[0045] FIG. 36 depicts a synthetic sequence for preparing maytansin-N-methyl-L-alanine-N-(3-hydroxy-4-amino)benzamide.

[0046] FIG. 37 depicts a synthetic sequence for preparing maytansin-N-methyl-L-alanine-N-(2-amino)benzamide.

[0047] FIG. 38 depicts a synthetic sequence for preparing maytansin-N-methyl-L-alanine-N-(4-methoxy-2-amino)benzamide.

[0048] FIG. 39 depicts a synthetic sequence for preparing maytansin-N-methyl-L-alanine-N-(3-morpholino-4-amino)benzamide.

[0049] FIG. 40 depicts a synthetic sequence for preparing maytansin-N-methyl-L-alanine-N-(3-acetamido-4-amino)benzamide.

[0050] FIG. 41 depicts a synthetic sequence for preparing maytansin-N-methyl-L-alanine-N-4-aminobenzamide-Cit-Val-cap-diBromomethylacrylamide.

[0051] FIG. 42 depicts the deconvoluted mass spectroscopy (MS) spectrum of the antibody drug conjugate, PRLR-Q-**63** conjugate from EXAMPLE 43.

[0052] FIG. 43 depicts the deconvoluted MS spectrum of the Isotype Control-Q-**63** conjugate from EXAMPLE 43.

[0053] FIG. 44 depicts the plot of % Cell Viability vs. Log_{10} [M] of certain compounds tested in EXAMPLE 45.

[0054] FIG. 45 depicts the plot of % Cell Viability vs. Log_{10} [M] of certain compounds tested in EXAMPLE 45.

[0055] FIG. 46 depicts the plot of % Cell Viability vs. Log10 [M] of certain compounds tested in EXAMPLE 45.

[0056] FIG. 47 depicts the plot of % Cell Viability vs. Log10 [M] of certain compounds tested in EXAMPLE 45.

DETAILED DESCRIPTION

A. DEFINITIONS

[0057] As used herein, "alkyl" refers to a monovalent and saturated hydrocarbon radical moiety. Alkyl is optionally substituted and can be linear, branched, or cyclic, *i.e.*, cycloalkyl. Alkyl includes, but is not limited to, those having 1-20 carbon atoms, *i.e.*, C_{1-20} alkyl; 1-12 carbon atoms, *i.e.*, C_{1-12} alkyl; 1-8 carbon atoms, *i.e.*, C_{1-8} alkyl; 1-6 carbon atoms,

and can be monocyclic or polycyclic, *e.g.*, bicyclic or tricyclic. Examples of aryl moieties include, but are not limited to those having 6 to 20 ring carbon atoms, *i.e.*, C_{6-20} aryl; 6 to 15 ring carbon atoms, *i.e.*, C_{6-15} aryl, and 6 to 10 ring carbon atoms, *i.e.*, C_{6-10} aryl. Examples of aryl moieties include, but are limited to phenyl, naphthyl, fluorenyl, azulenyl, anthryl, phenanthryl, and pyrenyl.

[0065] As used herein, "arylene" refers to a divalent moiety of an aromatic compound wherein the ring atoms are only carbon atoms. Arylene is optionally substituted and can be monocyclic or polycyclic, *e.g.*, bicyclic or tricyclic. Examples of arylene moieties include, but are not limited to those having 6 to 20 ring carbon atoms, *i.e.*, C_{6-20} arylene; 6 to 15 ring carbon atoms, *i.e.*, C_{6-15} arylene, and 6 to 10 ring carbon atoms, *i.e.*, C_{6-10} arylene.

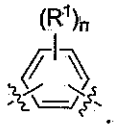
[0066] As used herein, "alkaryl" refers to an aryl that is substituted with at least one alkyl. Alkaryl is optionally substituted.

[0067] As used herein, "heteroalkyl" refers to an alkyl in which one or more carbon atoms are replaced by heteroatoms. As used herein, "heteroalkenyl" refers to an alkenyl in which one or more carbon atoms are replaced by heteroatoms. As used herein, "heteroalkynyl" refers to an alkynyl in which one or more carbon atoms are replaced by heteroatoms. Suitable heteroatoms include, but are not limited to, nitrogen, oxygen, and sulfur atoms. Heteroalkyl is optionally substituted. Examples of heteroalkyl moieties include, but are not limited to, aminoalkyl, sulfonylalkyl, sulfinylalkyl. Examples of heteroalkyl moieties also include, but are not limited to, methylamino, methylsulfonyl, and methylsulfinyl.

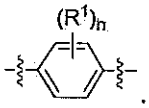
[0068] As used herein, "heteroaryl" refers to a monovalent moiety that is a radical of an aromatic compound wherein the ring atoms contain carbon atoms and at least one oxygen, sulfur, nitrogen, or phosphorus atom. Examples of heteroaryl moieties include, but are not limited to those having 5 to 20 ring atoms; 5 to 15 ring atoms; and 5 to 10 ring atoms. Heteroaryl is optionally substituted.

[0069] As used herein, "heteroarylene" refers to an arylene in which one or more ring atoms of the aromatic ring are replaced with an oxygen, sulfur, nitrogen, or phosphorus atom. Heteroarylene is optionally substituted.

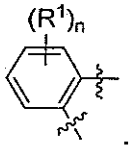
[0070] As used herein, "heterocycloalkyl" refers to a cycloalkyl in which one or more carbon atoms are replaced by heteroatoms. Suitable heteroatoms include, but are not limited to, nitrogen, oxygen, and sulfur atoms. Heterocycloalkyl is optionally substituted. Examples of heterocycloalkyl moieties include, but are not limited to, morpholinyl, piperidinyl,



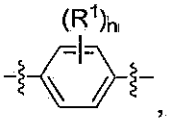
[0089] In some embodiments, A is:



[0090] In some embodiments, A is:

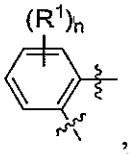


[0091] In some embodiments, A is:



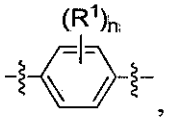
wherein n is 0, 1 or 2.

[0092] In some embodiments, A is:



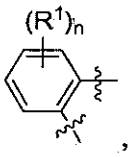
wherein n is 0, 1 or 2.

[0093] In some embodiments, A is:



wherein n is 0 or 1; and R^1 is alkoxy, halo, or haloalkyl.

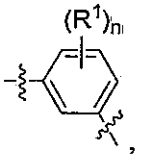
[0094] In some embodiments, A is:



wherein n is 0 or 1; and R^1 is alkoxy, halo, or haloalkyl. In some examples, R^1 is alkoxy.

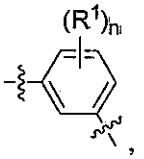
[0095] In some embodiments, A is:

[0141] In some embodiments, A is:



wherein n is 0, 1, 2, or 3.

[0142] In some embodiments, A is:

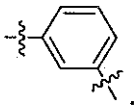


wherein:

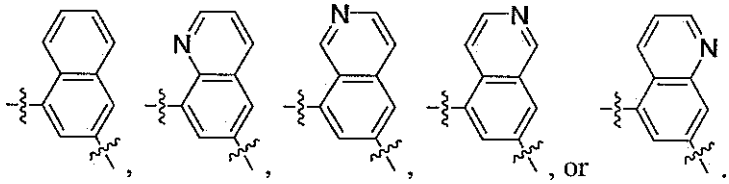
R^1 is C_{1-6} alkyl, C_{1-6} alkoxy, halo, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} heteroalkyl; and

n is 0, 1, 2, 3 or 4.

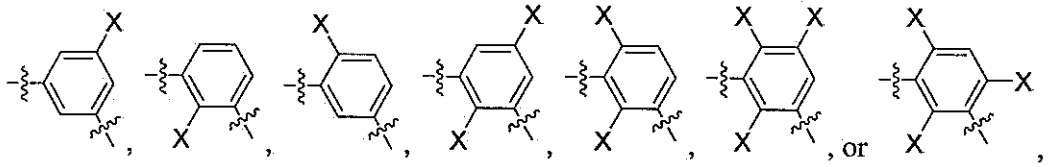
[0143] In some embodiments, A is:



[0144] In some embodiments, A is:



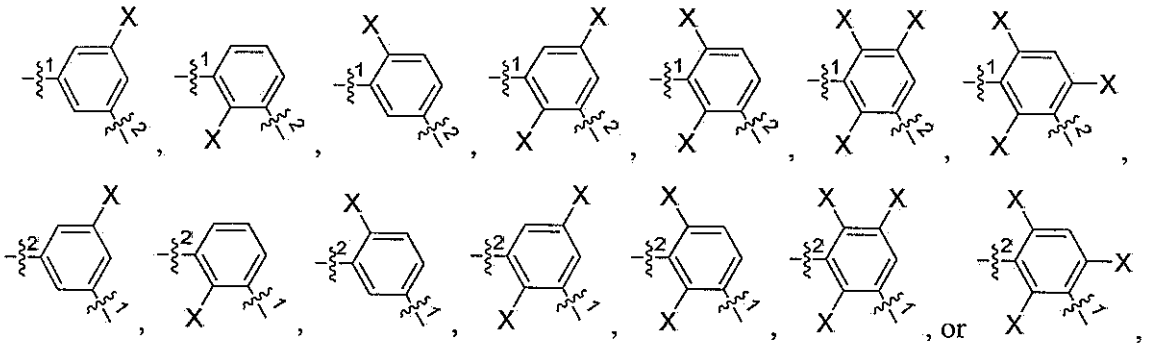
[0145] In some embodiments, A is:



wherein:

X is, independently at each occurrence, a hydrogen atom, alkyl, alkoxy, halo, haloalkoxy, haloalkyl, heteroalkyl. In some embodiments, X is fluoro, chloro, bromo, iodo, dimethylamino, methylamino, methoxy, ethoxy, or trifluoromethyl.

[0146] In some embodiments, A is:



wherein:

X is, independently at each occurrence, a hydrogen atom, alkyl, alkoxy, halo, haloalkoxy, haloalkyl, heteroalkyl. In some embodiments, X is fluoro, chloro, bromo, iodo, dimethylamino, methylamino, ethoxy, trifluoromethyl or methoxy;

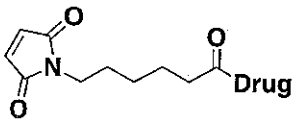
 is the bond to the nitrogen atom; and

 is the bond to the carbonyl.

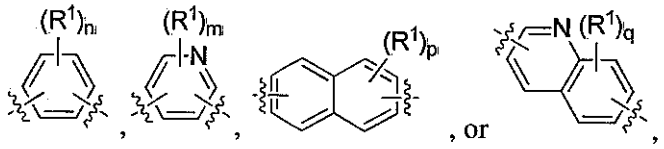
2. Linkers

[0147] The linker portion of the conjugates described herein is a divalent moiety that covalently links the binding agent to the maytansinoid derivatives described herein. Suitable linkers include those that release the maytansinoid portion in the presence of an enzyme or at a particular pH range or value.

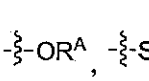
[0148] In some embodiments, the linker comprises an enzyme-cleavable moiety. Illustrative enzyme-cleavable moieties include, but are not limited to, peptide bonds, ester linkages, hydrazones, and disulfide linkages. In some embodiments, the linker comprises a cathepsin-cleavable linker.

[0149] In some embodiments, the linker comprises a non-cleavable moiety. In some embodiments, the non-cleavable linker is  or a residue thereof. In

[0208] In some embodiments, A is:



wherein:

R^1, independently at each occurrence, is alkyl, alkenyl, alkynyl, alkoxy, aryl, alkaryl, aralkyl, halo, haloalkoxy, haloalkyl, heteroaryl, heteroalkyl, heterocycloalkyl, hydroxyl, cyano, nitro, , or azido,

wherein R^A is alkyl or heteroalkyl;

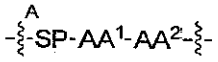
n is an integer from 0 to 4;

m is an integer from 0 to 3;

p is an integer from 0 to 6; and

q is an integer from 0 to 5; and

L is:



wherein:

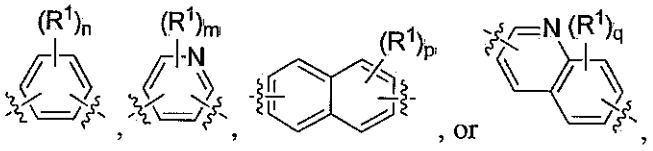
SP is a spacer;

 is one or more bonds to the binding agent;

AA^1 is an amino acid; and AA^2 is an amino acid.

[0209] In some embodiments,

A is:



wherein:

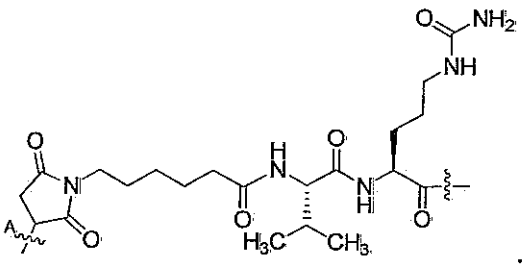
R^1, independently at each occurrence, is $C_{1\text{-}6}$ alkyl, $C_{1\text{-}6}$ haloalkyl, or halo;

n is an integer from 0 to 4;

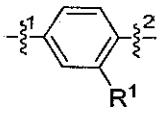
m is an integer from 0 to 3;

p is an integer from 0 to 6; and

q is an integer from 0 to 5; and



[0226] In some embodiments, A is:



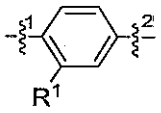
wherein:

R^1 is, independently at each occurrence, a hydrogen atom, alkyl, alkoxy, aryl, heteroalkyl, halo, haloalkyl, or haloalkoxy;

$-\overset{1}{\sim}-$ is the bond to the nitrogen atom; and

$-\overset{2}{\sim}-$ is the bond to the carbonyl. In some embodiments, R^1 is 1-methylethyl-thiol, phenyl, 2-fluorophenyl, pyridinyl, 4-pyridinyl, pyrrolidinyl, or 1-pyrrolidinyl. In some embodiments, R^1 is trifluoromethyl. In some embodiments, R^1 is methoxy. In some embodiments, R^1 is fluoro. In some embodiments, R^1 is hydrogen.

[0227] In some embodiments, A is:



wherein:

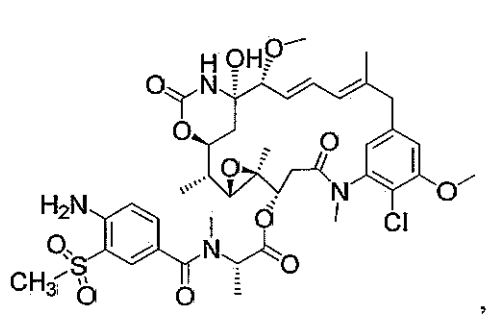
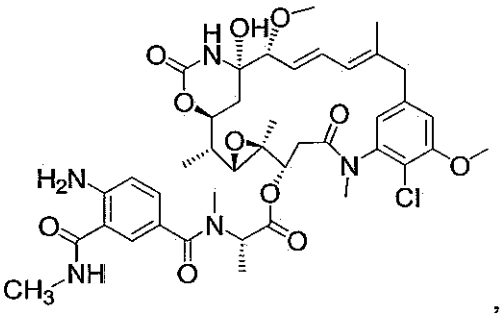
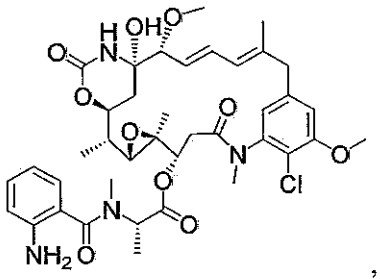
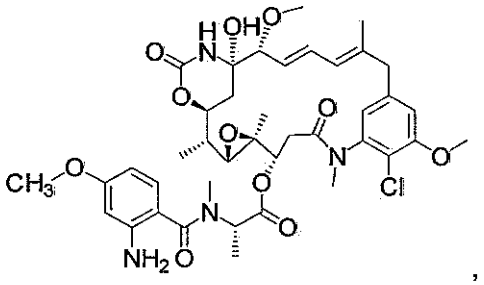
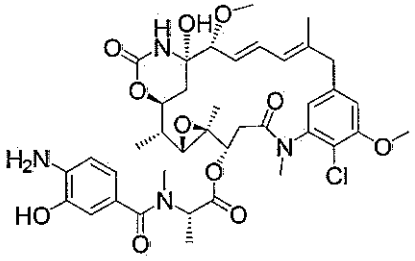
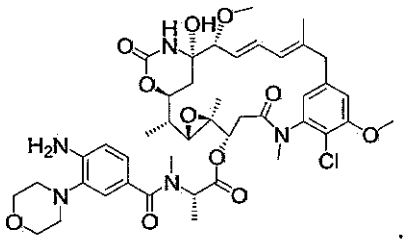
R^1 is, independently at each occurrence, a hydrogen atom, alkyl, alkoxy, aryl, heteroalkyl, halo, haloalkyl, haloalkoxy;

$-\overset{1}{\sim}-$ is the bond to the nitrogen atom; and

$-\overset{2}{\sim}-$ is the bond to the carbonyl. In some embodiments, R^1 is 1-methylethyl-thiol, phenyl, 2-fluorophenyl, pyridinyl, 4-pyridinyl, pyrrolidinyl, or 1-pyrrolidinyl. In some embodiments, R^1 is trifluoromethyl. In some embodiments, R^1 is methoxy. In some embodiments, R^1 is fluoro. In some embodiments, R^1 is hydrogen.

[0228] In some embodiments,

A is:

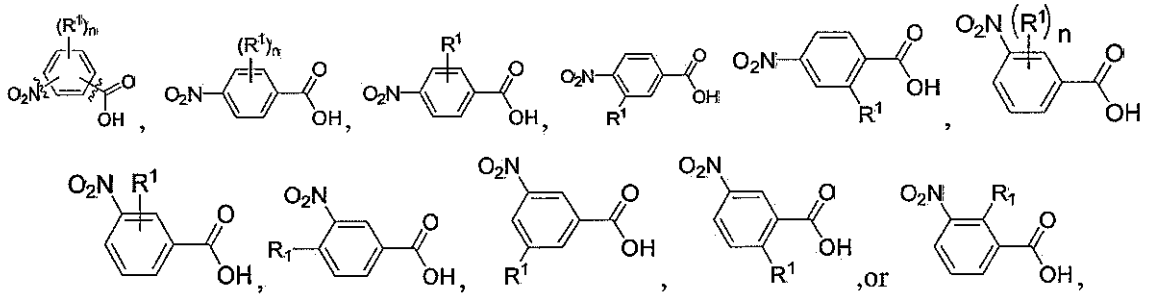
[0298] In some embodiments, the compound of Formula (II) is a compound selected from , , , , ,or .

D. PREPARATION OF COMPOUNDS

[0299] Compounds of Formula I can be synthesized by coupling compounds of Formula P1 with a binding agent, *e.g.*, antibody under standard conjugation conditions (*see*, *e.g*, Doronina *et al., Nature Biotechnology* 2003, 21, 7, 778, which is incorporated herein by reference). When the binding agent is an antibody, the antibody can be coupled to a compound of Formula P1 via one or more cysteine or lysine residues of the antibody. Compounds of Formula P1 can be coupled to cysteine residues, for example, by subjecting the antibody to a reducing agent, *e.g.*, dithiotheritol, to cleave the disulfide bonds of the antibody, purifying the reduced antibody, *e.g.*, by gel filtration, and subsequently reacting the antibody with a compound of formula P1 containing a reactive moiety, *e.g.*, a maleimido group. Suitable solvents include, but are not limited to

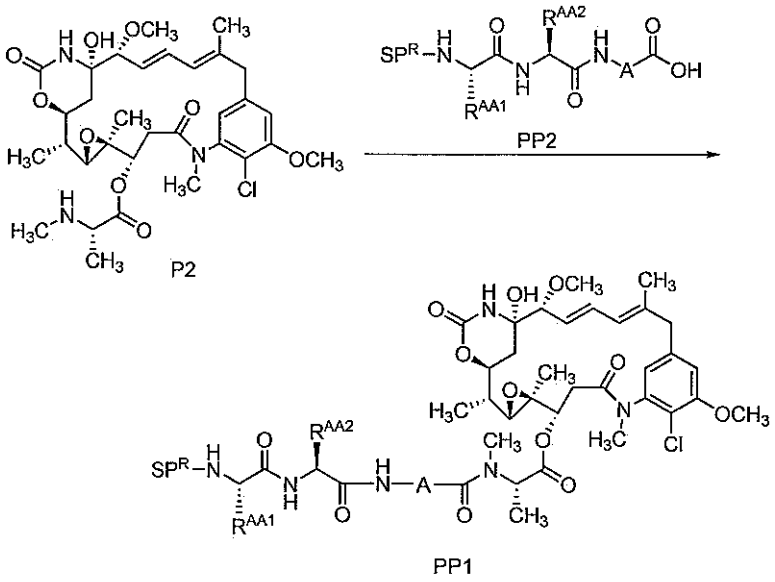
nitro-benzoic acid, 2,6-difluoro-3-nitro-benzoic acid, 2-chloro-6-fluoro-3-nitro-benzoic acid, 6-chloro-2-fluoro-3-nitro-benzoic acid, 2-chloro-4-fluoro-5-nitro-benzoic acid, 4-chloro-2-fluoro-5-nitro-benzoic acid, 2-ethoxy-5-nitro-benzoic acid, 2-(methylamino)-3-nitro-benzoic acid, 6-nitro-8-quinolinecarboxlic acid, 4-(dimethylamino)-3-nitro-benzoic acid hydrochloride (1:1), 2-methyl-nitro-benzoic acid, 3-methyl-4-nitro-benzoic acid, 4-nitro-1-naphthalenecarboxylic acid, 2,6-dimethyl-4-nitro-benzoic acid, 3-fluoro-4-nitro-benzoic acid, 3-chloro-4-nitro-benzoic acid, 3-bromo-4-nitro-benzoic acid, 3-cyano-4-nitro-benzoic acid, 3-cyclopropyl-4-nitro-benzoic acid, 3-methoxy-4-nitro-benzoic acid, 2-methoxy-4-nitro-benzoic acid, 5-chloro-2-methyl-4-nitro-benzoic acid, 8-nitro-5-isoquinolinecarboxylic acid, 5-nitro-8-quinolinecarboxylic acid, 8-nitro-5-quinolinecarboxylic acid, 2,5-difluoro-4-nitro-benzoic acid, 2-(dimethylamino)-4-nitro-benzoic acid,, 2-chloro-5-fluoro-4-nitro-benzoic acid, 3-(dimethylamino)-4-nitro-benzoic acid, 2-[(1-methylethyl)thio]-4-nitro-benzoic acid, 4-nitro-3-(trifluoromethyl)-benzoic acid, 4-nitro-2-(trifluoromethyl)-benzoic acid, 3,5-dimethoxy-4-nitro-benzoic acid, 4-nitro-2-(propylamino)-benzoic acid, 3-(difluoromethoxy)-4-nitro-benzoic acid, 2-(2-fluoro-phenyl)-4-nitro-benzoic acid, 4-nitro-2-(4-pyridinyl)-benzoic acid, 4-nitro-3-(4-pyridinyl)-benzoic acid, or 4-nitro-2-(1-pyrrolidinyl)-benzoic acid.

[0391] Suitable compounds of Formula PP6 include compounds having any one of the following formula:



wherein R^1 is, independently at each occurrence, C_{1-6} alkyl, C_{1-6} alkoxy, halo, C_{1-6} haloalkyl, or C_{1-6} haloalkoxy, wherein n is 0, 1, 2, 3, or 4. In certain of these embodiments, R^1 is methoxy or methyl. In some specific embodiments, R^1 is methoxy, fluoro, or trifluoromethyl. In certain embodiments, n is 1 or 2. In some of these embodiments, n is 1. In some embodiments, R^1 is fluoro, chloro, bromo, or iodo.

[0397] Compounds of Formula PP1 can be prepared by contacting a compound of Formula PP2 with the compound of Formula P2:



wherein:

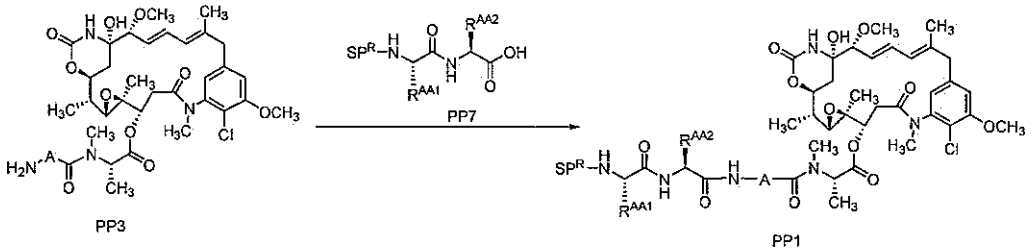
SP^R is a reactive linker;

R^{AA1} is an amino acid side chain;

R^{AA2} is an amino acid side chain; and

A is arylene or heteroarylene.

[0398] Compounds of Formula PP1 can be prepared by contacting a compound of Formula PP3 with the compound of Formula PP7:



wherein:

SP^R is a reactive linker;

R^{AA1} is an amino acid side chain;

R^{AA1} is an amino acid side chain; and

A is arylene or heteroarylene.

[0399] Compounds of Formula PP2 can be prepared by contacting a compound of Formula PP8 with a bifunctional spacer:

(t, 1H, J = 12 Hz), 2.18 (dd, 1H, J = 14 Hz, 3 Hz), 1.66 (s, 3H), 1.63 (m, 2H), 1.51 – 1.45 (m, 2H), 1.41 (d, 3H, J = 7 Hz), 1.30 (d, 3H, J = 7 Hz), 1.26 (m, 1H), 0.84 (s, 3H).

EXAMPLE 9

[0478] Compound **35** was synthesized as described below and as depicted in **FIG 13.**

Maytansin-N-methyl-L-alanine-N-(3-trifluoromethyl-4-amino)benzamide (35)

Step A: Maytansin-N-methyl-L-alanine-(3-trifluoromethyl-4-nitro)benzamide:

[0479] The title compound was prepared from maytansin-N-methyl-L-alanine (**9**, 46 mg, 0.071 mmol) and 3-trifluoromethyl-4-nitrobenzoic acid (**34**) (25 mg, 0.106 mmol), using the method from Step A of Example 5, to give a light yellow solid (37 mg, 61%). MS (ESI, pos.): calc'd for $C_{40}H_{46}N_4O_{12}ClF_3$, 866.3; found 849.2 (M-$H_2O$+H), 867.2 (M+H), 889.2 (M+Na).

Step B: Maytansin-N-methyl-L-alanine-N-(3-trifluoromethyl-4-amino)benzamide (**35**):

[0480] The title compound was prepared from the product of the preceding step (36 mg, 0.042 mmol), using the method from Step B of Example 5, to give a white solid (17 mg, 46%). MS (ESI, pos.): calc'd for $C_{40}H_{48}N_4O_{10}ClF_3$, 836.3; found 819.2 (M-$H_2O$+H), 837.2 (M+H), 859.2 (M+Na). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.54 (s, 1H), 7.37 (d, 1H, J = 8 Hz), 6.91 (br s, 1H), 6.83 (s, 1H), 6.70 (d, 1H, J = 11 Hz), 6.66 (d, 1H, J = 8 Hz), 6.45 (dd, 1H, J = 15 Hz, 11 Hz), 6.28 (s, 1H), 5.73 (dd, 1H, J = 16 Hz, 9 Hz), 5.44 (m, 1H), 4.88 (dd, 1H, J = 12 Hz, 3 Hz), 4.40 (s, 2H), 4.30 (t, 1H, J = 11 Hz), 3.99 (s, 3H), 3.63 (d, 1H, J = 13 Hz), 3.52 (d, 1H, J = 9 Hz), 3.36 (s, 3H), 3.12 (d, 1H, J = 13 Hz), 3.03 (m, 4H), 2.92 (s, 3H), 2.69 (m, 1H), 2.21 (dd, 1H, J = 14 Hz, 3 Hz), 1.65 (m, 4H), 1.52 – 1.44 (m, 4H), 1.31 (d, 3H, J = 6 Hz), 1.26 (m, 2H), 0.85 (s, 3H).

Example 10

[0481] Compound 37 was synthesized as described below and as depicted in **FIG 14.**

Maytansin-N-methyl-L-alanine-N-(2-chloro-4-amino-5-fluoro)benzamide (37)

Step A: Maytansin-N-methyl-L-alanine-(2-chloro-4-nitro-5-fluoro)benzamide:

[0482] The title compound was prepared from maytansin-N-methyl-L-alanine (**9**, 46 mg, 0.071 mmol) and 3-trifluoromethyl-4-nitrobenzoic acid (**36,**26 mg, 0.118 mmol), using the method from Step A of Example 5, to give a white solid (33 mg, 55%). MS (ESI, pos.): calc'd for $C_{39}H_{45}N_4O_{12}Cl_2F$, 850.2; found 833.1 (M-$H_2O$+H), 851.1 (M+H), 873.1 (M+Na).

Step B: Maytansin-N-methyl-L-alanine-N-(2-chloro-4-amino-5-fluoro)benzamide (37):

[0483] The title compound was prepared from the product of the preceding step (36 mg, 0.042 mmol), using the method from Step B of Example 5, to give a white solid (17 mg, 46%). MS (ESI, pos.): calc'd for $C_{39}H_{47}N_4O_{10}Cl_2F$, 820.3; found 803.2 (M-$H_2O$+H), 821.2 (M+H), 843.2 (M+Na). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 6.88 (d, 2H, J = 13 Hz), 6.83 (d, 1H, J = 11 Hz), 6.77 (d, 1H, J = 8 Hz), 6.72 (d, 1H, J = 10 Hz), 6.46 (dd, 1H, J = 15 Hz, 11 Hz), 6.25 (s, 1H), 5.71 (dd, 1H, J = 16 Hz, 10 Hz), 5.52 (m, 1H), 4.85 (dd, 1H, J = 12 Hz, 3 Hz), 4.30 (t, 1H, J = 11 Hz), 4.01 (s, 3H), 3.92 (s, 2H), 3.73 (d, 1H, J = 13 Hz), 3.52 (d, 1H, J = 9 Hz), 3.37 (s, 3H), 3.15 (d, 1H, J = 13 Hz), 3.10 (s, 3H), 3.03 (d, 1H, J = 10 Hz), 2.75 (s, 3H), 2.68 (dd, 1H, J = 14 Hz, 12 Hz), 2.22 (dd, 1H, J = 15 Hz, 3 Hz), 1.67 (s, 3H), 1.61 (m, 1H), 1.50 – 1.43 (m, 5H), 1.31 (d, 3H, J = 6 Hz), 1.27 – 1.24 (m, 1H), 0.86 (s, 3H).

Example 11

[0484] Compound **39** was synthesized as described below and as depicted in **FIG 16.**

Maytansin-N-methyl-L-alanine-N-(2,5-difluoro-4-amino)benzamide (39)

Step A: Maytansin-N-methyl-L-alanine-(2,5-difluoro-4-nitro)benzamide:

[0485] The title compound was prepared from maytansin-N-methyl-L-alanine (**9**, 48 mg, 0.074 mmol) and 2,5-difluoro-4-nitrobenzoic acid (**38,** 27 mg, 0.133 mmol), using the method from Step A of Example 5, to give a yellow solid (37 mg, 60%). MS (ESI, pos.): calc'd for $C_{39}H_{45}N_4O_{12}ClF_2$, 834.3; found 817.2 (M-$H_2O$+H), 835.2 (M+H), 857.2 (M+Na).

Step B: Maytansin-N-methyl-L-alanine-(2,5-difluoro-4-amino)benzamide (39):

[0486] The title compound was prepared from the product of the preceding step (36 mg, 0.043 mmol), using the method from Step B of Example 5, to give a white solid (22 mg, 59%). MS (ESI, pos.): calc'd for $C_{39}H_{47}N_4O_{10}ClF_2$, 804.3; found 787.3 (M-$H_2O$+H), 805.3 (M+H), 827.3 (M+Na). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 6.89 – 6.84 (m, 3H), 6.77 (d, 1H, J = 11 Hz), 6.49 – 6.41 (m, 2H), 6.24 (s, 1H), 5.72 (dd, 1H, J = 16 Hz, 9 Hz), 5.47 (q, 1H, J = 7

Maytansin-N-methyl-L-alanine-(3-chloro-4-amino)benzamide (43)

Step A: Maytansin-N-methyl-L-alanine-(3-chloro-4-nitro)benzamide:

[0491] The title compound was prepared from maytansin-N-methyl-L-alanine (**9**, 45 mg, 0.069 mmol) and 3-chloro-4-nitrobenzoic acid (**42**) (26 mg, 0.129 mmol), using the method from Step A of Example 5, to give a yellow solid (36 mg, 62%). MS (ESI, pos.): calc'd for $C_{39}H_{46}N_4O_{12}Cl_2$, 832.2; found 815.2 (M-$H_2O$+H), 833.2 (M+H), 855.2 (M+Na).

Step B: Maytansin-N-methyl-L-alanine-(3-chloro-4-amino)benzamide (**43**):

[0492] The title compound was prepared from the product of the preceding step (35 mg, 0.042 mmol), using the method from Step B of Example 5, to give a white solid (24 mg, 67%). MS (ESI, pos.): calc'd for $C_{39}H_{48}N_4O_{10}Cl_2$, 802.3; found 785.2 (M-$H_2O$+H), 803.2 (M+H), 825.1 (M+Na). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.35 (s, 1H), 7.17 (d, 1H, J = 8 Hz), 6.90 (s, 1H), 6.83 (d, 1H, J = 2 Hz), 6.68 (m, 2H), 6.44 (dd, 1H, J = 15 Hz, 11 Hz), 6.30 (s, 1H), 5.73 (dd, 1H, J = 15 Hz, 9 Hz), 5.42 (m, 1H), 4.87 (dd, 1H, J = 12 Hz, 3 Hz), 4.32 – 4.27 (m, 3H), 3.99 (s, 3H), 3.60 (d, 1H, J = 13 Hz), 3.51 (d, 1H, J = 10 Hz), 3.44 (bs s, 1H), 3.36 (s, 3H), 3.10 (m, 4H), 3.03 (d, 1H, J = 10 Hz), 2.92 (s, 3H), 2.69 (m, 1H), 2.21 (dd, 1H, J = 15 Hz, 3 Hz), 1.65 (s, 3H), 1.63 (m, 1H), 1.52 – 1.45 (m, 1H), 1.43 (d, 3H, J = 7 Hz), 1.31 (d, 3H, J = 7 Hz), 1.27 (m, 1H), 0.83 (s, 3H).

Example 14

[0493] Compound **45** was synthesized as described below and as depicted in **FIG 19**.

Maytansin-N-methyl-L-alanine-(5-amino-8-carboxyquinoline)carboxamide (45)

Step A: Maytansin-N-methyl-L-alanine-(5-nitro-8-carboxyquinoline)carboxamide :

[0494] The title compound was prepared from maytansin-N-methyl-L-alanine (**9**, 45 mg, 0.069 mmol) and 5-nitro-8-carboxyquinoline (**44**) (24 mg, 0.110 mmol), using the method from Step A of Example 5, to give a pale yellow solid (26 mg, 44%). MS (ESI, pos.): calc'd for $C_{42}H_{48}N_5O_{12}Cl$, 849.3; found 832.2 (M-H_2O+H), 850.2 (M+H), 872.2 (M+Na).

Step B: Maytansin-N-methyl-L-alanine-(5-amino-8-carboxyquinoline)carboxamide (**45**):

[0495] The title compound was prepared from the product of the preceding step (25 mg, 0.029 mmol), using the method from Step B of Example 5, to give a pale yellow solid (8 mg, 31%). MS (ESI, pos.): calc'd for $C_{42}H_{50}N_5O_{10}Cl$, 819.3; found 802.3 (M-H_2O+H), 820.3 (M+H). ^{1}H-NMR (500 MHz, DMSO-d_6): δ 8.80 (br s, 1H), 8.54 (d, 1H, *J* = 10 Hz), 7.39 (br s, 1H), 7.28 (s, 1H), 7.05 – 7.00 (br m, 2H), 6.90 (s, 1H), 6.84 (m, 1H), 6.62 (dd, 1H, *J* = 15 Hz, 11 Hz), 6.52 (br m, 1H), 6.22 (s, 2H), 5.98 (s, 1H), 5.62 (br m, 2H), 4.56 (br m, 1H), 4.11 (m, 1H), 3.98 (s, 3H), 3.64 (d, 1H, *J* = 13 Hz), 3.53 (d, 1H, *J* = 9 Hz), 3.27 (s, 3H), 2.92 – 2.88 (m, 3H), 2.81 (d, 1H, *J* = 10 Hz), 2.42 (br s, 2H), 2.07 – 2.04 (m, 1H), 1.75 (m, 2H), 1.66 (s, 3H), 1.55 – 1.45 (m, 3H), 1.42 (d, 3H, *J* = 7 Hz), 1.32 (d, 1H, *J* = 14 Hz), 1.24 (s, 1H), 1.14 (d, 3H, *J* = 7 Hz), 0.84 (s, 3H).

Example 15

[0496] Compound **47** was synthesized as described below and as depicted in **FIG 20.**

Maytansin-N-methyl-L-alanine-(3-bromo-4-amino)benzamide (47)

Step A: Maytansin-N-methyl-L-alanine-(3-bromo-4-nitro)benzamide :

[0497] The title compound was prepared from maytansin-N-methyl-L-alanine (**9**, 49 mg, 0.075 mmol) and 3-bromo-4-nitrobenzoic acid (**46**) (30 mg, 0.122 mmol), using the method from Step A of Example 5, to give a yellow solid (38 mg, 58%). MS (ESI, pos.): calc'd for $C_{39}H_{46}N_4O_{12}BrCl$, 876.2/878.2; found 861.1 (M-H_2O+H), 879.1 (M+H), 901.1 (M+Na) for the most abundant isotopes.

Step B: Maytansin-N-methyl-L-alanine-(3-bromo-4-amino)benzamide (47):

[0498] The title compound was prepared from the product of the preceding step (37 mg, 0.042 mmol), using the method from Step B of Example 5, to give a white solid (28 mg, 74%). MS (ESI, pos.): calc'd for $C_{39}H_{48}N_4O_{10}BrCl$, 846.2/848.2; found 831.1 (M-H_2O+H), 849.1 (M+H), 871.2 (M+Na) for the most abundant isotopes. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.51 (s, 1H), 7.20 (d, 1H, *J* = 8 Hz), 6.90 (s, 1H), 6.83 (s, 1H), 6.68 (m, 2H), 6.44 (dd, 1H, *J* = 15 Hz, 11 Hz), 6.33 (s, 1H), 5.74 (dd, 1H, *J* = 15 Hz, 10 Hz), 5.42 (m, 1H), 4.88 (dd, 1H, *J* = 12 Hz, 3 Hz), 4.31 (m, 3H), 3.99 (s, 3H), 3.60 (d, 1H, *J* = 13 Hz), 3.51 (d, 1H, *J* = 9 Hz), 3.46 (br s, 1H), 3.36 (s, 3H), 3.10 (s, 3H), 3.09 (m, 1H), 3.03 (d, 1H, *J* = 10 Hz), 2.70 (t, 1H,

J = 13 Hz), 2.21 (dd, 1H, J = 15 Hz, 3 Hz), 1.65 (s, 3H), 1.51 – 1.45 (m, 2H), 1.43 (d, 3H, J = 7 Hz), 1.30 (d, 3H, J = 6 Hz), 1.27 (m, 1H), 0.85 (s, 3H).

Example 16

[0499] Compound **49** was synthesized as described below and as depicted in **FIG 21.**

Maytansin-N-methyl-L-alanine-(3-methoxy-4-amino)benzamide (49)

Step A: Maytansin-N-methyl-L-alanine-(3-methoxy-4-nitro)benzamide :

[0500] The title compound was prepared from maytansin-N-methyl-L-alanine (**9**, 49 mg, 0.075 mmol) and 3-methoxy-4-nitrobenzoic acid (**48**) (23 mg, 0.117 mmol), using the method from Step A of Example 5, to give a yellow solid (34 mg, 55%). MS (ESI, pos.): calc'd for $C_{40}H_{49}N_4O_{13}Cl$, 828.3; found 811.2 (M-H_2O+H), 829.3 (M+H), 851.3 (M+Na).

Step B: Maytansin-N-methyl-L-alanine-(3-methoxy-4-amino)benzamide (**49**):

[0501] The title compound was prepared from the product of the preceding step (33 mg, 0.040 mmol), using the method from Step B of Example 5, to give a white solid (25 mg, 74%). MS (ESI, pos.): calc'd for $C_{40}H_{51}N_4O_{11}Cl$, 798.3; found 781.2 (M-H_2O+H), 799.2 (M+H). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 6.94 (s, 1H), 6.92 (s, 1H), 6.85 (d, 1H, J = 8 Hz), 6.81 (s, 1H), 6.74 (br d, 1H, J = 10 Hz), 6.54 (d, 1H, J = 10 Hz), 6.44 (dd, 1H, J = 15 Hz, 11 Hz), 6.33 (s, 1H), 5.76 (m, 1H), 5.43 (br s, 1H), 4.87 (dd, 1H, J = 12 Hz, 3 Hz), 4.31 (t, 1H, J = 11 Hz), 3.98 (s, 3H), 3.70 (s, 3H), 3.64 (br d, 1H, J = 13 Hz), 3.36 (s, 3H), 3.11 – 3.02 (m, 5H), 2.94 (s, 3H), 2.68 (m, 1H), 2.20 (dd, 1H, J = 14 Hz, 3 Hz), 1.67 (m, 1H), 1.65 (s, 3H), 1.49 (dd, 1H, J = 9 Hz, 7 Hz), 1.44 (d, 3H, J = 7 Hz), 1.30 (d, 3H, J = 7 Hz), 1.27 (m, 1H), 0.85 (s, 3H).

Example 17

[0502] Compound **51** was synthesized as described below and as depicted in **FIG 22.**

Maytansin-N-methyl-L-alanine-(2-methyl-4-amino)benzamide (51)

Step A: Maytansin-N-methyl-L-alanine-(2-methyl-4-nitro)benzamide :

[0503] The title compound was prepared from maytansin-N-methyl-L-alanine (**9**, 49 mg, 0.075 mmol) and 2-methyl-4-nitrobenzoic acid (**50**) (24 mg, 0.132 mmol), using the method from Step A of Example 5, to give a pale yellow solid (32 mg, 52%). MS (ESI, pos.): calc'd for $C_{40}H_{49}N_4O_{12}Cl$, 812.3; found 795.3 (M-H_2O+H), 813.3 (M+H), 835.3 (M+Na).

