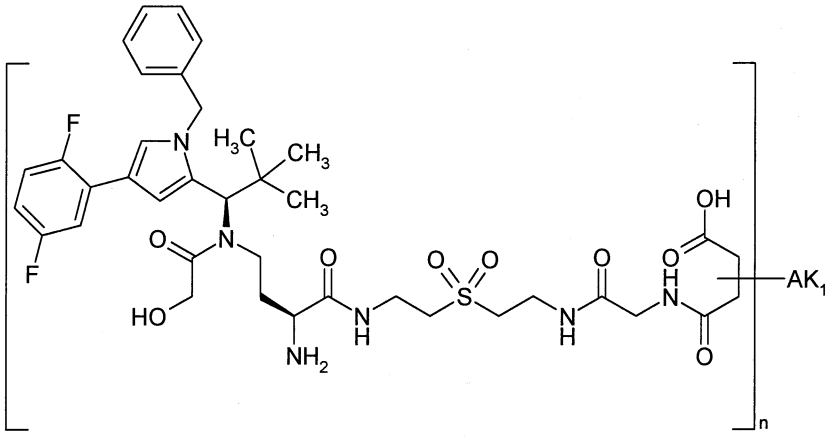


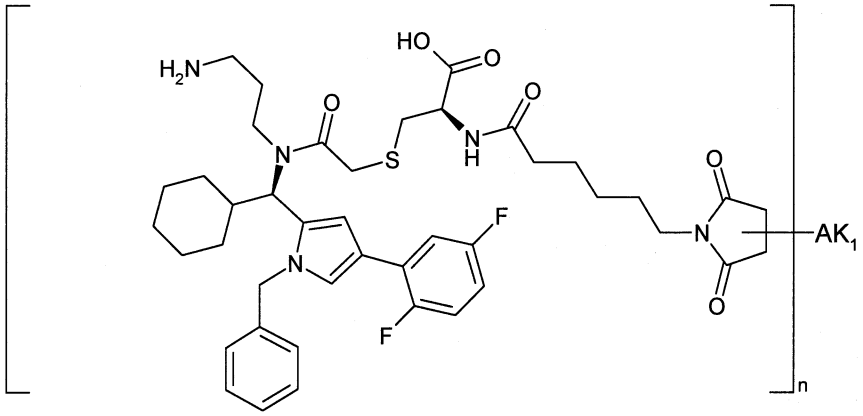


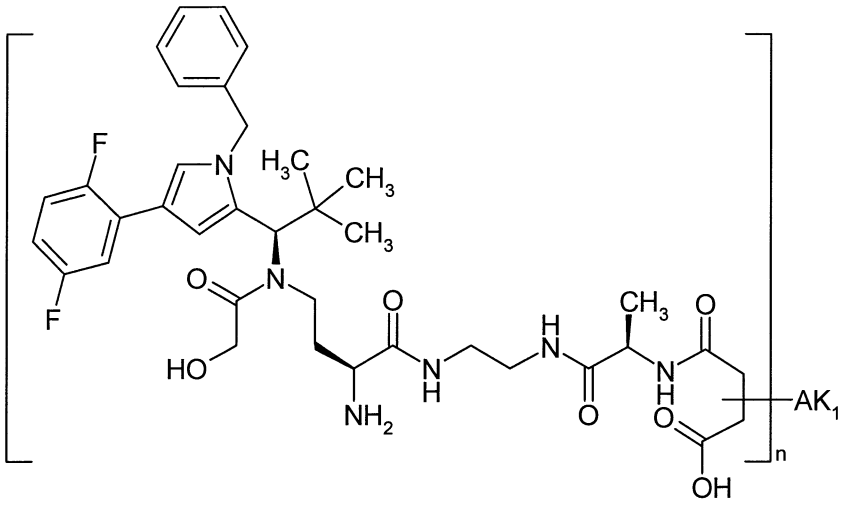


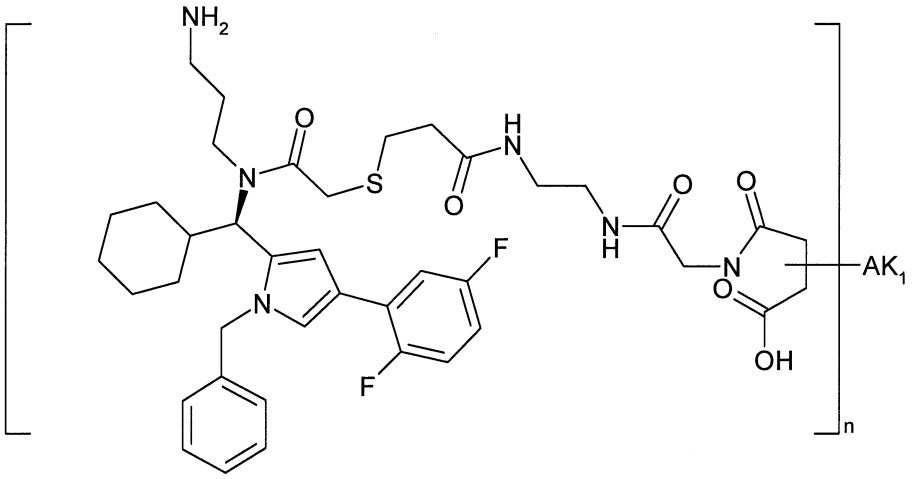








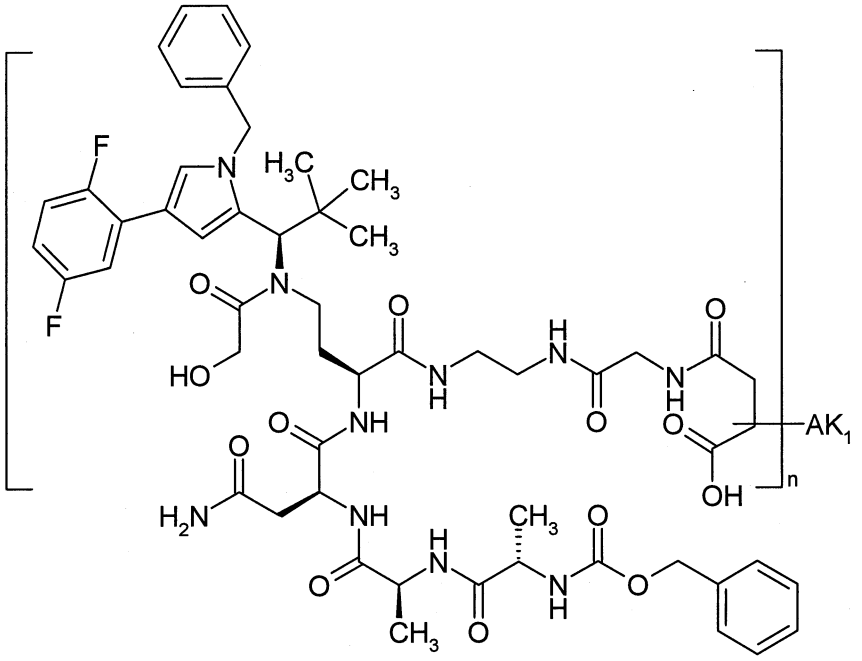


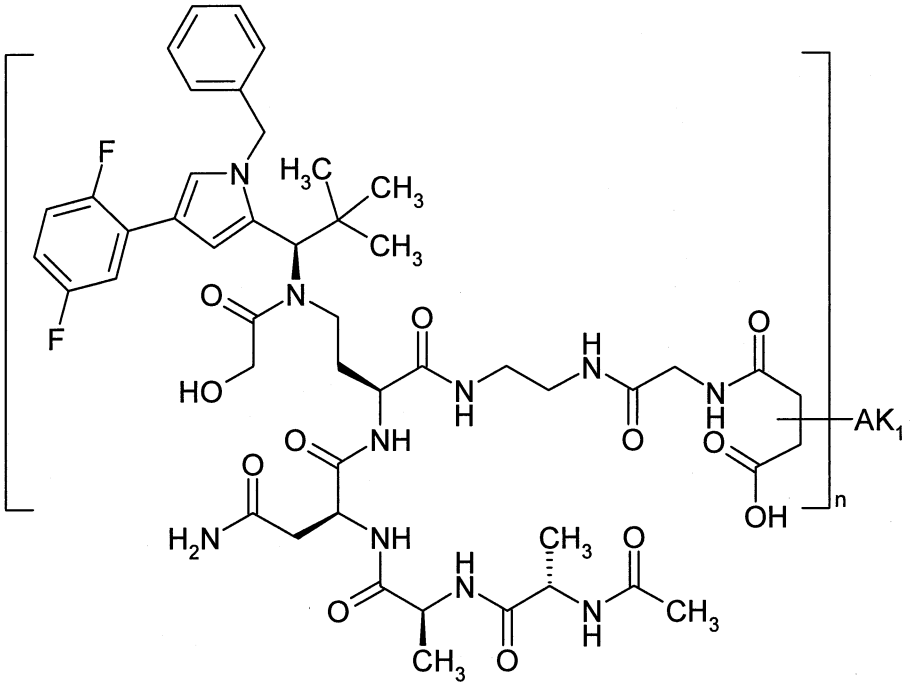


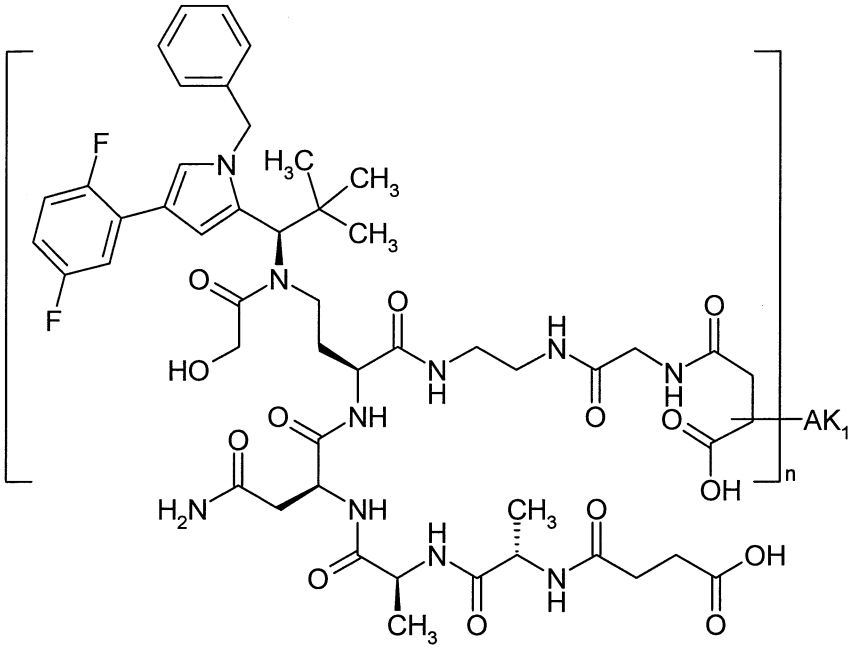
where n is a number from 1 to 20,

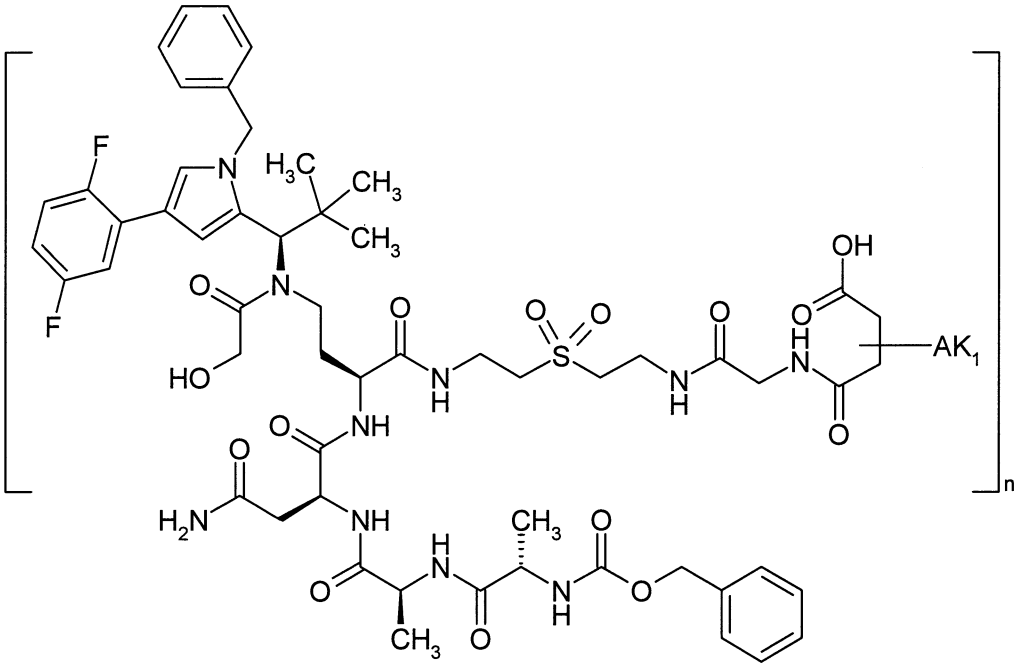
AK1 represents a cysteine-bonded antibody.