*Step B: Maytansin-N-methyl-L-alanine-(2-methyl-4-amino)benzamide (**51**):*

[0504] The title compound was prepared from the product of the preceding step (30 mg, 0.037 mmol), using the method from Step B of Example 5, to give a white solid (17 mg, 55%). MS (ESI, pos.): calc'd for $C_{40}H_{51}N_4O_{10}Cl$, 782.3; found 765.2 (M-H_2O+H), 783.2 (M+H). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 6.93 (s, 1H), 6.85 (s, 1H), 6.81 (d, 1H, J = 8 Hz), 6.77 (d, 1H, J = 11 Hz), 6.49 (s, 1H), 6.45 (dd, 1H, J = 15 Hz, 11 Hz), 6.34 (d, 1H, J = 7 Hz), 6.28 (s, 1H), 5.74 (dd, 1H, J = 15 Hz, 9 Hz), 5.38 (m, 1H), 4.90 (m, 1H), 4.32 (t, 1H, J = 11 Hz), 4.00 (s, 3H), 3.69 (d, 1H, J = 13 Hz), 3.51 (d, 1H, J = 9 Hz), 3.36 (s, 3H), 3.15 (m, 1H), 3.12 (s, 3H), 3.01 (d, 1H, J = 10 Hz), 2.73 (s, 3H), 2.69 (m, 1H), 2.22 (m, 1H), 2.18 (s, 3H), 1.68 (m, 1H), 1.66 (s, 3H), 1.51 (m, 1H), 1.47 (d, 3H, J = 7 Hz), 1.30 (d, 3H, J = 6 Hz), 1.28 (m, 1H), 0.87 (s, 3H).

Example 18

[0505] Compound **53** was synthesized as described below and as depicted in **FIG 23**.

*Maytansin-N-methyl-L-alanine-(3-methyl-4-amino)benzamide (**53**)*

Step A: Maytansin-N-methyl-L-alanine-(3-methyl-4-nitro)benzamide :

[0506] The title compound was prepared from maytansin-N-methyl-L-alanine (**9**, 49 mg, 0.075 mmol) and 3-methyl-4-nitrobenzoic acid (**52**) (26 mg, 0.143 mmol), using the method from Step A of Example 5, to give a yellow solid (34 mg, 56%). MS (ESI, pos.): calc'd for $C_{40}H_{49}N_4O_{12}Cl$, 812.3; found 795.2 (M-H_2O+H), 813.2 (M+H).

*Step B: Maytansin-N-methyl-L-alanine-(3-methyl-4-amino)benzamide (**53**):*

[0507] The title compound was prepared from the product of the preceding step (33 mg, 0.041 mmol), using the method from Step B of Example 5, to give a white solid (24 mg, 71%). MS (ESI, pos.): calc'd for $C_{40}H_{51}N_4O_{10}Cl$, 782.3; found 765.2 (M-H_2O+H), 783.2 (M+H). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.15 (s, 1H), 7.09 (d, 1H, J = 8 Hz), 6.94 (s, 1H),

Maytansin-N-methyl-L-alanine-(3-methoxy-4-amino)benzamido-Cit-Val-Cap-Mal (60)

Step A: Boc-L-valine-L-citrulline-(3-methoxy-4-amino)benzoic acid t-butyl ester (57):

[0512] The title compound was prepared from Boc-L-valine-L-citrulline (**3**, 100 mg, 0.267 mmol) and 4-amino-3-methoxybenzoic acid tert-butyl ester (**56**, 61 mg, 0.273 mmol), using the method from Step A of Example 2, to give a white solid (74 mg, 48%). MS (ESI, pos.): calc'd for $C_{28}H_{45}N_5O_8$, 579.3; found 580.4 (M+H), 602.6 (M+Na).

Step B: L-valine-L-citrulline-(3-methoxy-4-amino)benzoic acid (58):

[0513] The title compound was prepared from the product of the preceding step (**57**, 72 mg, 0.124 mmol), using the method from Step C of Example 1, to give an off-white solid (68 mg, 100%). MS (ESI, pos.): calc'd for $C_{19}H_{29}N_5O_6$, 423.2; found 424.4 (M+H), 847.4 (2M+H).

Step C: 6-(Maleimidyl-caprolyl)-L-valine-L-citrulline-(3-methoxy-4-amino)benzoic acid (59):

[0514] The title compound was prepared from the product of the preceding step (**58**, 67 mg, 0.124 mmol), using the method from Step D of Example 1, to give a white solid (45 mg, 59%). MS (ESI, pos.): calc'd for $C_{29}H_{40}N_6O_9$, 616.3; found 617.5 (M+H), 639.6 (M+Na).

Step D: Maytansin-N-methyl-L-alanine-(3-methoxy-4-amino)benzamido-Cit-Val-Cap-Mal (60):

[0515] The title compound was prepared from the product of the preceding step (**59**, 44 mg, 0.071 mmol) and maytansin-N-methyl-L-alanine (**9**, 49 mg, 0.075 mmol), using the method from Step E of Example 1, to give a white solid (14 mg, 16%). MS (ESI, pos.): calc'd for $C_{61}H_{82}N_9O_{17}Cl$, 1247.6; found 1231.1 (M-H_2O+H), 1249.1 (M+H), 1271.1 (M+Na). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 8.48 (s, 1H), 8.24 (d, 1H, J = 8 Hz), 7.11 (d, 1H, J = 8 Hz), 6.96 – 6.93 (m, 3H), 6.83 (s, 1H), 6.72 – 6.68 (m, 3H), 6.45 (dd, 1H, J = 16 Hz, 11 Hz), 6.25 (s, 1H), 6.18 (d, 1H, J = 9 Hz), 5.77 (dd, 1H, J = 15 Hz, 10 Hz), 5.44 (m, 1H), 5.03 (br s 1H), 4.90 (d, 1H, J = 10 Hz), 4.62 (m, 1H), 4.54 (br s, 2H), 4.33 – 4.28 (m, 2H), 3.99 (s, 3H), 3.75 (s, 3H), 3.61 (d, 1H, J = 13 Hz), 3.52 – 3.48 (m, 3H), 3.36 (s, 3H), 3.24 (m, 2H), 3.11 (d, 1H, J = 13 Hz), 3.07 (s, 3H), 3.03 (d, 1H, J = 10 Hz), 2.90 (s, 3H), 2.70 (m, 1H), 2.26

[0565] The title compound was prepared from the product of the preceding step (35 mg, 0.042 mmol), using the method from Step B of Example 5, to give a white solid (19 mg, 57%). MS (ESI, pos.): calc'd for $C_{41}H_{52}N_5O_{11}Cl$, 825.3; found 808.4 (M-H_2O), 826.4 (M+H). ^{1}H-NMR (500 MHz, DMSO-d_6): δ 9.05 (s, 1H), 7.30 (s, 1H), 7.17 (s, 1H), 6.98 (d, 1H, J = 9 Hz), 6.91 (s, 1H), 6.79 (s, 1H), 6.58 (m, 3H), 5.97 (s, 1H), 5.64 (br s, 1H), 5.34 (m, 3H), 4.60 (d, 1H, J = 12 Hz), 4.10 (t, 1H, J = 12 Hz), 3.93 (s, 3H), 3.50 (d, 1H, J = 9 Hz), 3.33 (s, 3H), 3.29 (m, 1H), 3.26 (s, 3H), 3.16 (d, 1H, J = 12 Hz), 2.97 (s, 3H), 2.79 (m, 4H), 2.07 (d, 1H, J = 13 Hz), 1.95 (s, 2H), 1.59 (s, 3H), 1.51 – 1.42 (m, 2H), 1.29 (m, 3H), 1.13 (d, 3H, J = 6 Hz), 0.81 (s, 3H).

Example 36

[0566] Compound **100** was synthesized as described below and as depicted in **FIG 41**.

Maytansin-N-methyl-L-alanine-N-4-aminobenzamide-Cit-Val-cap-diBromomethylacrylamide (100)

Step A: 3-Bromo-2-bromomethyl-propionyl chloride (92):

[0567] To a 10 mL round bottom flask equipped with a magnetic stirrer and nitrogen inlet was charged 3-bromo-2-bromomethyl-propionic acid (**91**, 1.0 g; 4.1 mmol) and thionyl chloride (3.0 mL). This solution was heated to reflux for 3 hours and concentrated to 0.90 g (84% yield) as a brown oil. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 3.85 – 3.75 (m, 4H), 3.60 (pentet, 1H, J = 9 Hz).

Step B: 6-Amino-hexanoic acid tert-butyl ester (94):

[0568] To a 50 mL round bottom flask equipped with a magnetic stirrer and nitrogen inlet was charged 6-aminohexanoic acid (**93**, 2.0 g; 15 mmol) and thionyl chloride (5.0 mL; 69 mmol; 4.5 equiv.). This solution was stirred at or below 30 °C for 2 hours and concentrated *in vacuo* to dryness. To the tan semi-solid a slurry of sodium bicarbonate (2.6 g; 30 mmol; 2.0 equiv.) in *t*-BuOH (5.0 mL; 87 mmol; 5.7 equiv.) was added and the slurry was stirred at ambient temperature for another 2 h. The butanol was removed *in vacuo* at 40 °C. The thick white slurry was diluted with ethyl acetate and washed with 4 portions of 1 N NaOH, 3 portions of H_2O, 1 portion of brine. The organics were dried over Na_2SO_4, filtered

[0571] The title compound was prepared from the product of Example 1, Step D (**6**, 100 mg, 0.254 mmol) and di-tert-butyl dicarbonate (61 mg, 0.279 mmol), which were weighed into a round-bottom flask and treated with 1 M NaOH (2 mL) in THF (3 mL) and H_2O (1.5 mL). The flask was sealed via rubber septum and the reaction was stirred at ambient temperature overnight, concentrated in vacuo and neutralized to pH 7 with dropwise addition of 1 M HCl (2 mL). The aqueous the reaction with ethyl acetate, dried the organic layer over Na_2SO_4, filter and concentrated to give an off-white solid (93 mg, 74%). MS (ESI, pos.): calc'd for $C_{23}H_{35}N_5O_7$, 493.5; found 394.2 (M+1-Boc), 494.2 (M+H), 516.2 (M+Na).

Step F: Maytansin-N-methyl-L-alanine-N-4-aminobenzamide-Cit-Val-Boc (98):

[0572] The title compound was prepared from the product of the preceding step Boc-Val-Cit-4-aminobenzoic acid (**97**, 76 mg, 0.154 mmol) and maytansin-N-methyl-L-alanine (**9**, 50 mg, 0.077 mmol) using the method from Step A of Example 5, to give a white solid (22 mg, 26%). MS (ESI, pos.): calc'd for $C_{55}H_{77}ClN_8O_{15}$,1124.5; found 1107.2 (M-H_2O), 1125.3 (M+H), 1147.2 (M+Na).

*Step G: Maytansin-N-methyl-L-alanine-N-4-aminobenzamide-Cit-Val (**99**):*

[0573] The title compound was prepared from the product of the preceding step (**98**, 20 mg, 0.018 mmol) weighed into a round-bottom flask dissolved in ACN (3 mL) and H_2O (1 mL) and treated with TFA (1 mL). The flask was sealed via rubber septum, purged with nitrogen, and the reaction was stirred at ambient temperature. After 48 h the reaction was purified directly on a 30 g C18 RediSep Gold Aq column via ISCO system (gradient elution: 10 – 65% MeCN in water, 0.05% acetic acid in both, over 20 min). The product-containing fractions were combined, partially concentrated in vacuo, frozen on dry ice, and lyophilized to give an off-white solid (8 mg, 46%). MS (ESI, pos.): calc'd for $C_{50}H_{69}ClN_8O_{13}$, 1024.5; found 1007.2 (M-H_2O), 1026.2 (M+H).

*Step H: Maytansin-N-methyl-L-alanine-N-4-aminobenzamide-Cit-Val-caproyl-bis(BrMe)acrylamide (**100**):*

[0574] The title compound was prepared from the product of the preceding step (**99**, 8 mg, 0.008 mmol) and 6-(3-Bromo-2-bromomethyl-propionylamino)-hexanoic acid (**96**), using the method from Step A of Example 5, to give a white solid (8 mg, 75%). MS (ESI,

Mix and Go competent cells, incubated on ice for 5 minutes and competent cells were plated on LB plates containing Carbenicillin, which were incubated overnight at 37°C.

[0590] The following day, a single colony was picked from each plate and grown in LB broth containing 100 µg/mL Carbenicillin for 3 to 4 hours. The sample was then diluted into LB broth containing 100 µg/ml Carbenicillin and transferred to a 37°C shaking incubator to grow overnight. A maxiprep DNA extraction was then performed on both plasmids and the full DNA open reading frames were sequenced. Once the sequences were confirmed, the heavy chain DNA along with previously cloned affiliated light chain DNA was stably transfected into a CHO cell line to produce each antibody.

[0591] The H1H6958N2 (international patent application WO 2015026907 A1) containing the N180Q Fc mutation is referred to as **PRLR-Q**, and the isotype control antibody recognizing an exogenous antigen also containing the N180Q Fc mutation is referred to as **ISOTYPE CONTROL-Q**.

Example 43

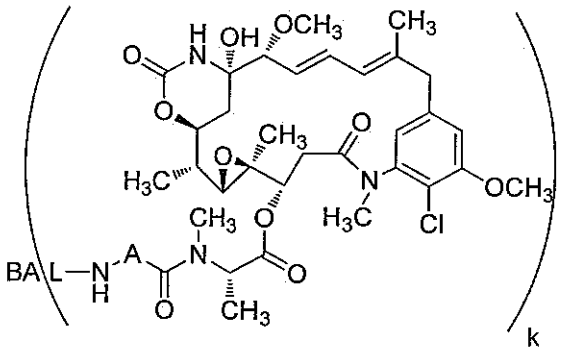
[0592] *Bacterial Transglutaminase Conjugation*

[0593] PRLR-Q (MW 145438 Da) and Isotype Control-Q (MW 144602 Da) antibodies were conjugated at 1-10 mg/mL in PBS pH 7.4. Linker payload **63** was added in a 10 to 25-fold molar excess over antibody and the enzymatic reaction was initiated by addition of 1-5 units of bacterial transglutaminase (Zedira, T1001) per mg antibody and incubated with shaking at 37°C for 4-16 hours. The conjugates were purified by size exclusion chromatography and sterile filtered. Protein and linker payload concentrations were determined by UV spectral analysis. Size-exclusion HPLC established that all conjugates used were >95% monomeric. Yields are reported in Table 1 based on protein. All conjugated antibodies were analyzed by UV for linker payload loading values according to Hamblett et al, Cancer Res 2004 10 7063. In addition, the conjugates were analyzed by ESI-MS for linker payload loadings using a Waters Synapt G2-Si QTOF mass spectrometry coupled with Acquity UPLC. The chromatographic separation was achieved on a C4 column (Waters protein BEH C4, 50 mm X 1 mm, 1.7 µm) in a 25 minute gradient (minute:percentage of mobile pahse B; 0:20%, 1:20%, 18:40%, 18.1:90%, 20:95%, 20.8:95%, 20.9:20% 25:20%). The mobile phase A was 0.1% formic acid in water and mobile phase B was 0.1% formic acid

CLAIMS

What is claimed is:

1. A compound of Formula (I):



(I)

or a pharmaceutically acceptable salt thereof,

wherein:

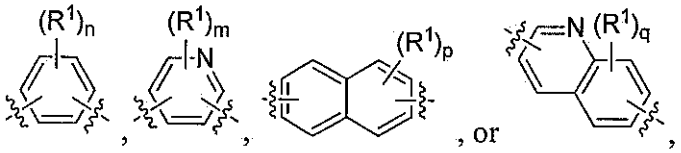
A is arylene or heteroarylene;

L is a linker;

BA is an antibody or an antigen binding fragment thereof; and

k is an integer from 1 to 30.

2. The compound of claim 1, wherein A is:



wherein:

R^1, independently at each occurrence, is alkyl, alkenyl, alkynyl, alkoxy, aryl, alkaryl, aralkyl, halo, haloalkyl, haloalkoxy, heteroaryl, heterocycloalkyl, hydroxyl, cyano, nitro, $-OR^A$, $-SO_2R^A$, $-C(=O)R^A$, or azido,

wherein R^A is alkyl or heteroalkyl;

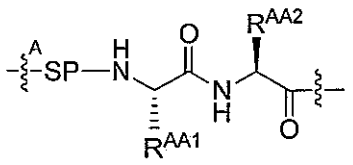
n is an integer from 0 to 4;

m is an integer from 0 to 3;

p is an integer from 0 to 6; and

q is an integer from 0 to 5.

3. The compound of any of claims 1-2, wherein L is:



wherein:

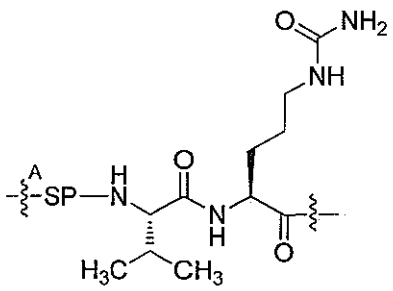
SP is a spacer;

 is one or more bonds to the antibody or antigen binding fragment thereof;

R^{AA1} is an amino acid side chain; and

R^{AA2} is an amino acid side chain.

4. The compound of claim 3, wherein L is:

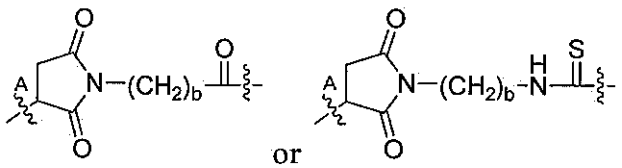


wherein:

SP is a spacer; and

 is one or more bonds to the antibody or antigen binding fragment thereof.

5. The compound of claim 4, wherein SP is:

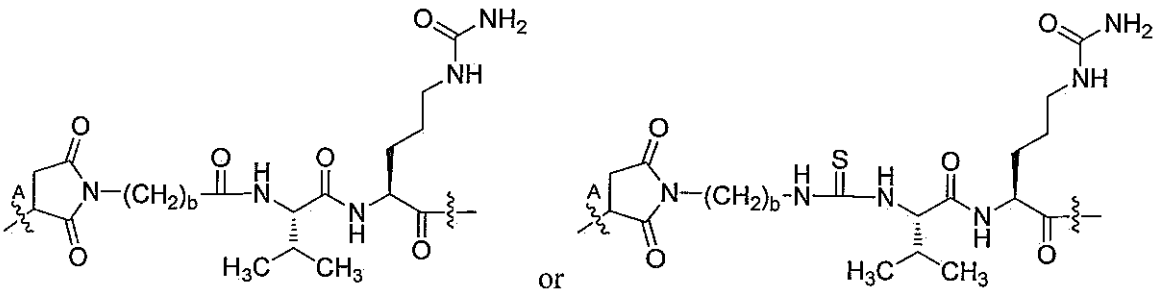


wherein:

$-\overset{A}{\sim}$ is a bond to the antibody or antigen binding fragment thereof; and

b is an integer from 2 to 8.

6. The compound of any of claims 1-2, wherein L is:

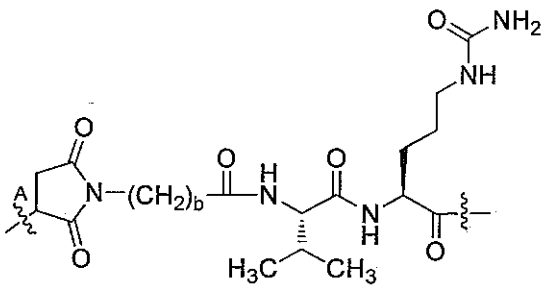


wherein:

$-\overset{A}{\sim}$ is a bond to the antibody or antigen binding fragment thereof; and

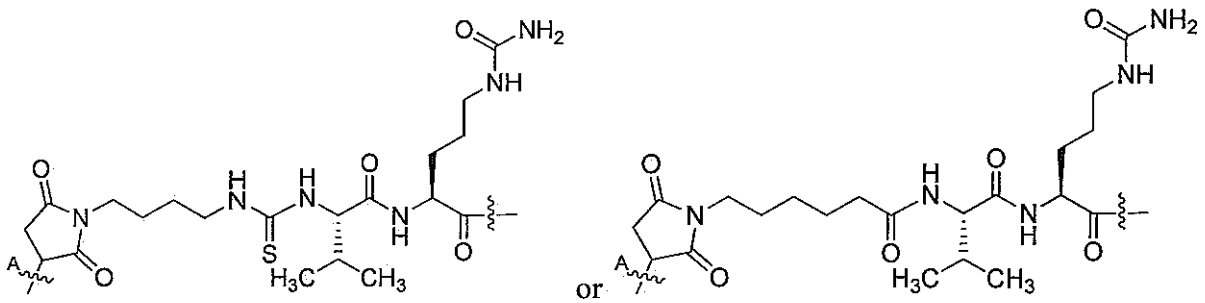
b is an integer from 2 to 8.

7. The compound of claim 6, wherein L is:



wherein $-\overset{A}{\sim}$ is a bond to the antibody or antigen binding fragment thereof.

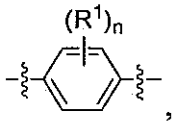
8. The compound of any of claims 1-2, wherein L is:



wherein $-\overset{A}{\sim}-$ is a bond to the antibody or antigen binding fragment thereof.

9. The compound of claim 1, wherein:

A is:

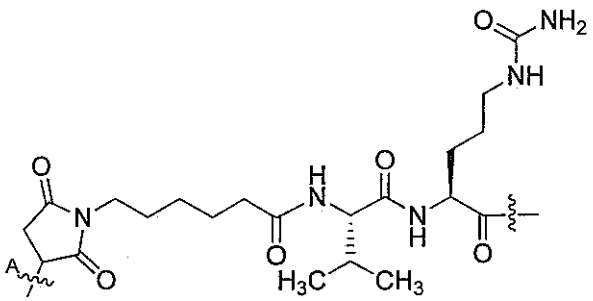


wherein:

n is 0, 1 or 2; and

R^1 is, independently at each occurrence, alkyl, alkoxy, haloalkyl, or halo; and

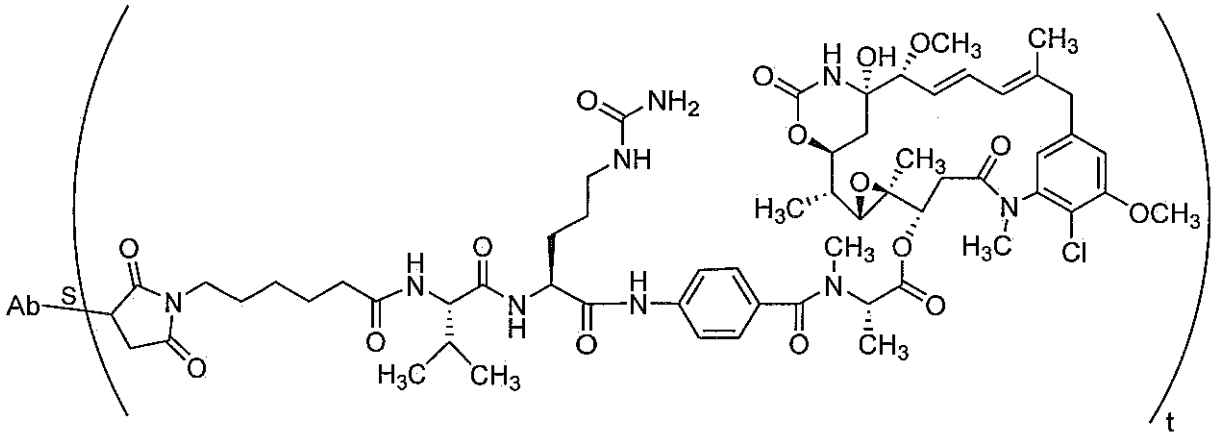
L is:



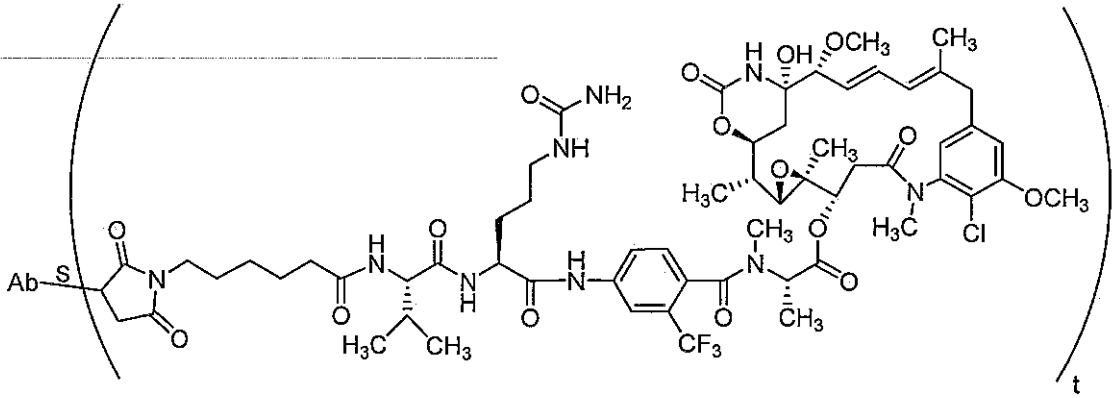
wherein:

$-\overset{A}{\sim}-$ is a bond to the antibody or antigen binding fragment thereof.

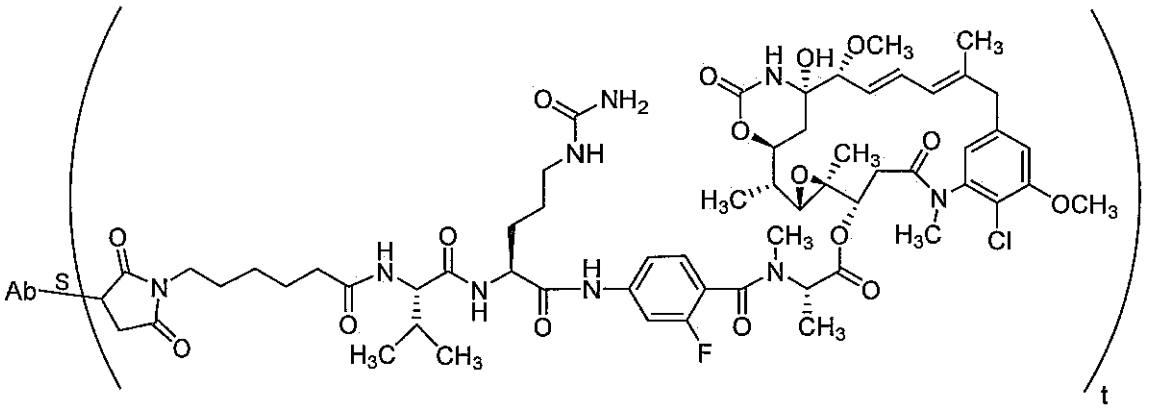
10. The compound of claim 1, wherein the compound is:



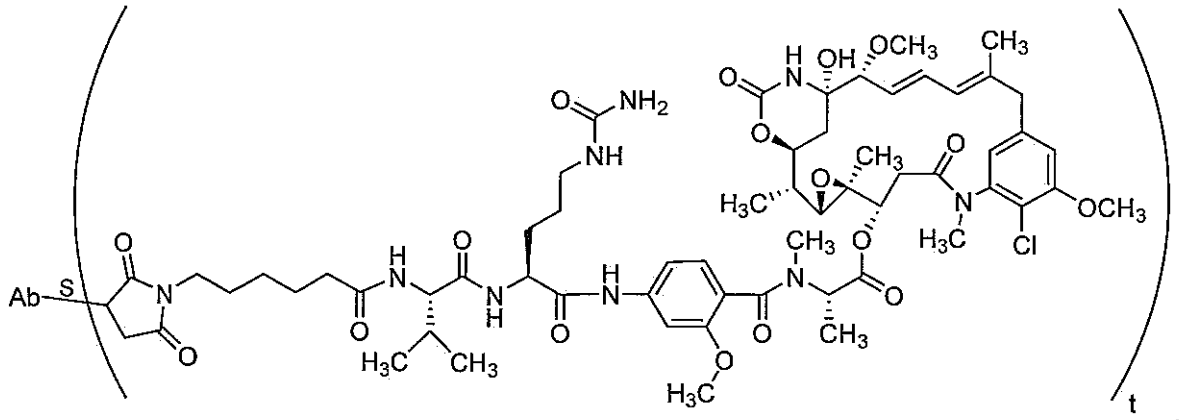
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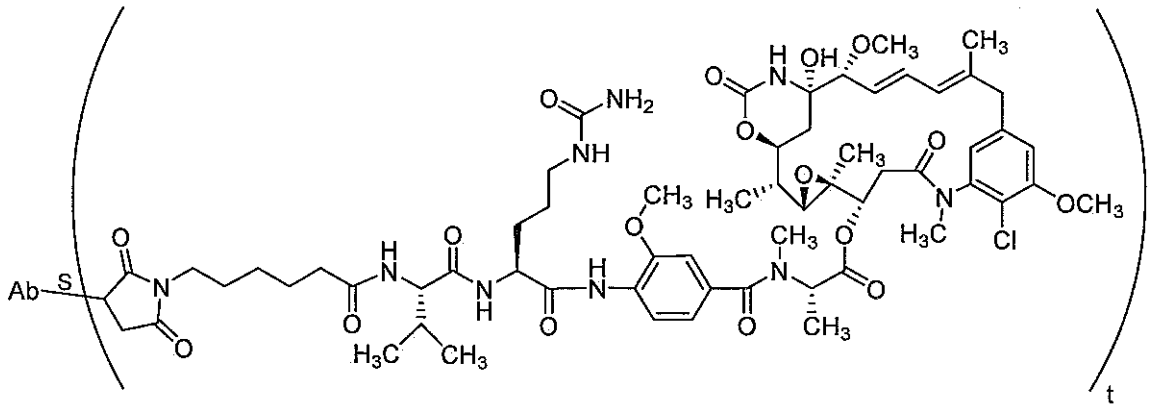


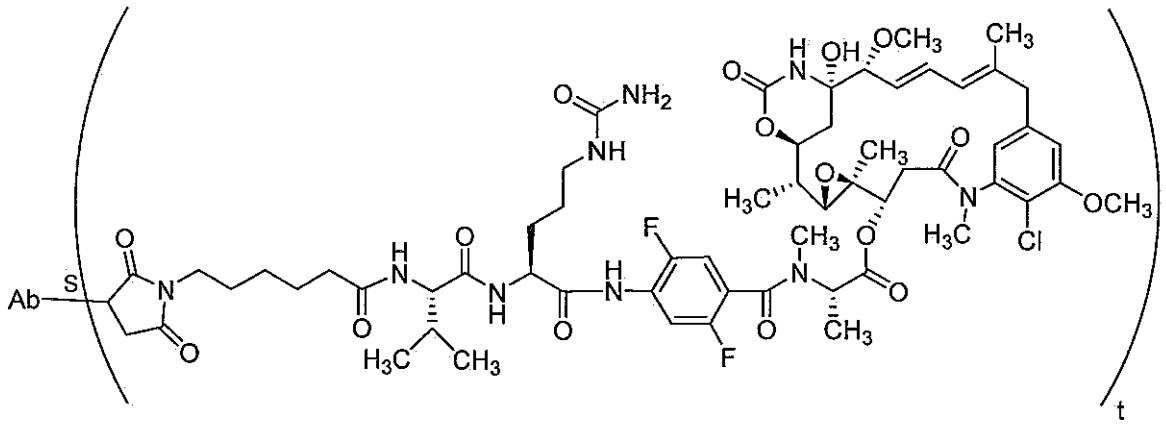
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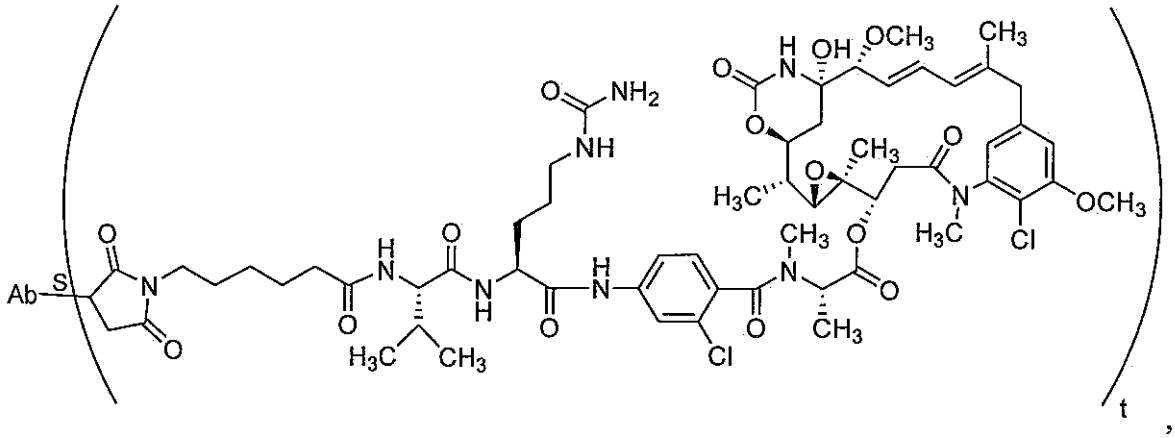


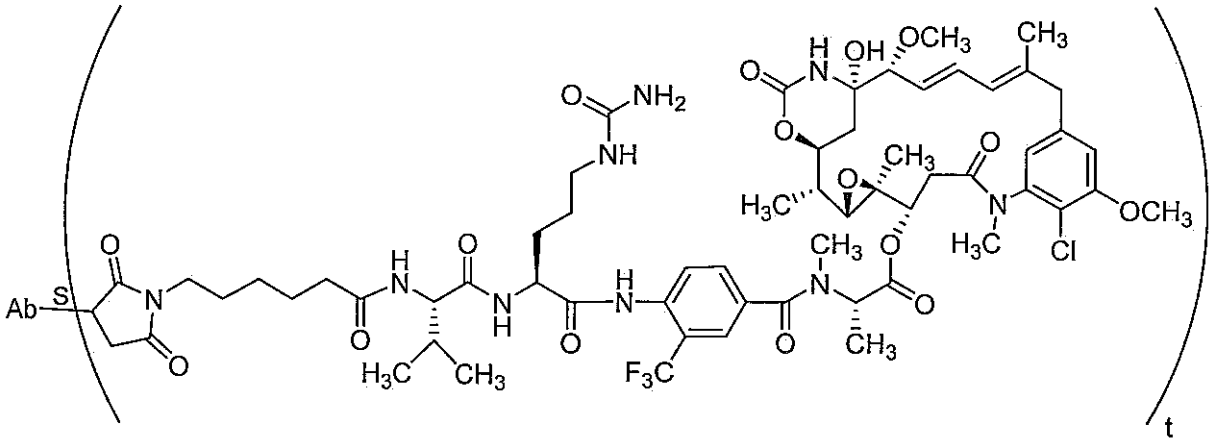
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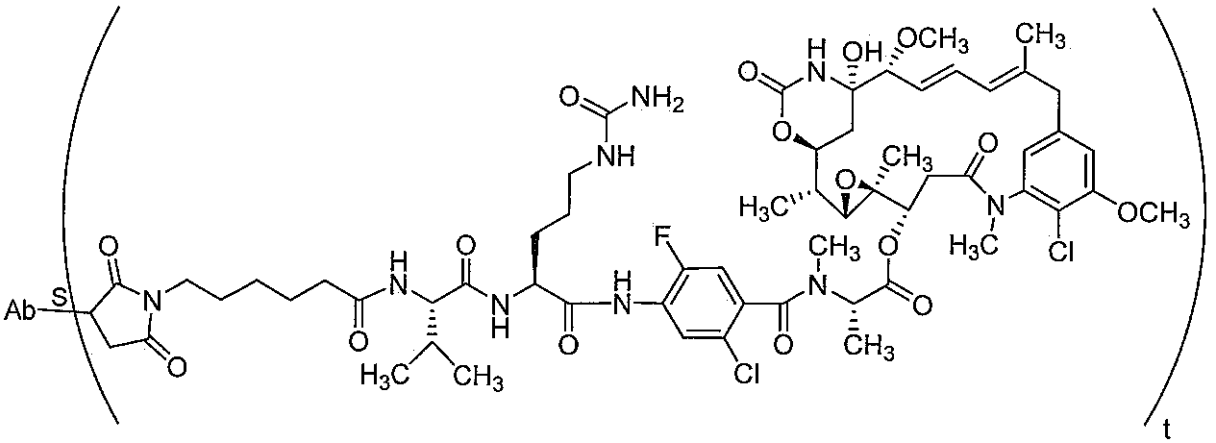