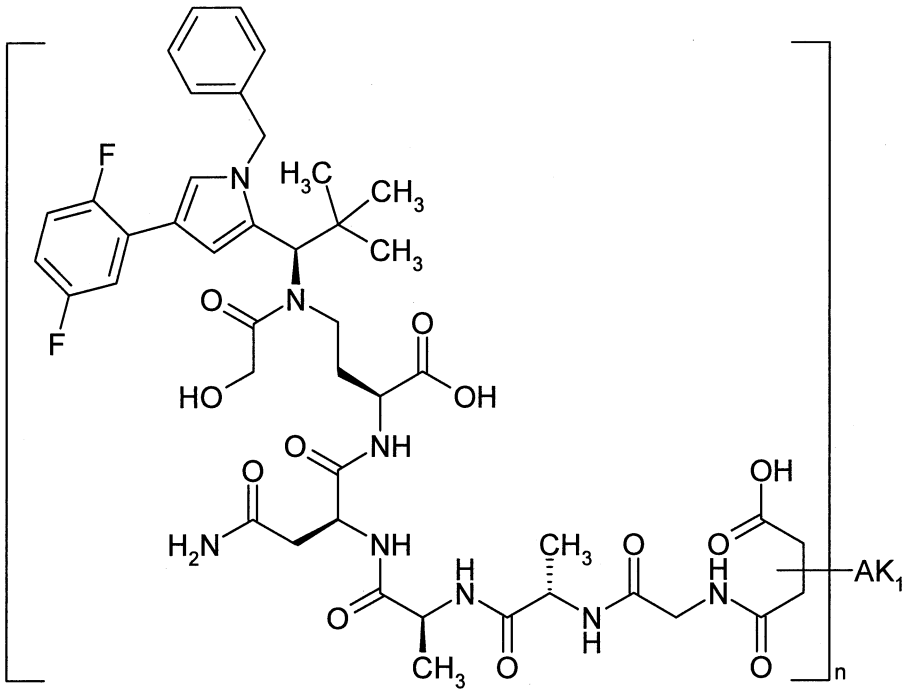
49. Antibody-prodrug conjugate according to one or more of Claims 1 to 47 where the antibody-prodrug conjugate satisfies one of the following formulae:

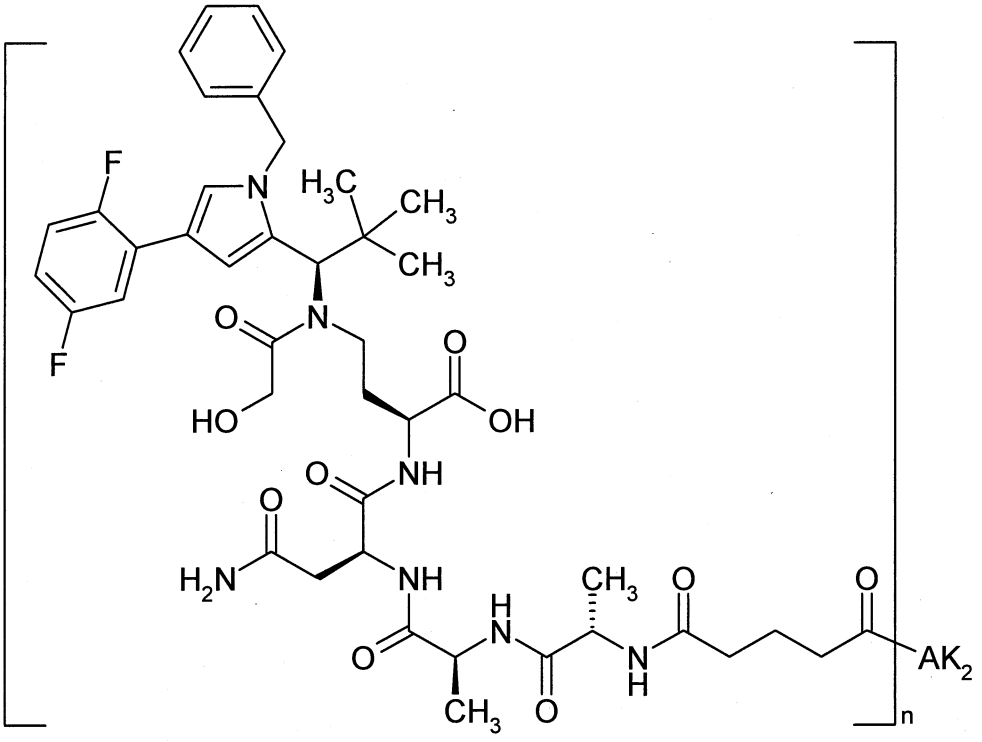


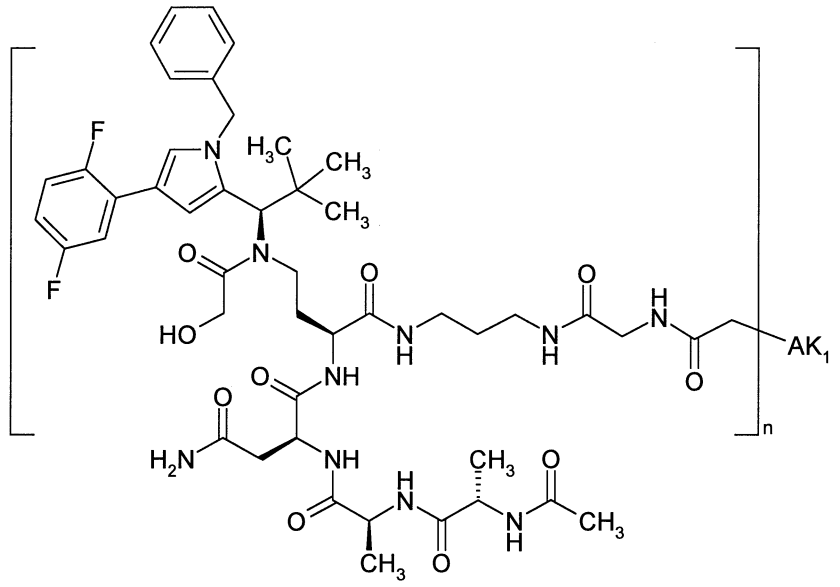


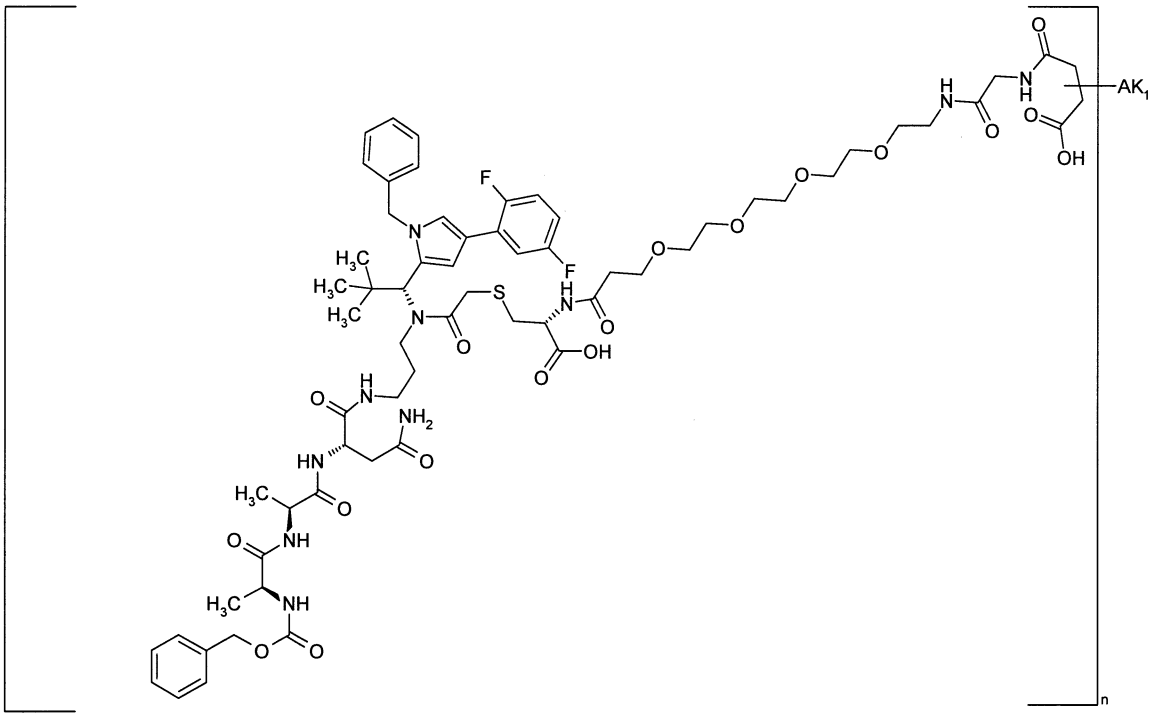


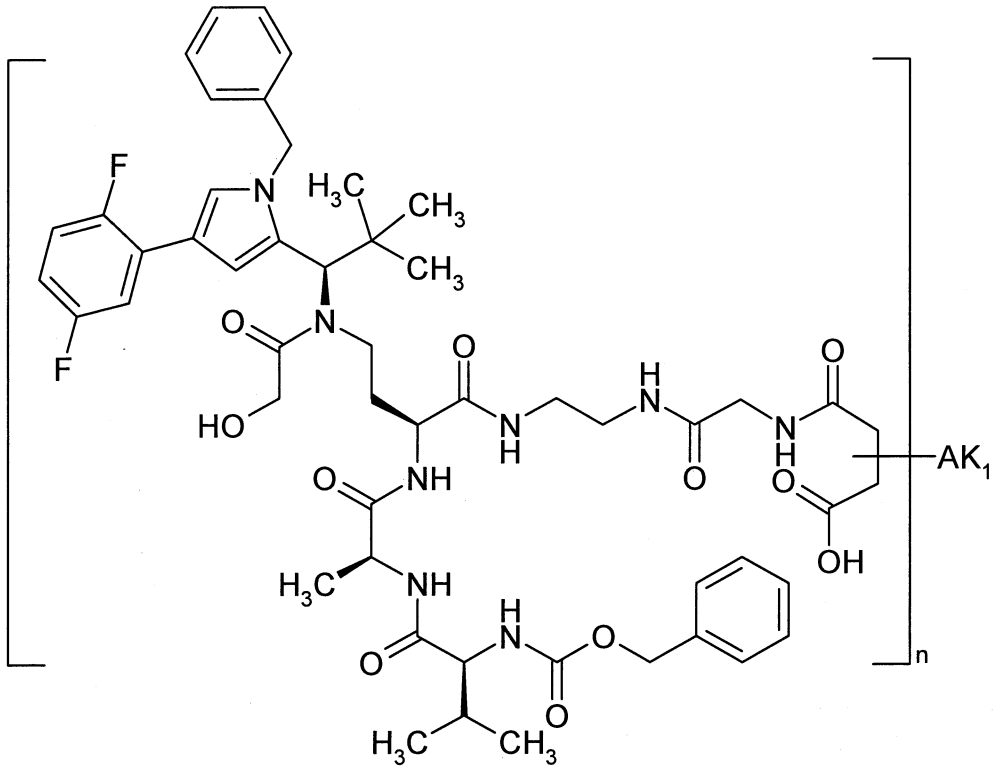


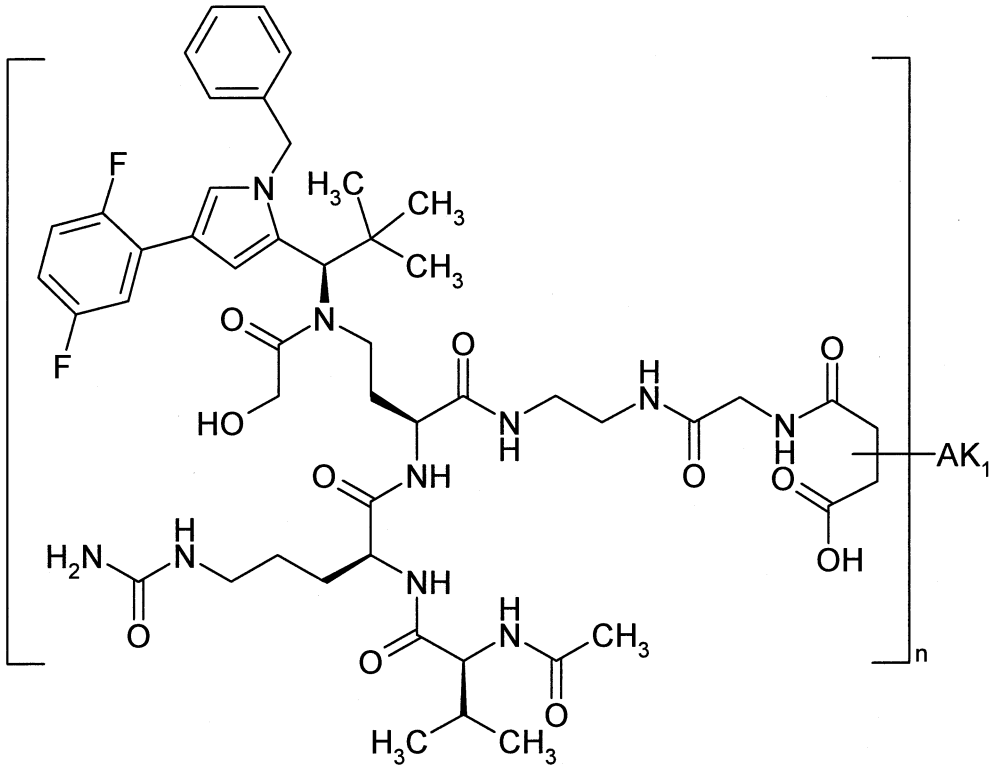


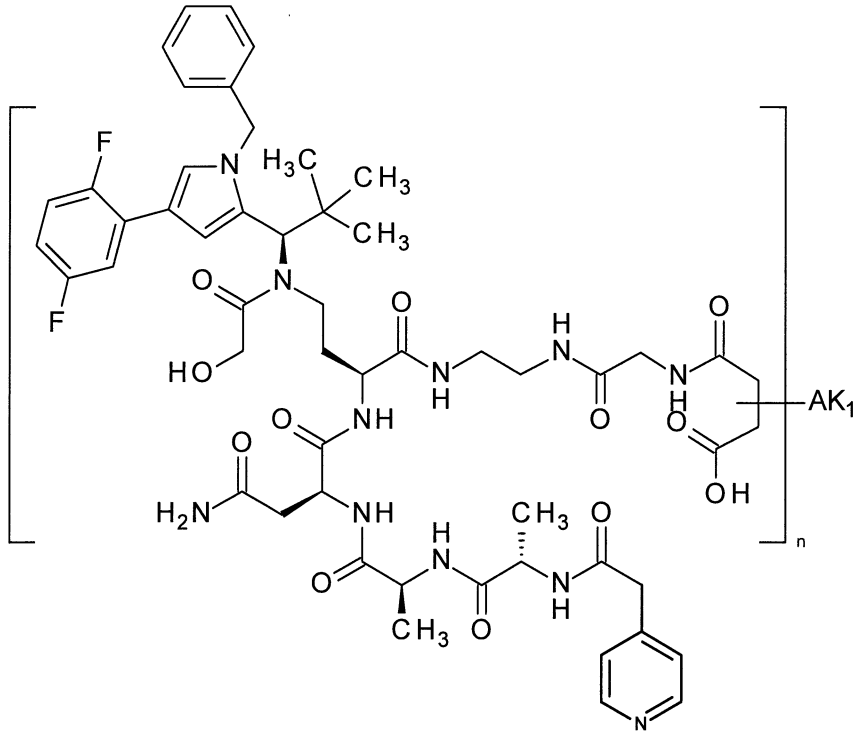


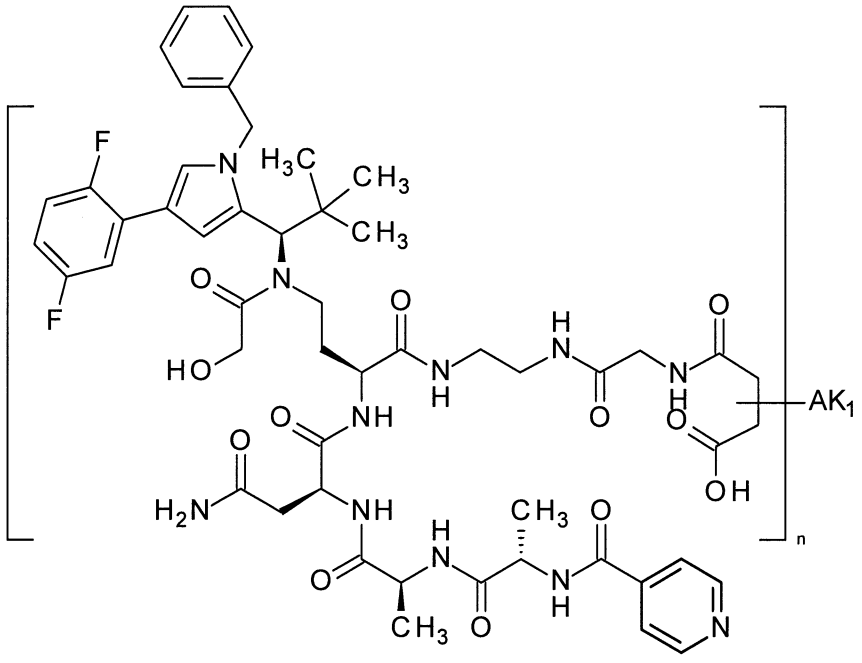


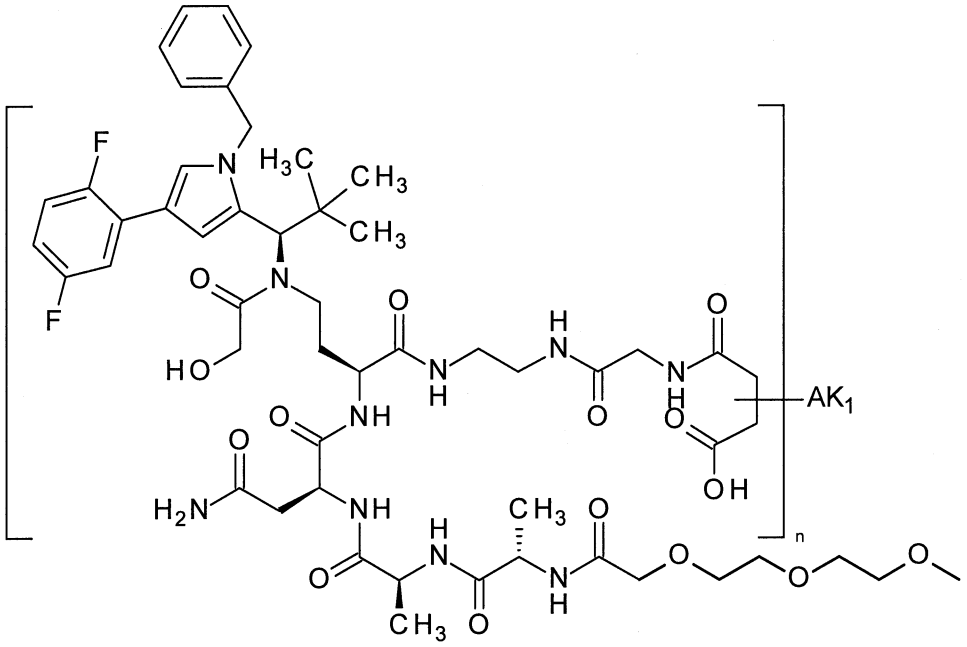


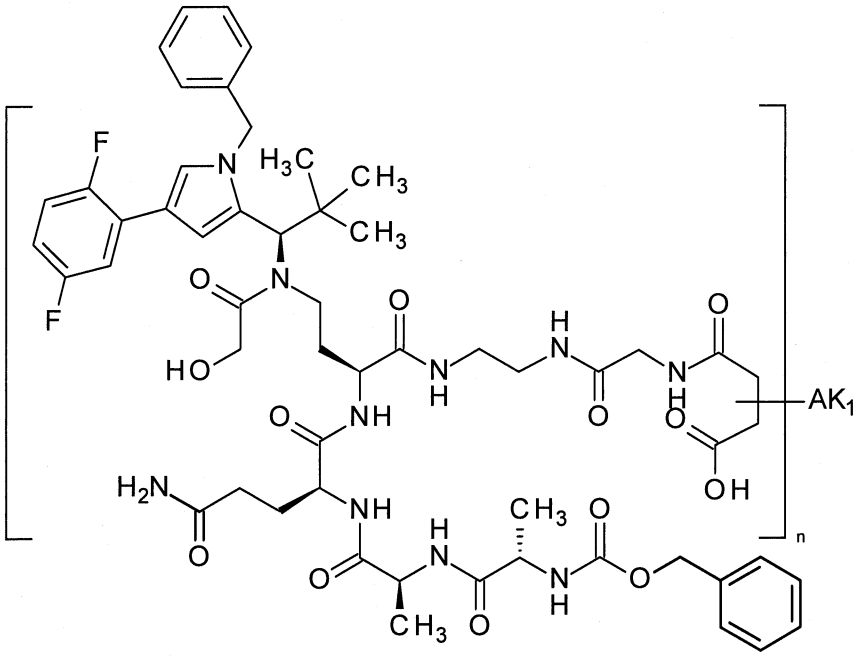