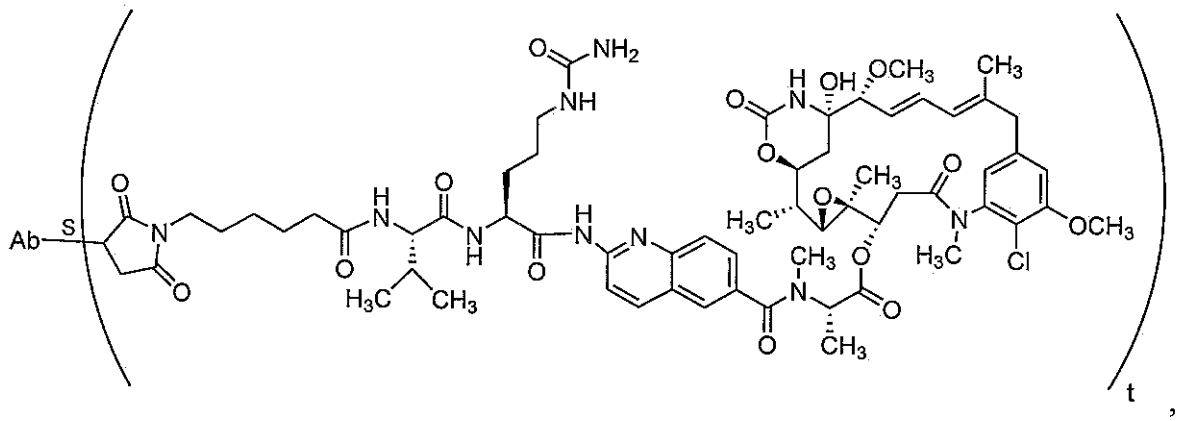


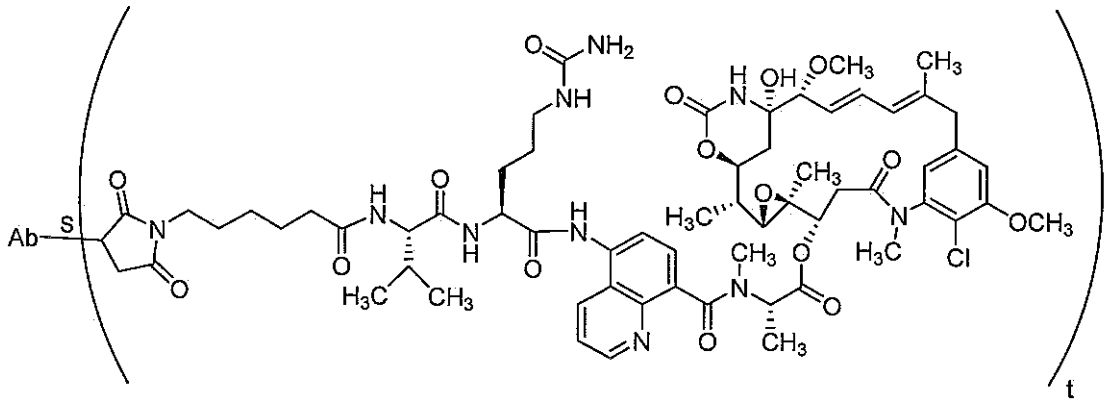


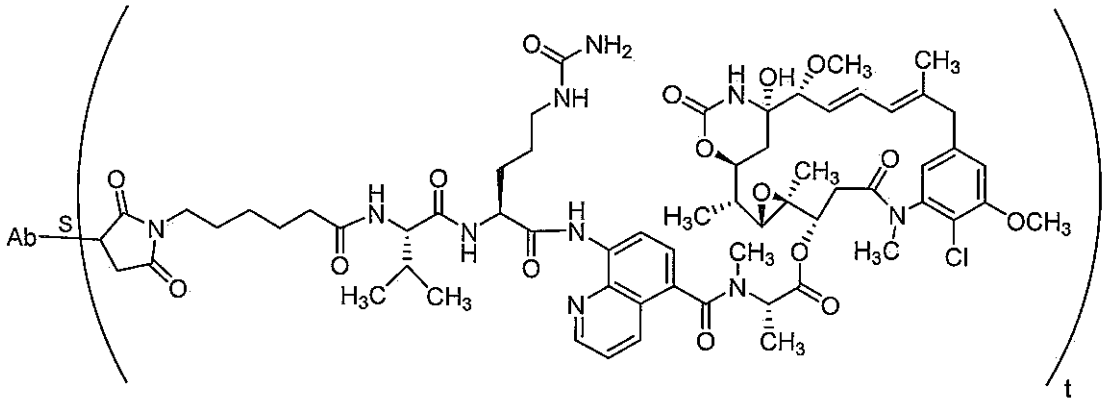


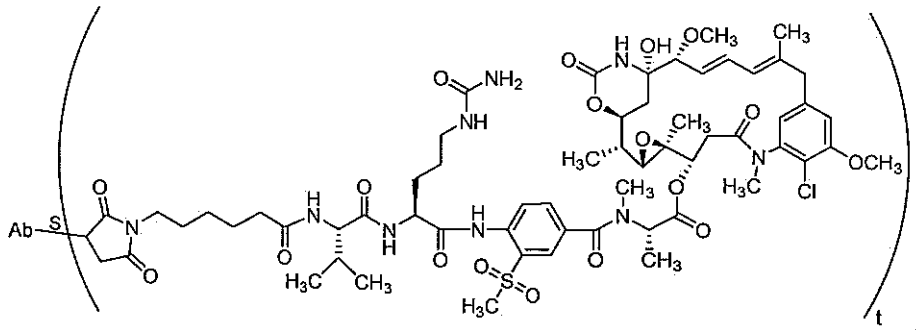


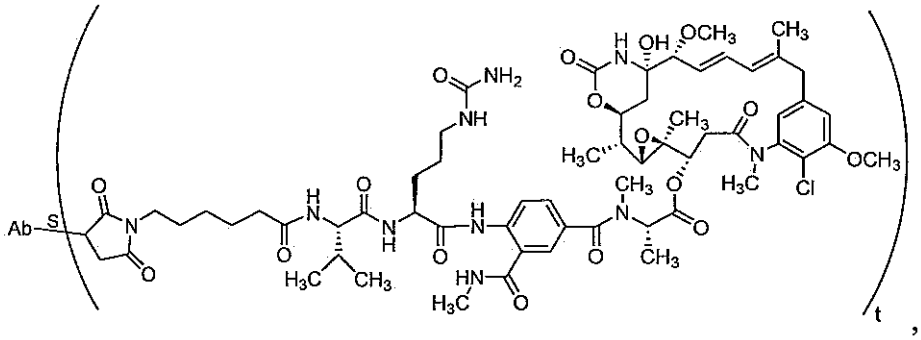




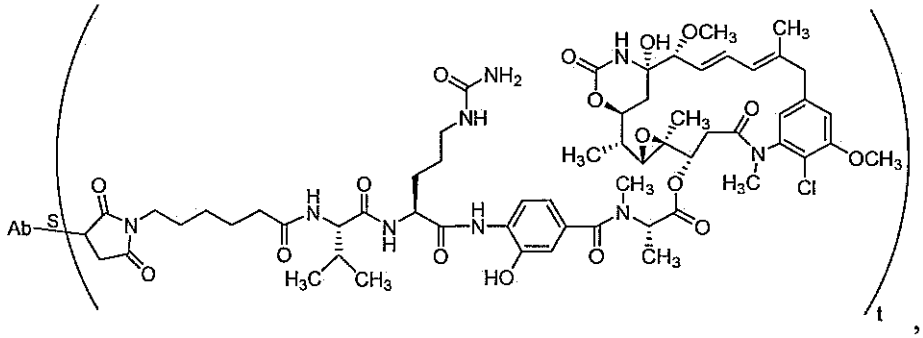




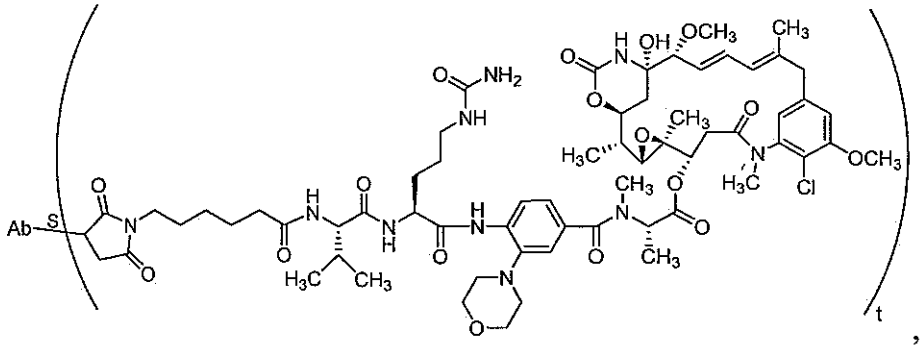




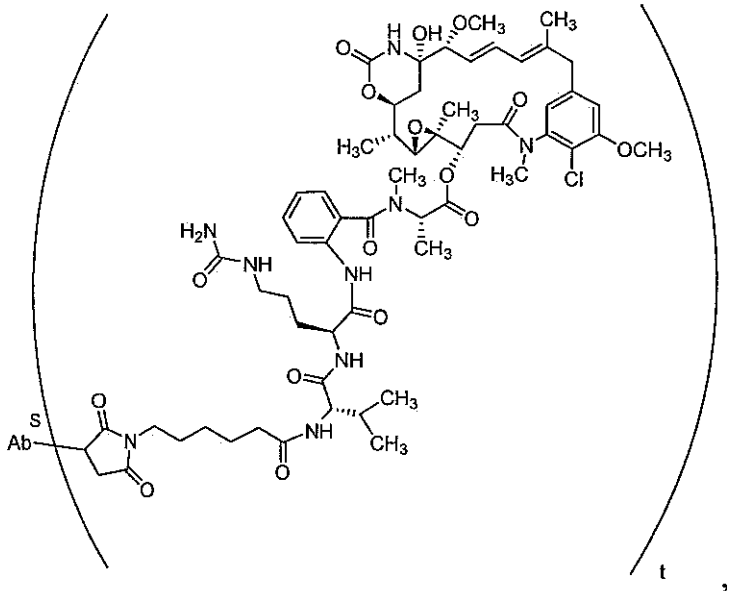
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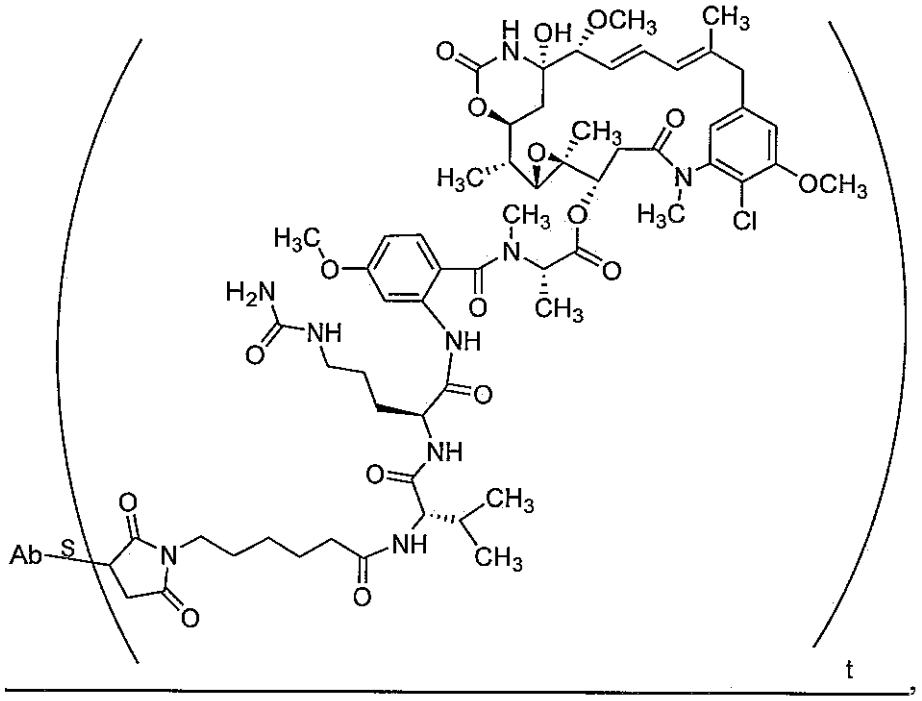
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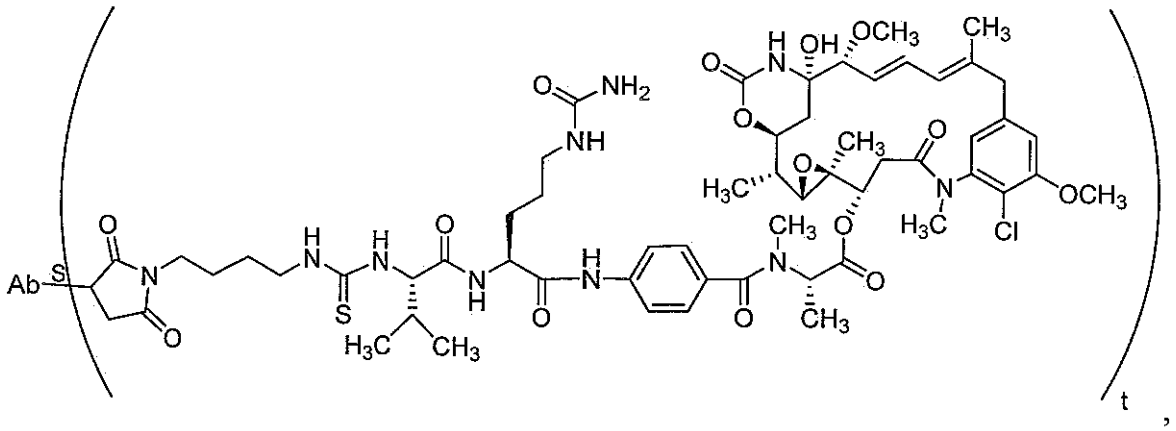


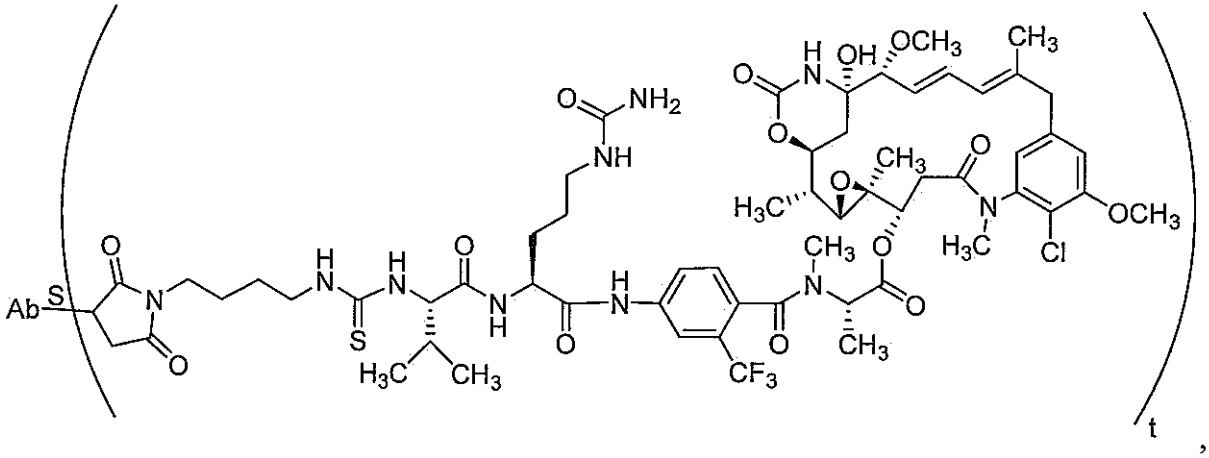
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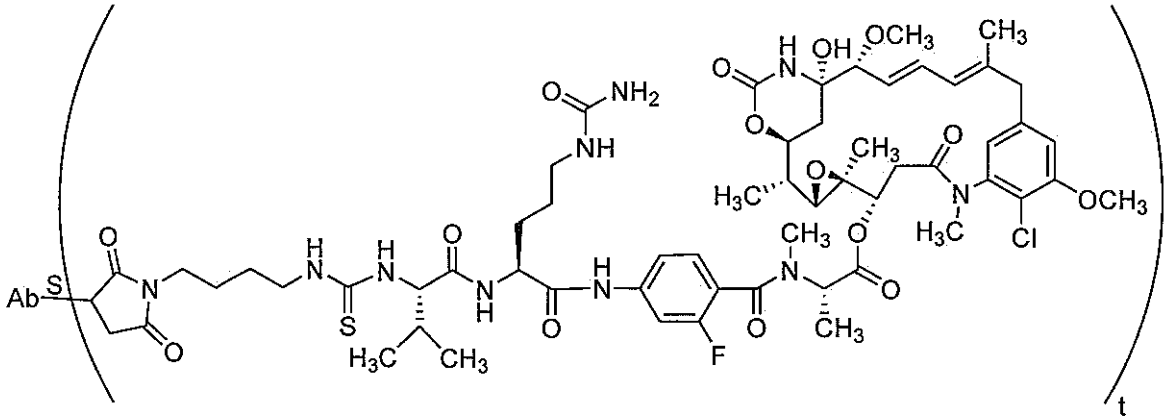


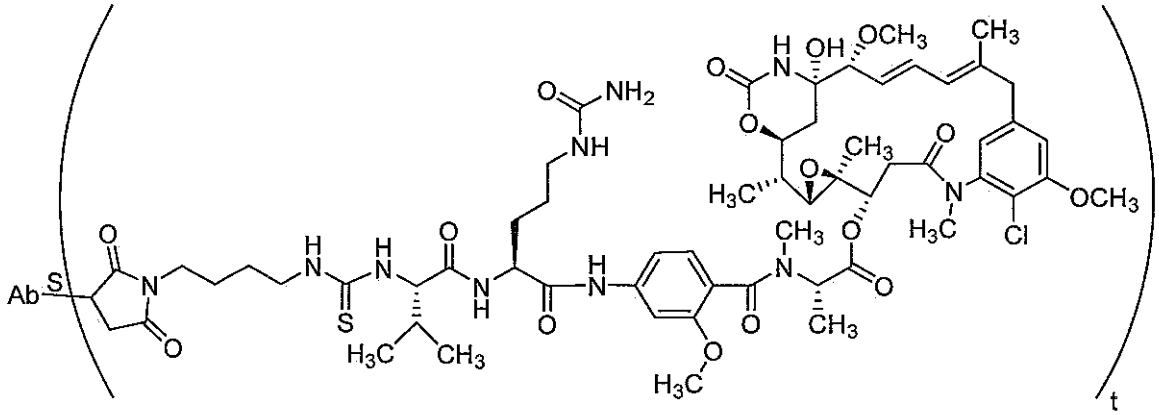
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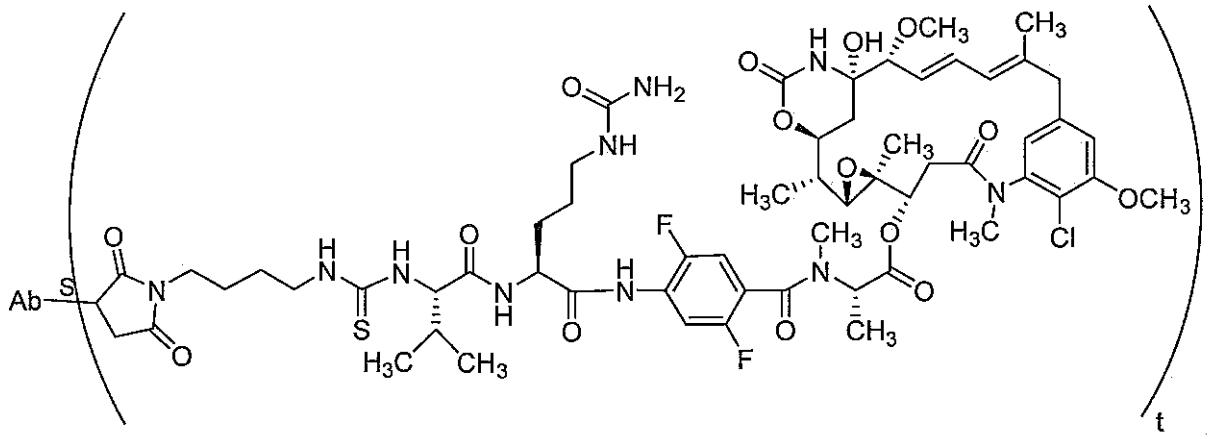


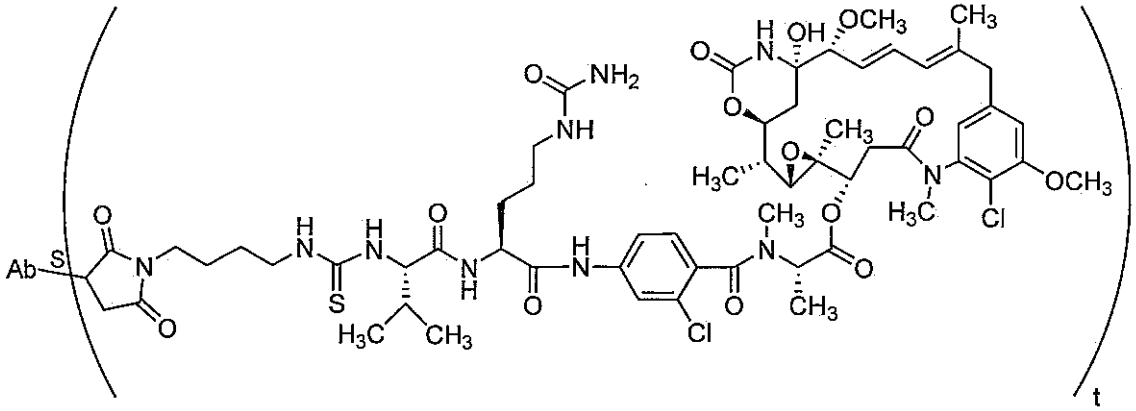




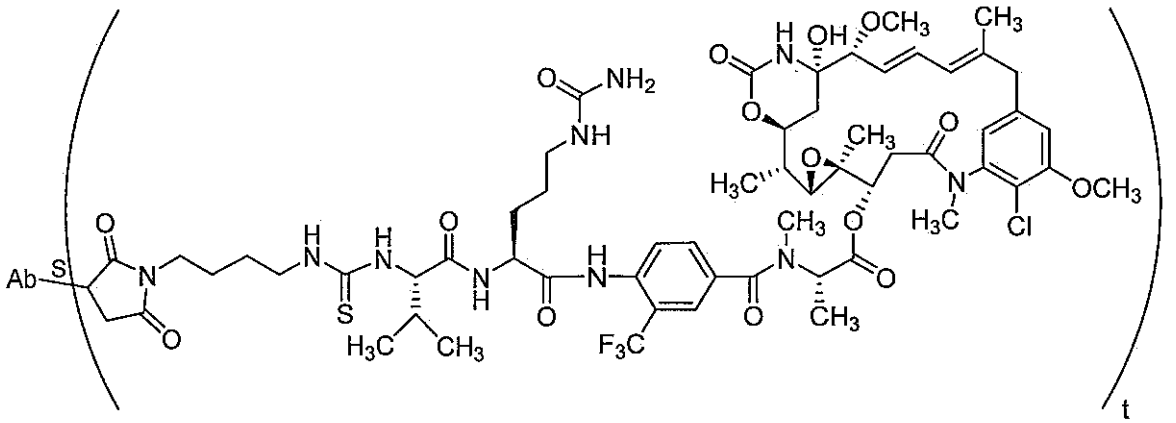




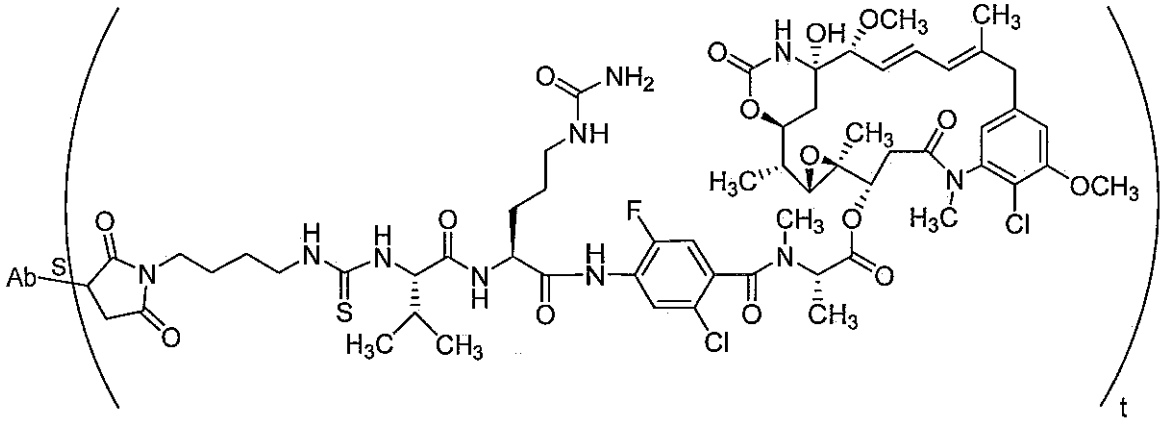



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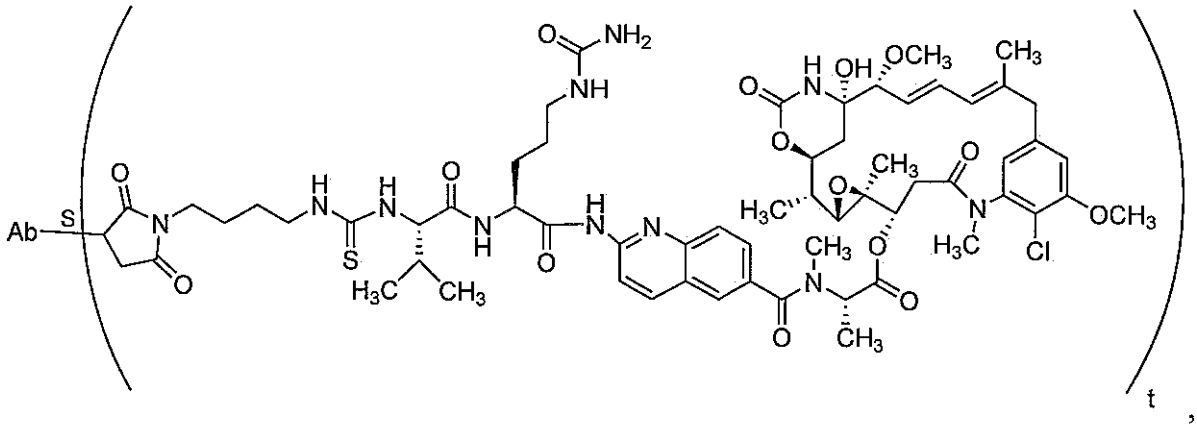
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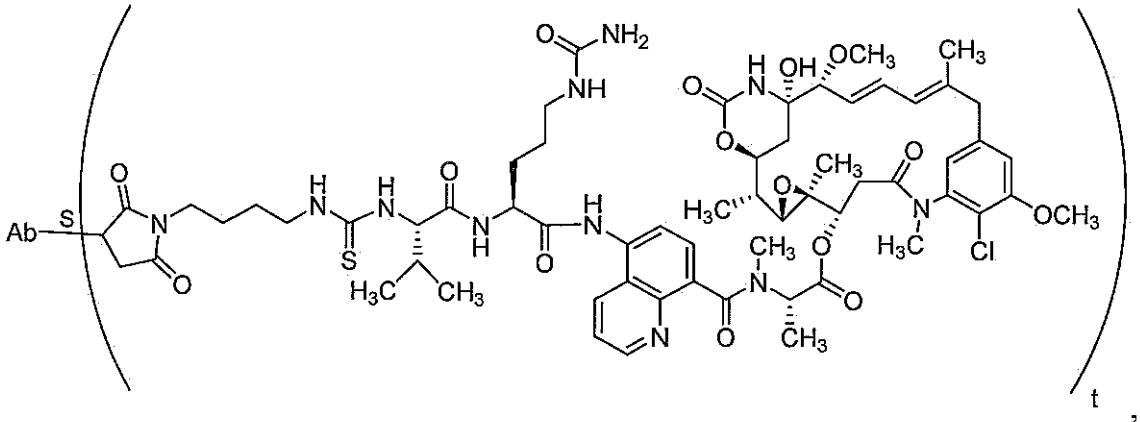
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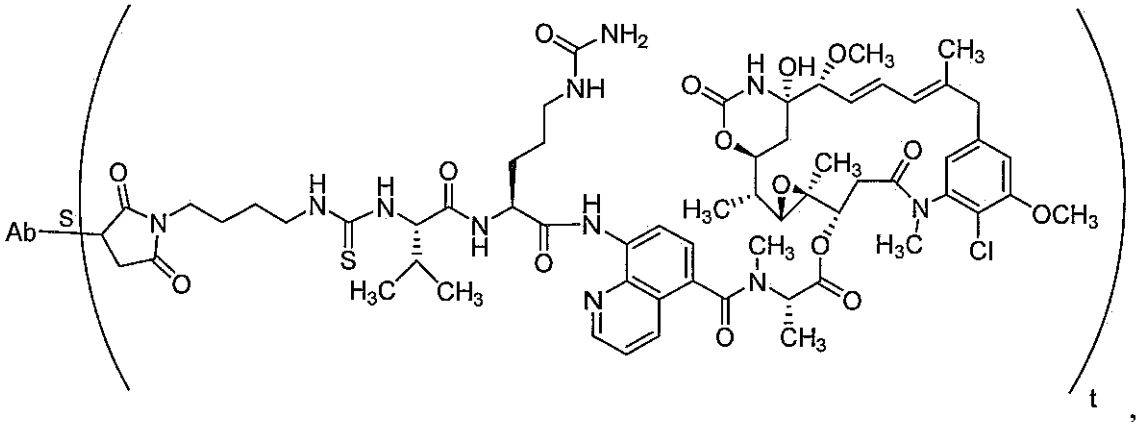
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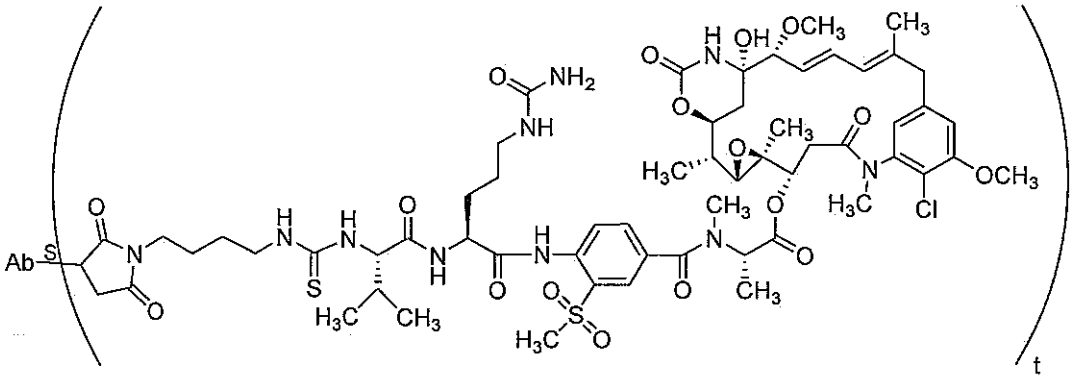
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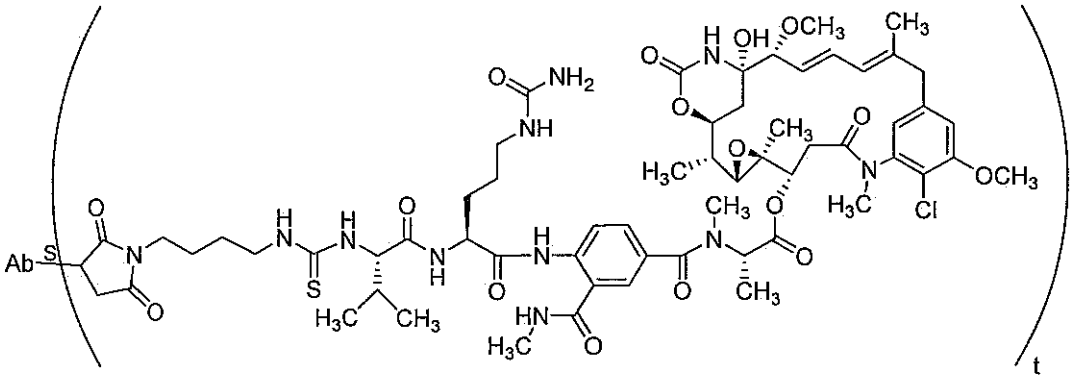


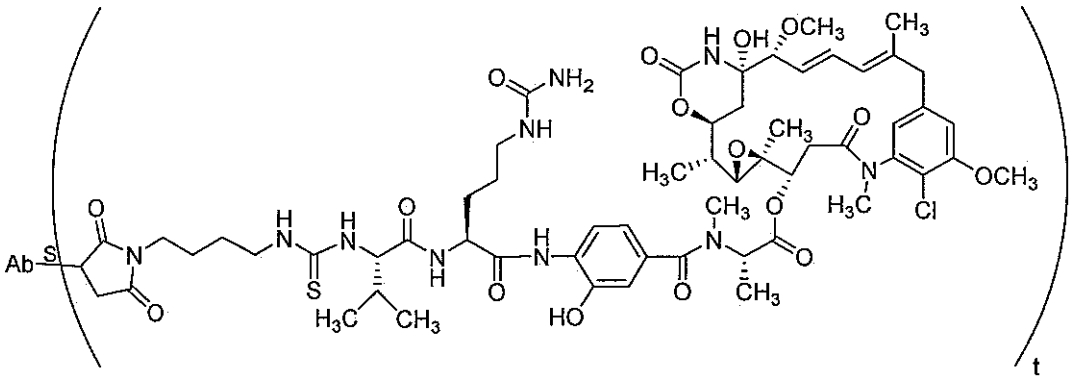
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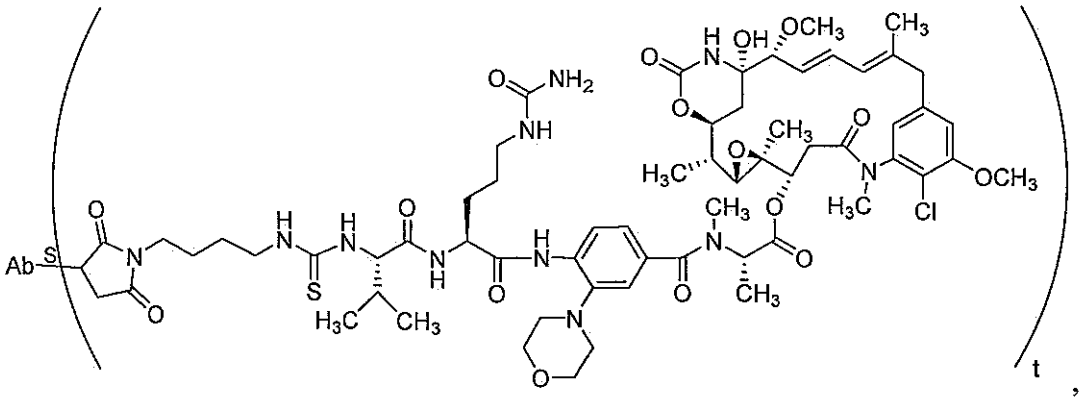


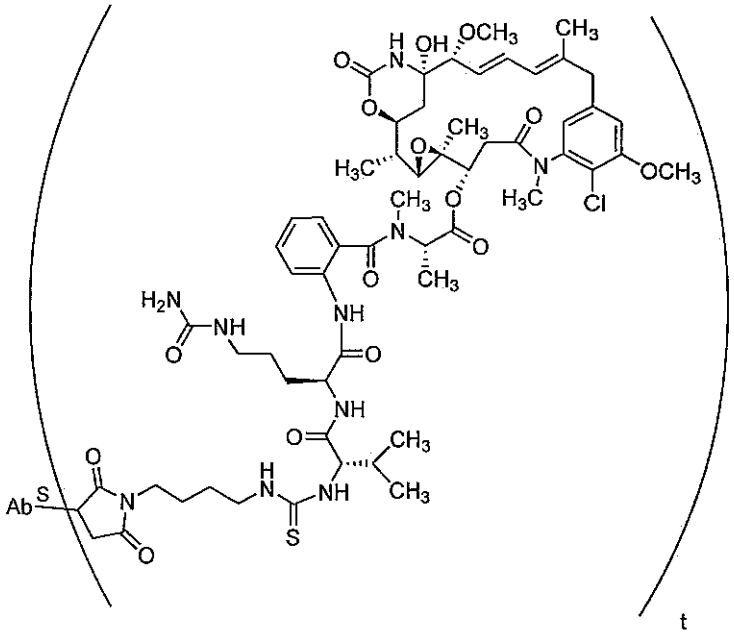
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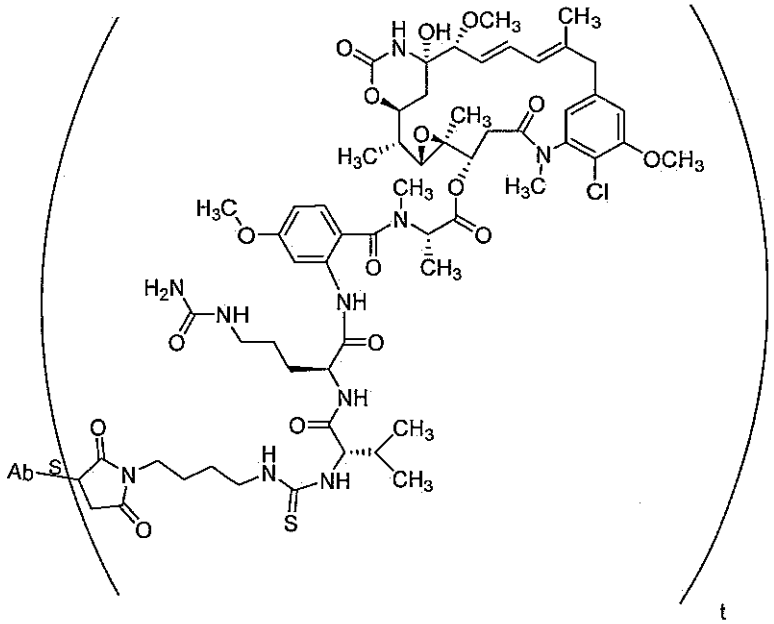




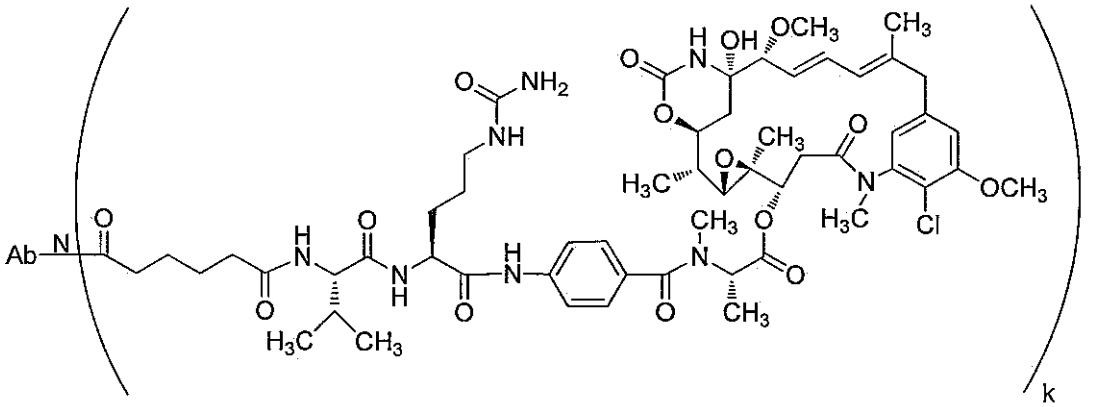


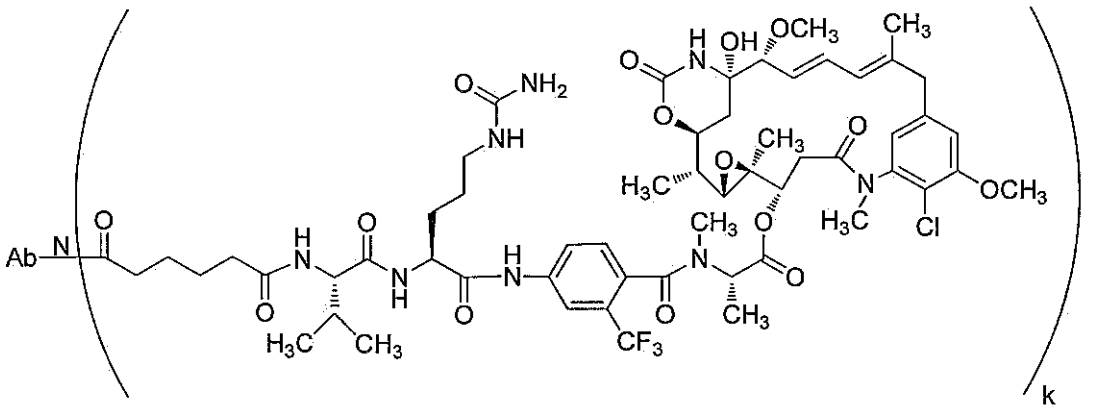


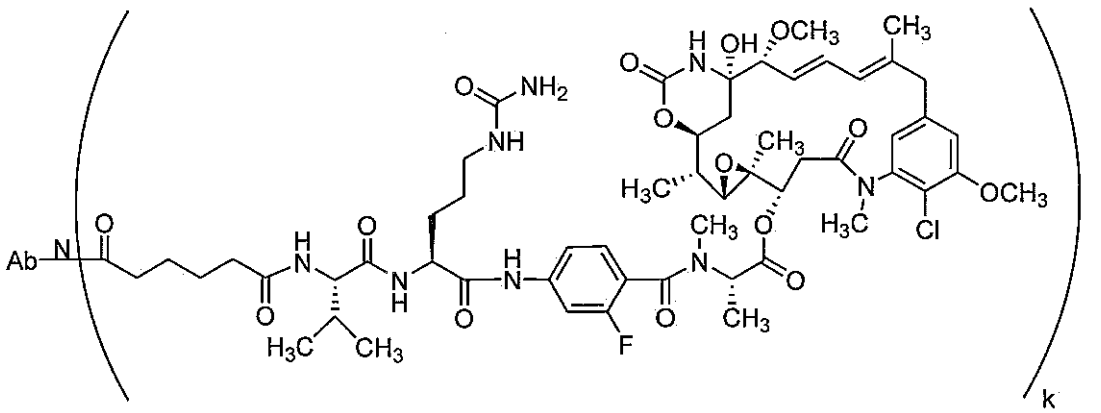
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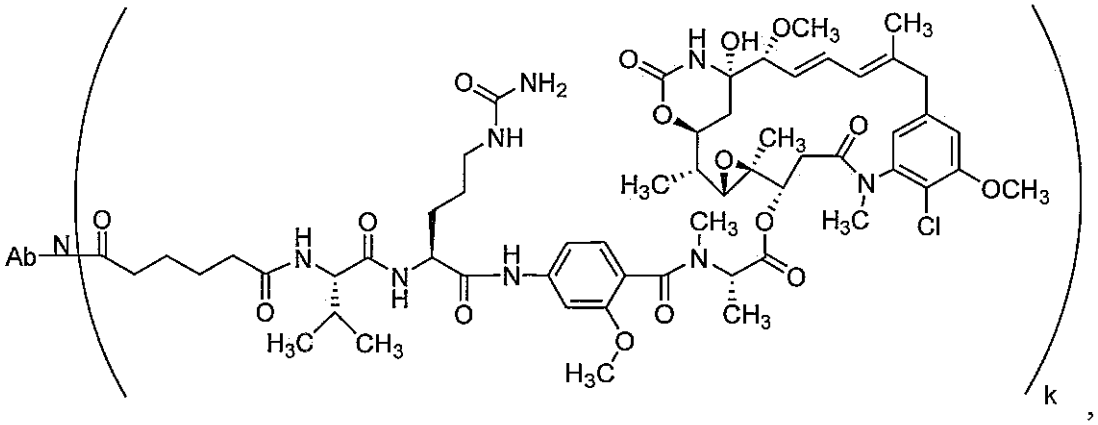


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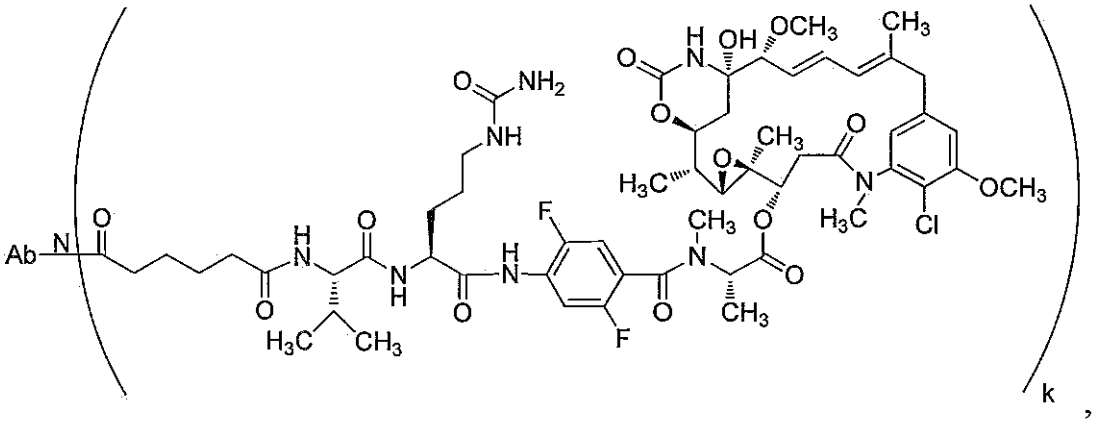




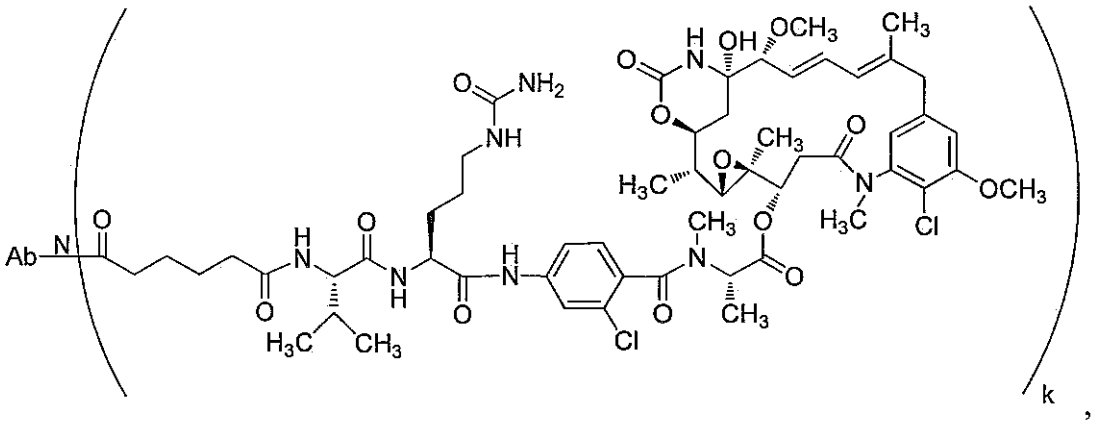



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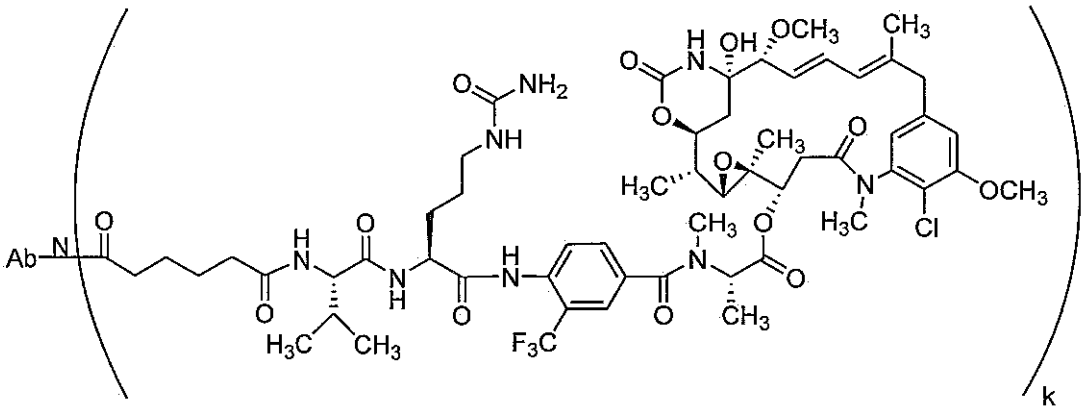
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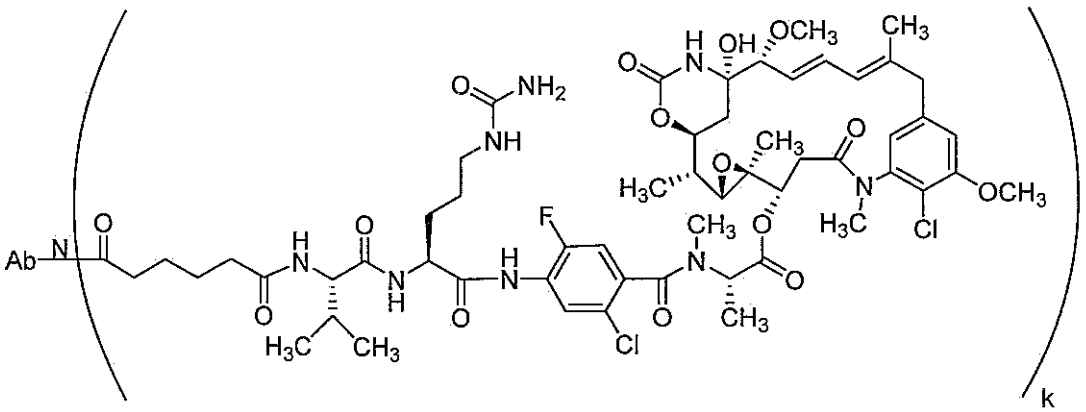

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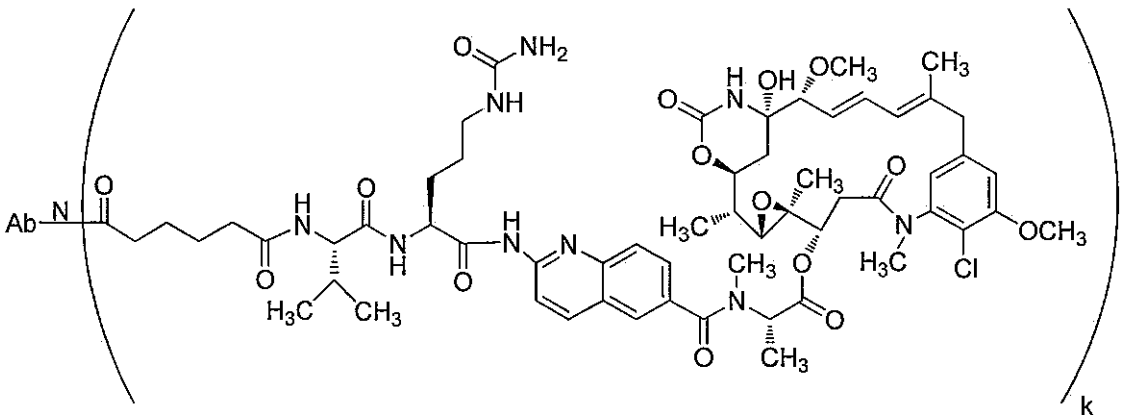
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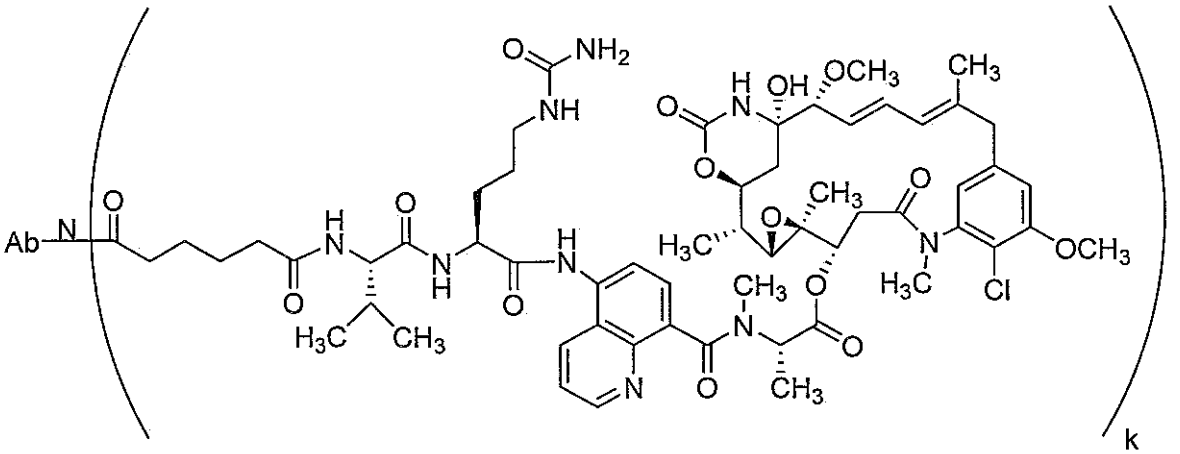

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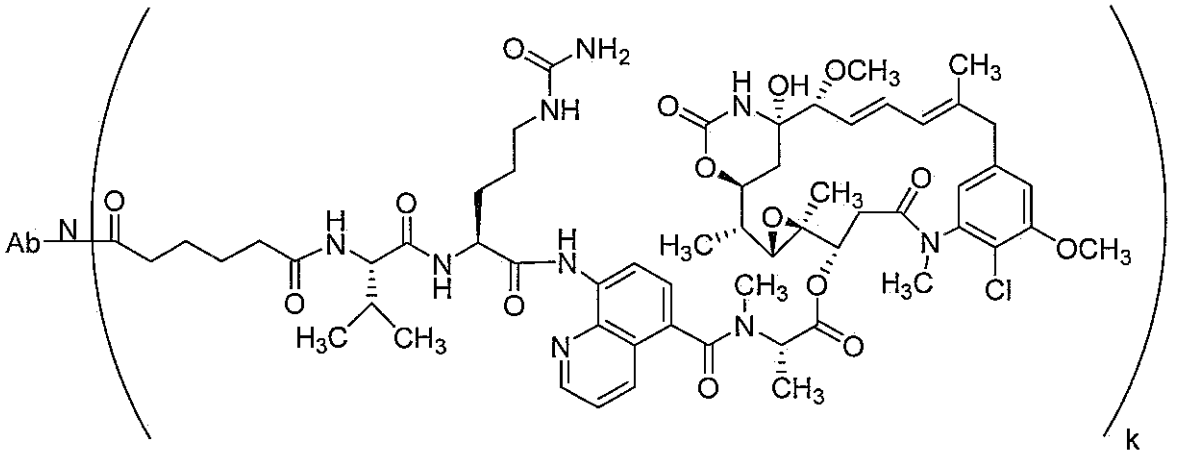




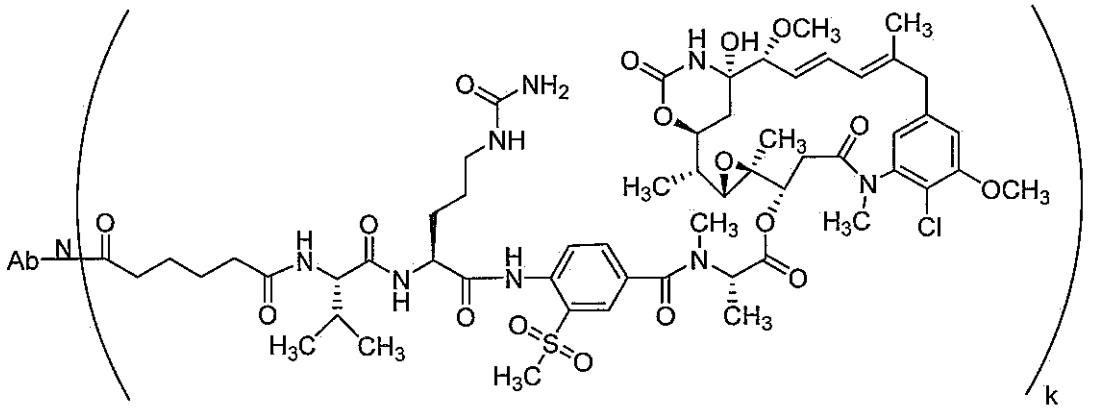



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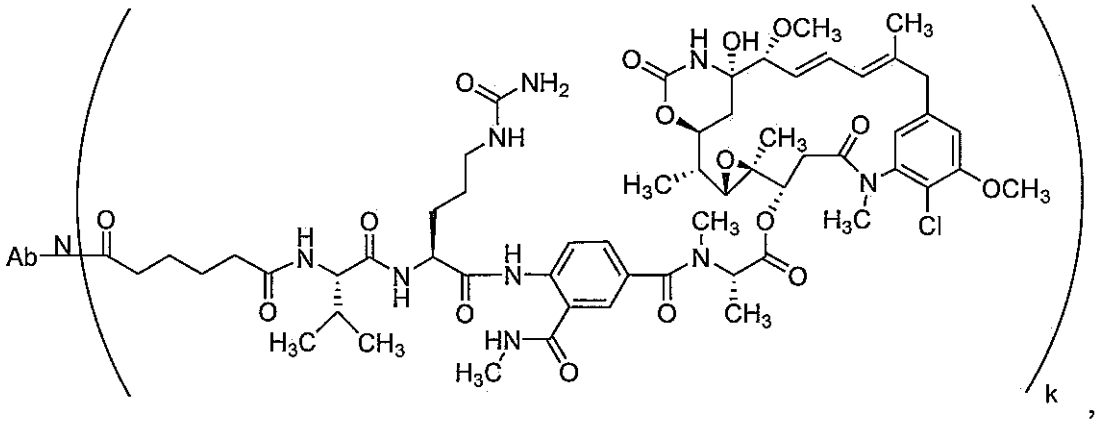
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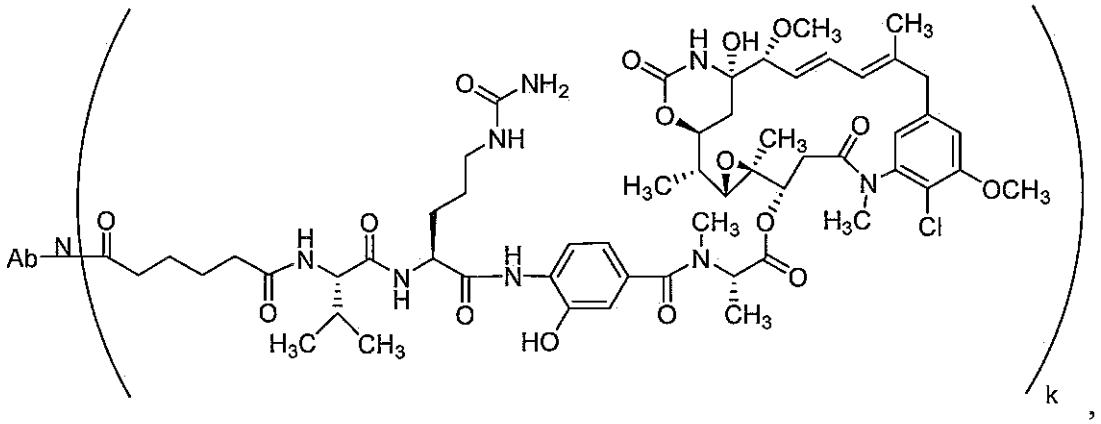
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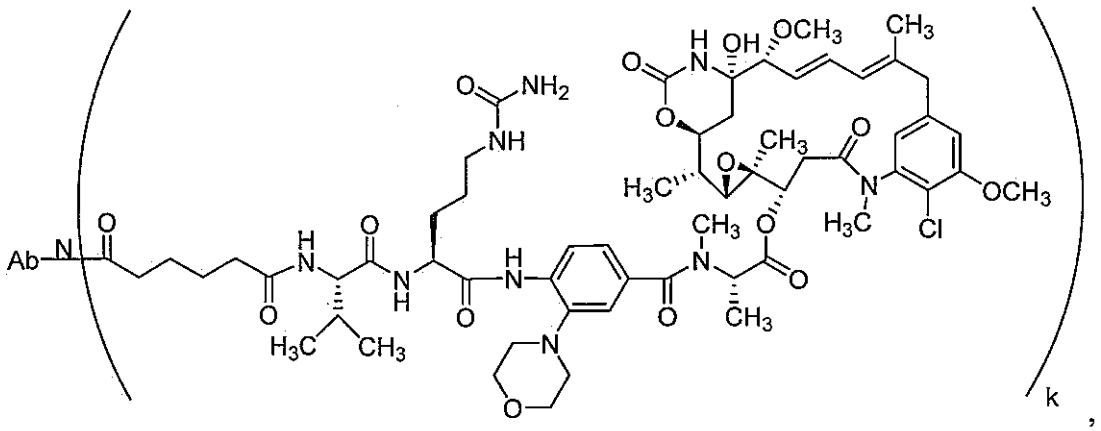
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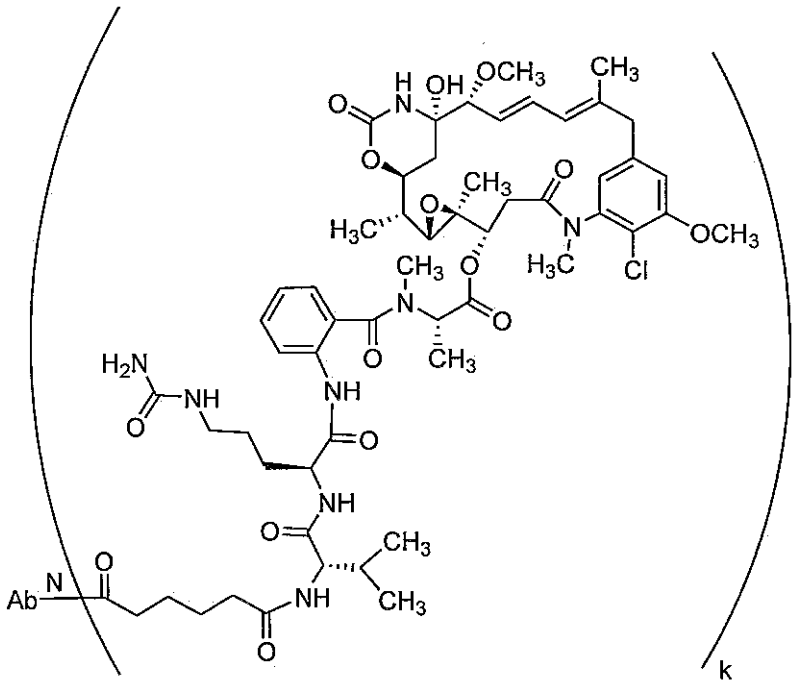
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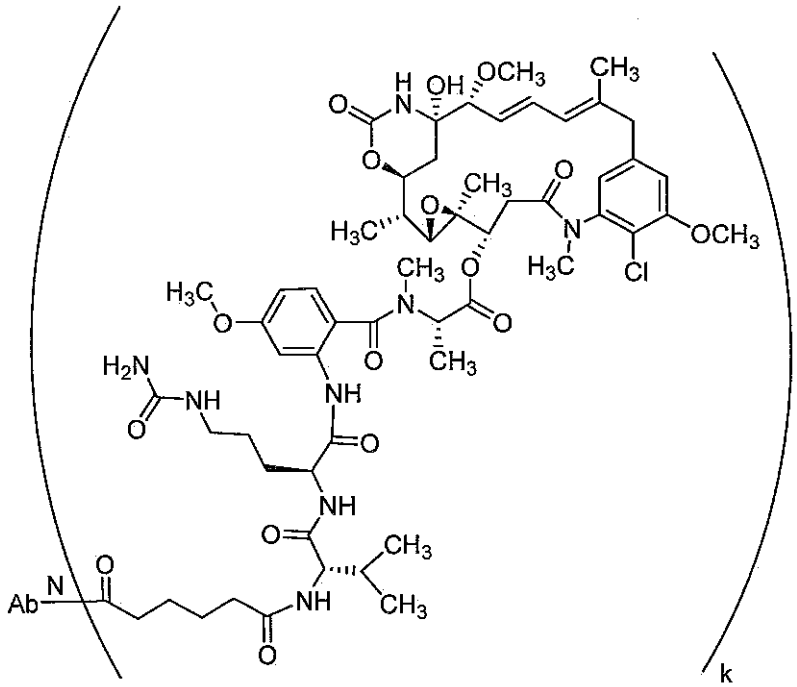
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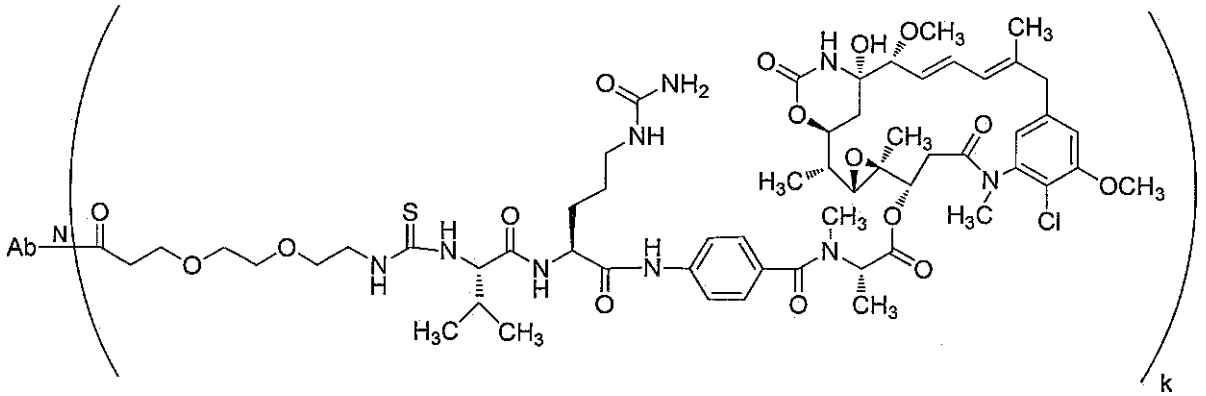
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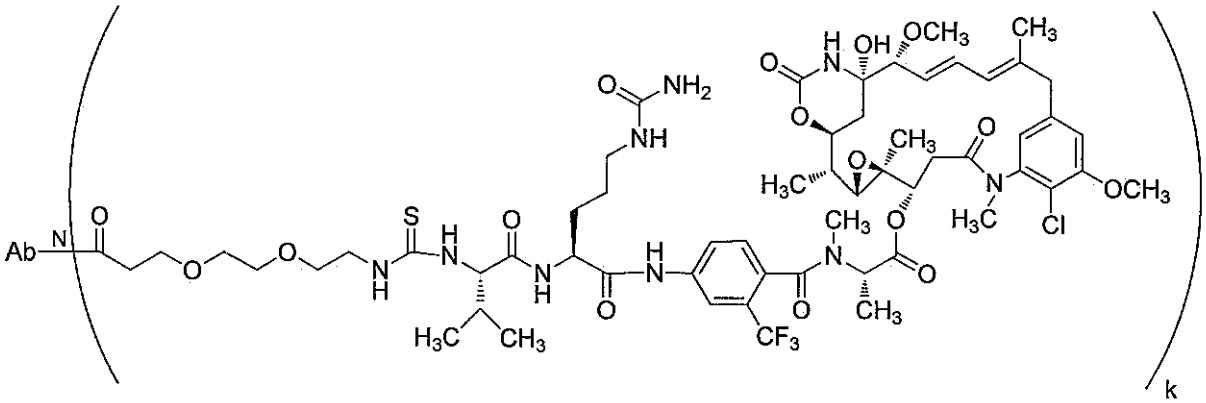

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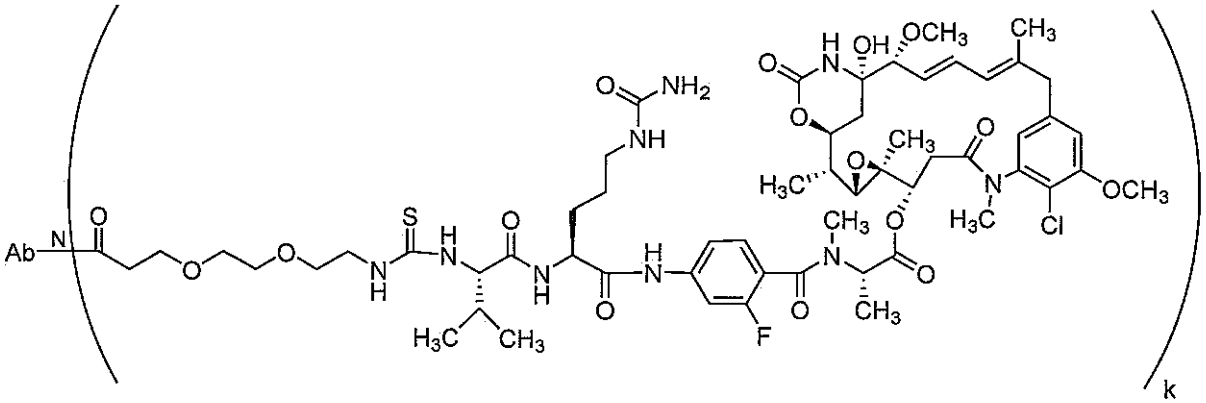
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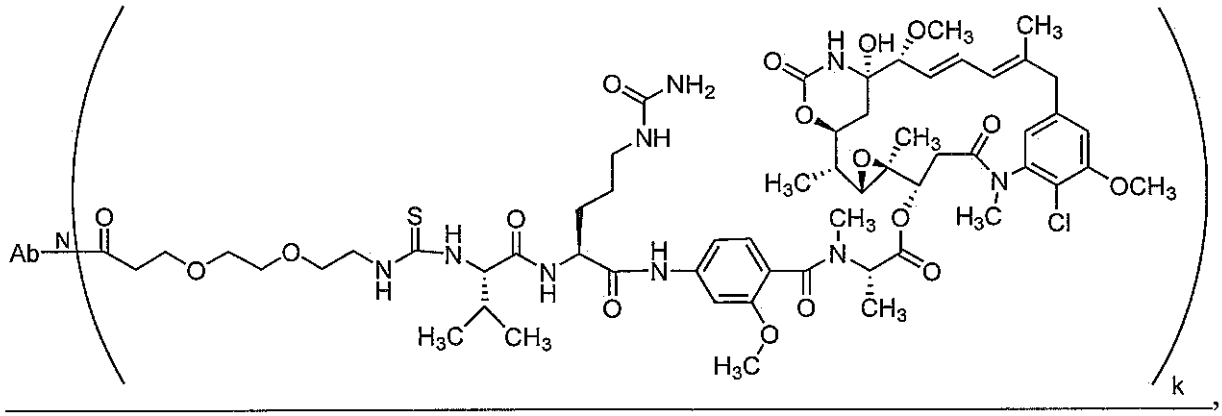

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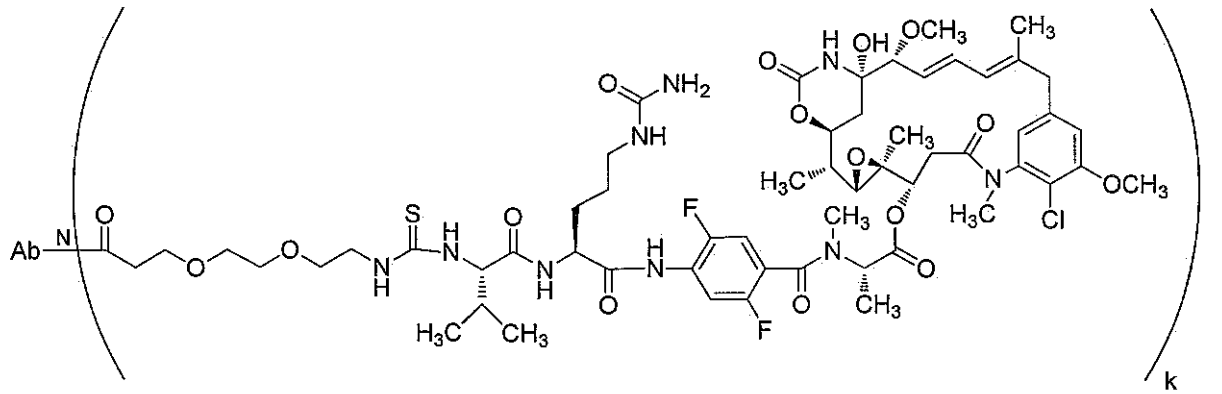
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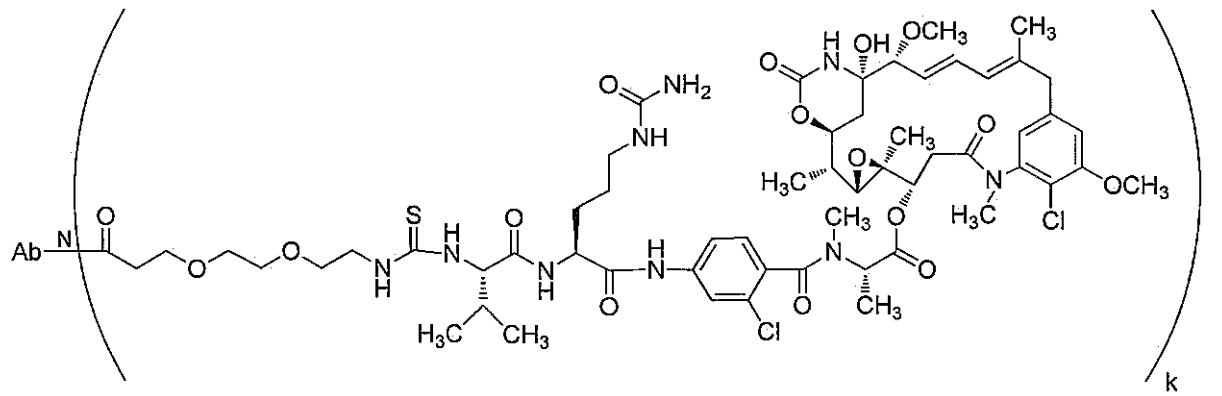