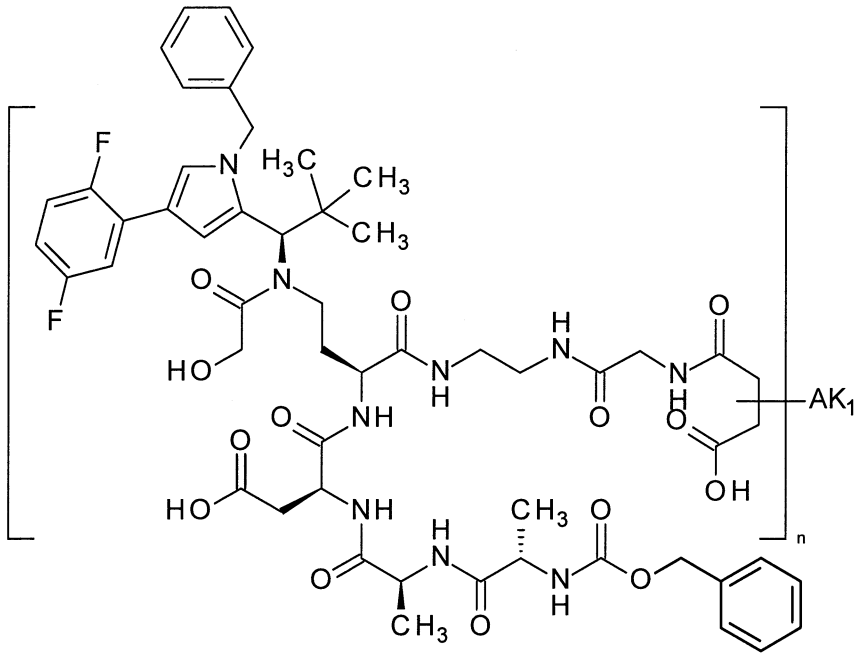


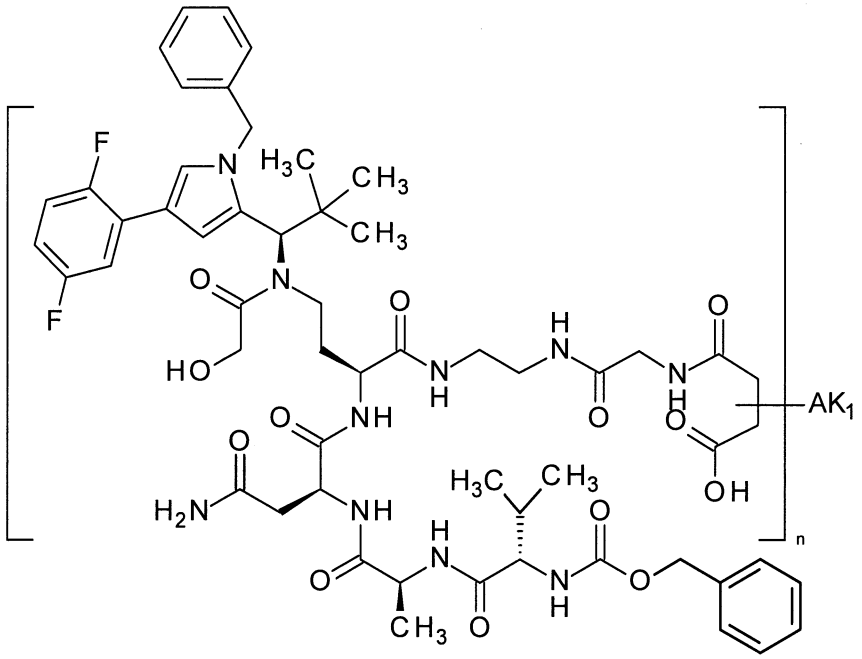


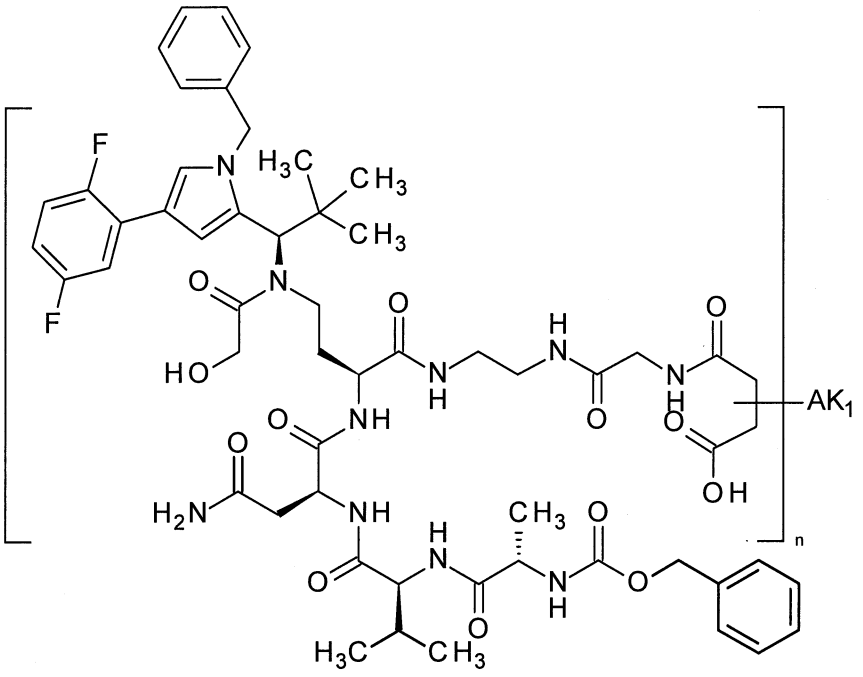


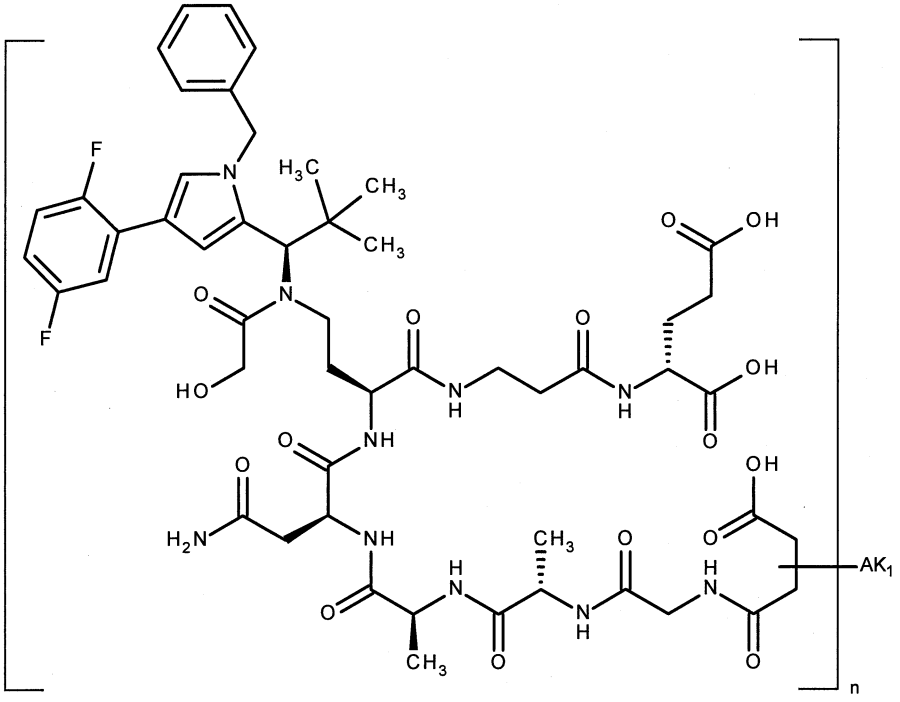


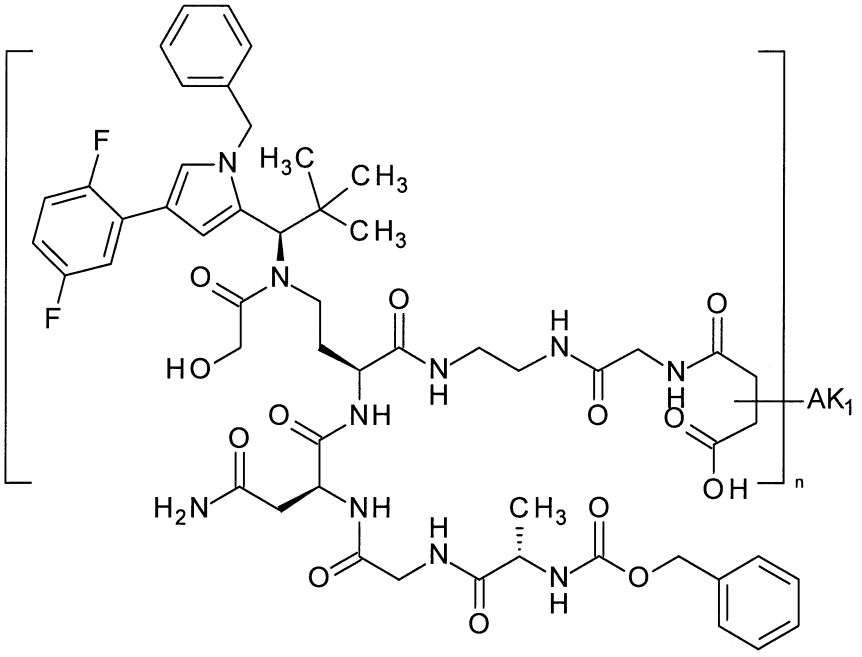


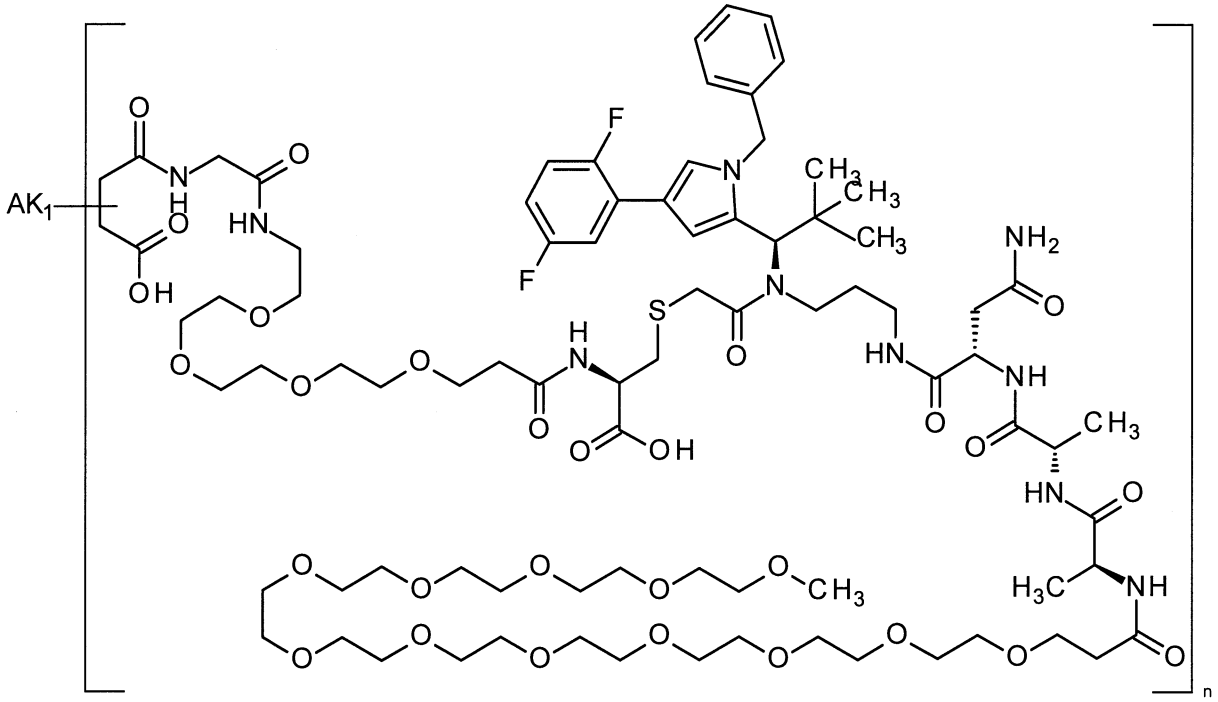


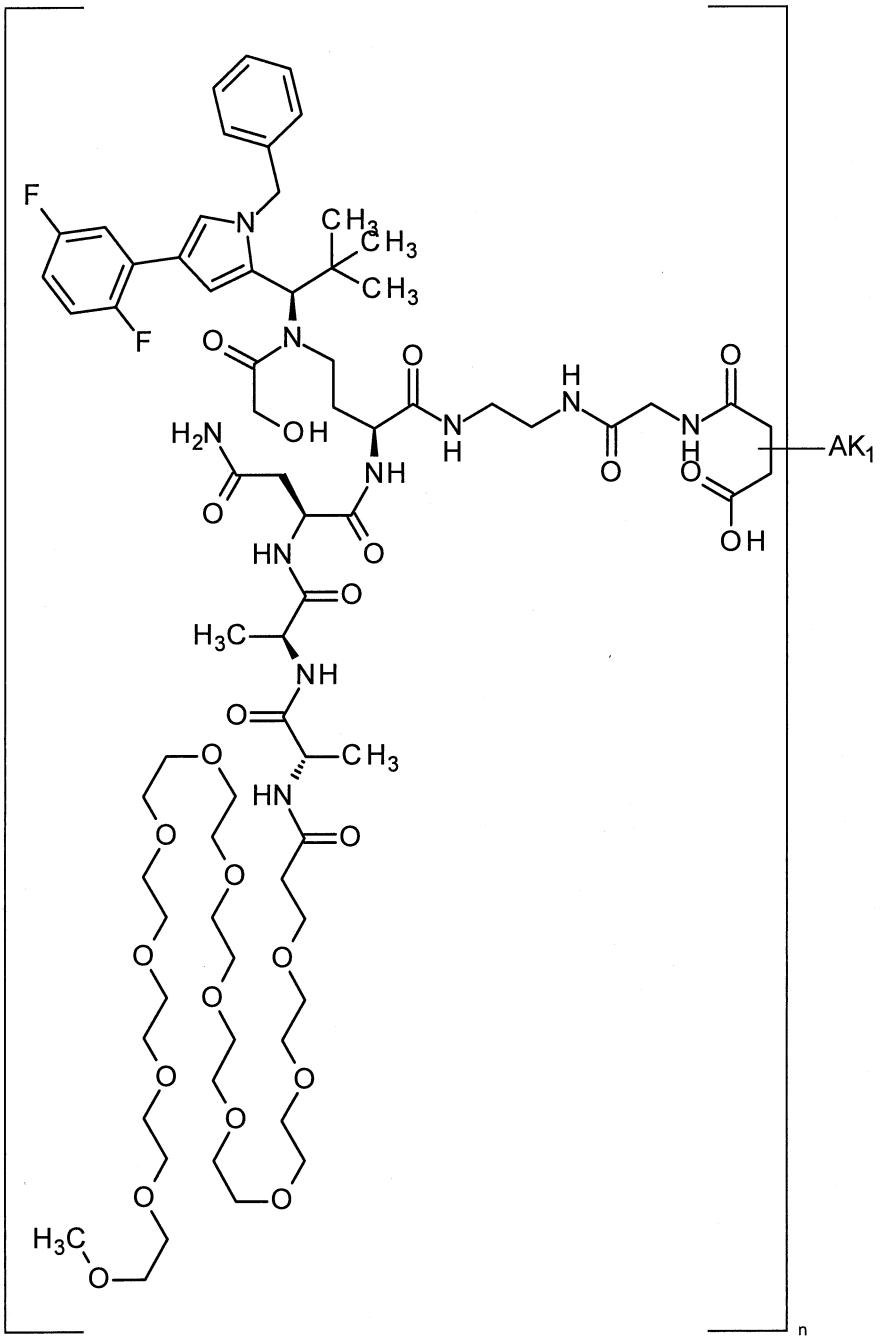


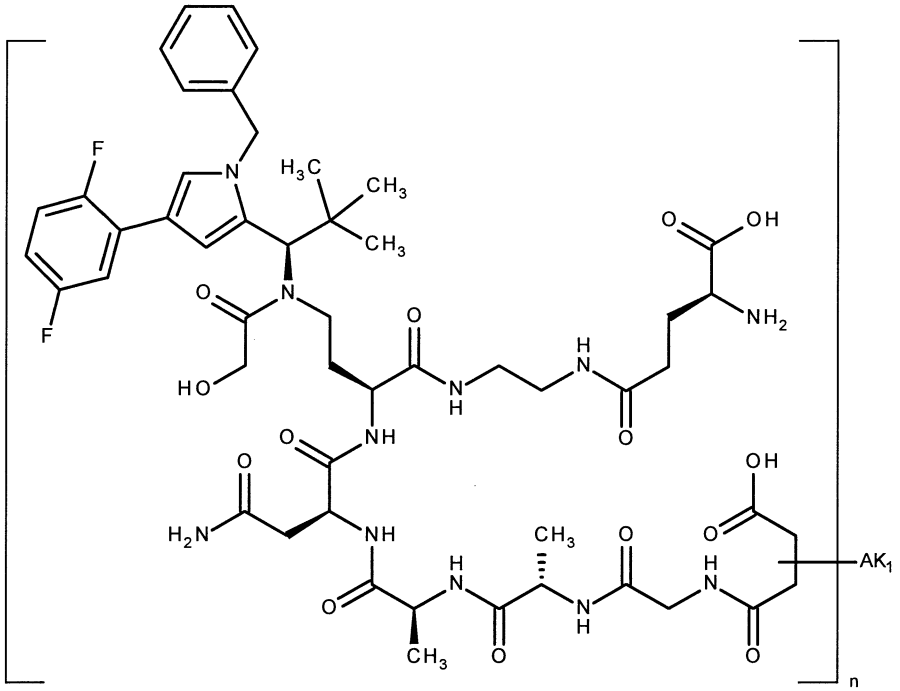


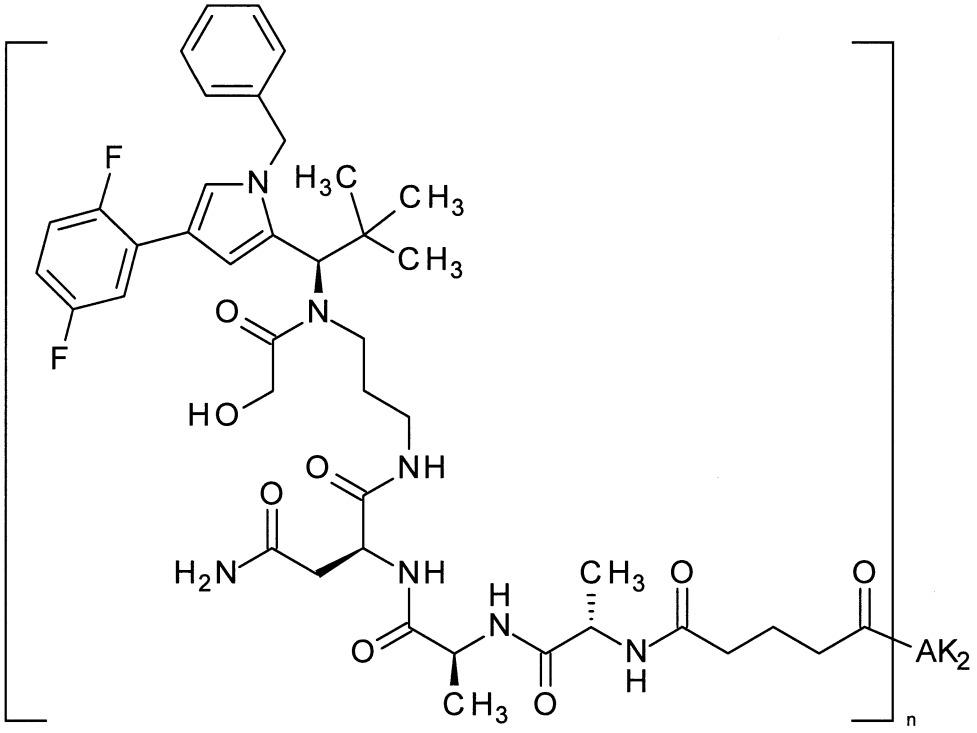