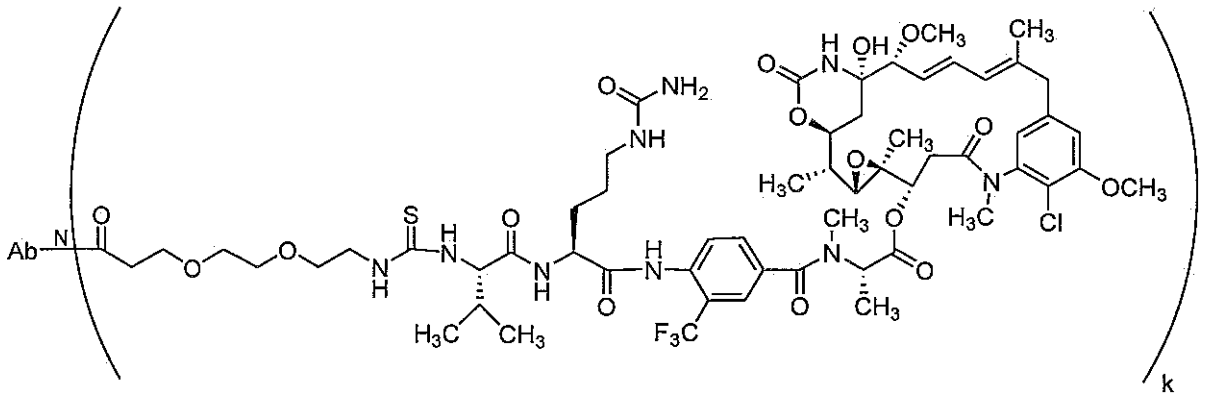


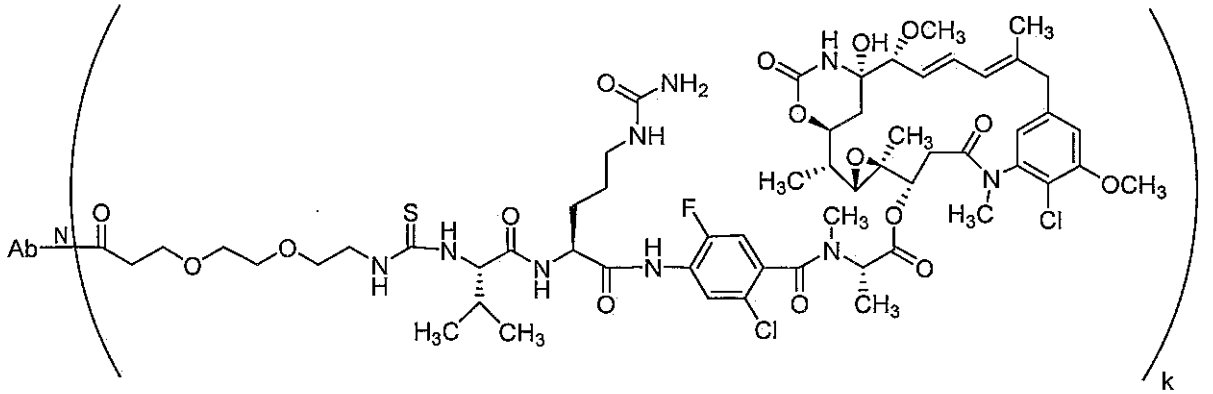


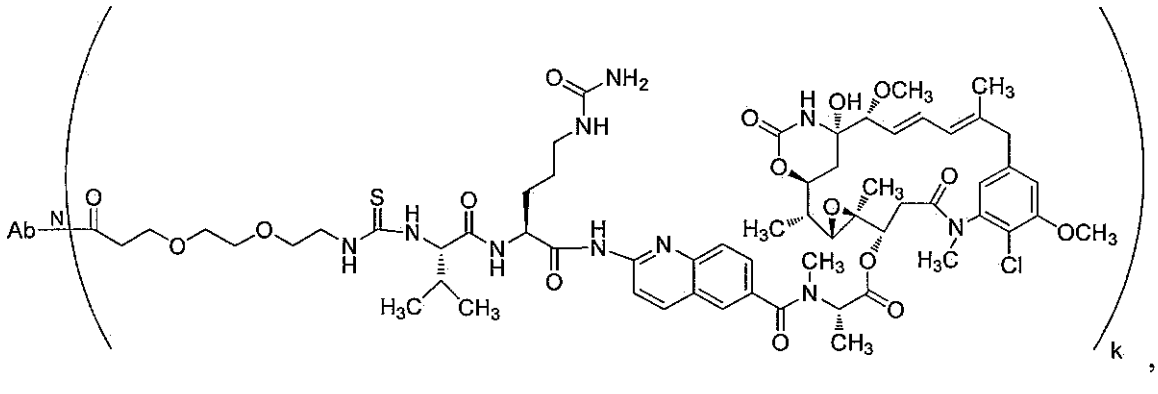


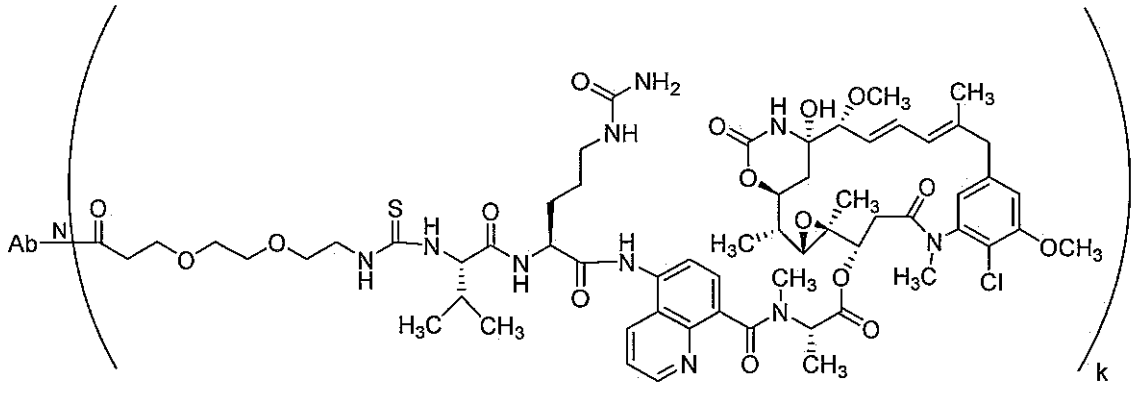


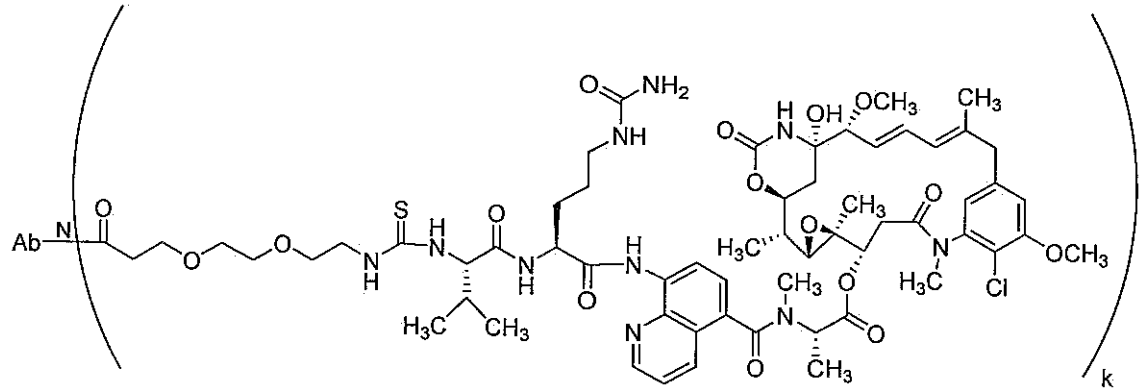


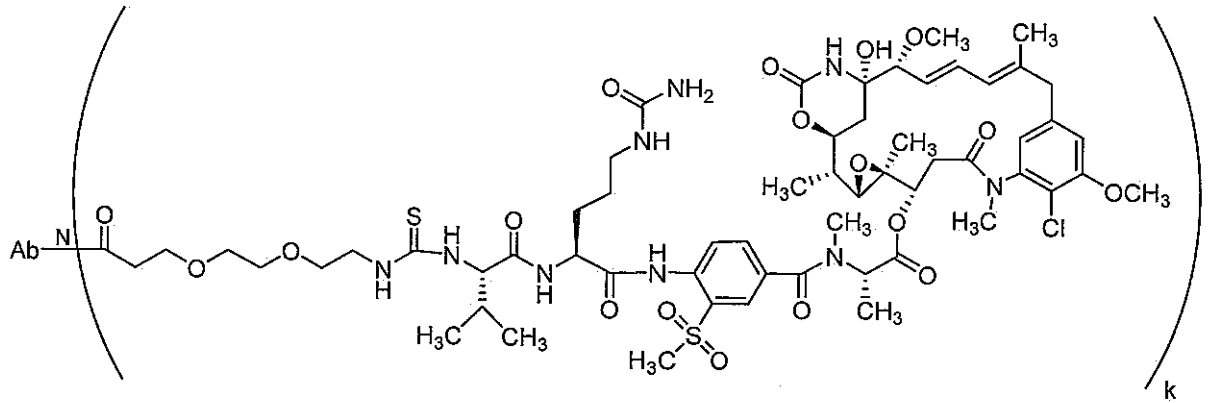


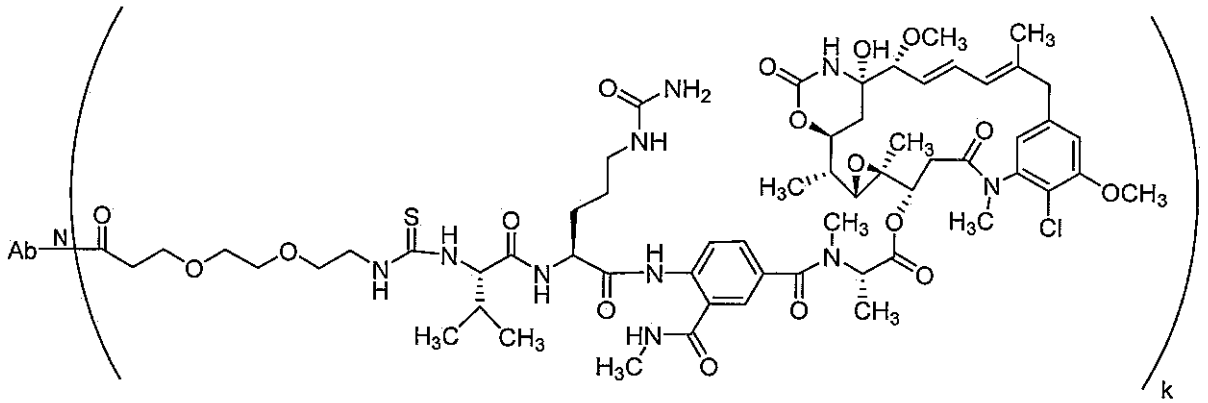


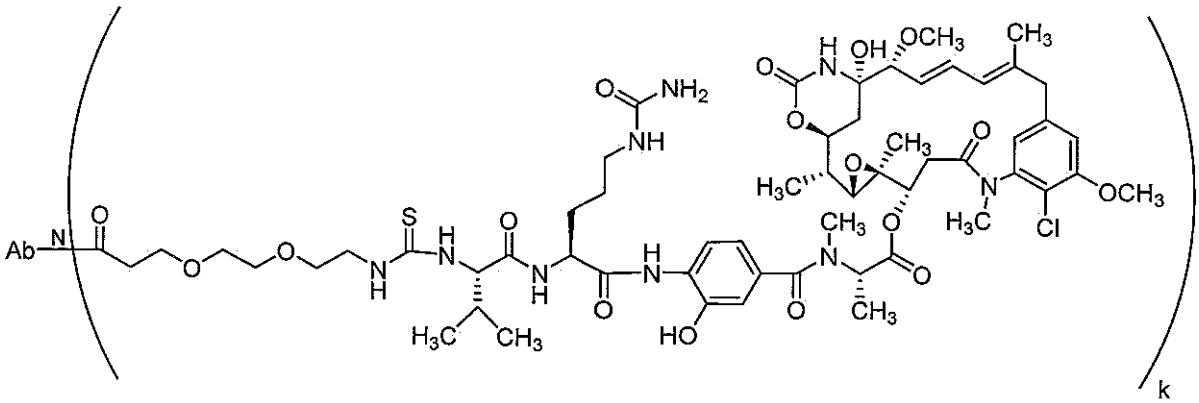


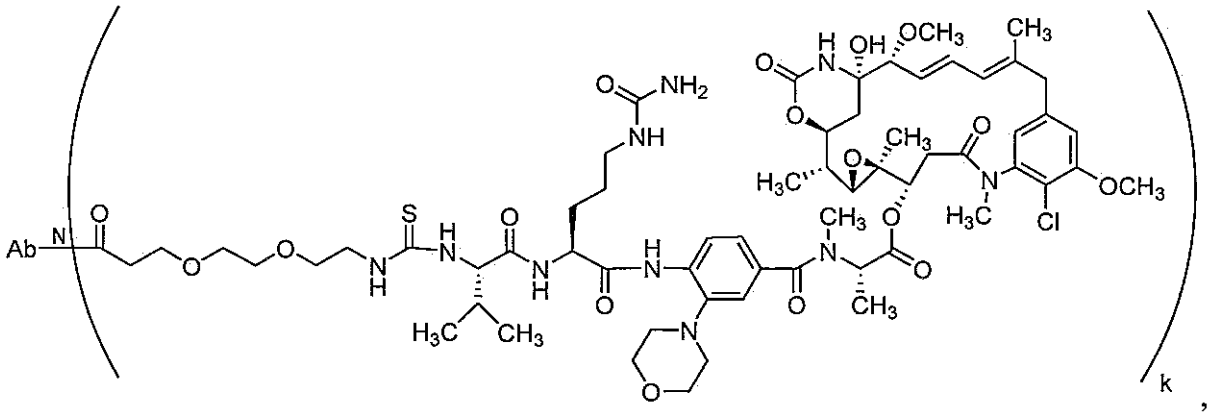


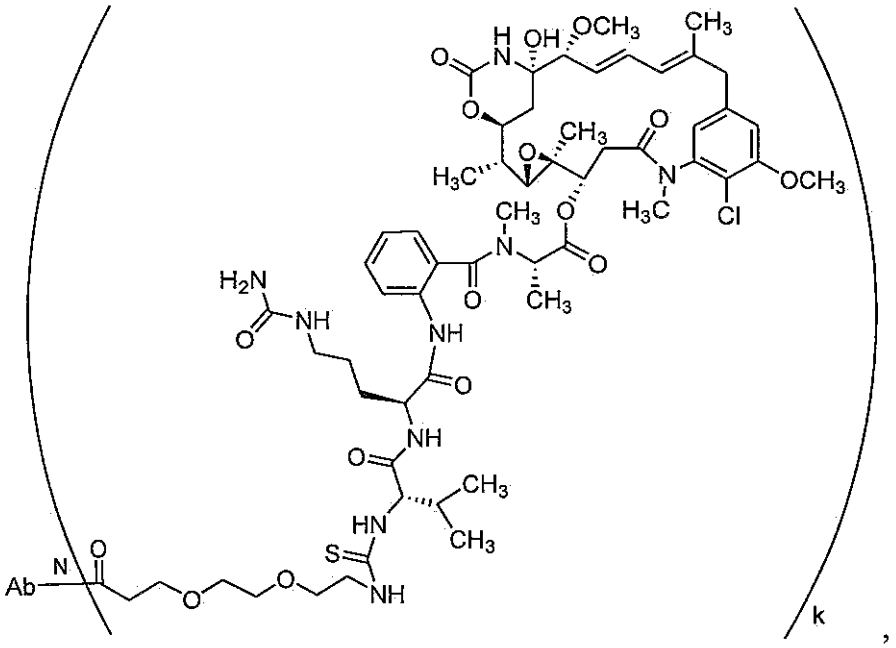




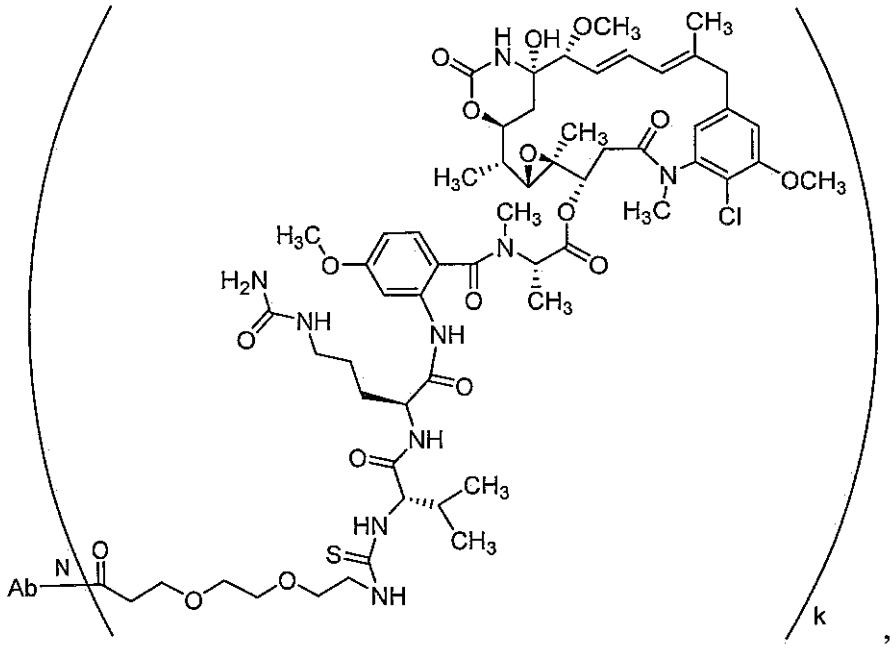




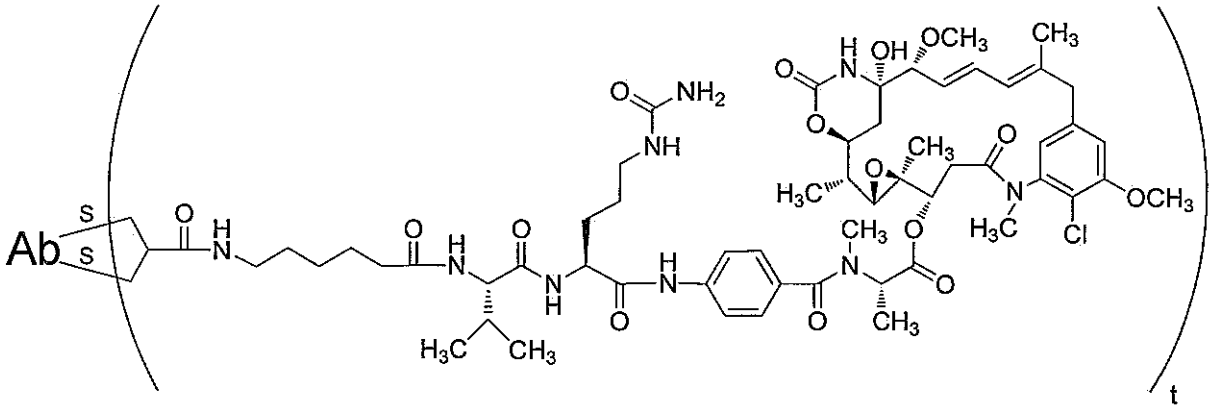




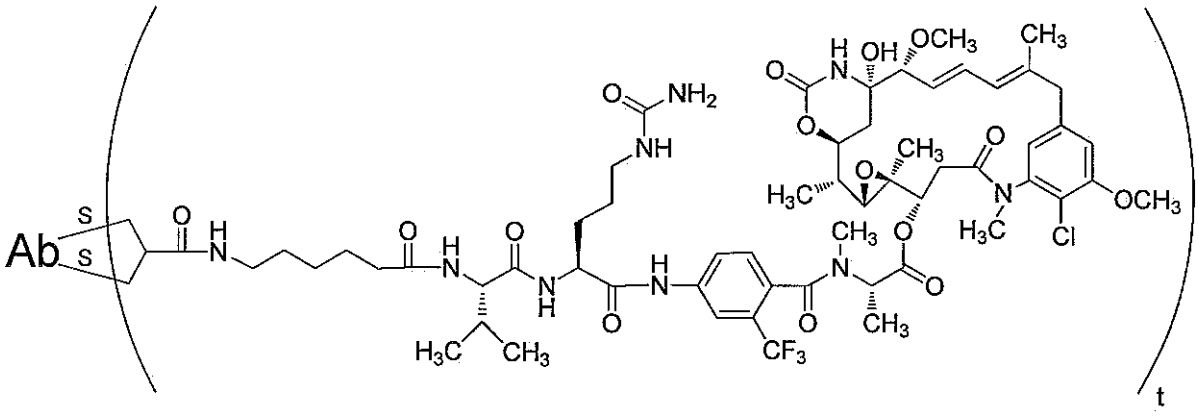
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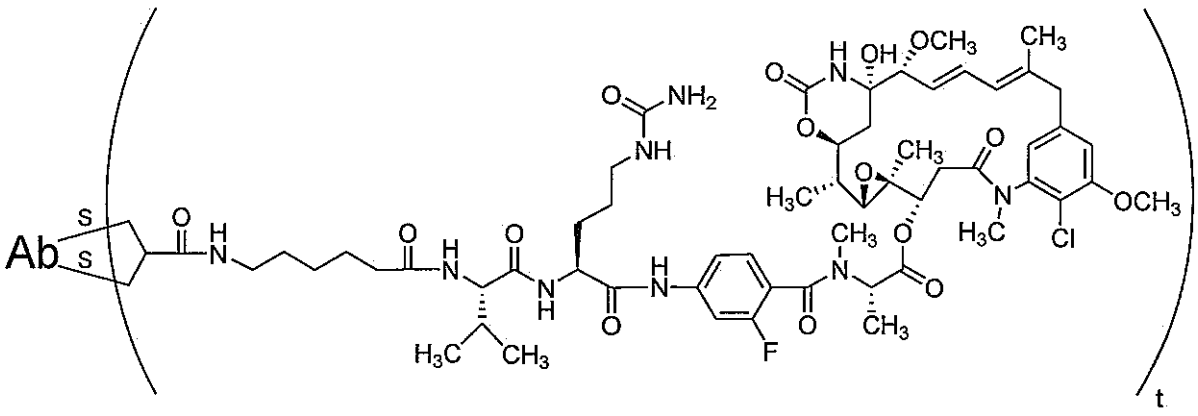
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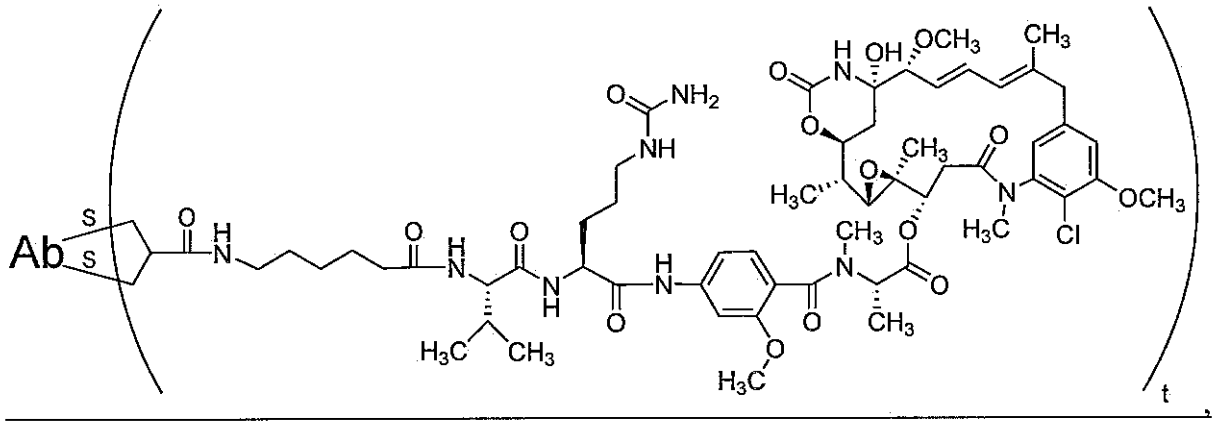
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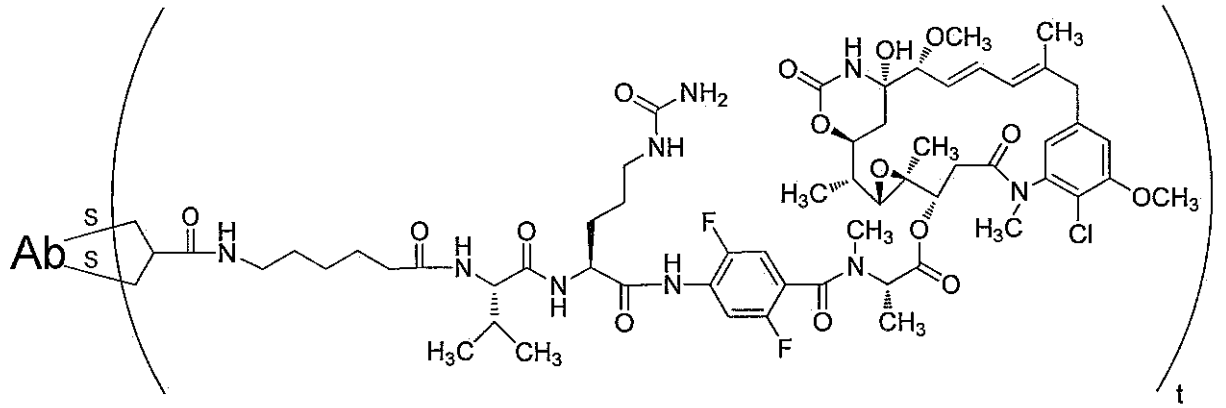


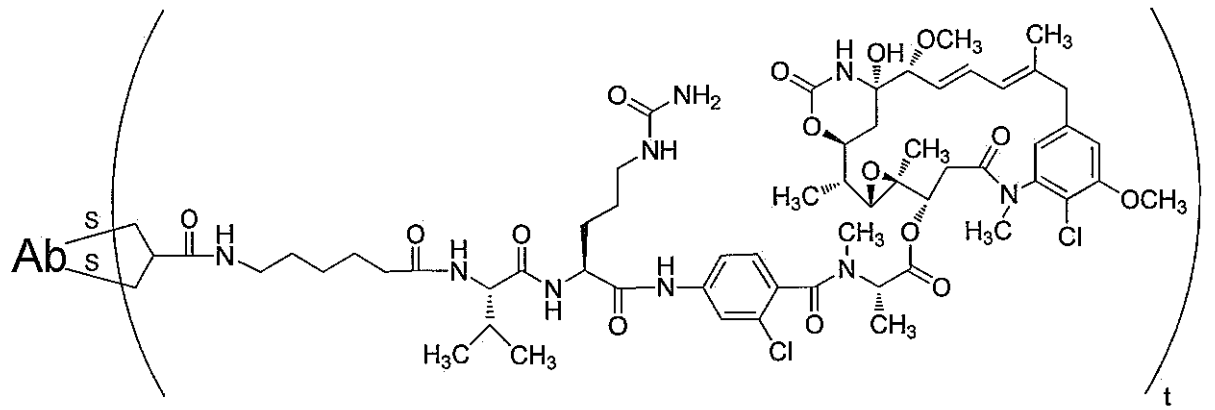
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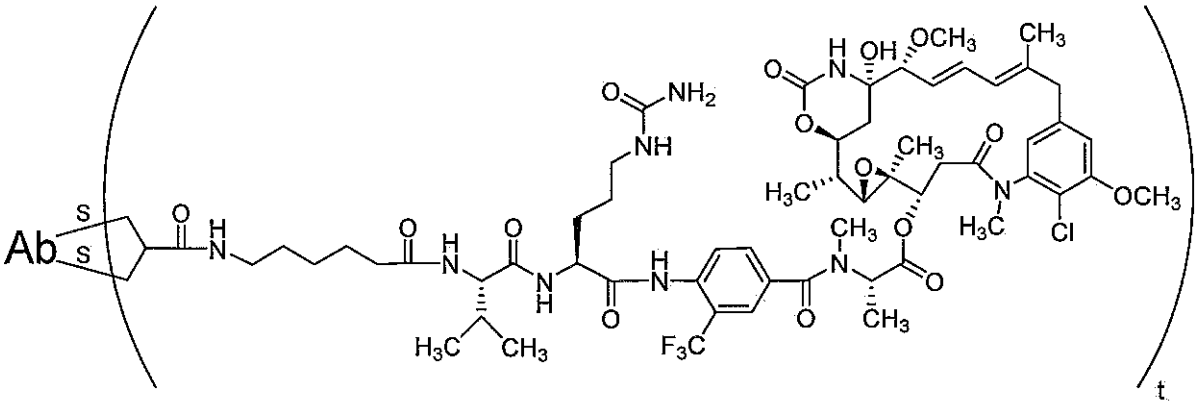


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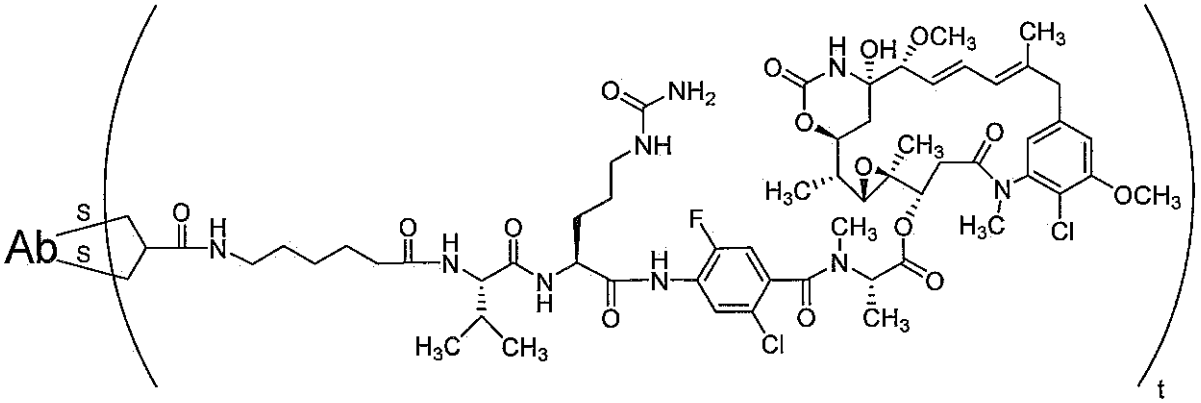




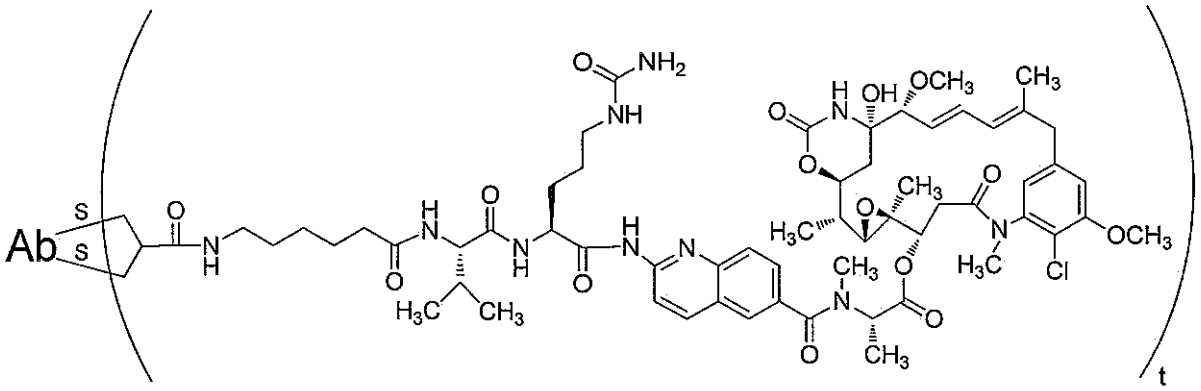



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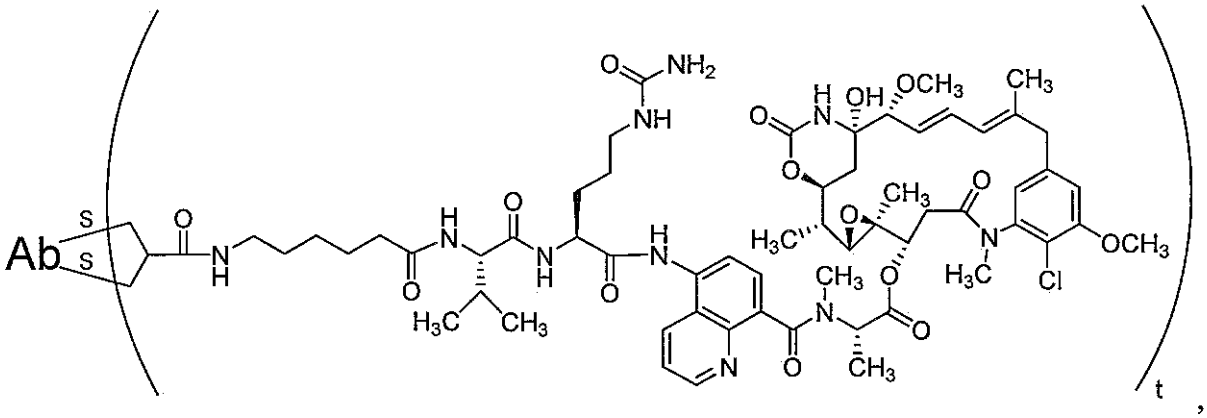
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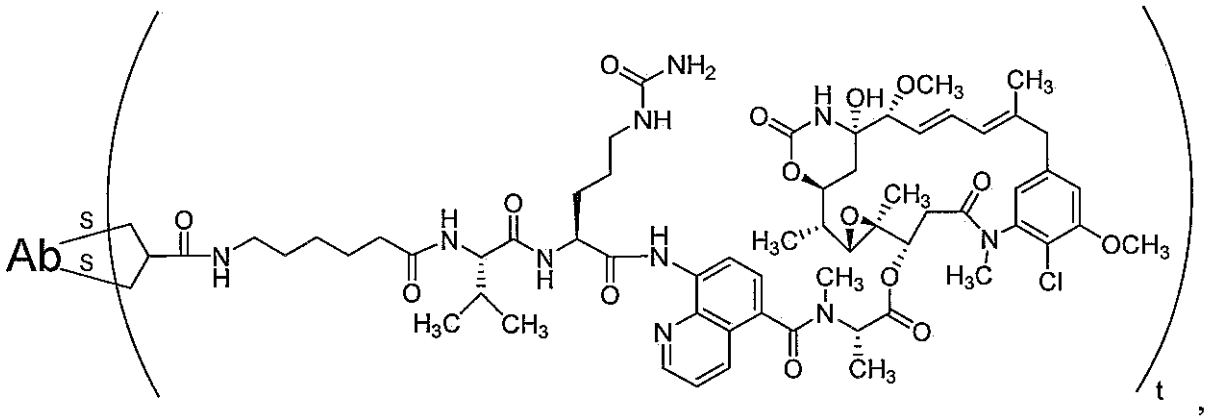

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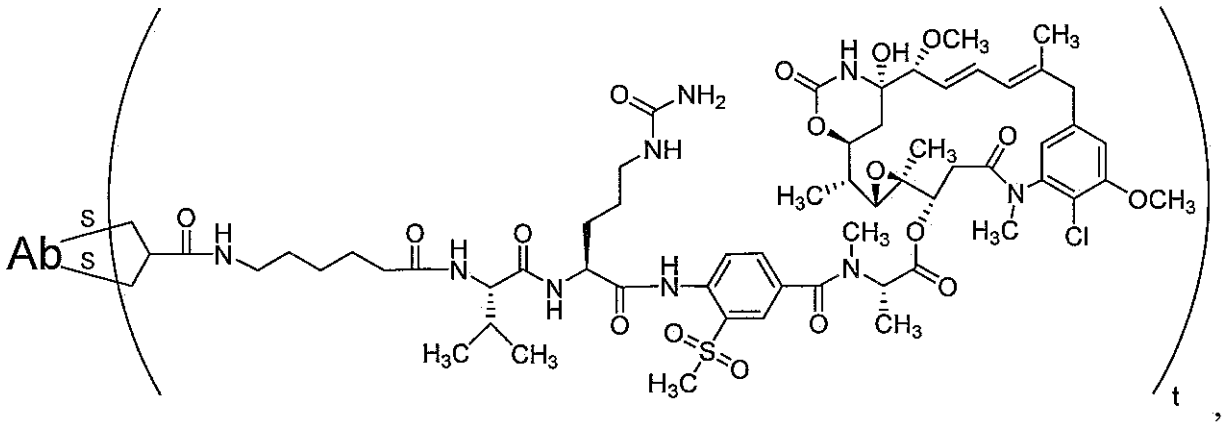
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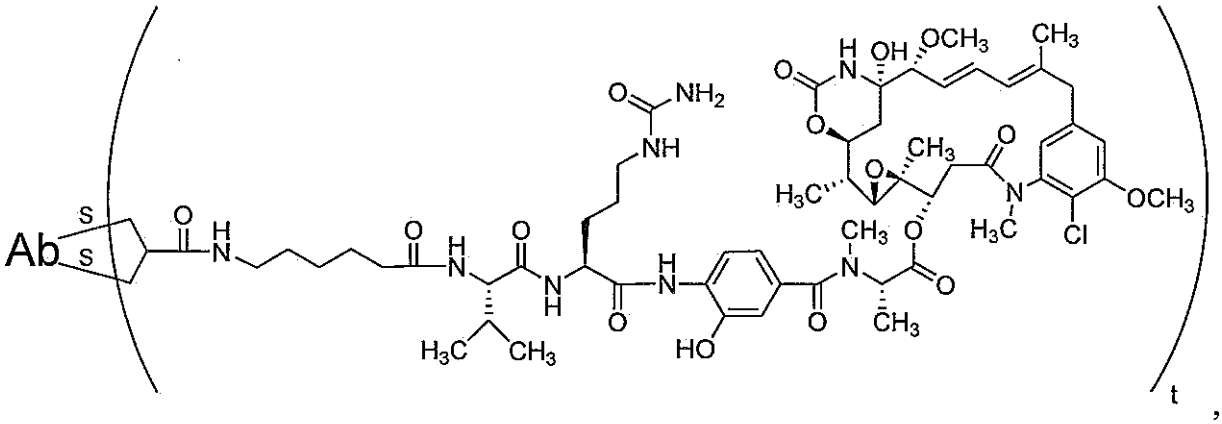

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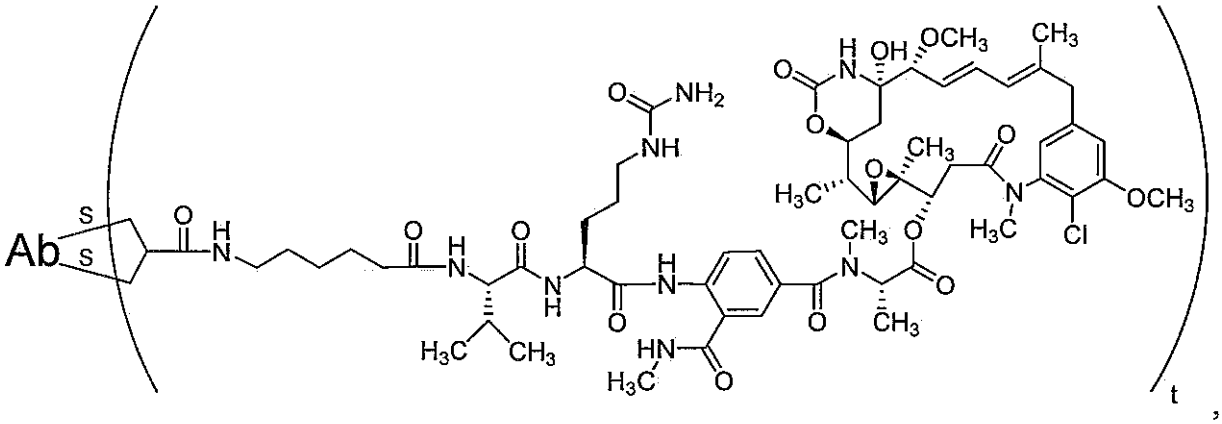
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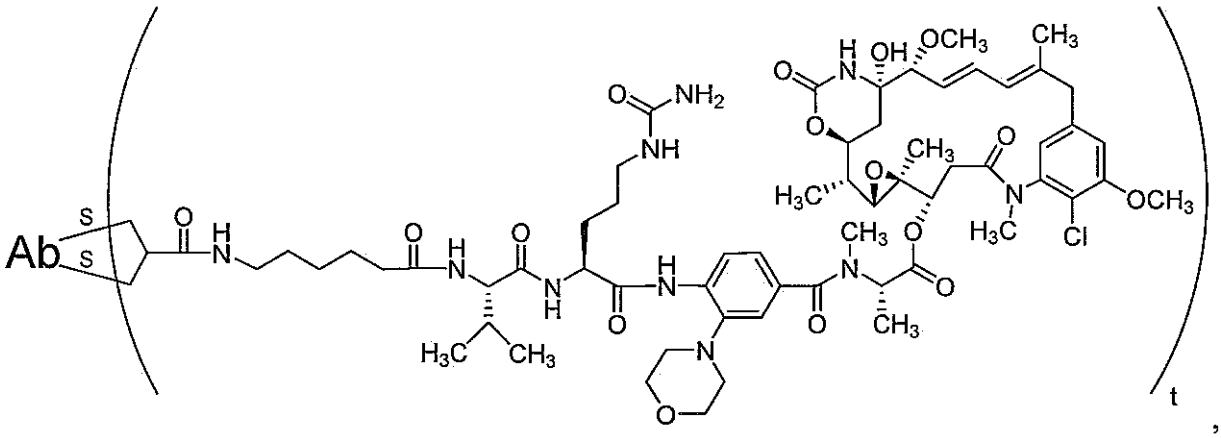


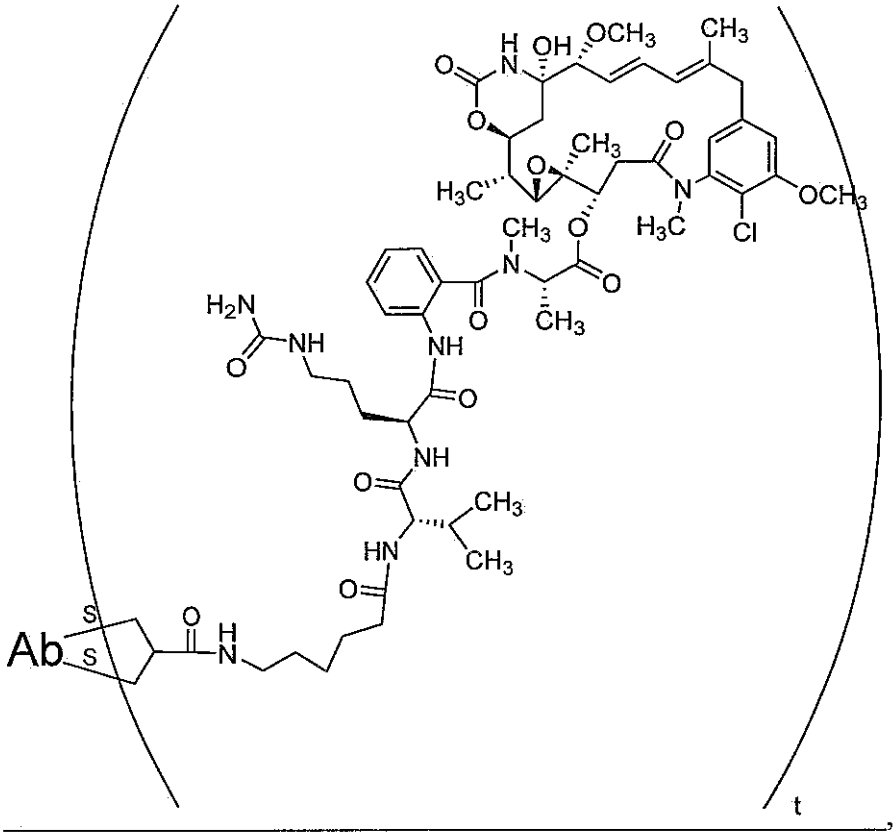


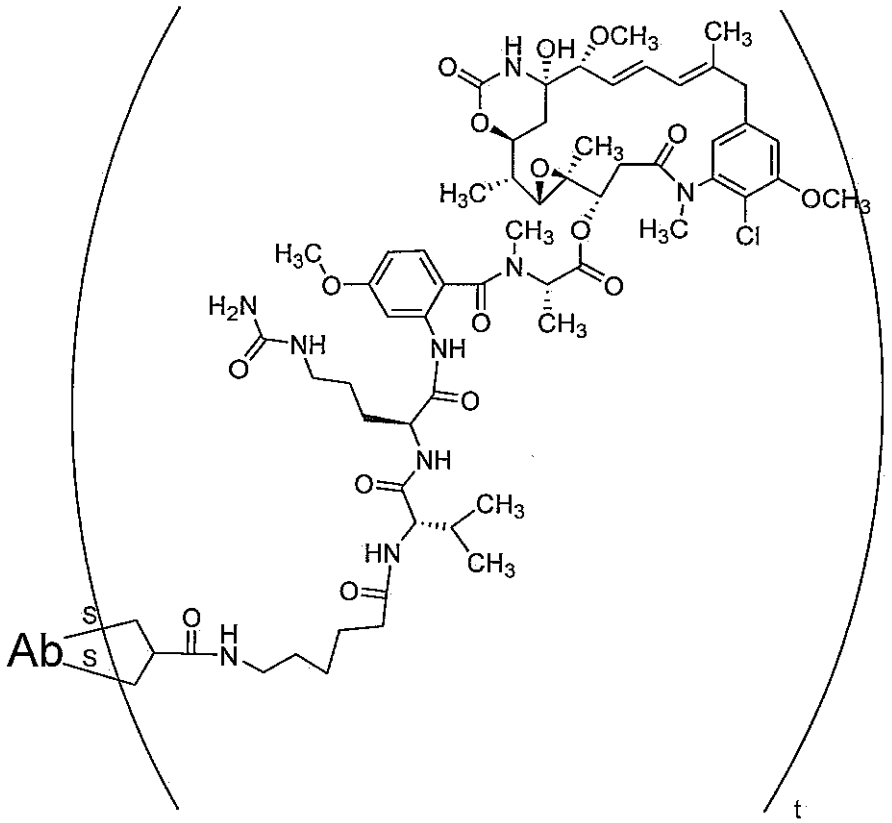




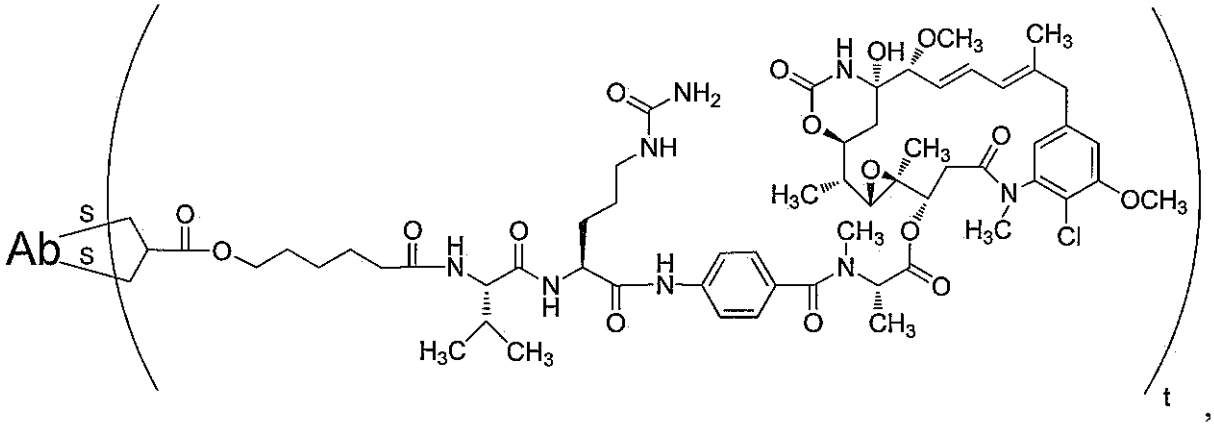




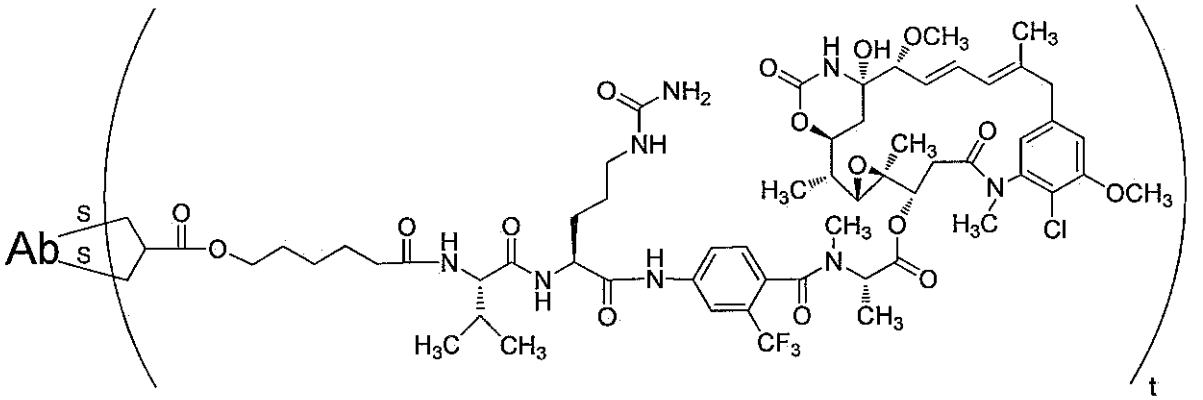

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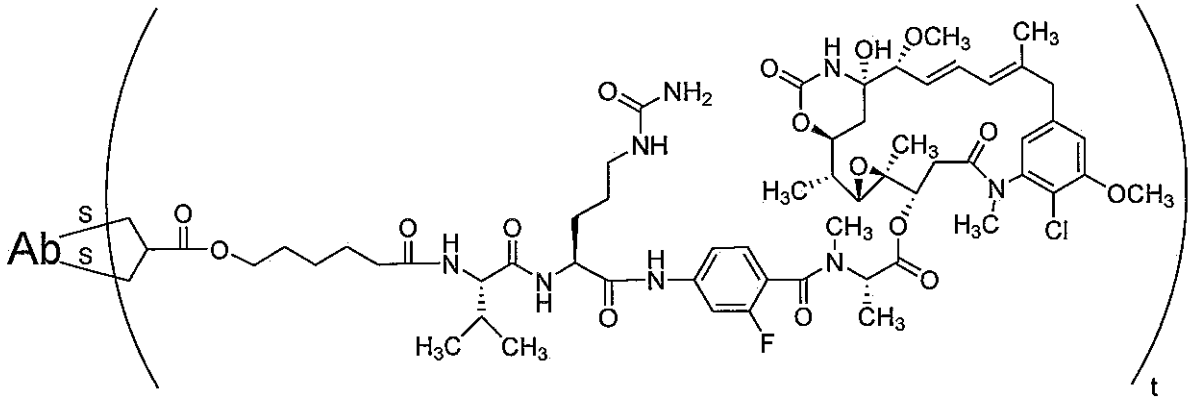
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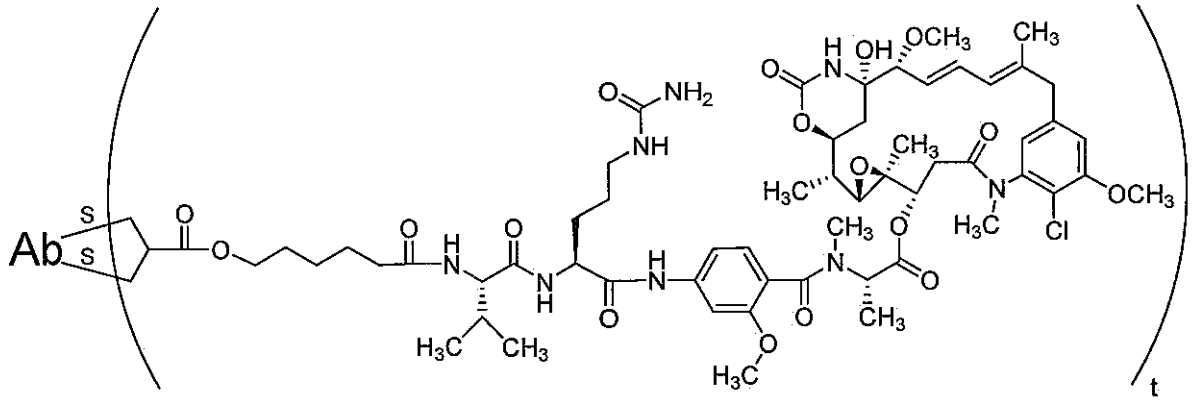
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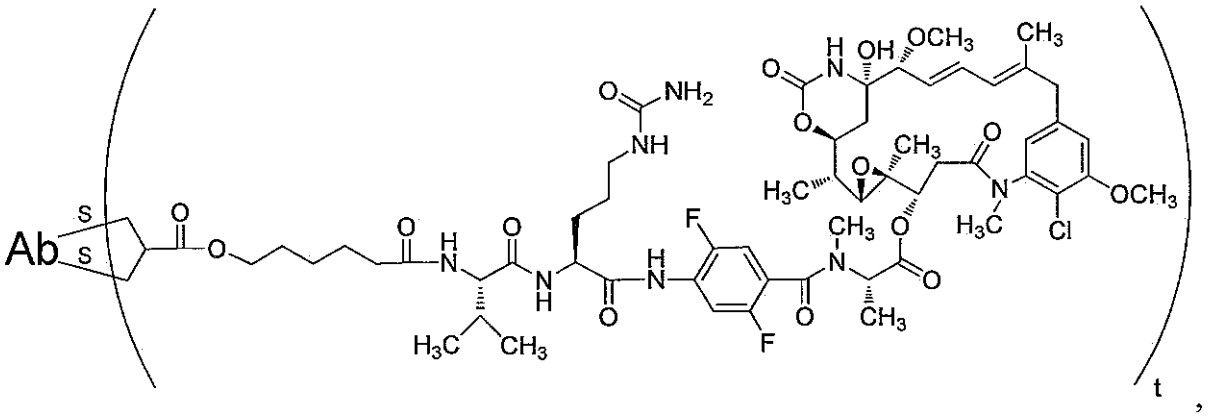
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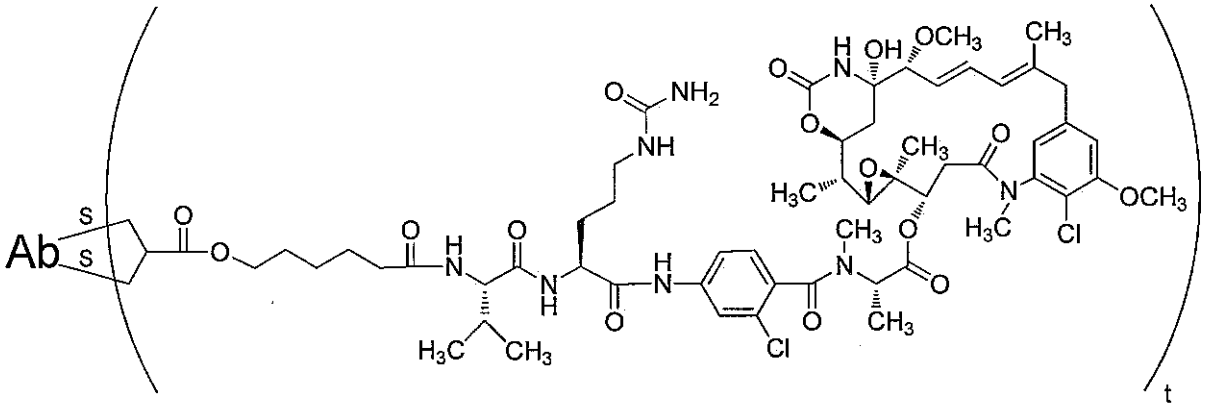

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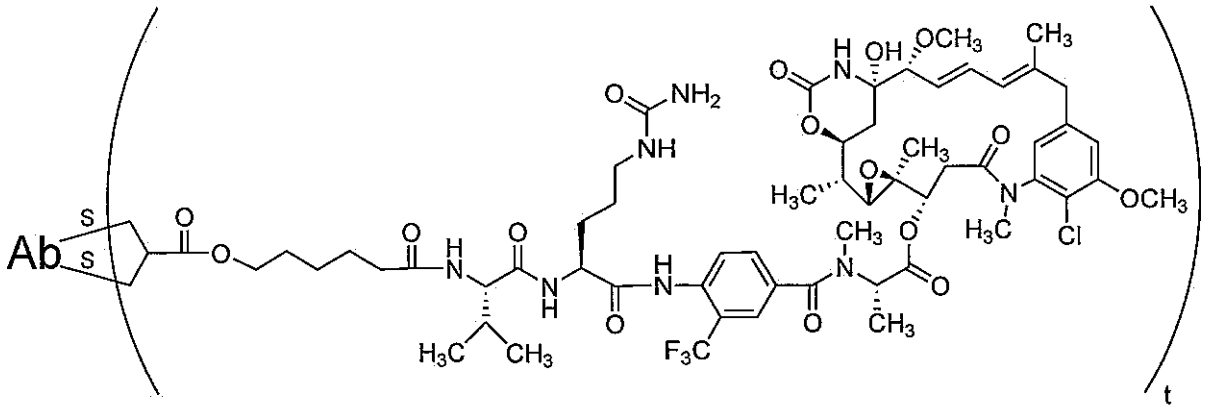
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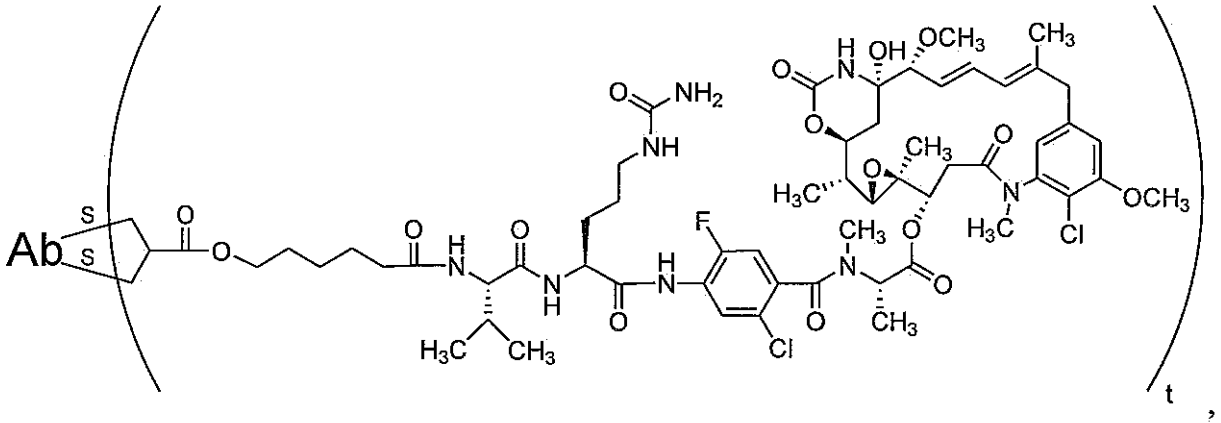