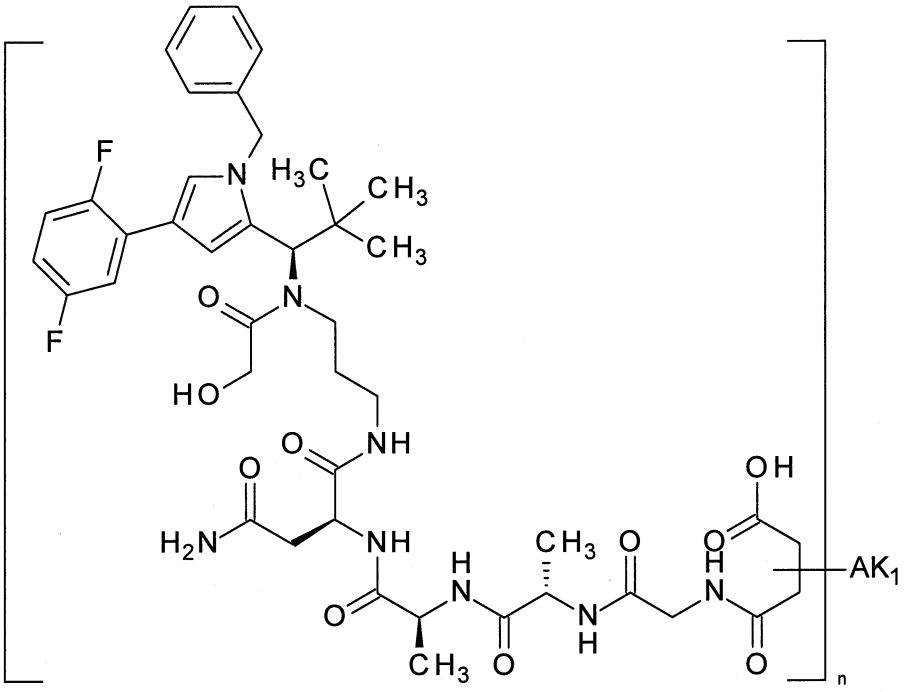


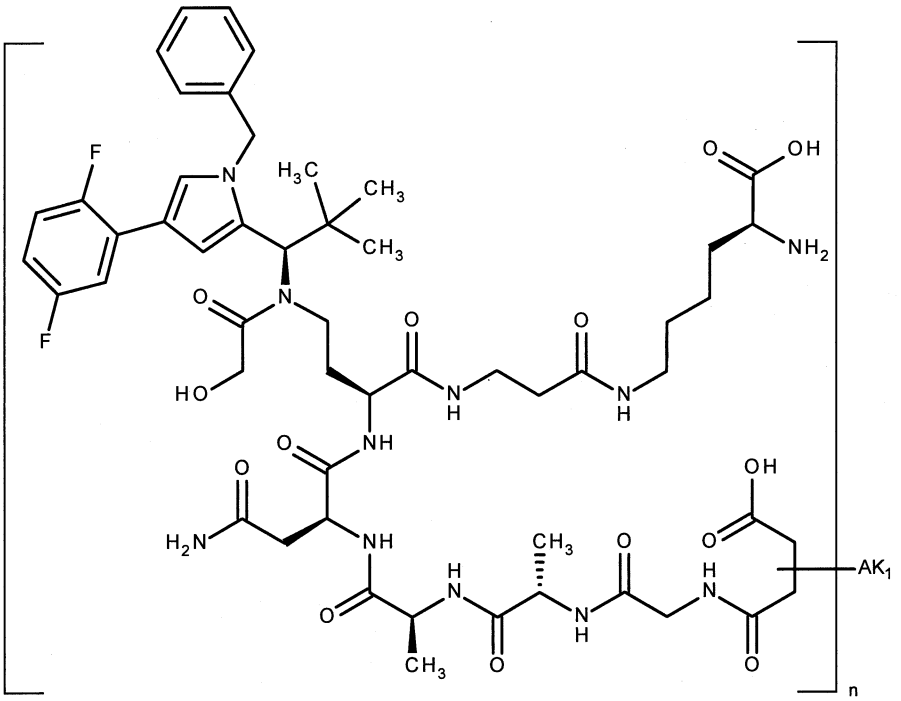


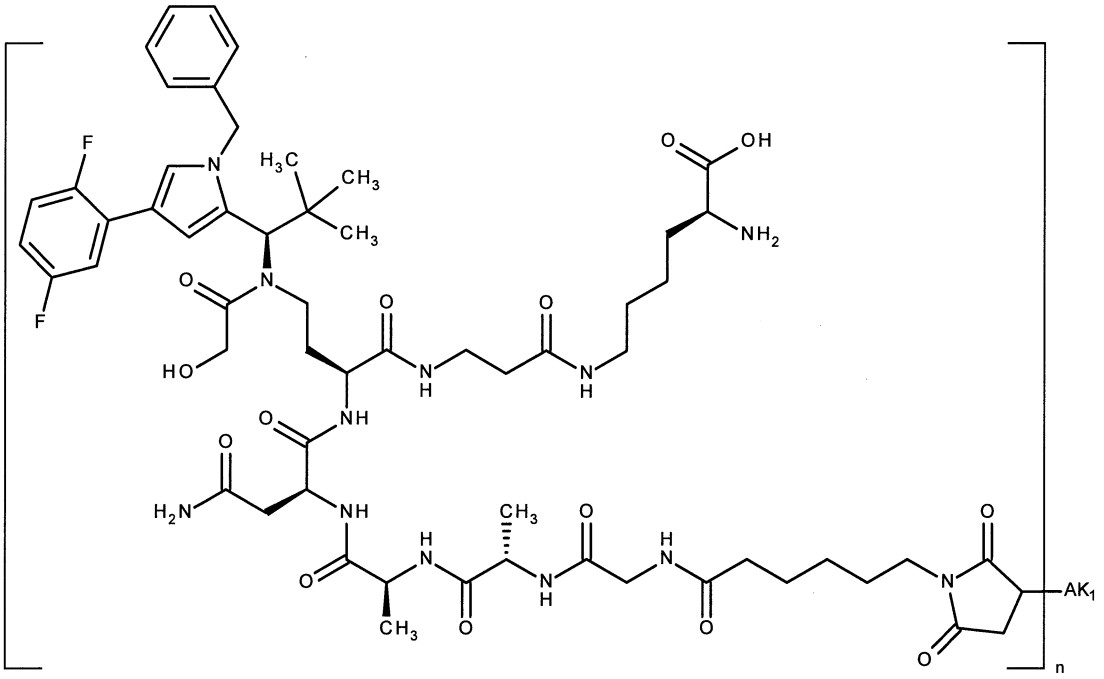


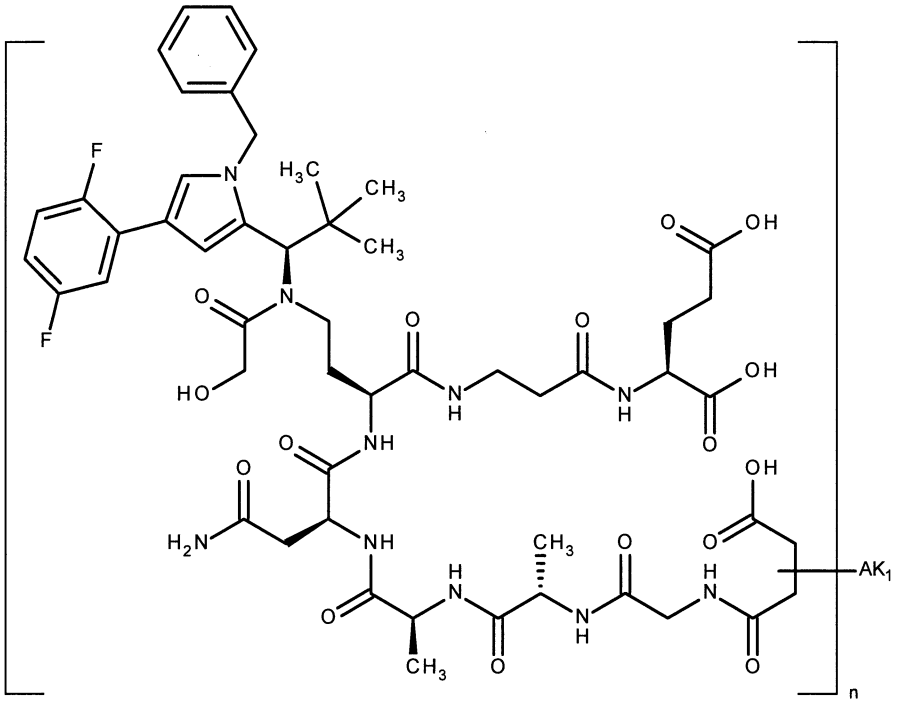

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F
N
H3C
CH3
CH3
O
N
HO
O
NH
O
H
N
O
OH
NH2
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H
N
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OH
AK1
n

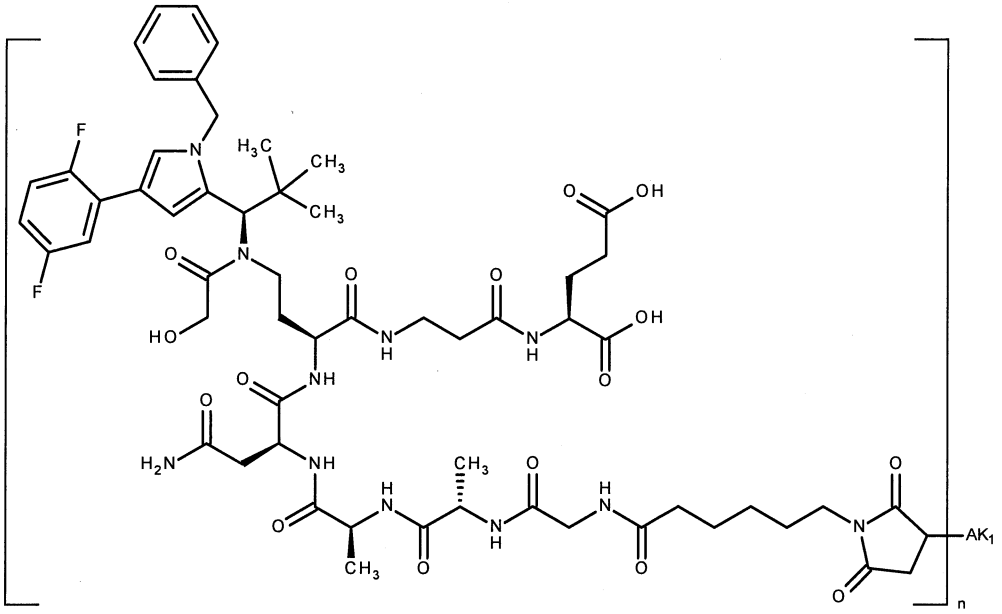

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AK2
n

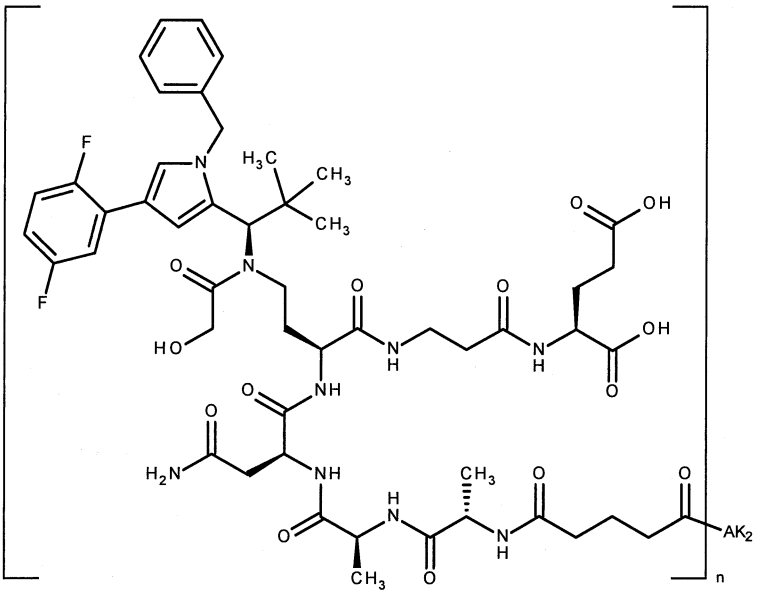


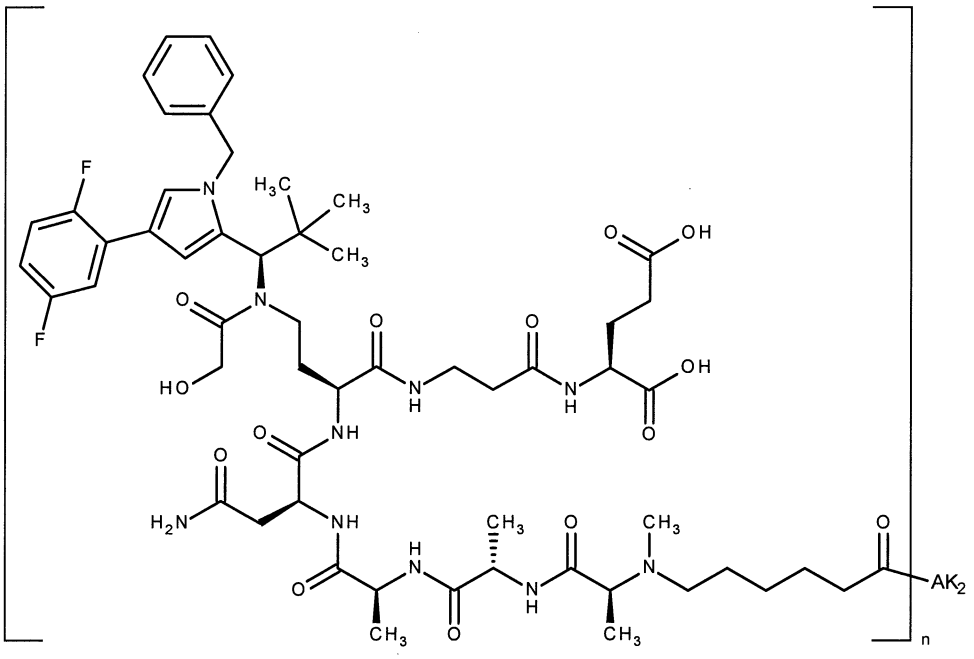


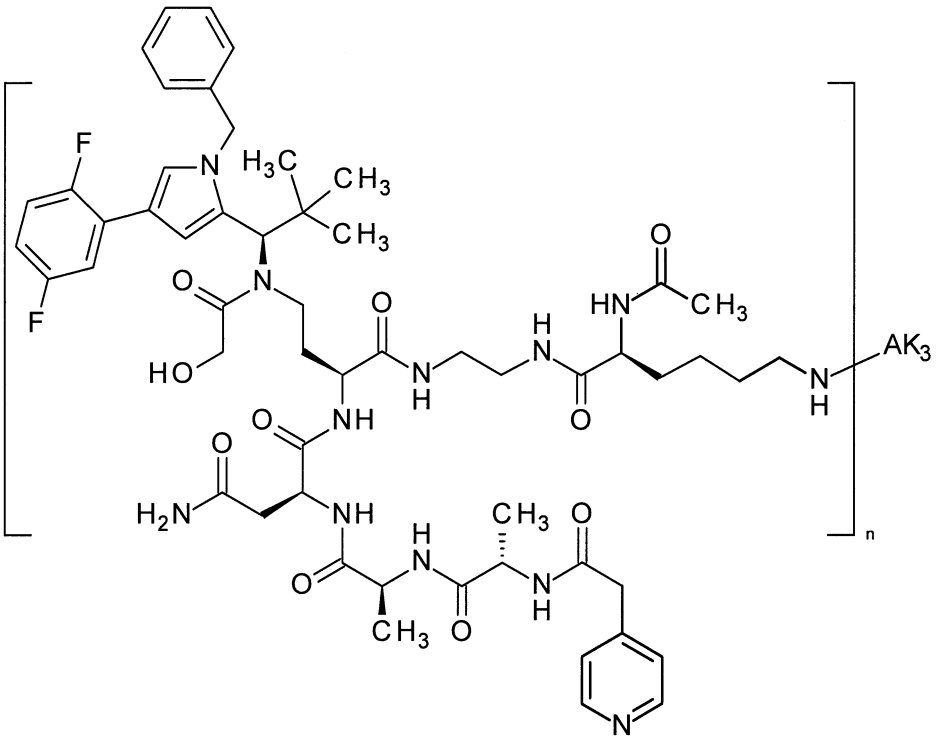


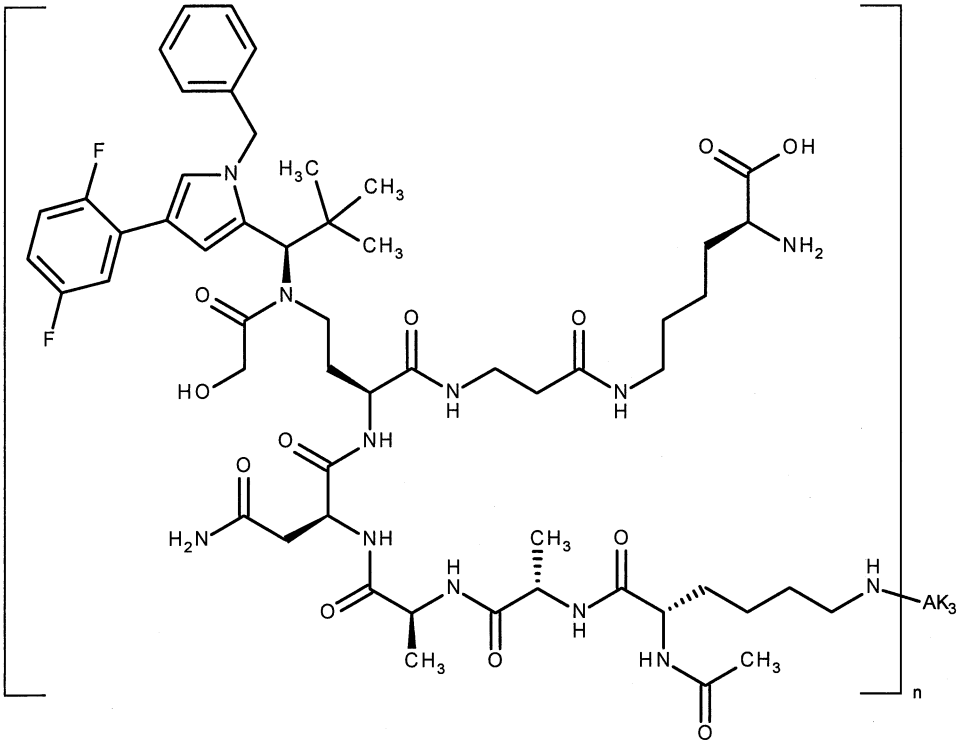


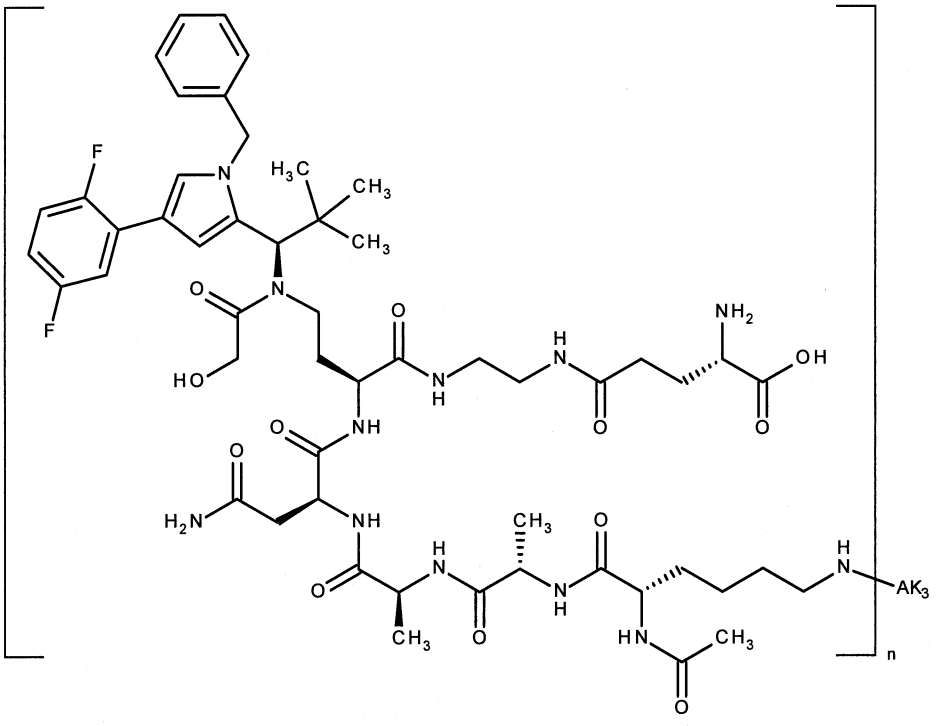


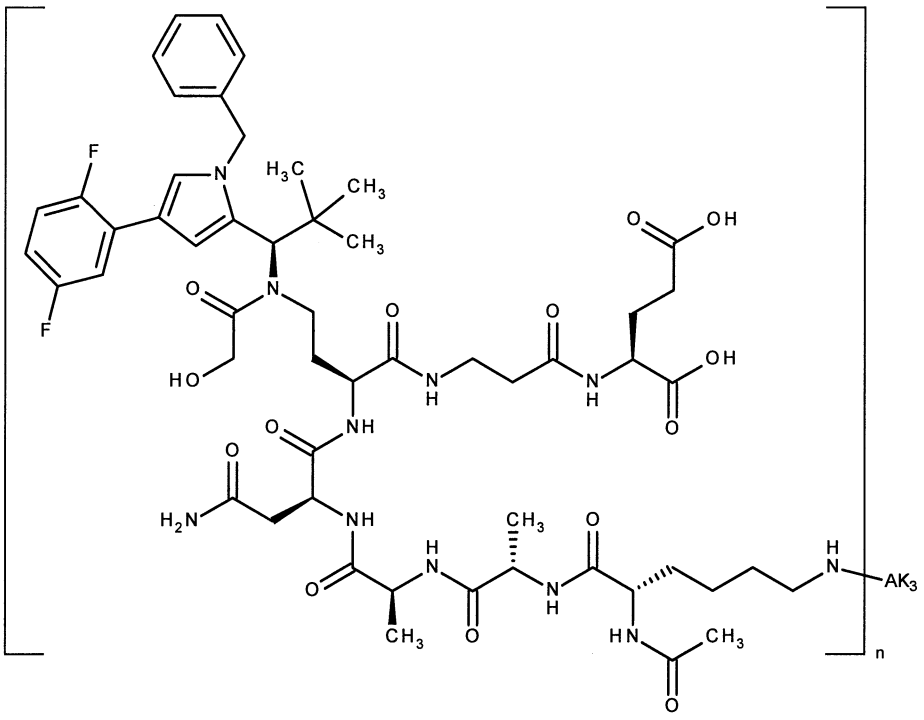


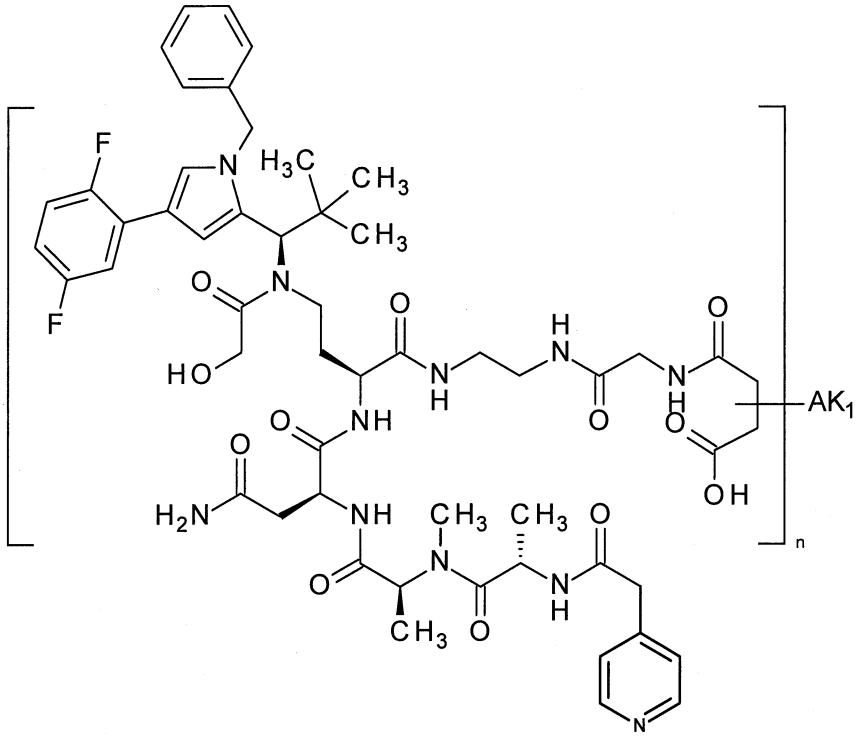


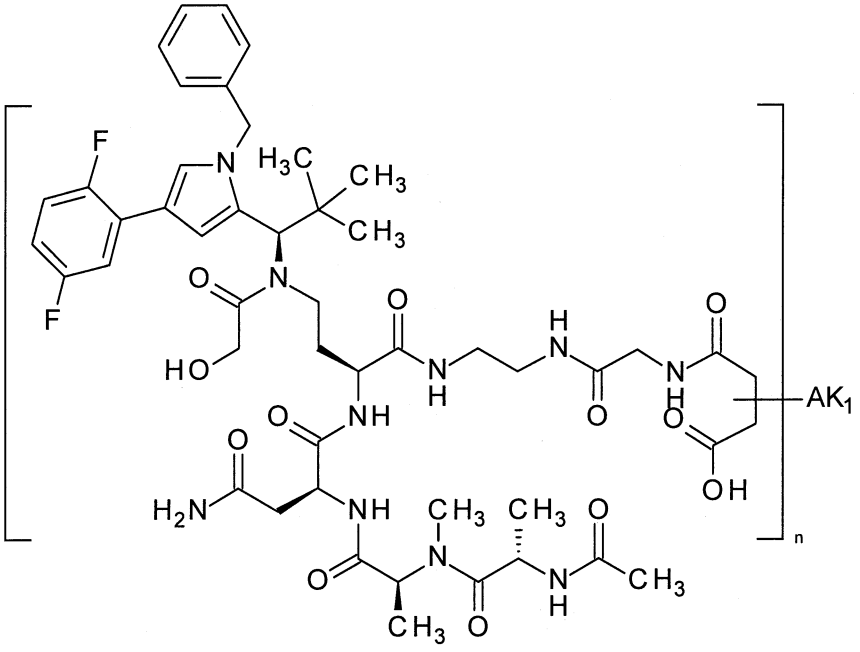


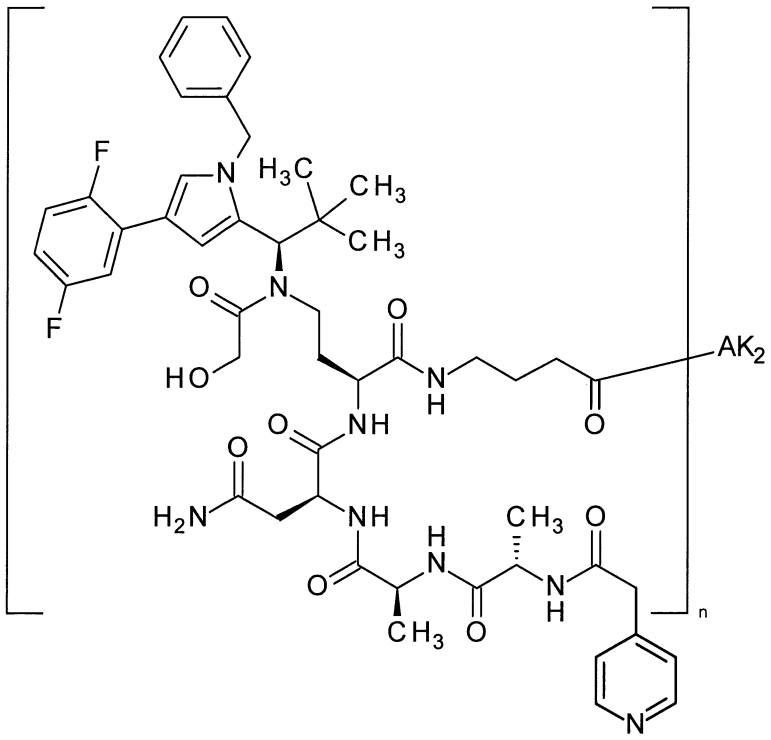


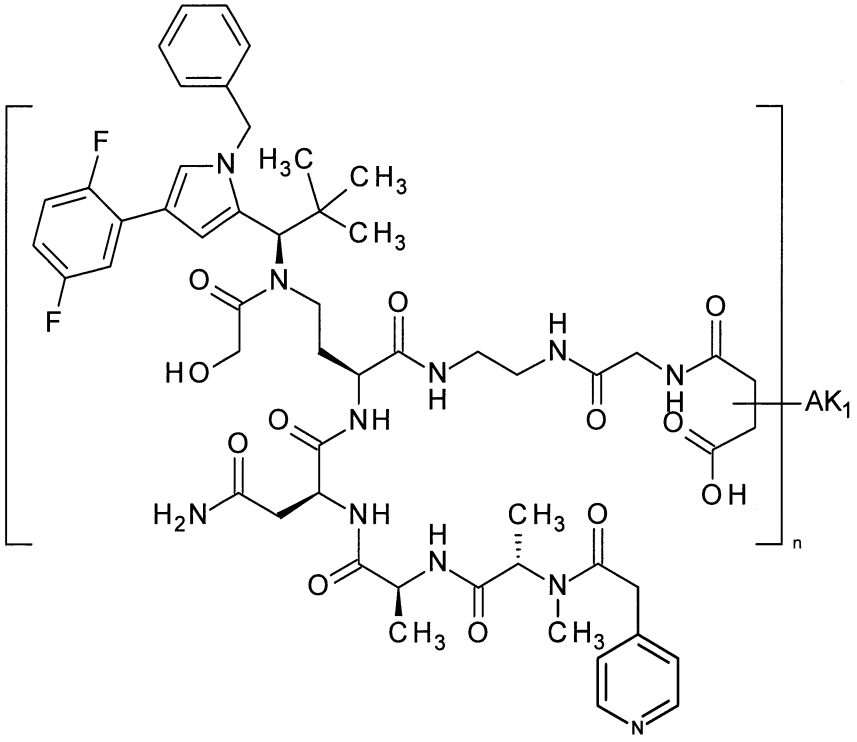


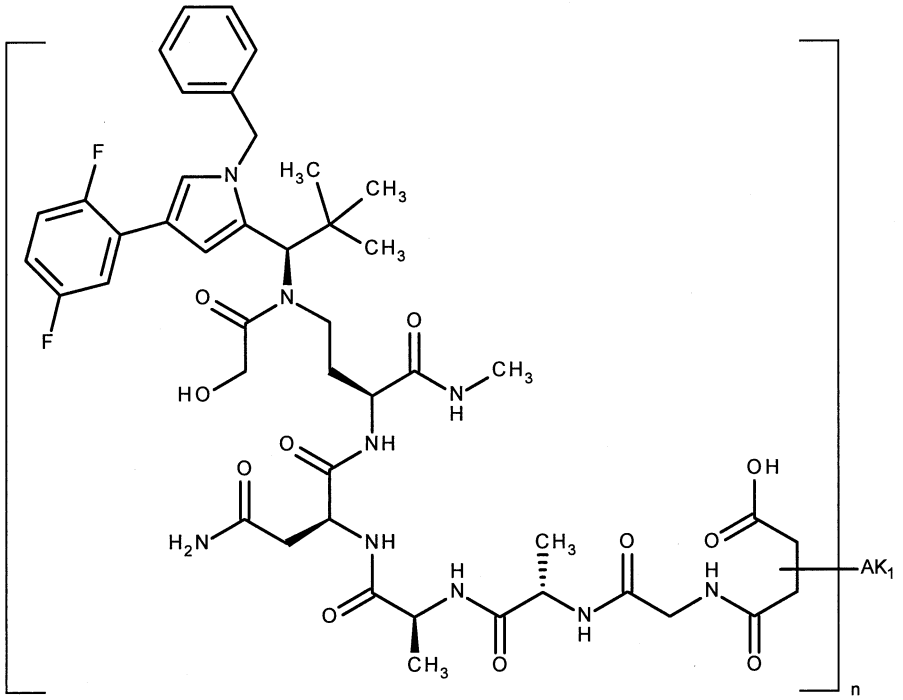


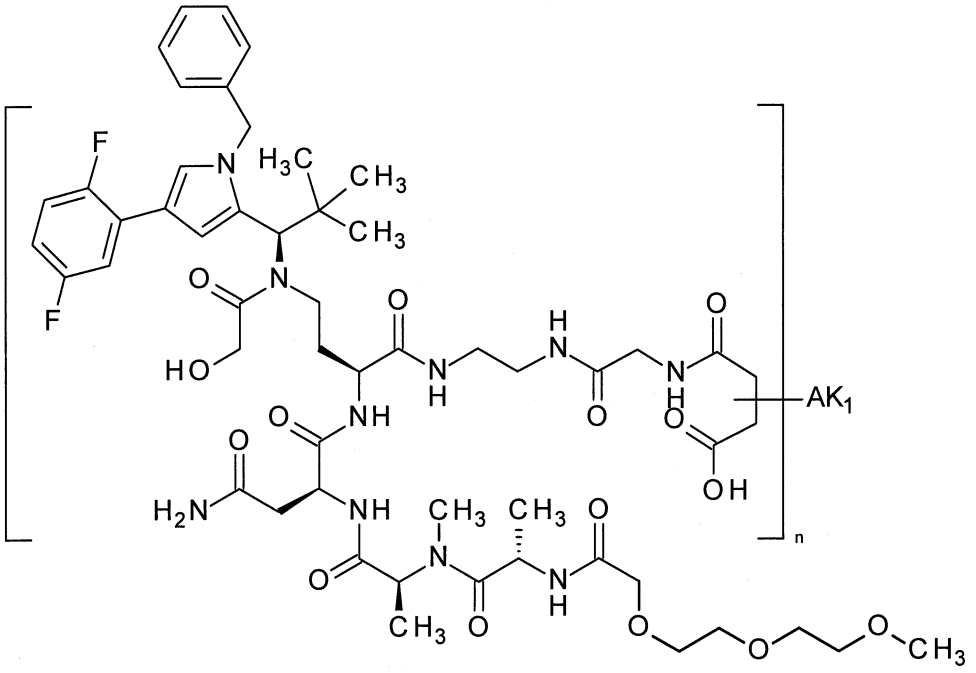


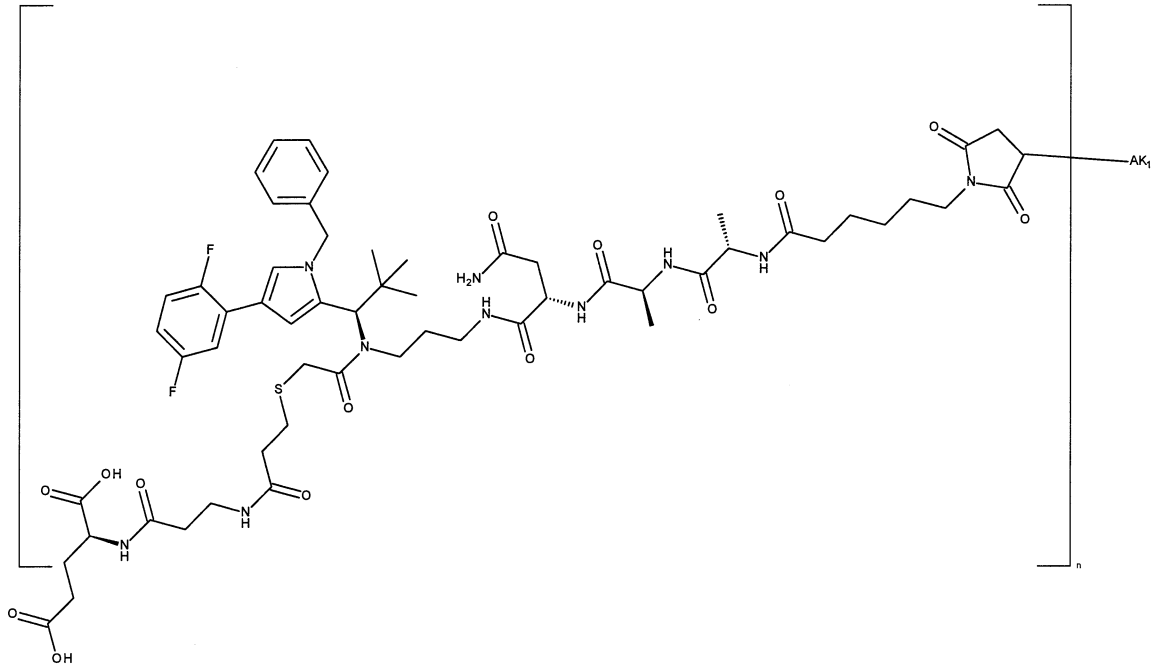


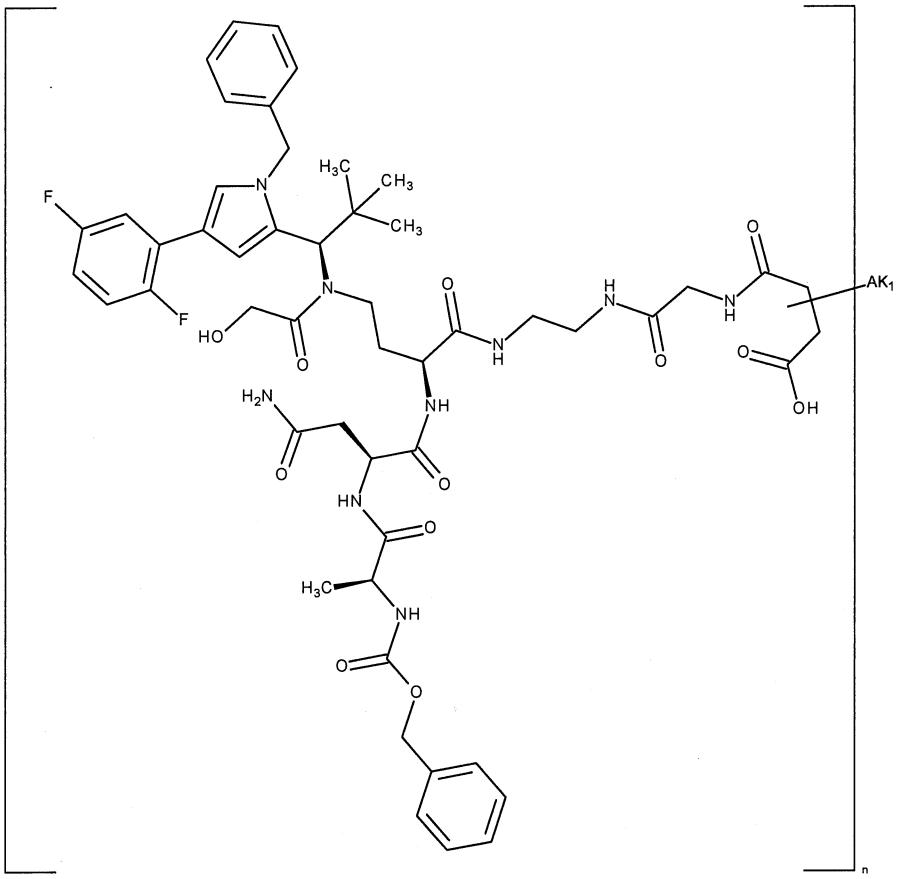


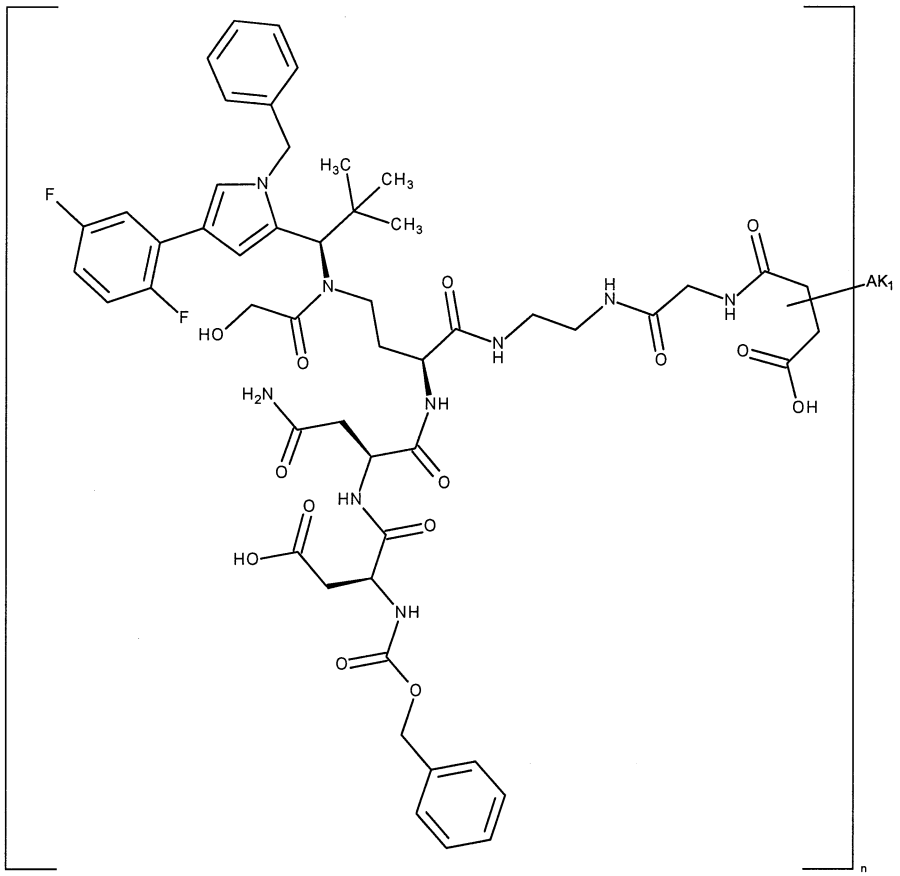


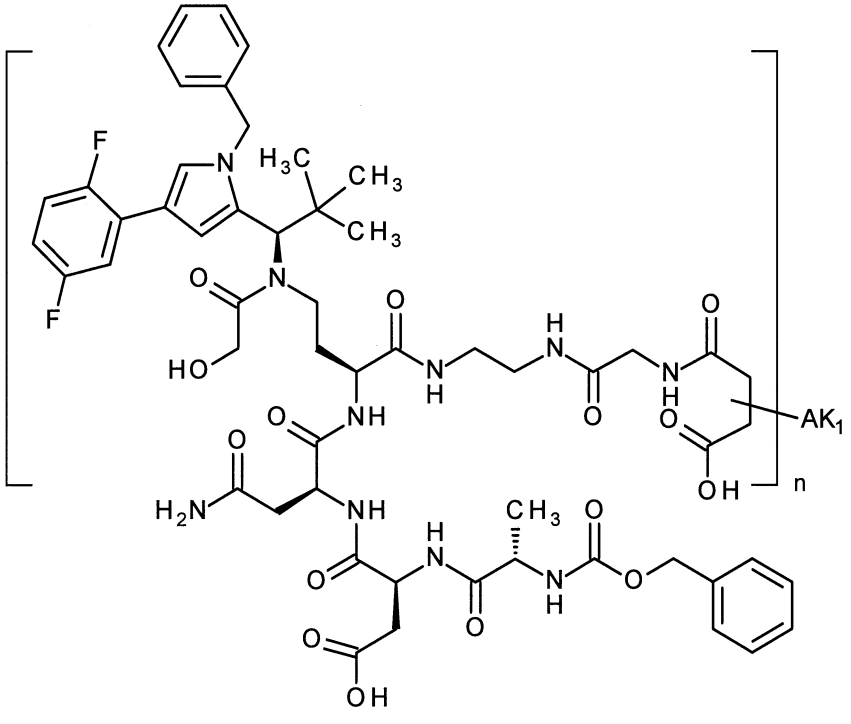










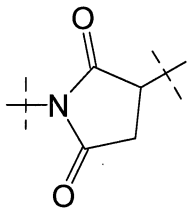


where

n	is a number from 1 to 20,
AK_1	is a cysteine-bonded antibody, and
AK_2	is a lysine-bonded antibody;
AK_3	is a glutamine-bonded antibody.

50. Antibody-prodrug conjugate according to one or more of Claims 1 to 49 where

n	is a number from 1 to 20,
AK1	represents a cysteine-bonded antibody, and
AK2	represents a lysine-bonded antibody,

where the antibody-prodrug conjugate contains a group 

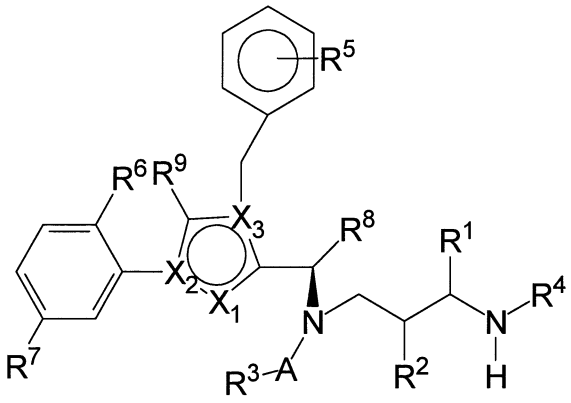
that is bonded to the antibody, or the hydrolysed open-chain succinamides of this group bonded to the antibody.

51. Conjugate according to one or more of the preceding claims for use in a method for the treatment and/or prophylaxis of diseases.

52. Use of a conjugate according to one or more of the preceding claims in the manufacture of a medicament in a method for the treatment of hyperproliferative and/or angiogenic disorders.

53. Pharmaceutical composition comprising a conjugate according to one or more of the preceding claims 1 to 51 in combination with an inert non-toxic pharmaceutically suitable auxiliary.

54. Kinesin spindle protein inhibitor prodrug of the following formula (III):



(III)

where

X_1 represents N, X_2 represents N and X_3 represents C; or

X_1 represents N, X_2 represents C and X_3 represents N; or

X_1 represents CH or CF, X_2 represents C and X_3 represents N; or

X_1 represents NH, X_2 represents C and X_3 represents C; or

X_1 represents CH, X_2 represents N and X_3 represents C;

(with X_1 representing CH, X_2 representing C and X_3 representing N being preferred);

R^1 represents -H, –MOD or $-(CH_2)_{0-3}Z$,

where Z represents -H, $-NHY^3$, $-OY^3$, $-SY^3$, halogen, $-C(=O)-NY^1Y^2$ or $-C(=O)-OY^3$,

where Y^1 and Y^2 independently of one another represent -H, $-NH_2$, $-(CH_2CH_2O)_{0-3}-(CH_2)_{0-3}Z'$ (e.g. $-(CH_2)_{0-3}Z'$) or $-CH(CH_2W)Z'$,

where Y^3 represents -H or $-(CH_2)_{0-3}Z'$,

where Z' represents -H, NH_2, SO_3H, -COOH, $-NH-C(=O)-CH_2-CH_2-CH(NH_2)COOH$ or $-(C(=O)-NH-CHY^4)_{1-3}COOH$,