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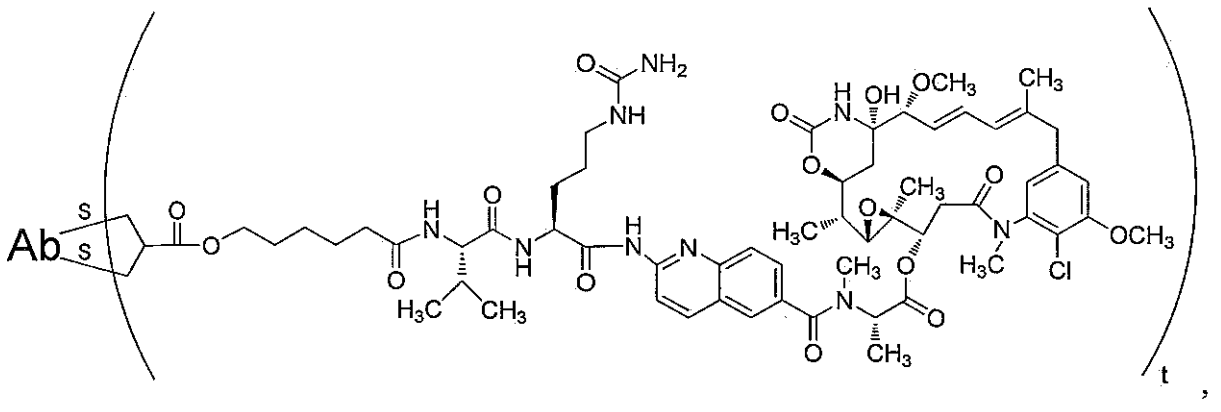
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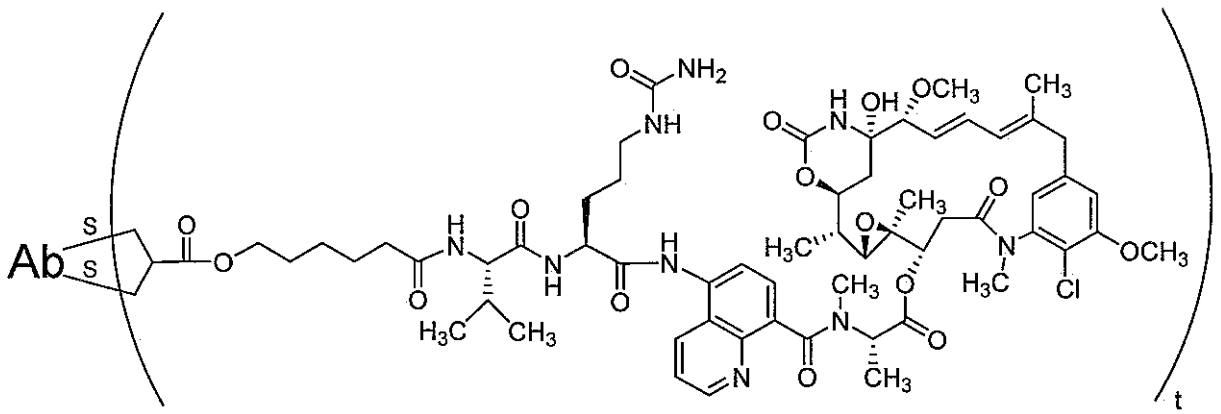


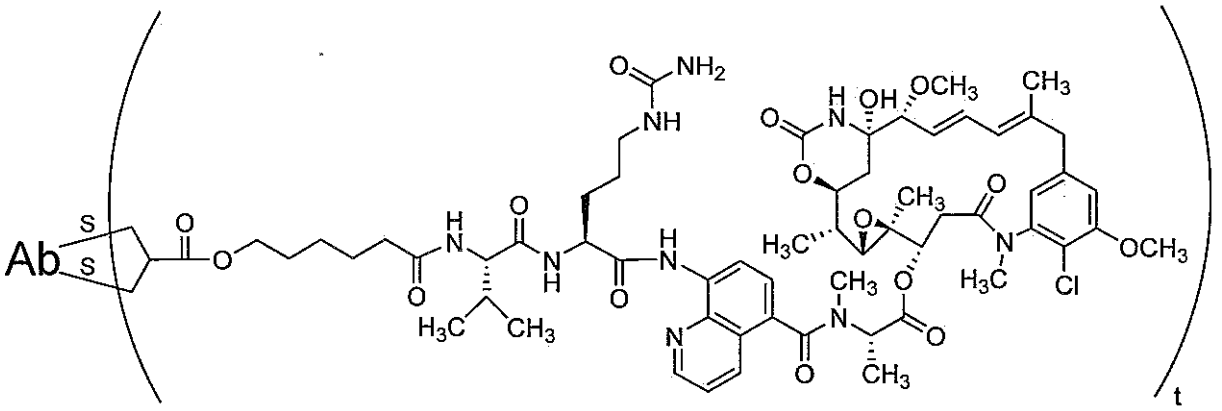


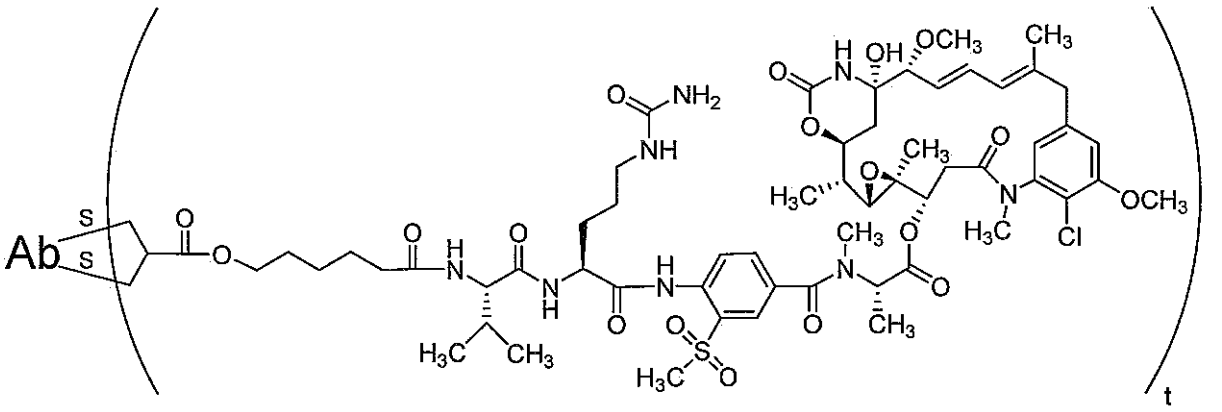


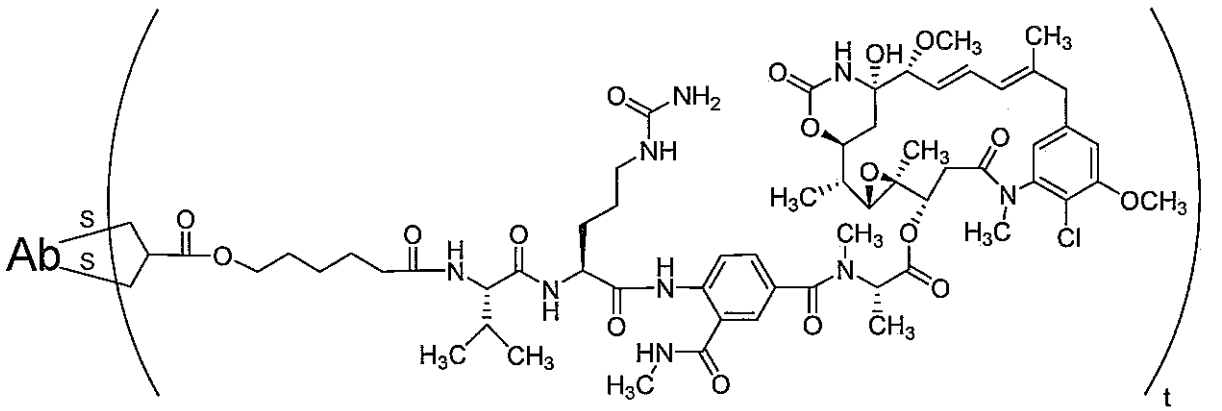


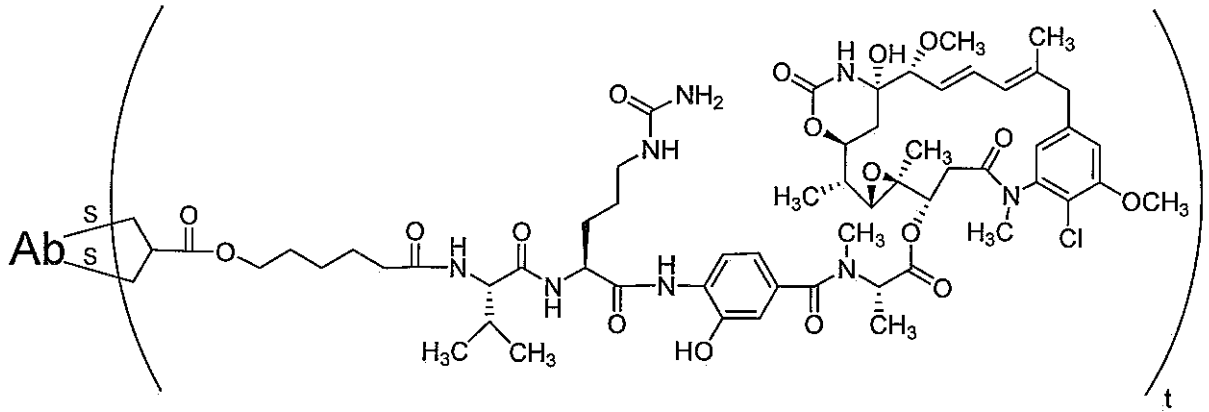




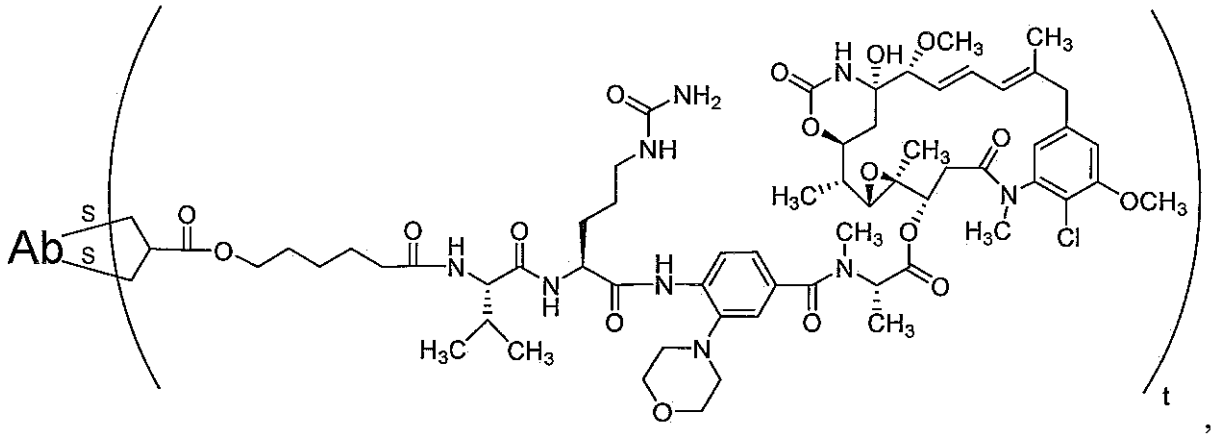




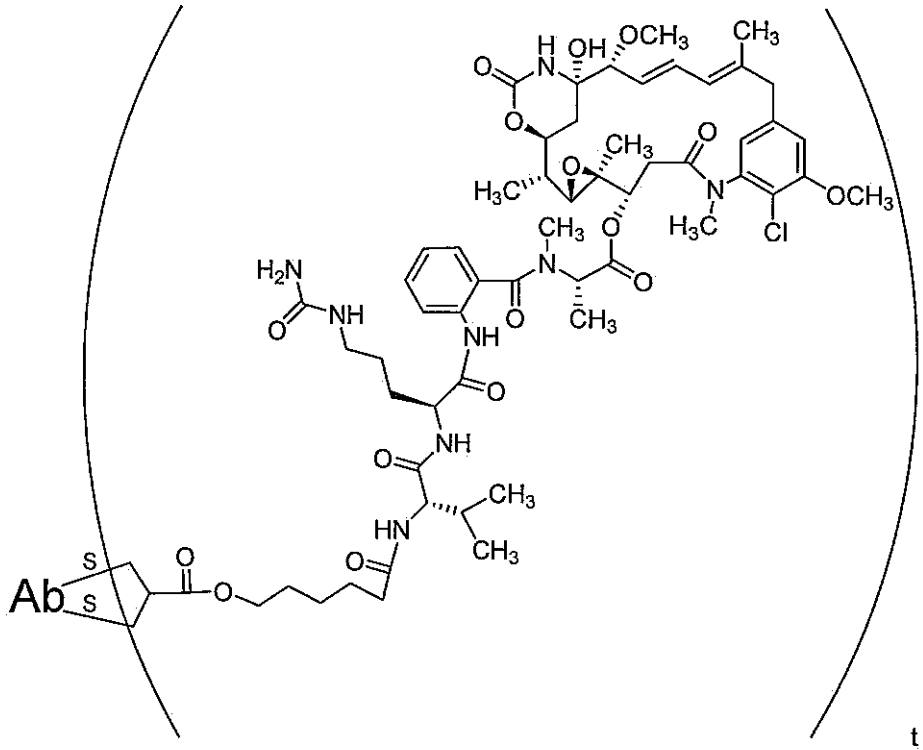




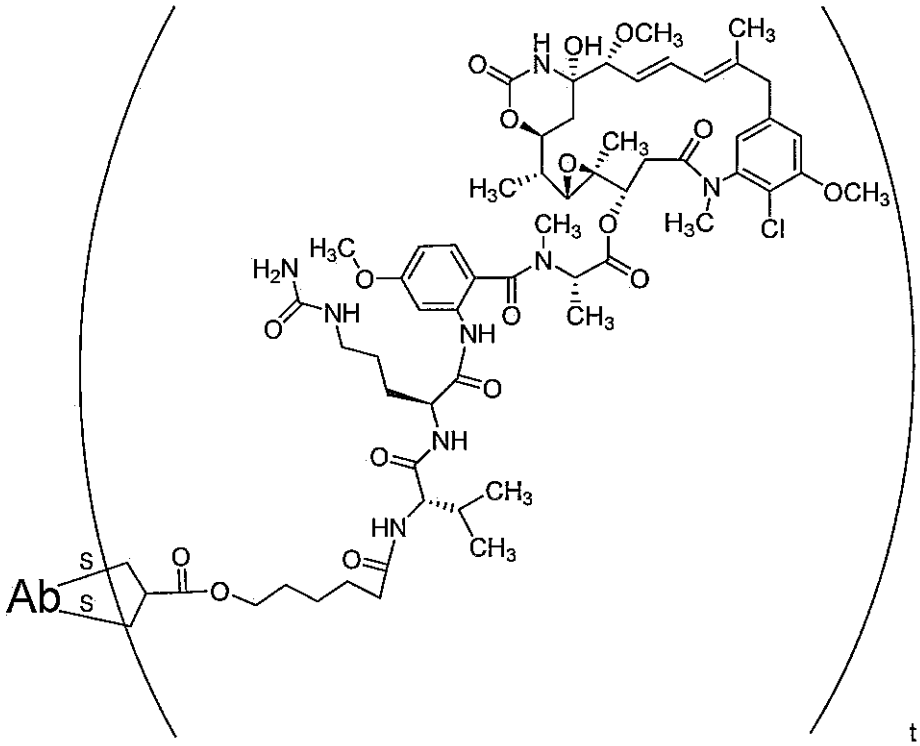
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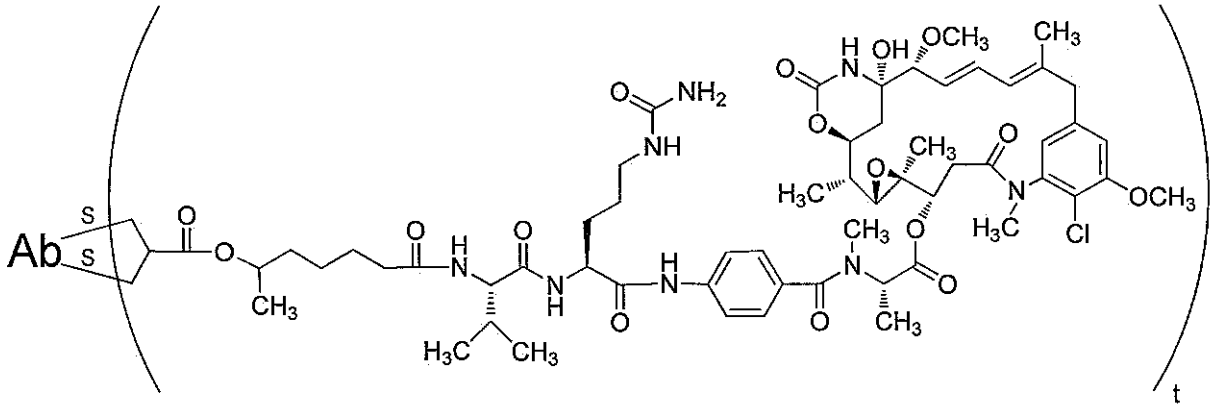
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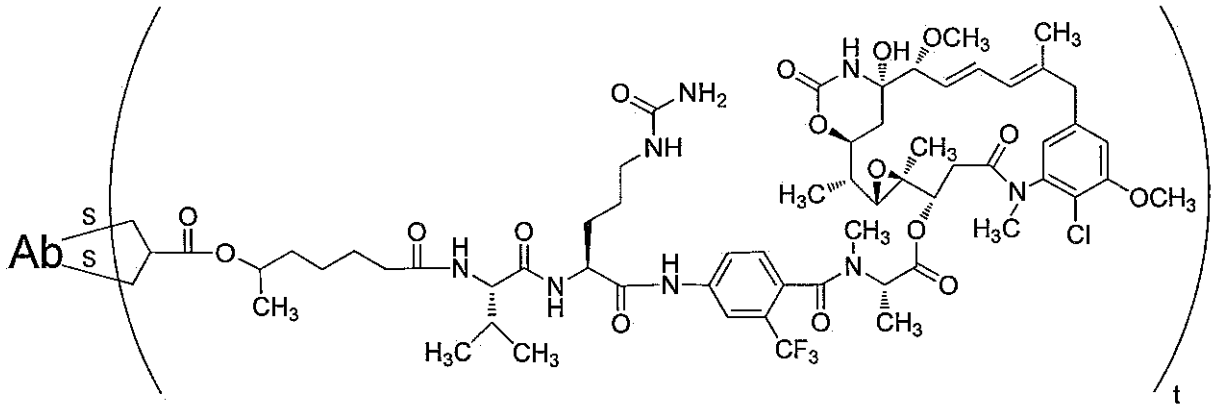
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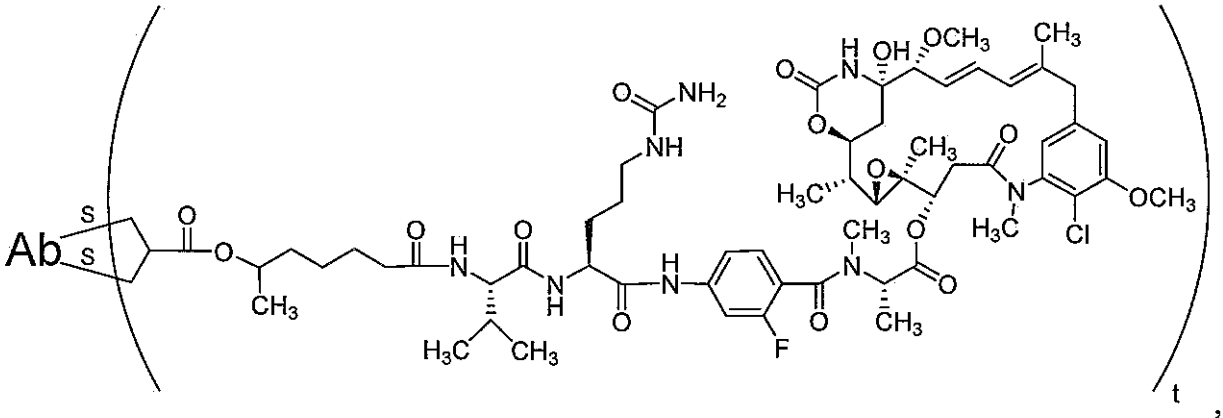
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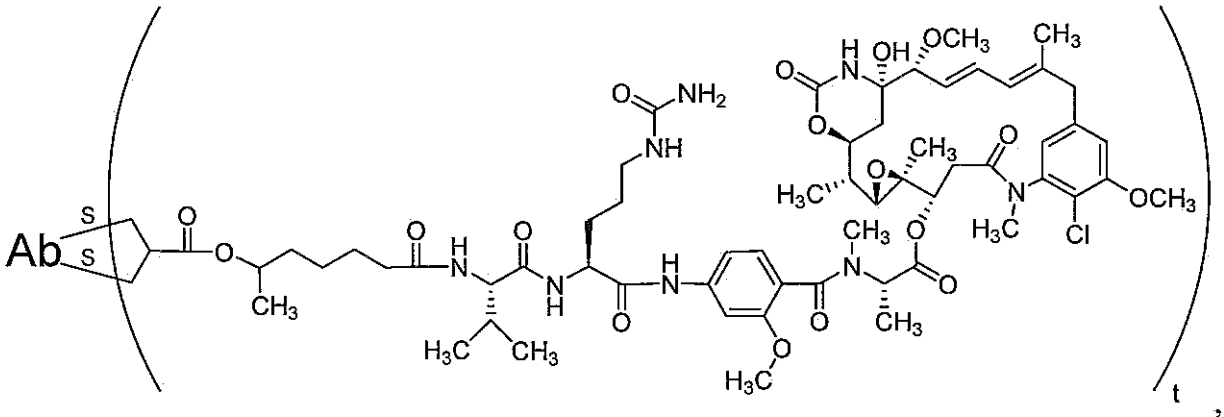
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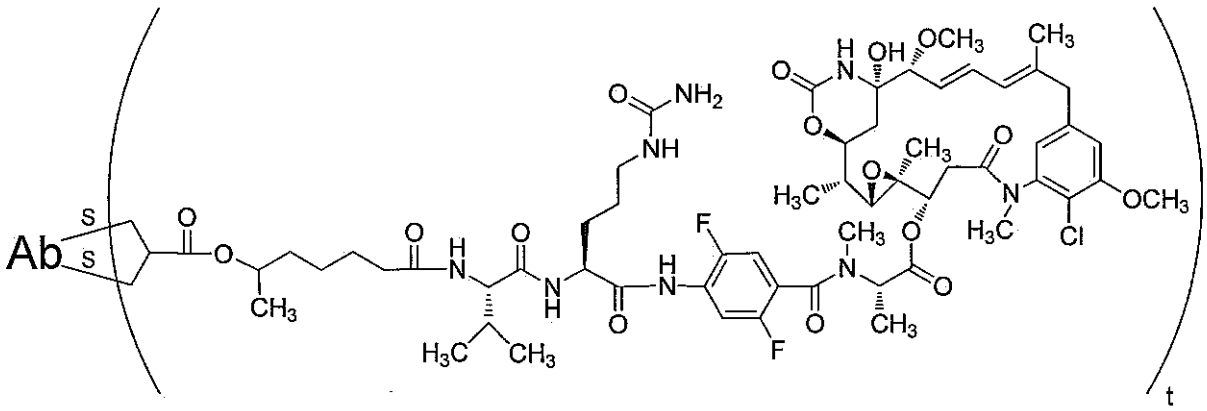
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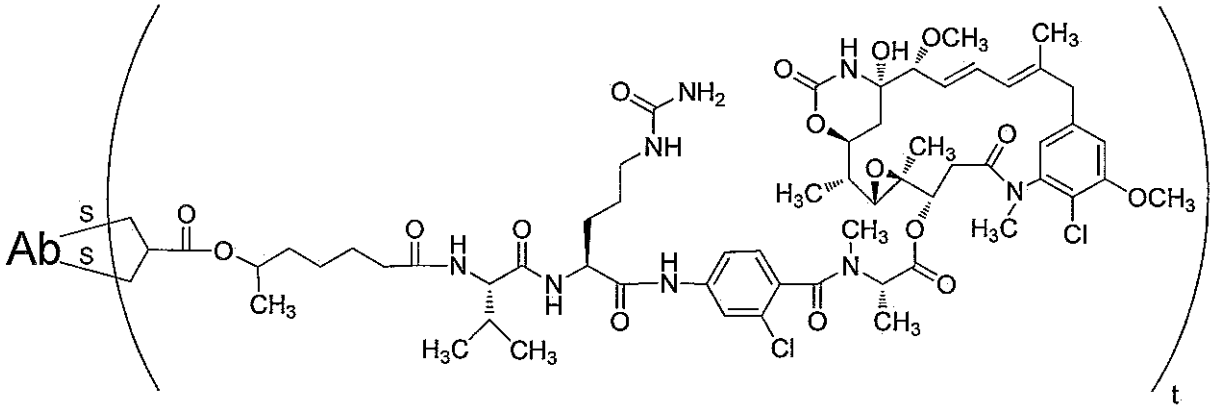
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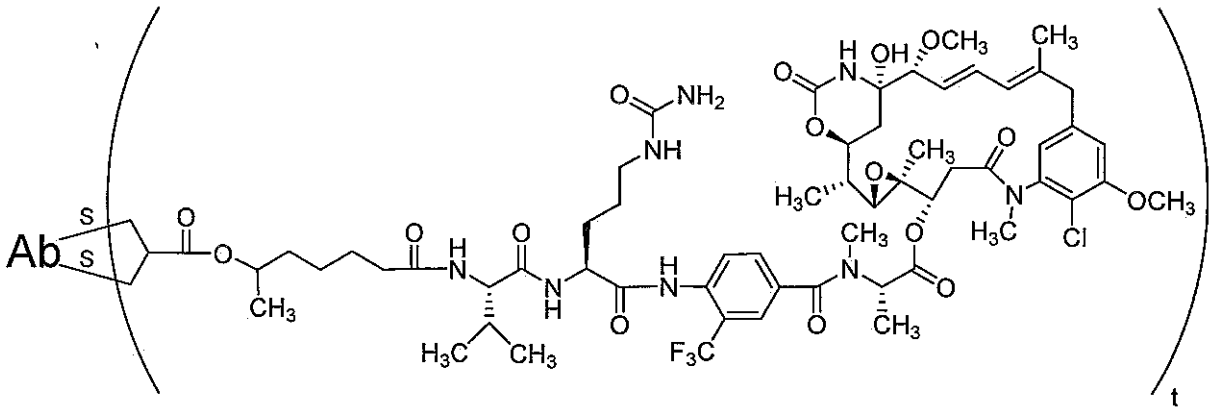


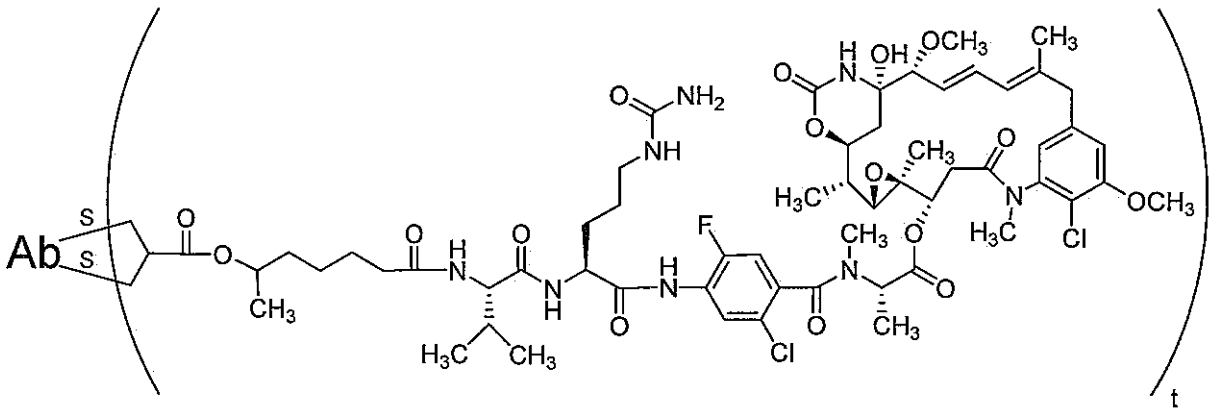
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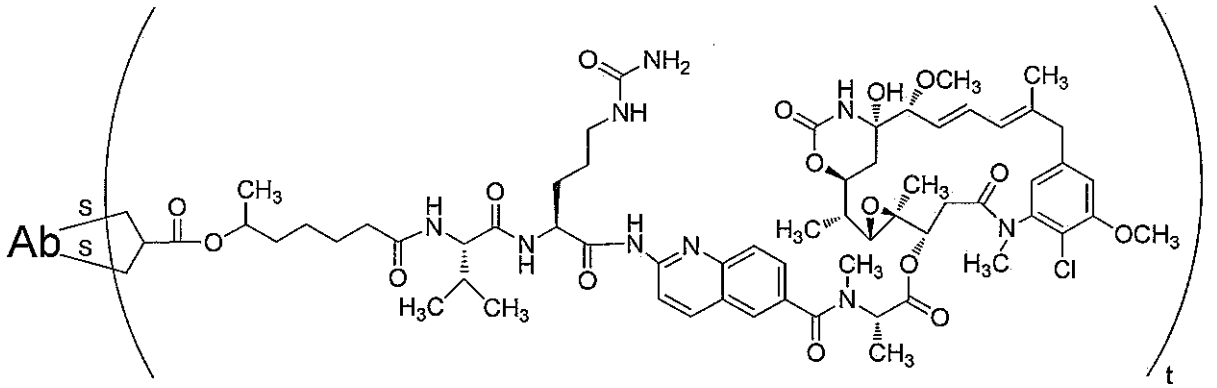


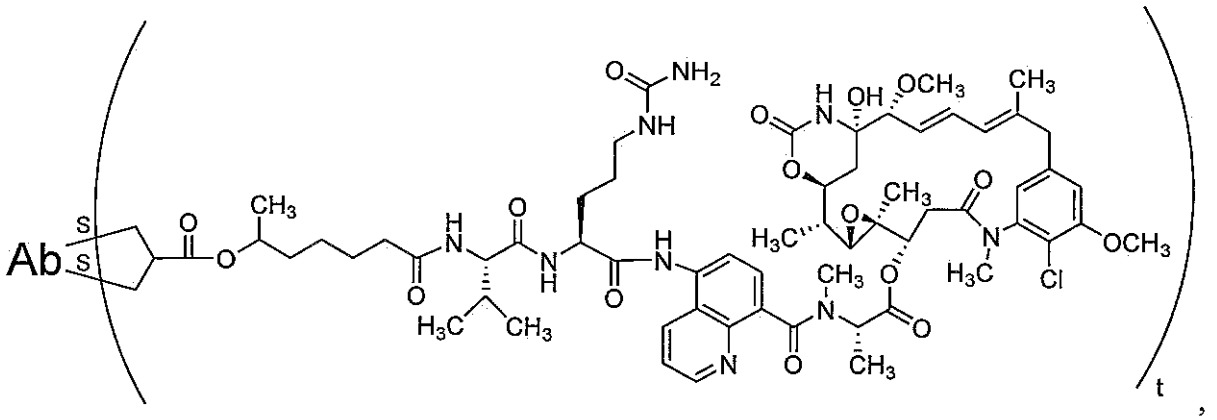
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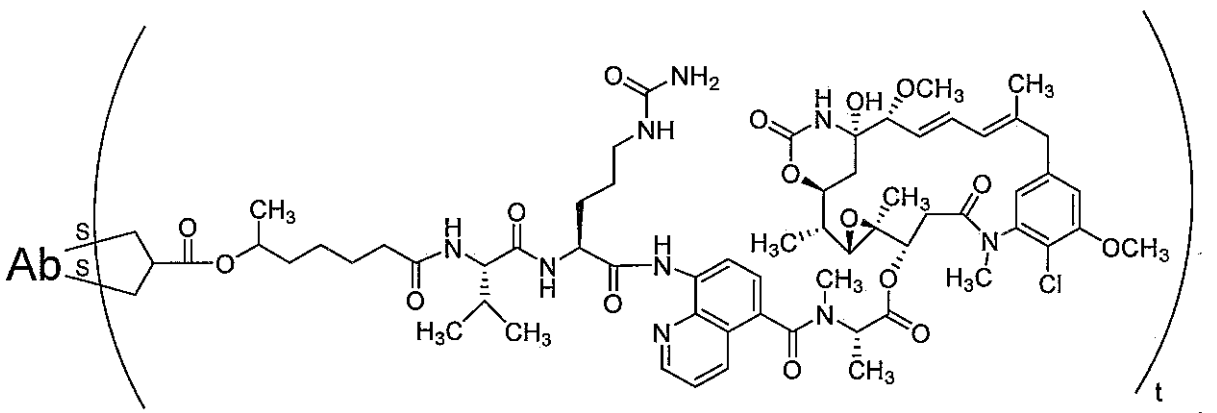