where W represents -H or -OH,

where Y^4 represents straight-chain or branched C_{1-6}-alkyl which is optionally substituted by $–NH-C(=O)-NH_2$, or represents aryl or benzyl which are optionally substituted by $–NH_2$;

R^2 represents -H, -MOD, $-C(=O)-CHY^4-NHY^5$ or $-(CH_2)_{0-3}Z$,

where Z represents -H, halogen, $-OY^3$, $-SY^3$, $-NHY^3$, $-C(=O)-NY^1Y^2$ or $-C(=O)-OY^3$,

where Y^1 and Y^2 independently of one another represent -H, $-NH_2$ or $-(CH_2)_{0-3}Z'$,

where Y^3 represents -H or $-(CH_2)_{0-3}Z'$,

where Z' represents -H, $-SO_3H$, $-NH_2$ or -COOH;

where Y^4 represents straight-chain or branched C_{1-6}-alkyl which is optionally substituted by $-NH-C(=O)-NH_2$, or represents aryl or benzyl which are optionally substituted by $-NH_2$,

where Y^5 represents -H or $-C(=O)-CHY^6-NH_2$,

where Y^6 represents straight-chain or branched C_{1-6}-alkyl;

R^4 represents a group of the formula $R^{21}-(C=O)_{(0-1)}-(P3)_{(0-2)}-P2-NH-CH(CH_2C(=O)-NH_2)-C(=O)-$ or the cathepsin-cleavable group of the formula $R^{21}-(C=O)_{(0-1)}-(P3)_{(0-2)}-P2-$,

where R^{21} represents a C_{1-10}-alkyl, C_{5-10}-aryl or C_{6-10}-aralkyl, C_{5-10}-heteroalkyl, C_{1-10}-alkyl-O-C_{6-10}-aryl, C_{5-10}-heterocycloalkyl, heteroaryl, heteroarylalkyl, C_{1-10}-alkoxy, C_{6-10}-aryloxy or C_{6-10}-aralkoxy, C_{5-10}-heteroalkoxy, C_{1-10}-alkyl-O-C_{6-10}-aryloxy, C_{5-10}-heterocycloalkoxy group which may be mono- or polysubstituted by $-NH_2$, -NH-alkyl, $-N(alkyl)_2$, $-NH-C(=O)-alkyl$, $-N(alkyl)-C(=O)-alkyl$, $-SO_3H$, $-S(=O)_2-NH_2$, $-S(=O)_2-N(alkyl)_2$, -COOH, $-C(=O)-NH_2$, $-C(=O)-N(alkyl)_2$, or –OH, -H or an $-O_x-(CH_2CH_2O)_v-R^{22}$ group,

where x is 0 or 1,

where v represents a number from 1 to 20,

where R^{22} represents –H, –alkyl (preferably C1-12-alkyl), $-CH_2-COOH$, $-CH_2-CH_2-COOH$, or $-CH_2-CH_2-NH_2$);

P2 is an amino acid selected from Gly, Pro, Ala, Val, Nva, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg, citrulline and His;

P3 is an amino acid selected from Gly, Pro, Ala, Val, Nva, Leu, Ile, Met, Phe, Tyr, Trp, Ser, Thr, Cys, Asn, Gln, Asp, Glu, Lys, Arg, citrulline and His or one of the respective N-alkyl amino acids, preferably N-methyl amino acids;

A represents -C(=O)-, -S(=O)-, -$S(=O)_2$-, -$S(=O)_2$-NH- or -C(=N-NH_2)-;

R^3 represents -MOD or an optionally substituted alkyl, cycloalkyl, aryl, heteroaryl, heteroalkyl, heterocycloalkyl group, a C_{1-10}-alkyl, C_{6-10}-aryl or C_{6-10}-aralkyl, C_{5-10}-heteroalkyl, C_{1-10}-alkyl-O-C_{6-10}-aryl or C_{5-10}-heterocycloalkyl group which may be substituted by 1-3 –OH groups, 1-3 halogen atoms, 1-3 halogenated alkyl groups (each having 1-3 halogen atoms), 1-3 -O-alkyl groups, 1-3 –SH groups, 1-3 -S-alkyl groups, 1-3 -O-CO-alkyl groups, 1-3 -O-C(=O)-NH-alkyl groups, 1-3 -NH-C(=O)-alkyl groups, 1-3 -NH-C(=O)-NH-alkyl groups, 1-3 -$S(=O)_n$-alkyl groups, 1-3 -$S(=O)_2$-NH-alkyl groups, 1-3 -NH-alkyl groups, 1-3 -N(alkyl)$_2$ groups, 1-3 -NH_2 groups or 1-3 -$(CH_2)_{0-3}$Z groups, (where "alkyl" preferably represents C_{1-10}-alkyl),

where Z represents -H, halogen, -OY^3, -SY^3, -NHY^3, -C(=O)-NY^1Y^2 or -C(=O)-OY^3,

where n represents 0, 1 or 2,

where Y^1 and Y^2 independently of one another represent -H, -NH_2 or -$(CH_2)_{0-3}$Z‘,

where Y^3 represents -H, -$(CH_2)_{0-3}$-CH(NH-C(=O)-CH_3)Z‘, -$(CH_2)_{0-3}$-CH(NH_2)Z‘, or -$(CH_2)_{0-3}$Z‘,

where Z‘ represents -H, -SO_3H, -NH_2 or –COOH,

R^5 represents -H, -NH_2, -NO_2, halogen (in particular -F, -Cl, -Br), -CN, -CF_3, -OCF_3, -CH_2F, -CH_2F, -SH or -$(CH_2)_{0-3}$Z,

where Z represents -H, -OY^3, -SY^3, halogen, -NHY^3, -C(=O)-NY^1Y^2 or -C(=O)-OY^3,

where Y^1 and Y^2 independently of one another represent -H, -NH_2 or -$(CH_2)_{0-3}$Z‘,

where Y^3 represents -H or -$(CH_2)_{0-3}$Z‘,

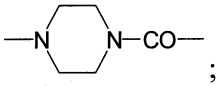
where Z‘ represents -H, -SO_3H, -NH_2 or -COOH;

R^6 and R^7 independently of one another represent -H, cyano, C_{1-10}-alkyl, fluoro-C_{1-10}-alkyl, C_{2-10}-alkenyl, fluoro-C_{2-10}-alkenyl, C_{2-10}-alkynyl, fluoro-C_{2-10}-alkynyl, hydroxy, -NO_2, NH_2, -COOH or halogen (in particular -F, -Cl, -Br),

R^8 represents C_{1-10}-alkyl, fluoro-C_{1-10}-alkyl, C_{2-10}-alkenyl, fluoro-C_{2-10}-alkenyl, C_{2-10}-alkynyl, fluoro-C_{2-10}-alkynyl, C_{4-10}-cycloalkyl, fluoro-C_{4-10}-cycloalkyl, or $-(CH_2)_{0-2}-(HZ^2)$,
where HZ^2 represents a 4- to 7-membered heterocycle having up to two heteroatoms selected from the group consisting of N, O and S, where each of these groups may be substituted by –OH, -COOH or -NH_2;

R^9 represents -H, -F, -CH_3, -CF_3, -CH_2F or -CHF_2;

–MOD represents $-(NR^{10})_n-(G1)_o-G2-H$,
where
R^{10} represents -H or C_1-C_3-alkyl;

G1 represents –NH-C(=O)- , -C(=O)NH- or 

;

n is 0 or 1;

o is 0 or 1; and

G2 represents a straight-chain and/or branched hydrocarbon group which has 1 to 10 carbon atoms and which may be interupted once or more than once identically or differently by the groups -O-, -S-, -S(=O)-, -$S(=O)_2$, -NR^y-, -$NR^yC(=O)$-, -$C(=O)NR^y$-, -NR^yNR^y-, -$S(=O)_2$-NR^yNR^y-, -$C(=O)$-NR^yNR^y-$C(=O)$-, -CR^x=N-O-,
where R_x represents –H, C_1-C_3-alkyl or phenyl,
where R^y represents -H, phenyl, C_1-C_{10}-alkyl, C_2-C_{10}-alkenyl or C_2-C_{10}-alkynyl, each of

which may be substituted by –NH-C(=O)-NH_2, -COOH, -OH, -NH_2, NH-CN-NH_2, sulphonamide, sulphone, sulphoxide or sulphonic acid), where the hydrocarbon chain including any side chains may be substituted by -NH-C(=O)-NH_2, -COOH, -OH, -NH_2, NH-CN-NH_2, sulphonamide, sulphone, sulphoxide or sulphonic acid, where the group –MOD preferably has at least one group -COOH;

and the salts, solvates, salts of the solvates and epimers thereof.