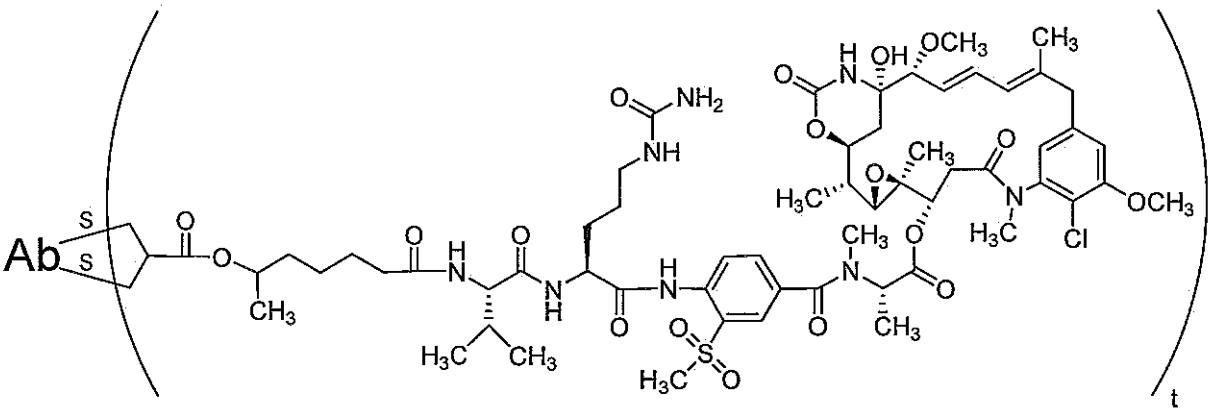


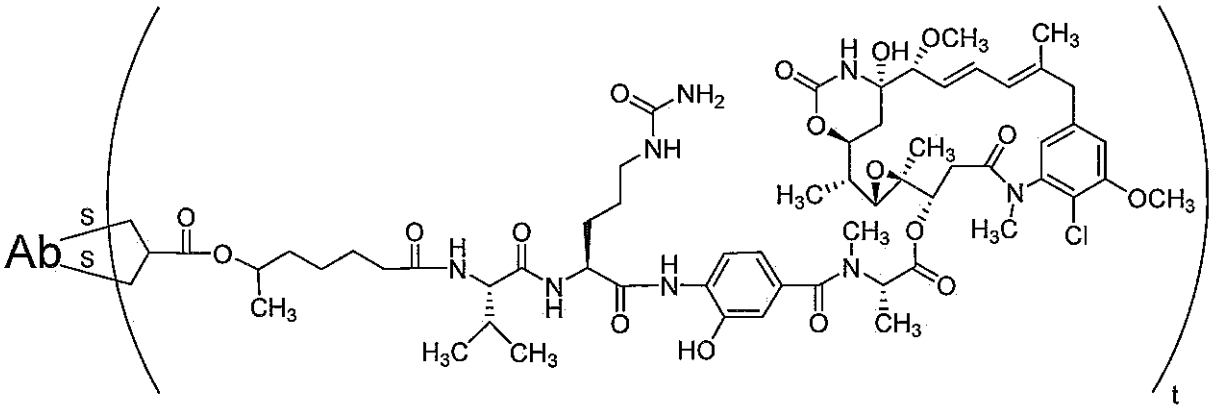


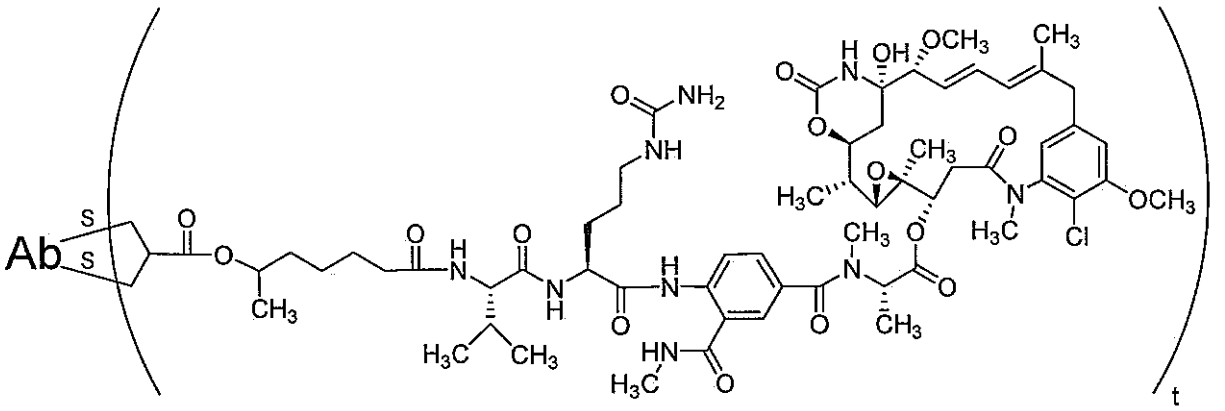


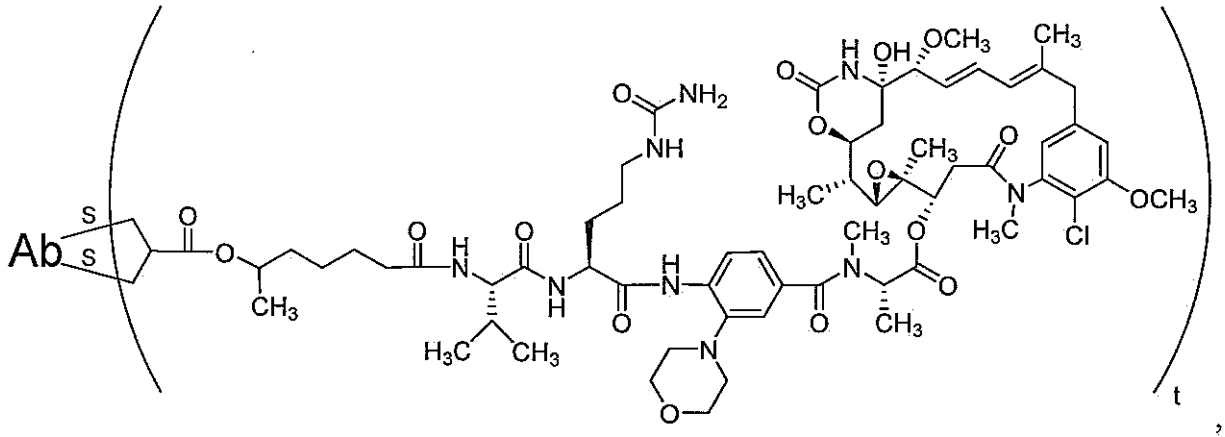


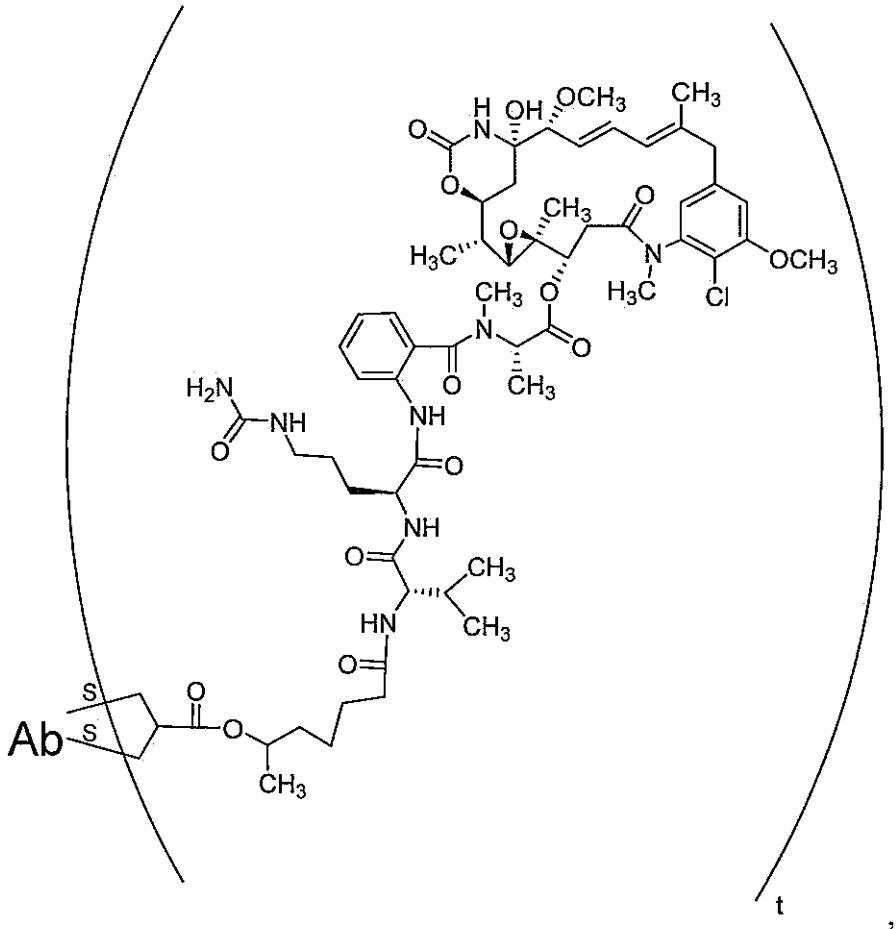


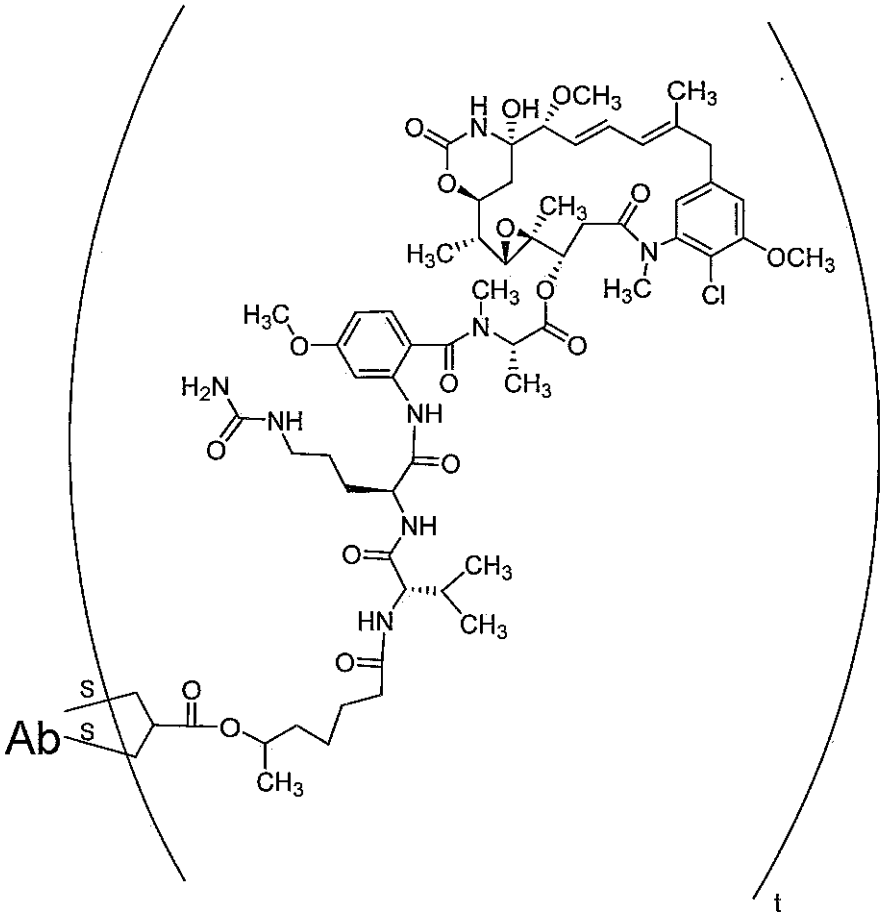




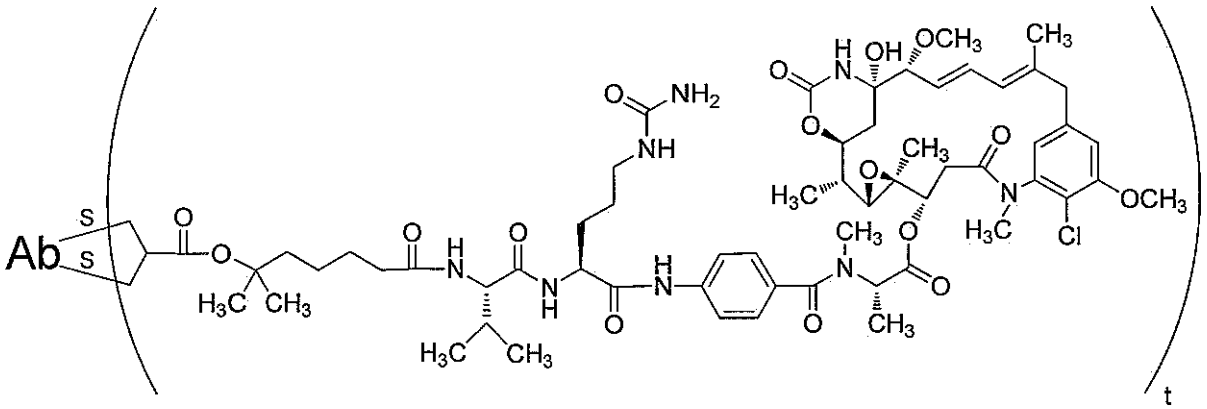




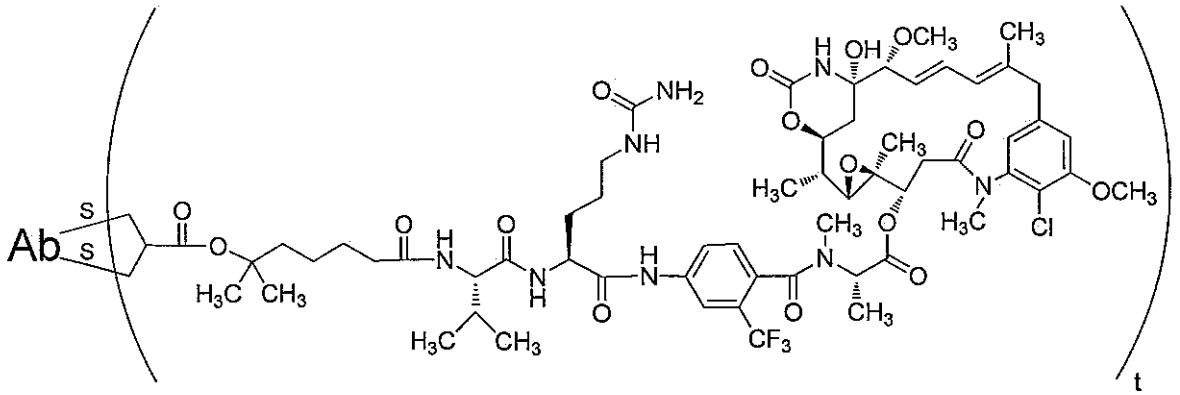



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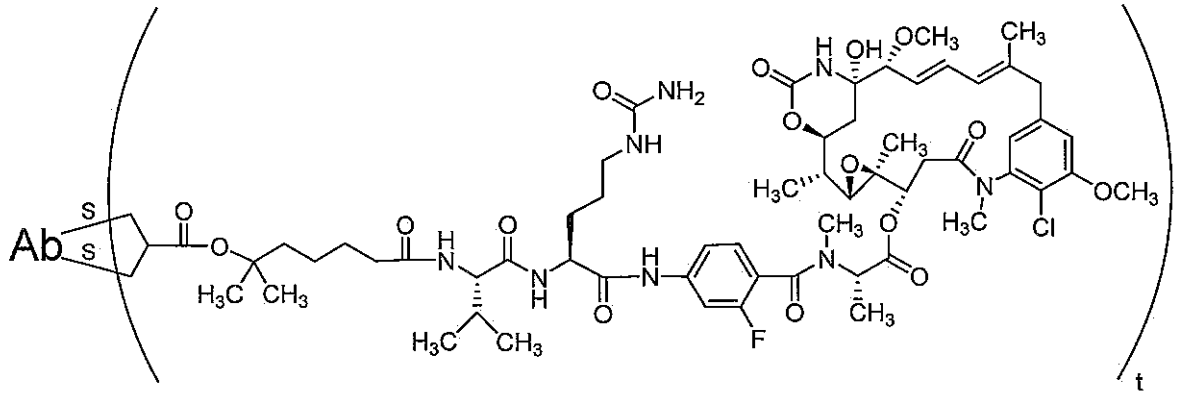
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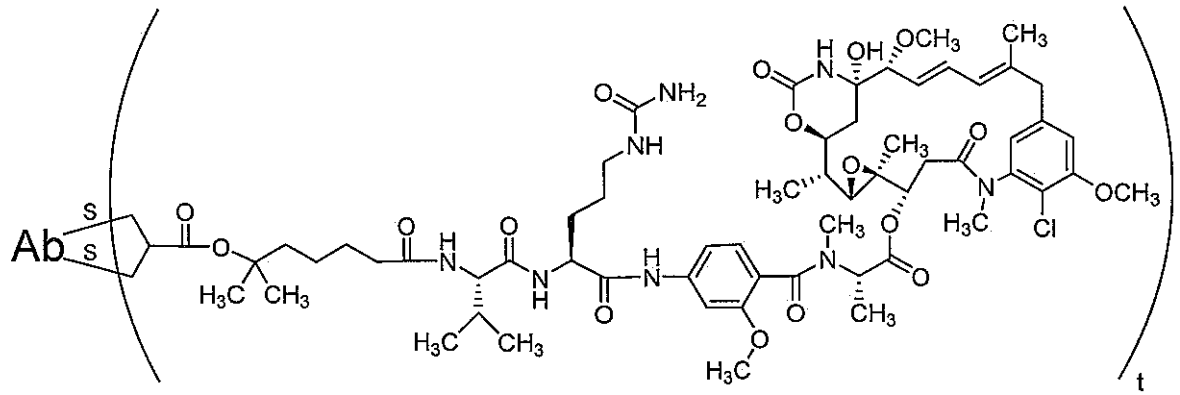
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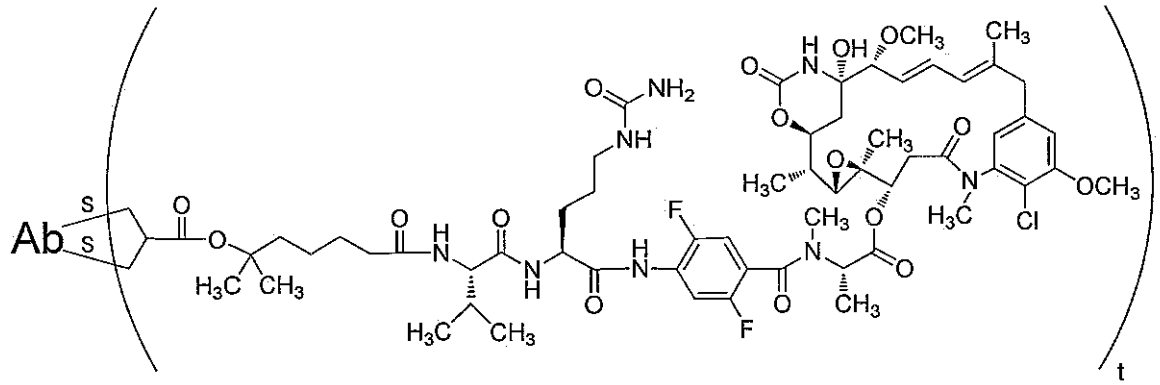
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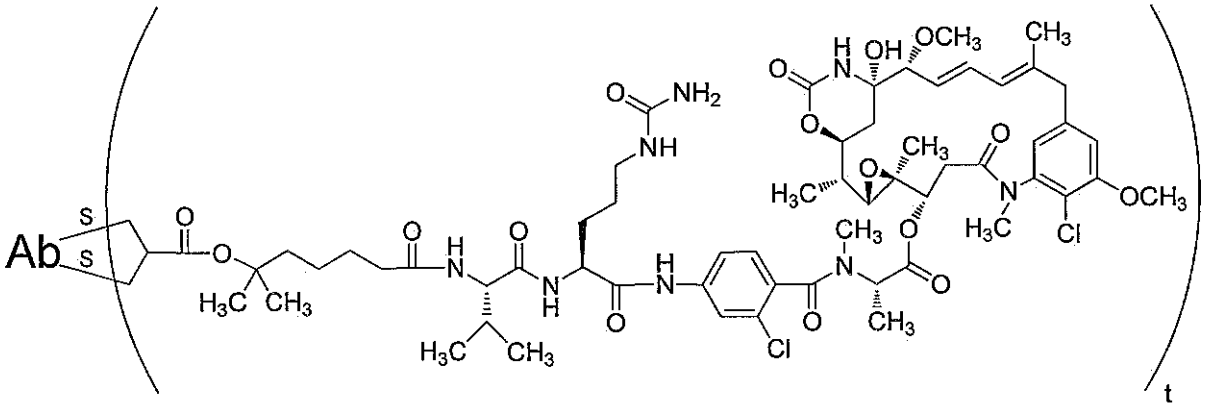
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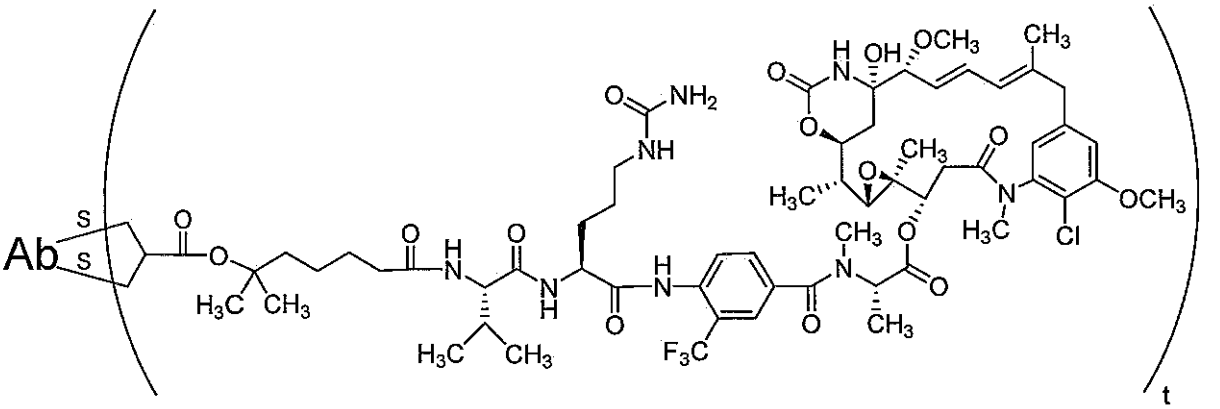
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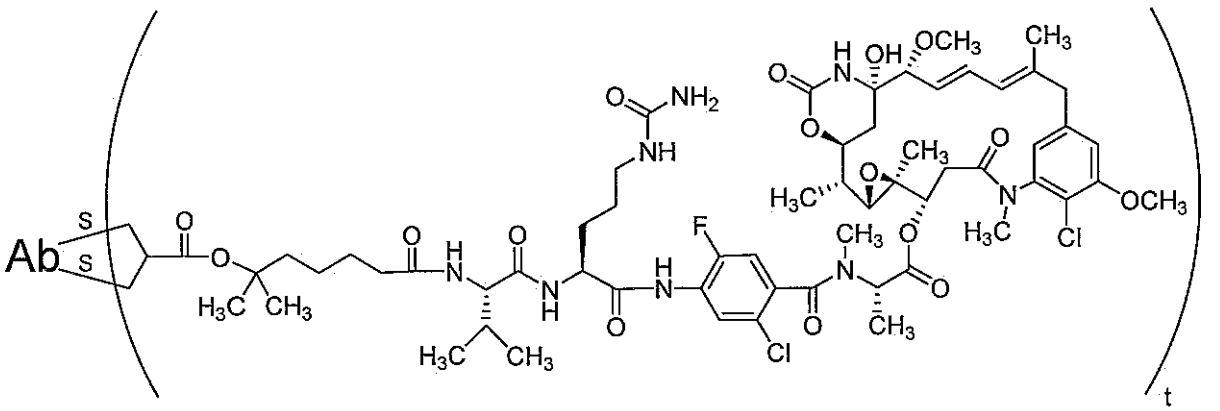


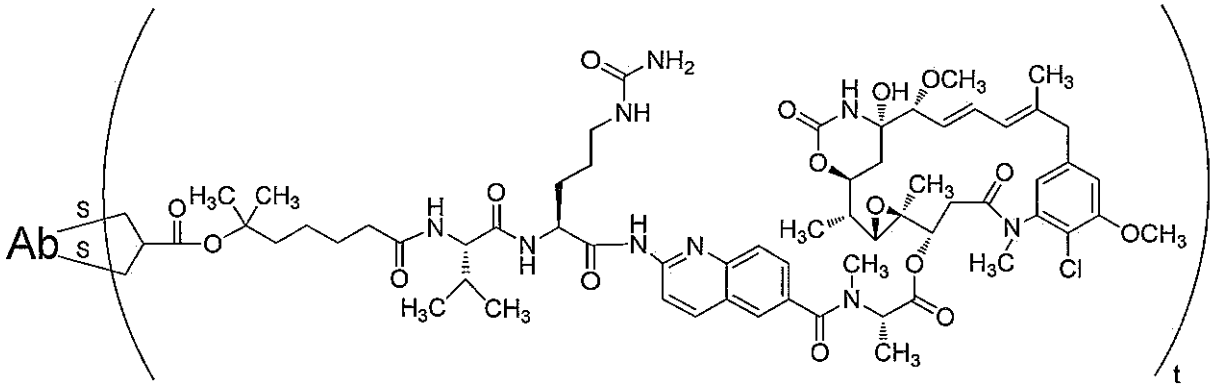
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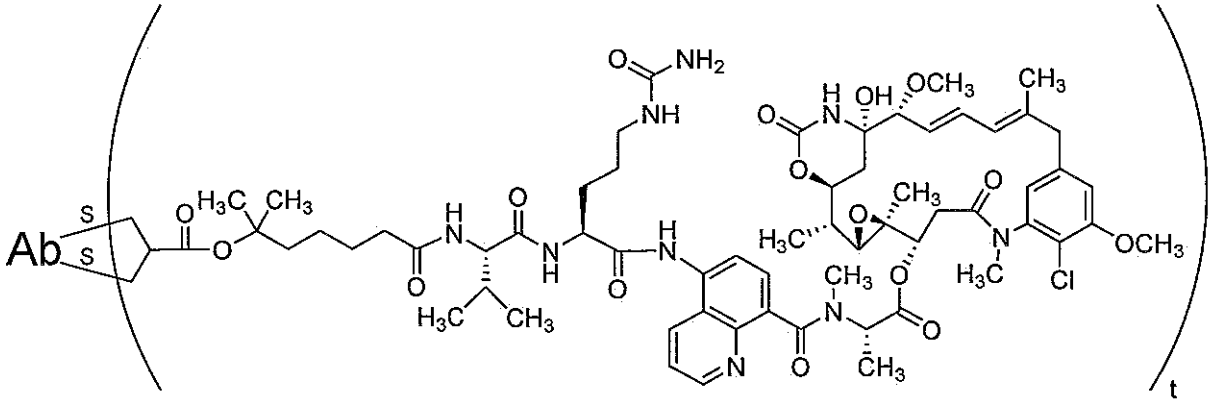
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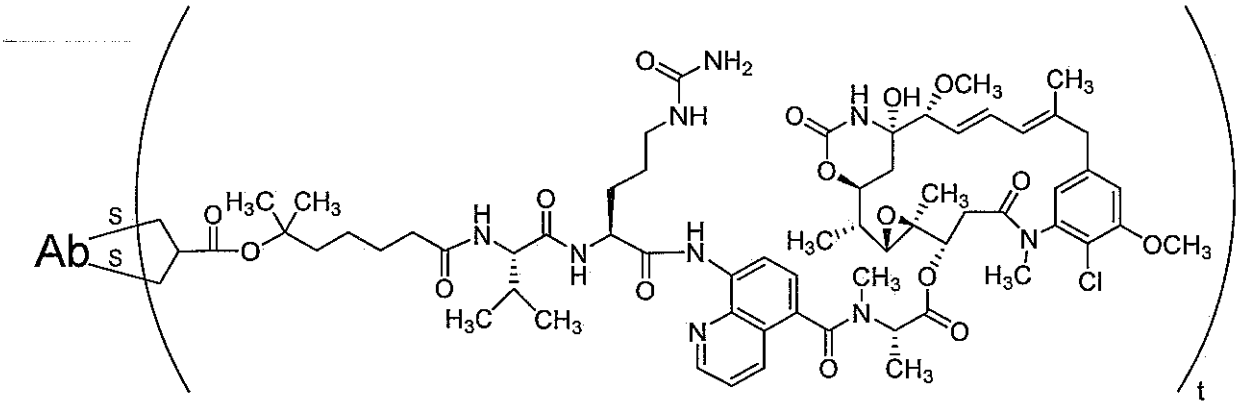



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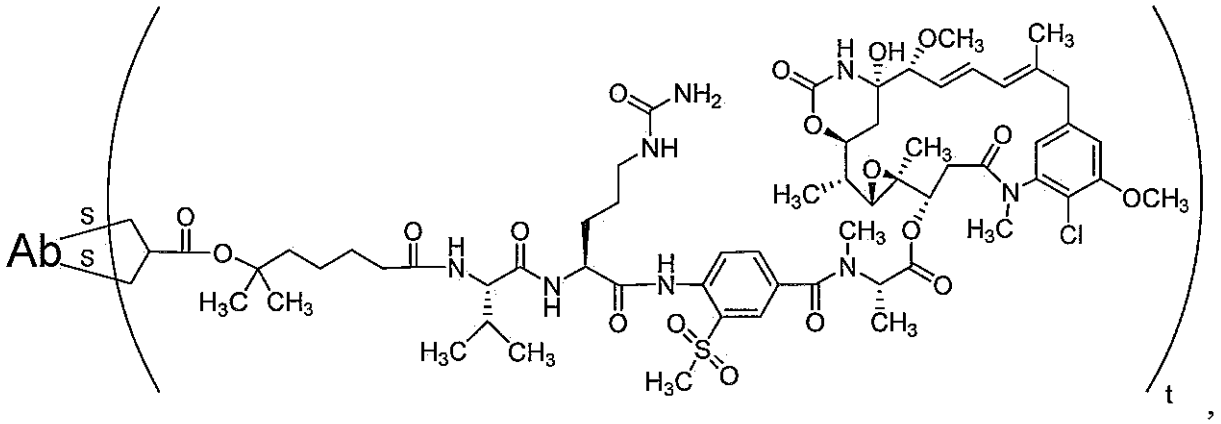
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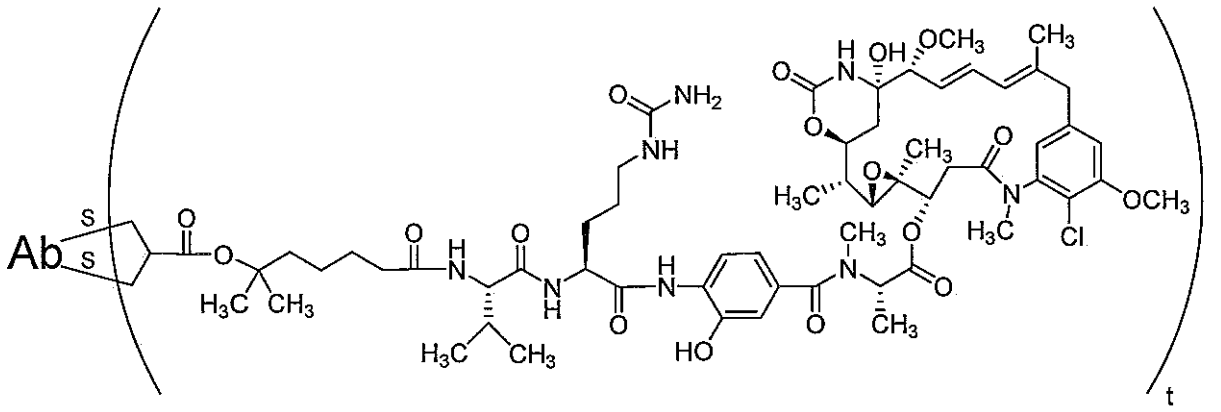
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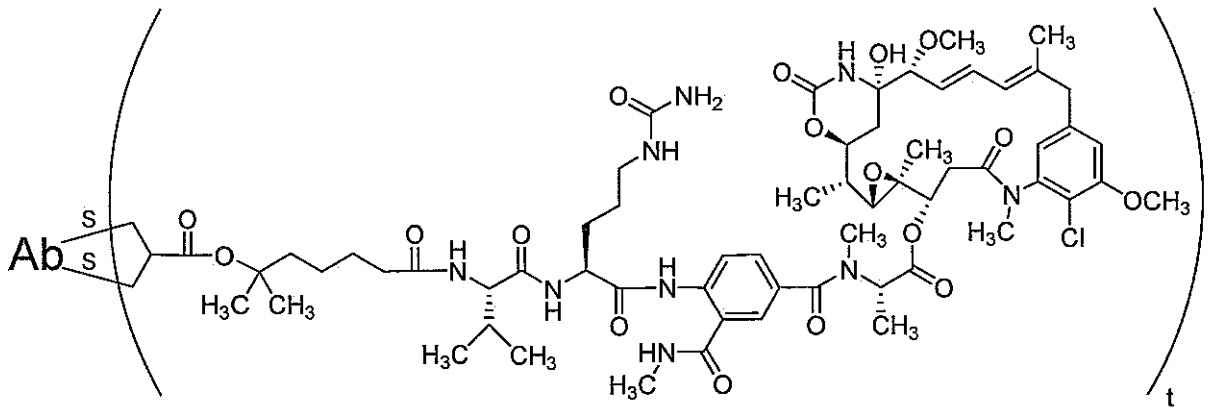
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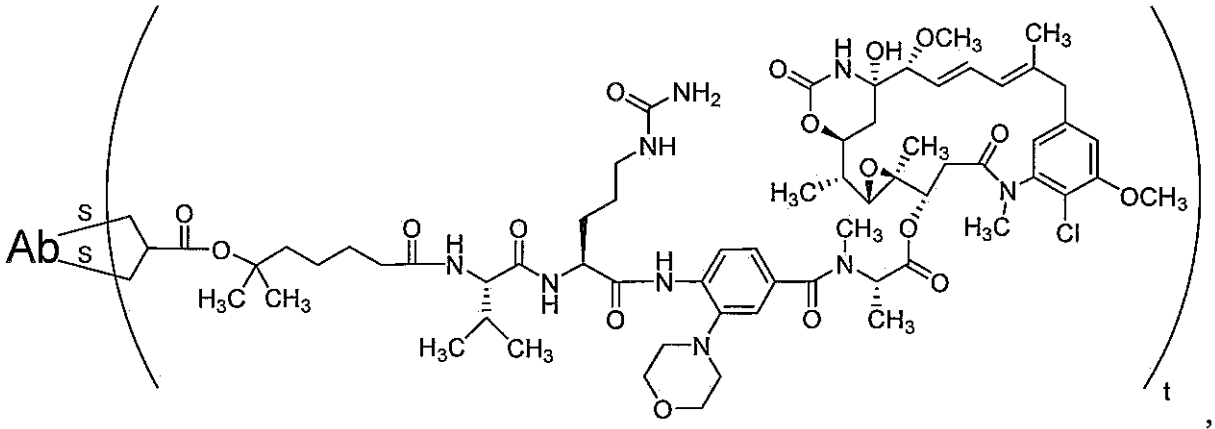
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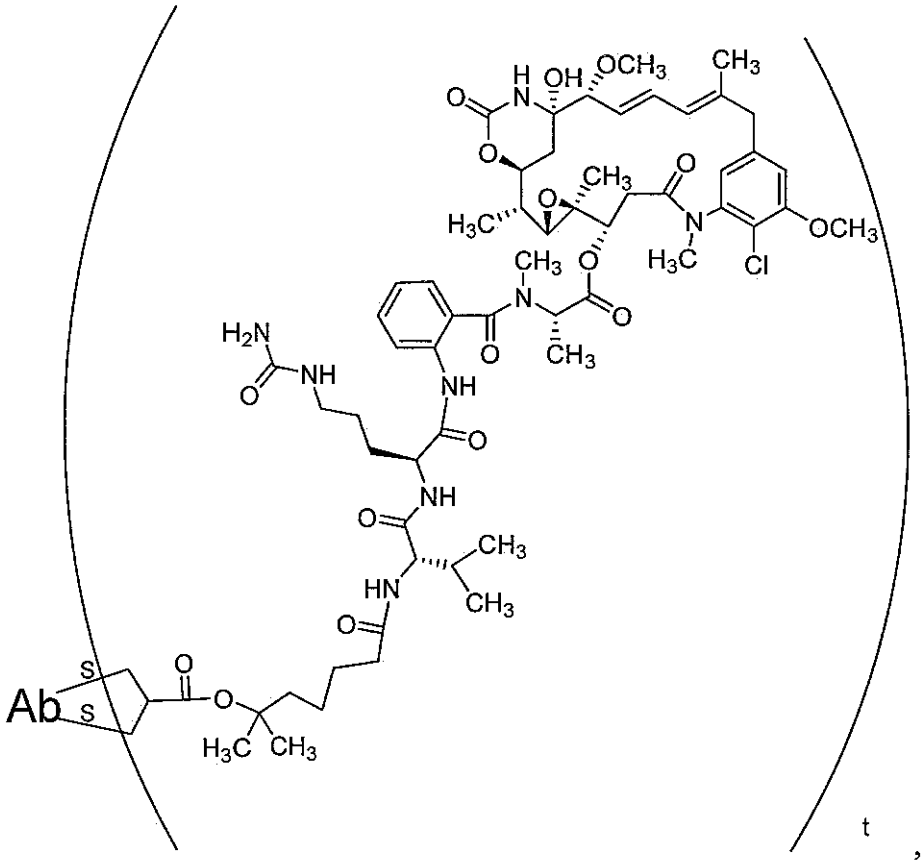
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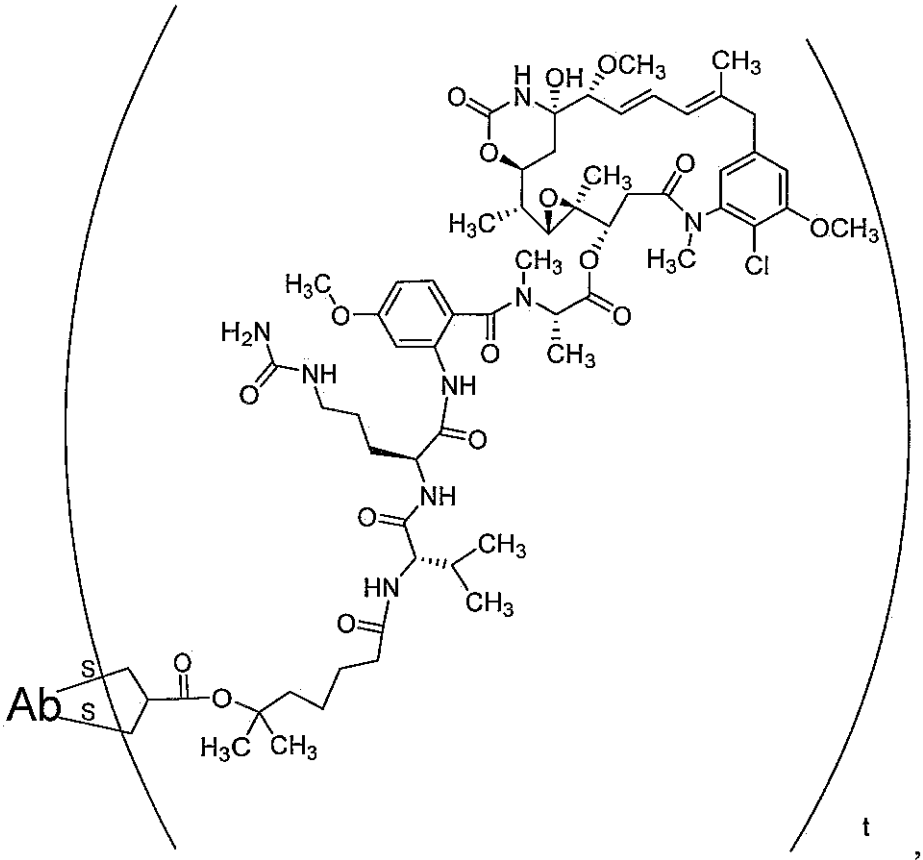
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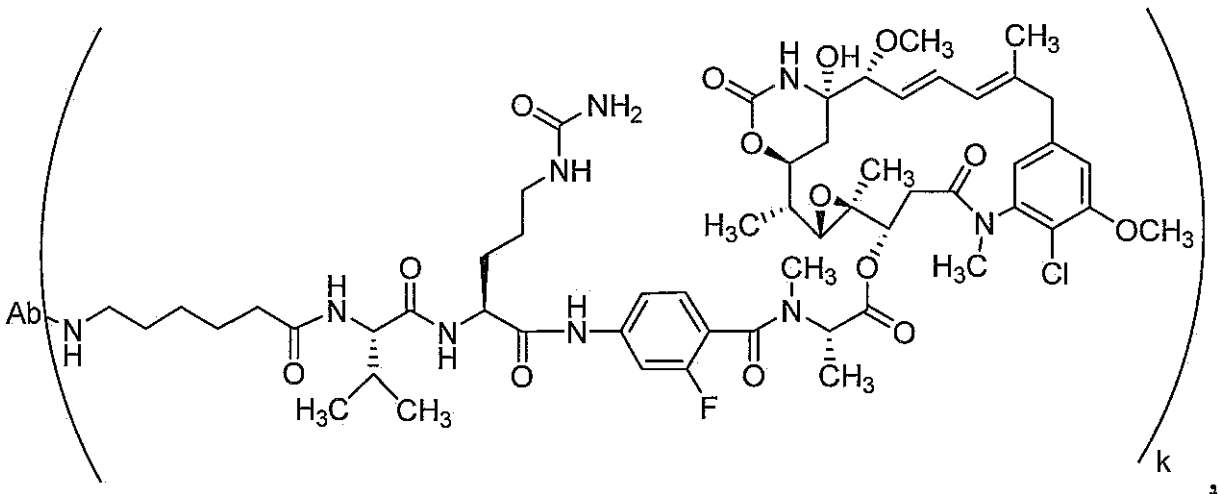
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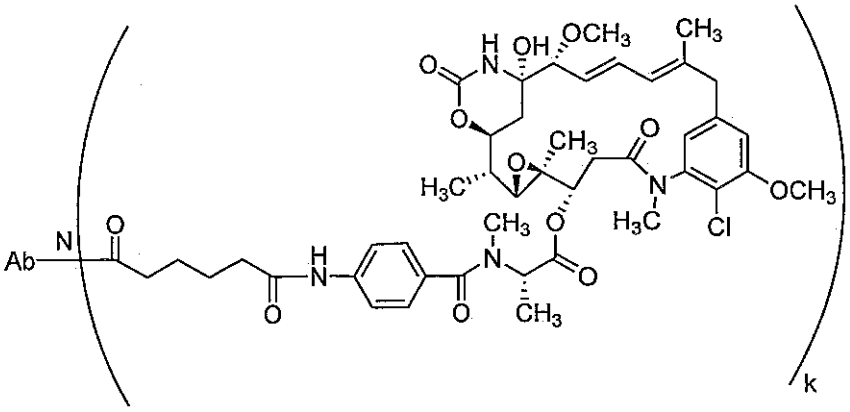
t ,


Ab
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O
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H2N
NH
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NH
O
NH
O
HN
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CH3
CH3
H3C
O
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CH3
O
O
H3C
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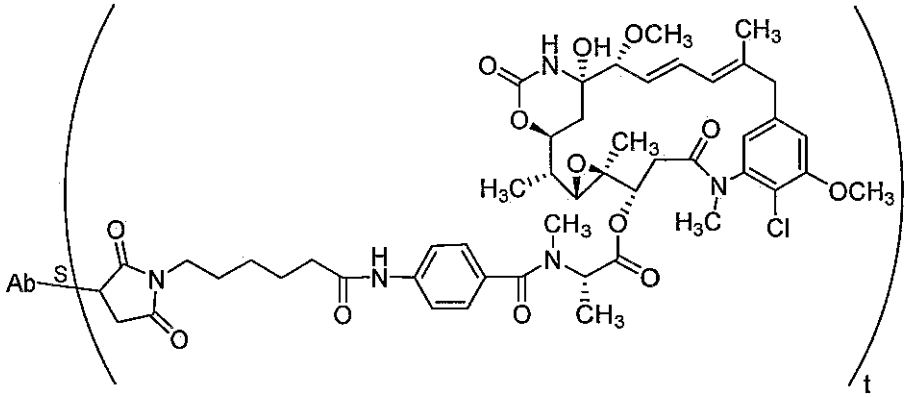
t ,


Ab
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CH3
H
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H
OH
OCH3
CH3
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k



, or



;

wherein:

Ab is an antibody or an antigen binding fragment thereof;

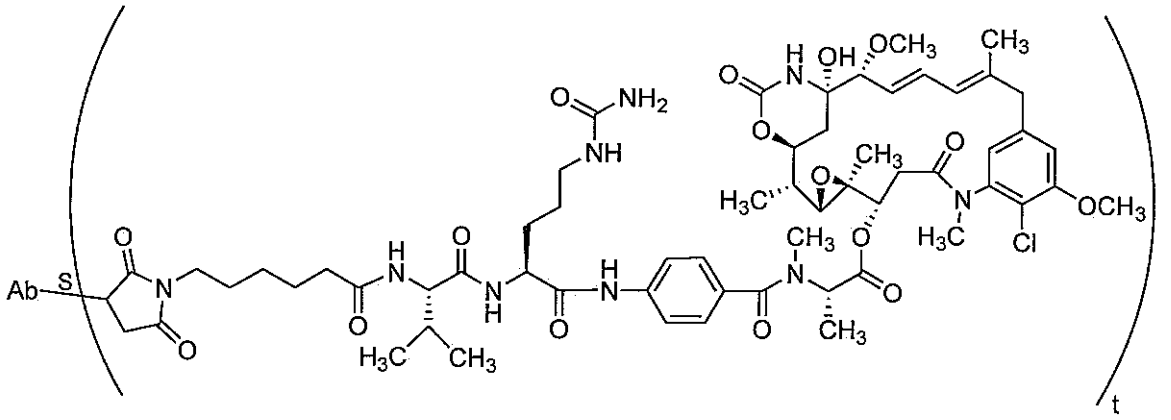
—S— is a bond to a cysteine of the antibody or an antigen binding fragment thereof;

—N— is a bond to a lysine of the antibody or an antigen binding fragment thereof;

k is an integer from 1 to 30; and

t is an integer from 1 to 8.

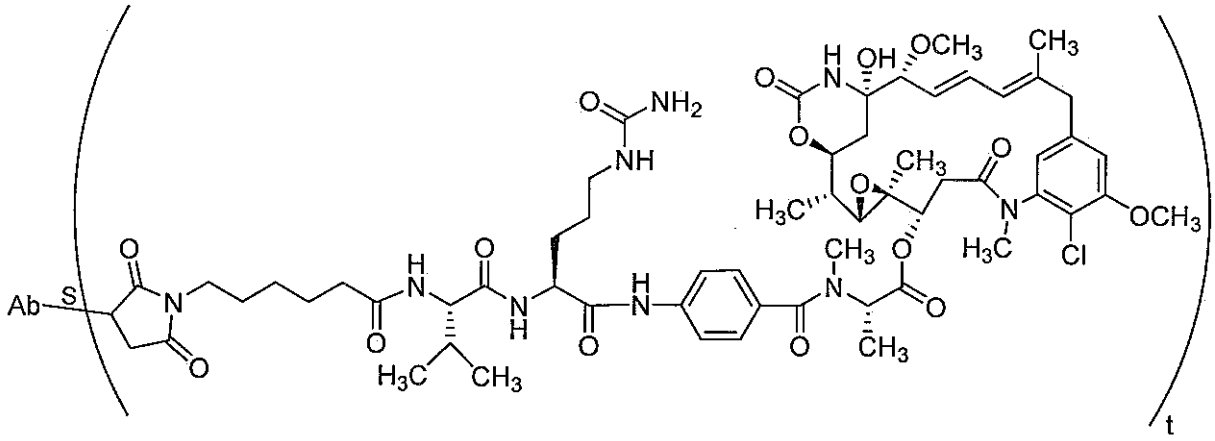
11. The compound of claim 10, wherein the compound is:

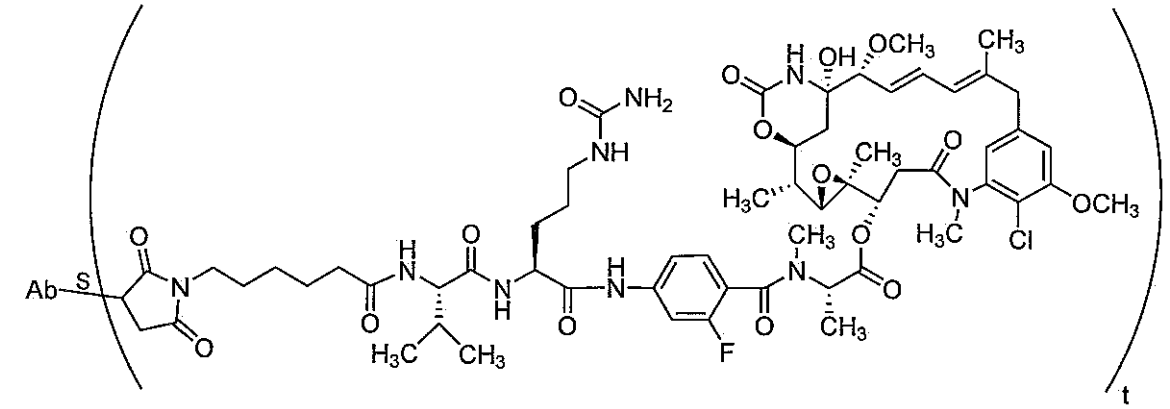


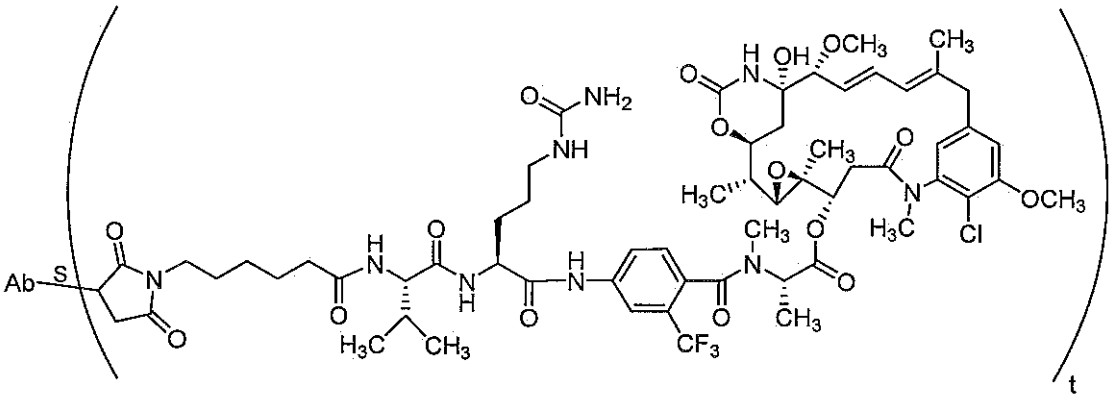
12. The compound of any of claims 1-11, wherein t is 1.

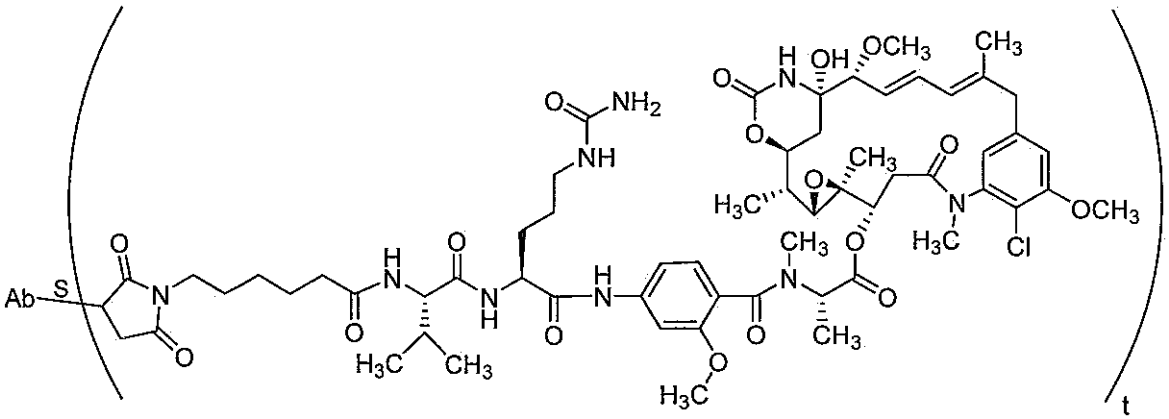
13. The compound of any of claims 1-12, wherein the antibody or an antigen binding fragment thereof is an anti-MUC16 antibody or anti-PSMA antibody.

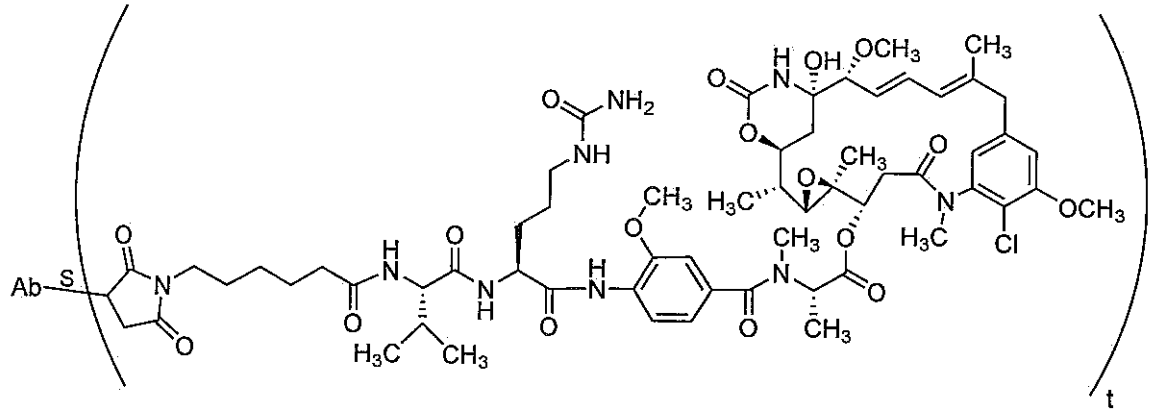
14. The compound of claim 1 selected from



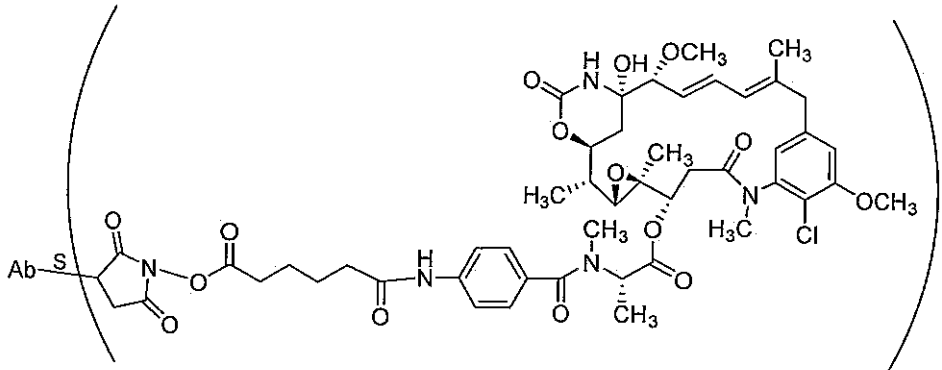




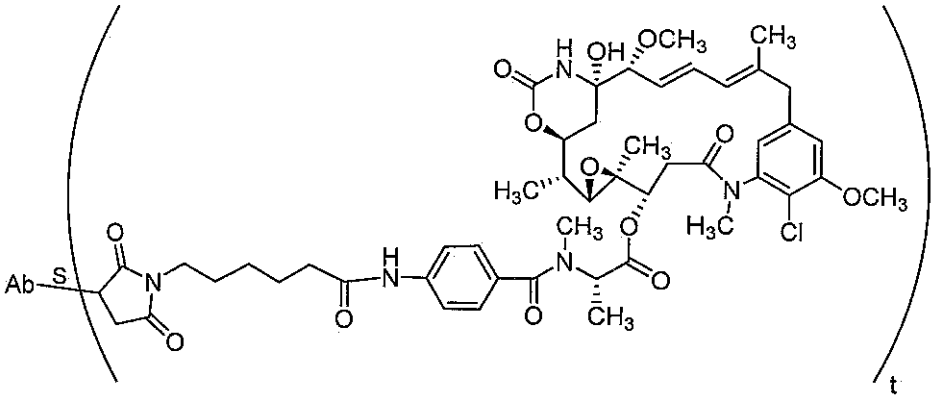




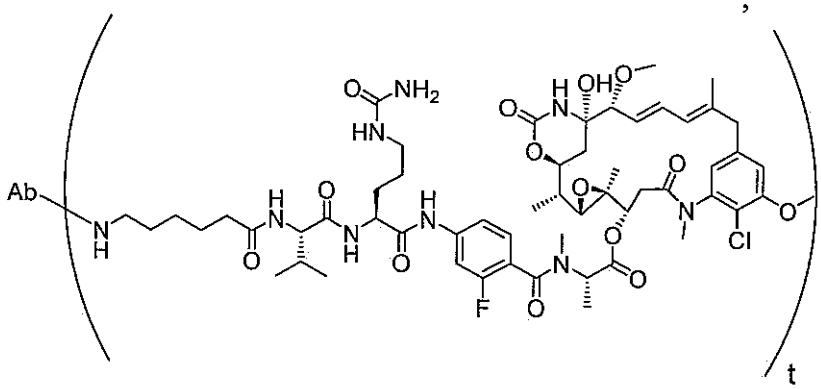
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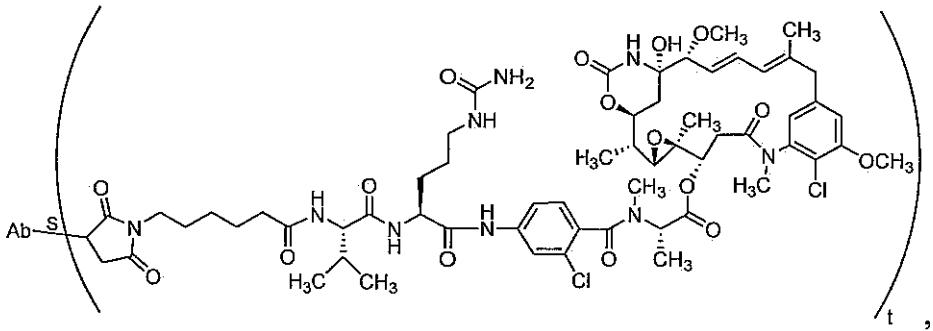
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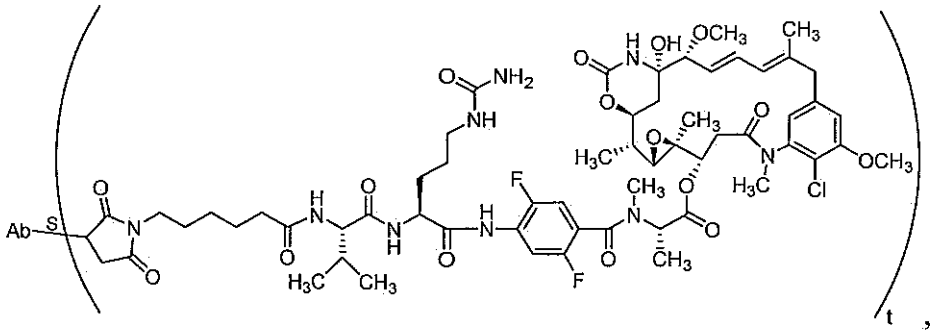


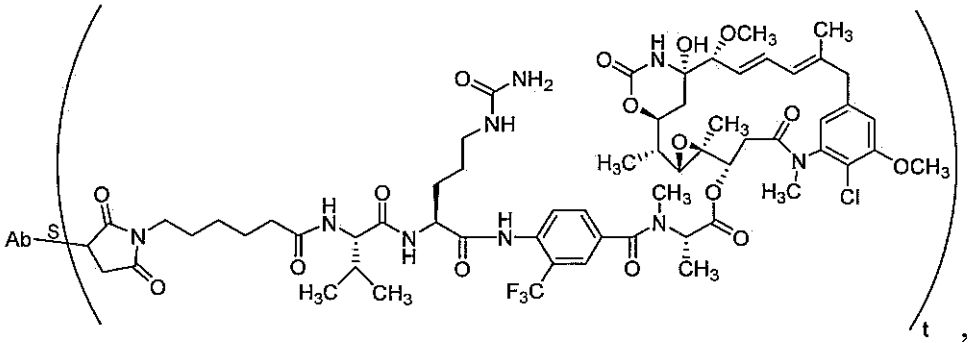
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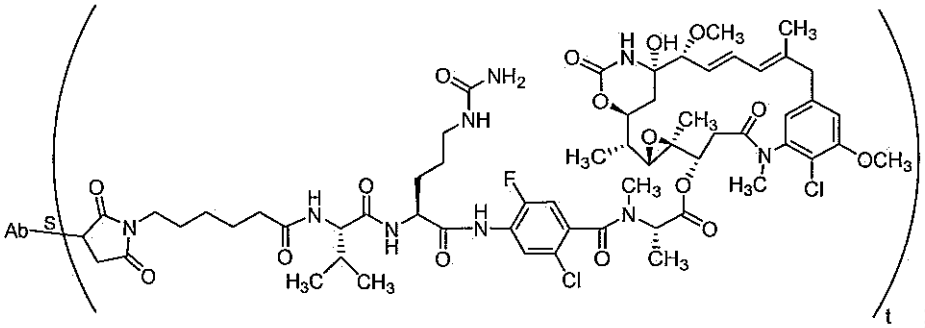


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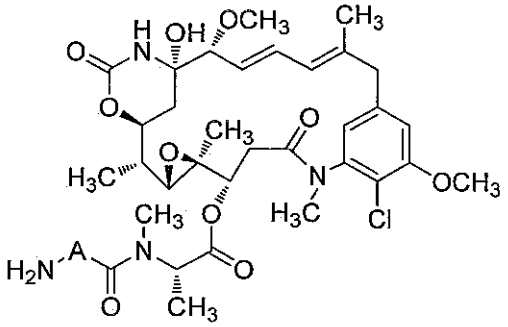

t ; and

t is an integer from 1 to 8.

15. The compound of any of claims 1-10 or 14 wherein t is 1.

16. The compound of any of claims 1-9, 12, or 14 wherein the antibody or antigen binding fragment thereof is an anti-MUC16 antibody or anti-PSMA antibody.

17. A compound of Formula II:



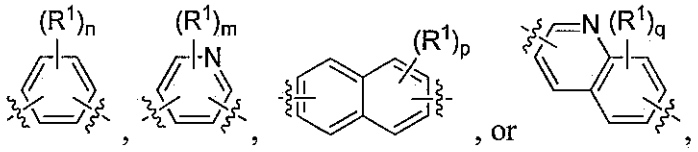
(II)

or a pharmaceutically acceptable salt thereof,

wherein A is arylene or heteroarylene.

18. The compound of claim 17, wherein:

A is:



wherein:

R^1 is, independently at each occurrence, alkyl, alkenyl, alkynyl, alkoxy, aryl, alkaryl, aralkyl, halo, haloalkyl, haloalkoxy, heteroaryl, heterocycloalkyl, cyano, nitro, $-OR^A$, $-SO_2R^A$, $-C(=O)R^A$, or azido,

wherein R^A is alkyl;

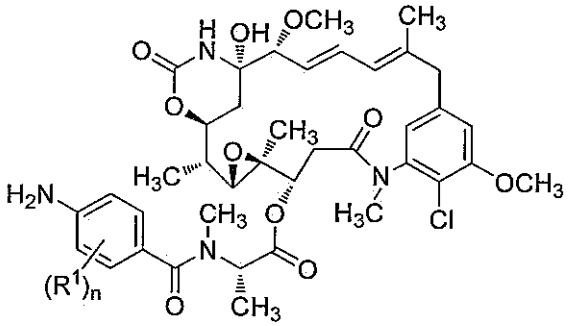
n is an integer from 0 to 4;

m is and integer from 0 to 3;

p is an integer from 0 to 6; and

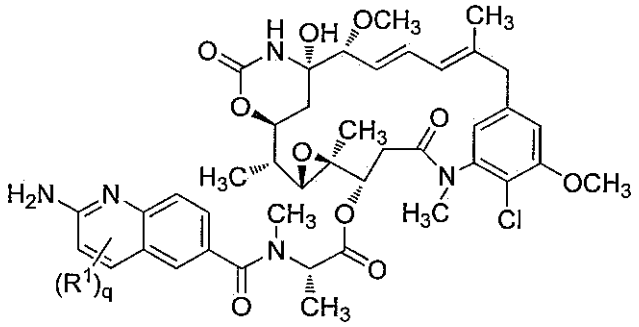
q is an integer from 0 to 5.

19. The compound of claim 17, wherein the compound of Formula (II) is a compound of the Formula (IIA):



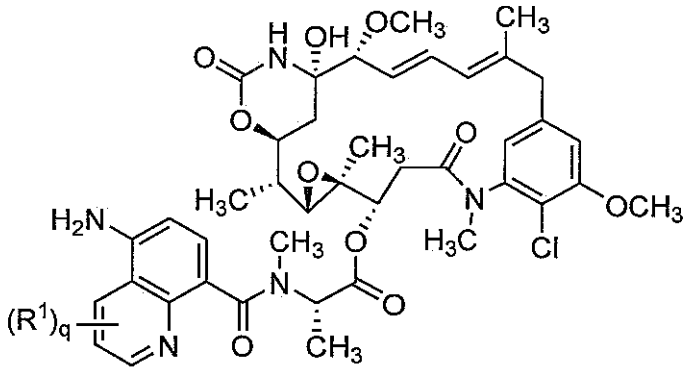
(IIA).

20. The compound of claim 17, wherein the compound of Formula (II) is a compound of the Formula (IIB):



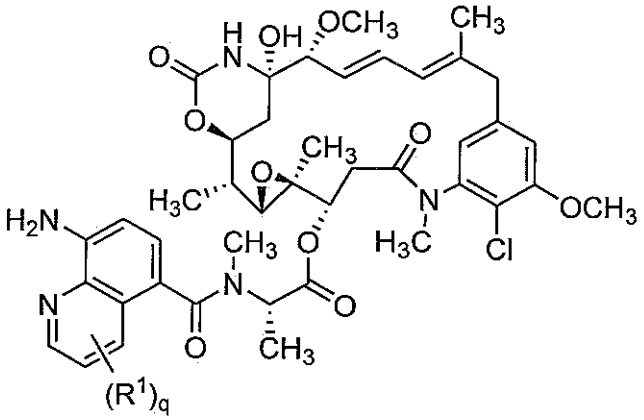
(IIB).

21. The compound of claim 17, wherein the compound of Formula (II) is a compound of the Formula (IIB2):



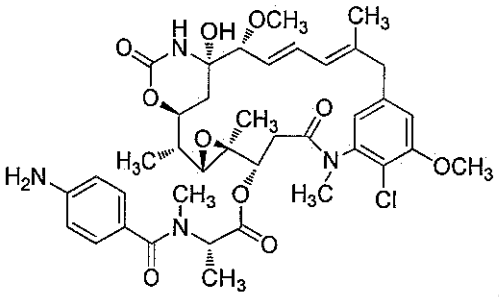
(IIB2).

22. The compound of claim 17, wherein the compound of Formula (II) is a compound of the Formula (IIB3):

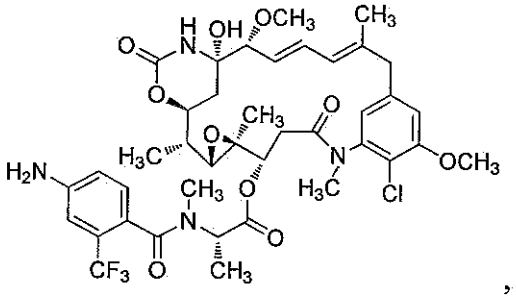


(IIB3).

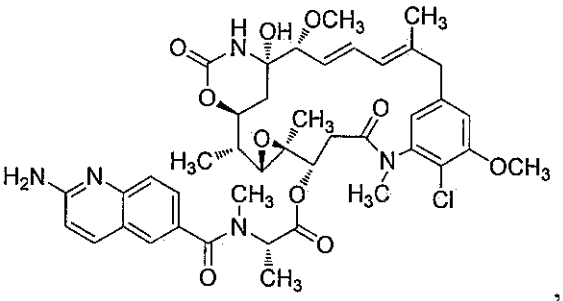
23. The compound of claim 17, wherein the compound is:



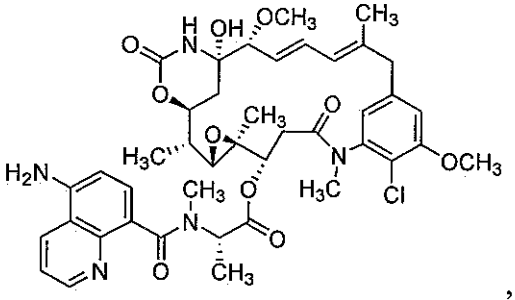
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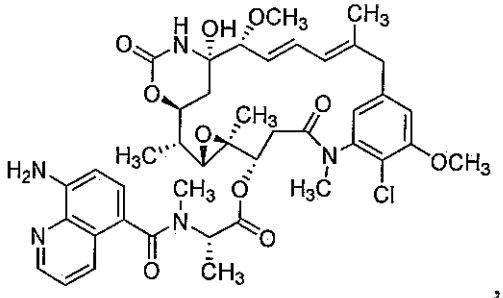
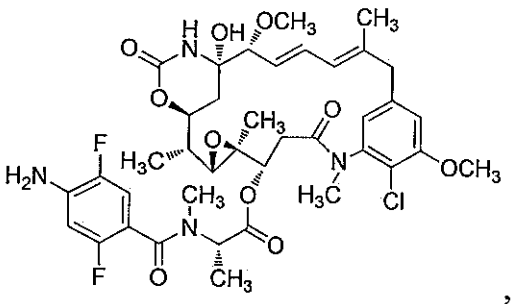
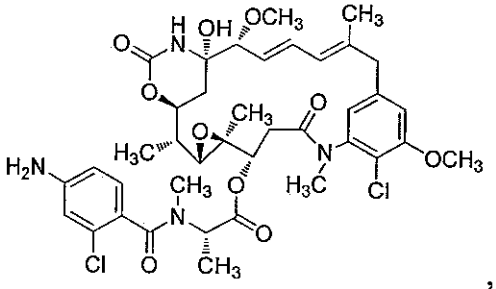
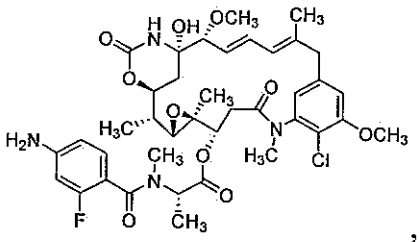
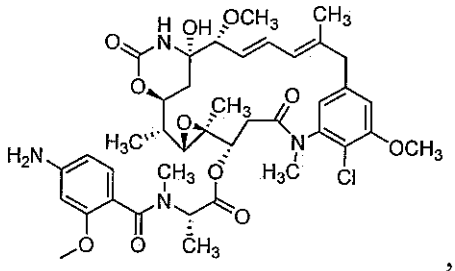
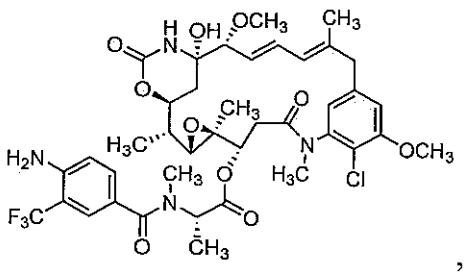
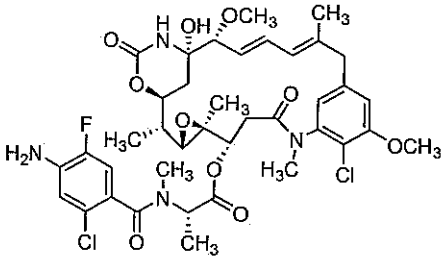
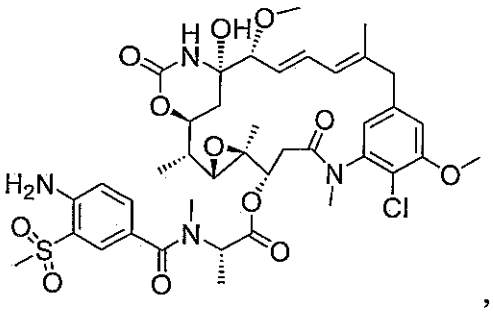
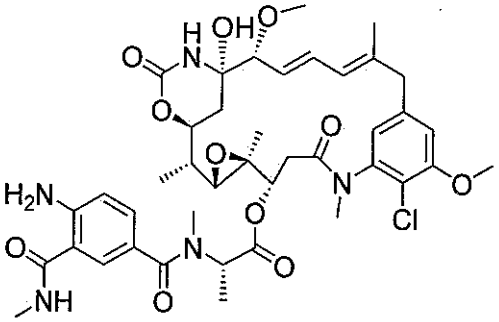
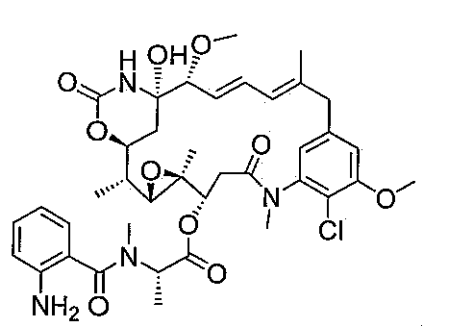
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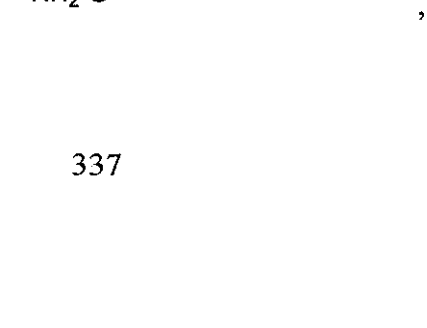


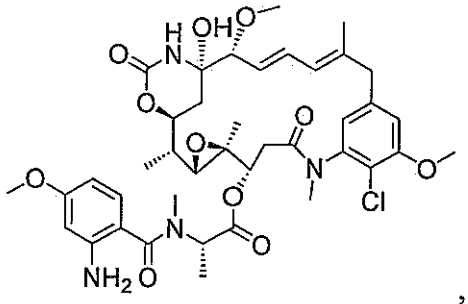
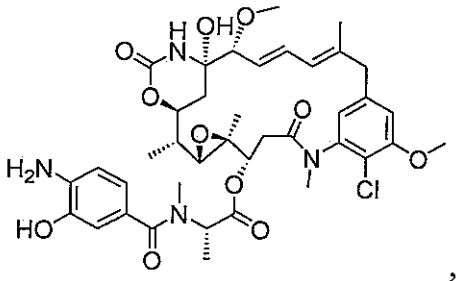
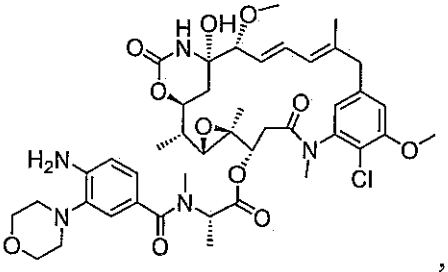
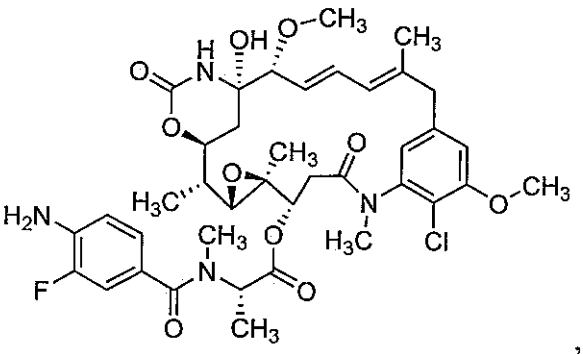
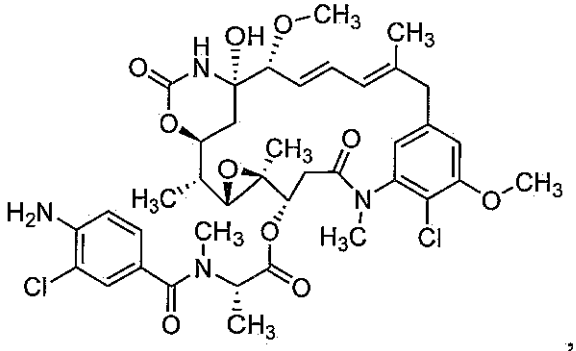
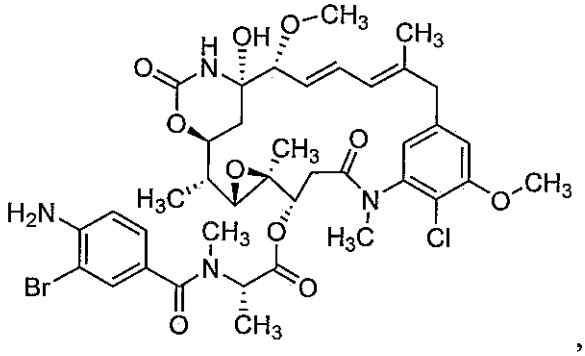
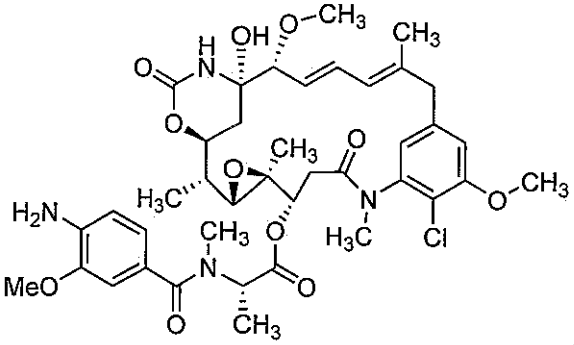
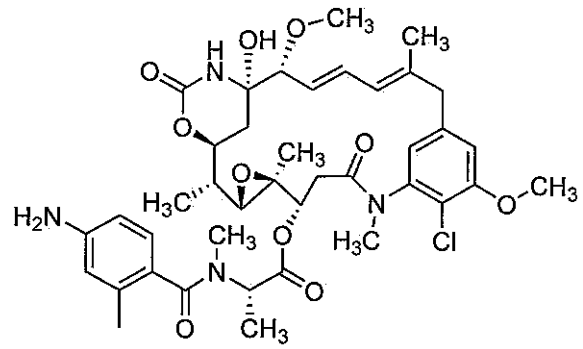
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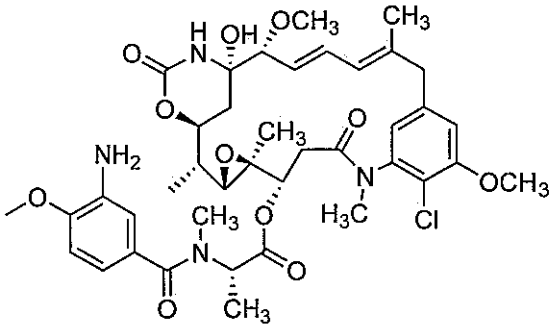
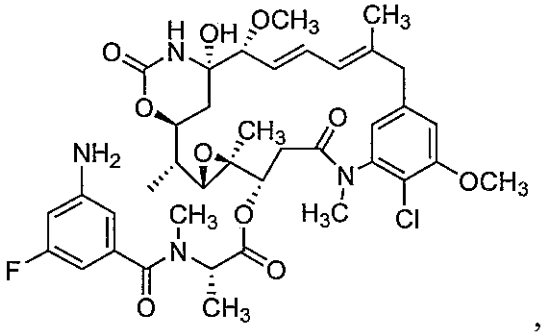
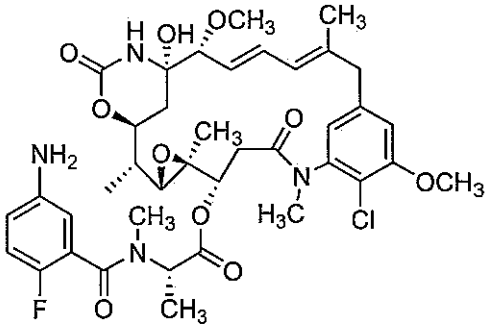
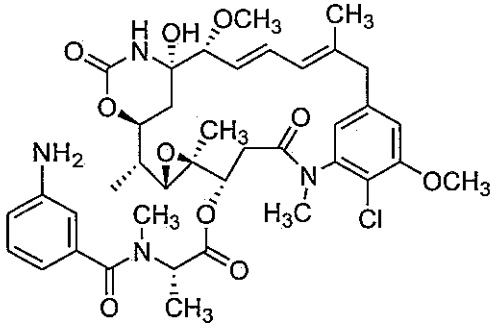
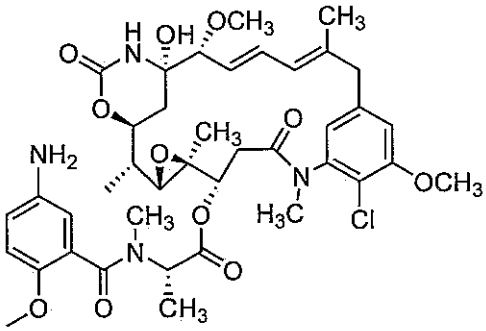
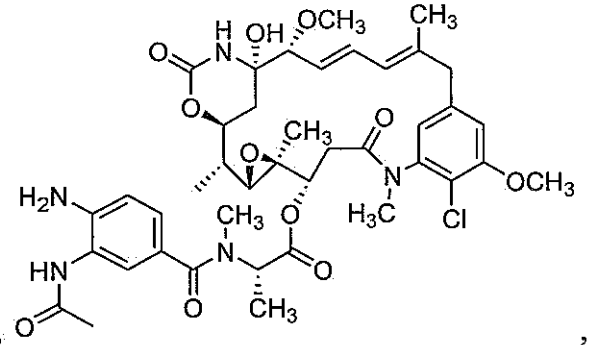
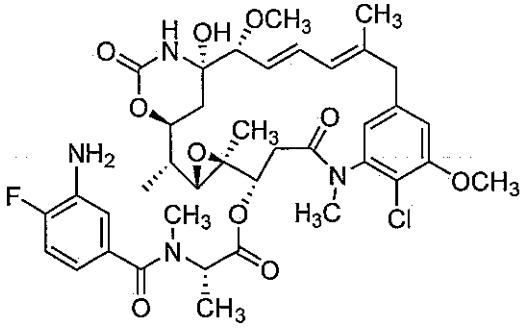


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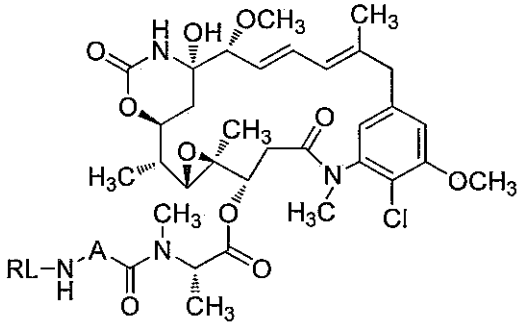

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24. A pharmaceutical composition comprising the compound of any of claims 1-23 and a pharmaceutically acceptable excipient

25. Use of a compound of any of claims 1-23 or a composition of claim 24 in the manufacture of a medicament for treating cancer .

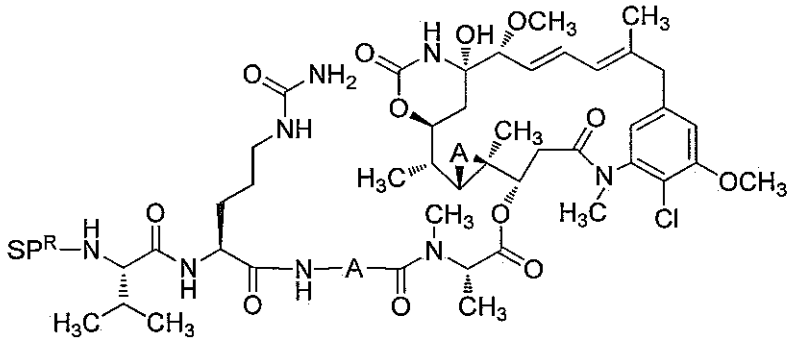
26. A compound of Formula P1:



P1

wherein A is arylene or heteroarylene and RL is a reactive linker.

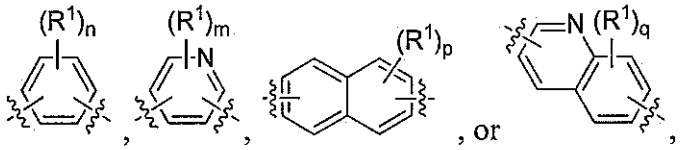
27. The compound of claim 26, wherein the compound of Formula P1 is a compound of Formula P1B:



P1B

wherein

A is:



wherein:

R^1 is alkyl, alkenyl, alkynyl, alkoxy, aryl, alkaryl, aralkyl, halo, haloalkyl, haloalkoxy, heteroaryl, heterocycloalkyl, cyano, nitro, $-OR^A$, $-SO_2R^A$, $-C(=O)R^A$, or azido,

wherein R^A is alkyl;

n is an integer from 0 to 4;

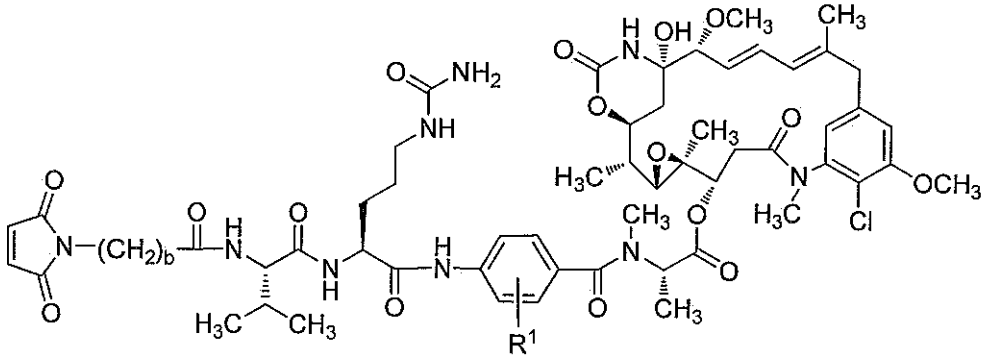
m is an integer from 0 to 3;

p is an integer from 0 to 6; and

q is an integer from 0 to 5; and

SP^R is a reactive spacer.

28. The compound of claim 26, wherein the compound of Formula P1 is a compound of Formula P1H:



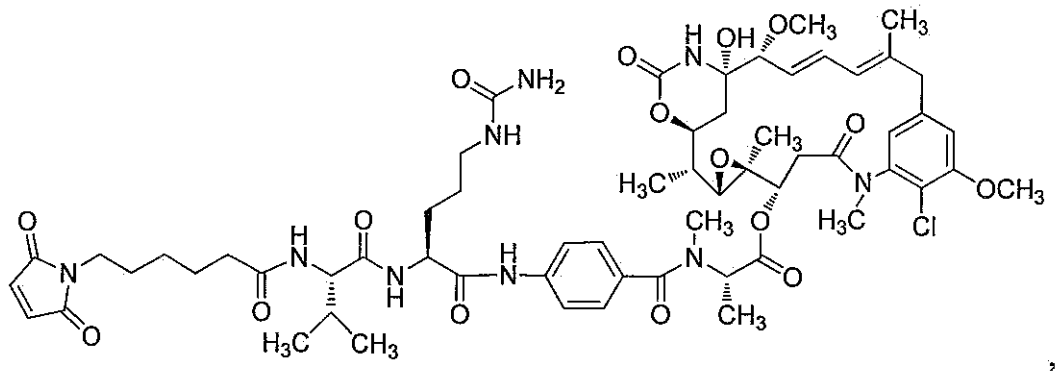
P1H

wherein:

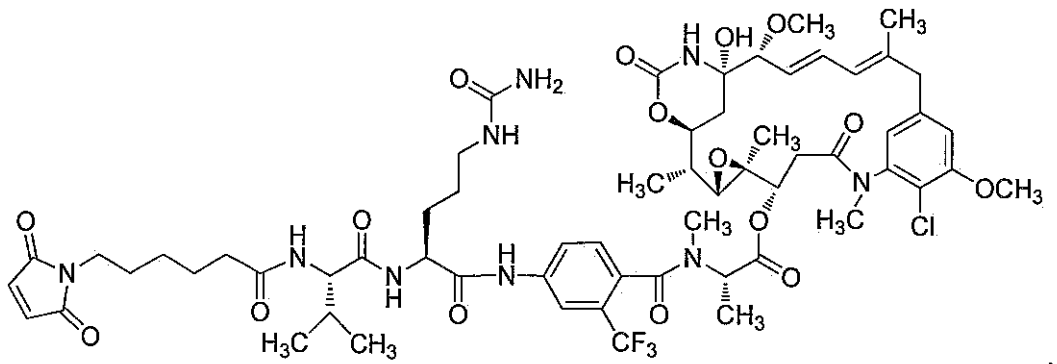
R^1 is hydrogen, alkoxy, halo, haloalkyl, or trifluoromethyl; and

b is an integer from 2 to 8.

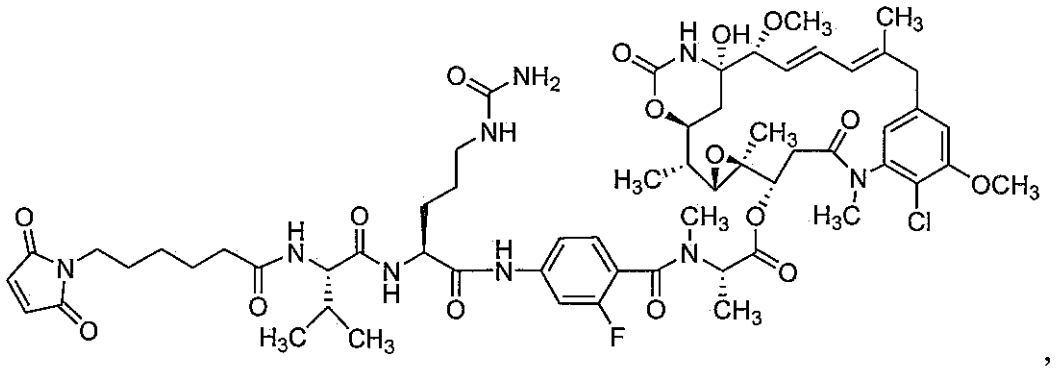
29. The compound of claim 26, wherein the compound is:



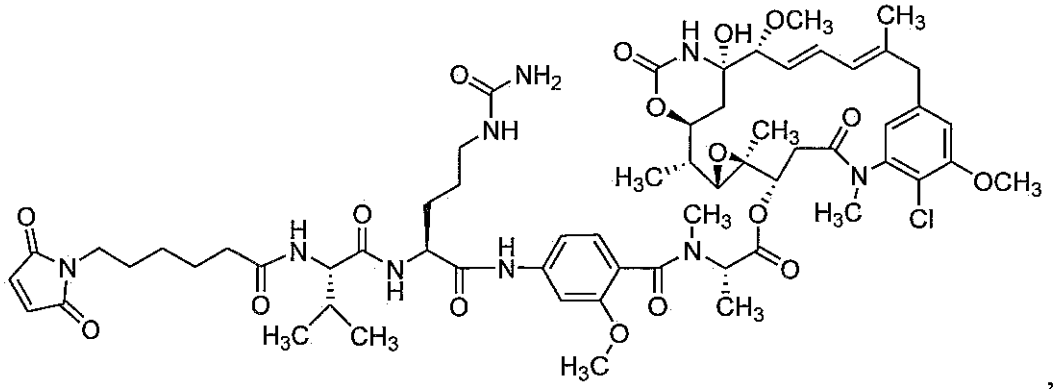
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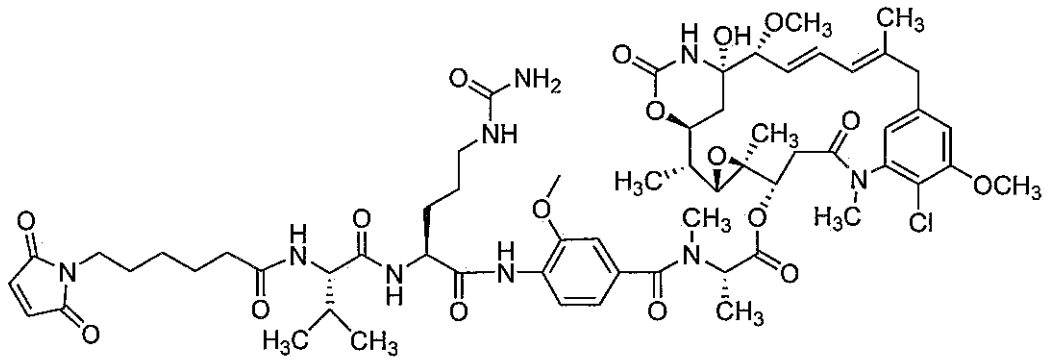
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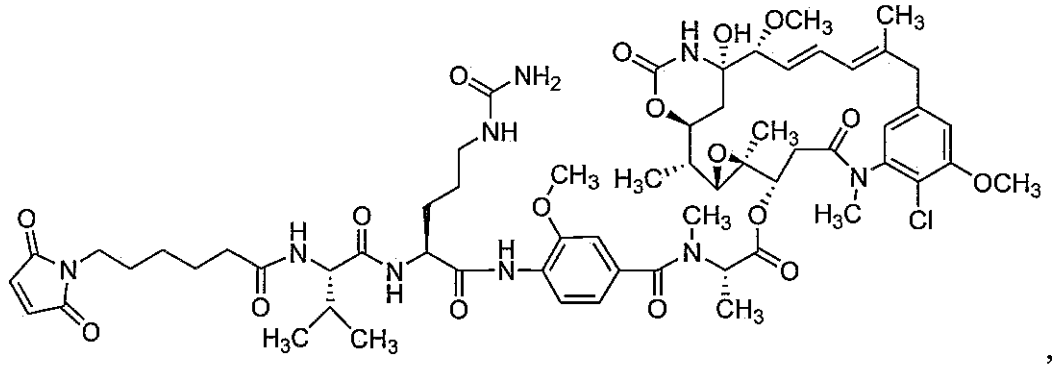
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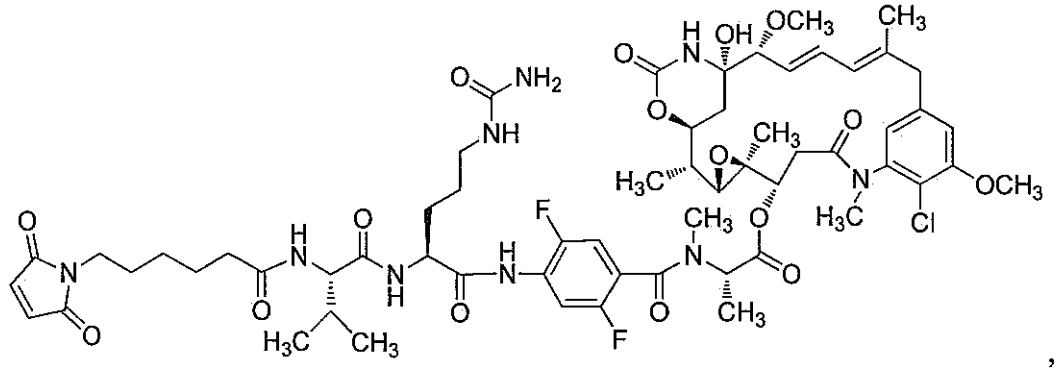
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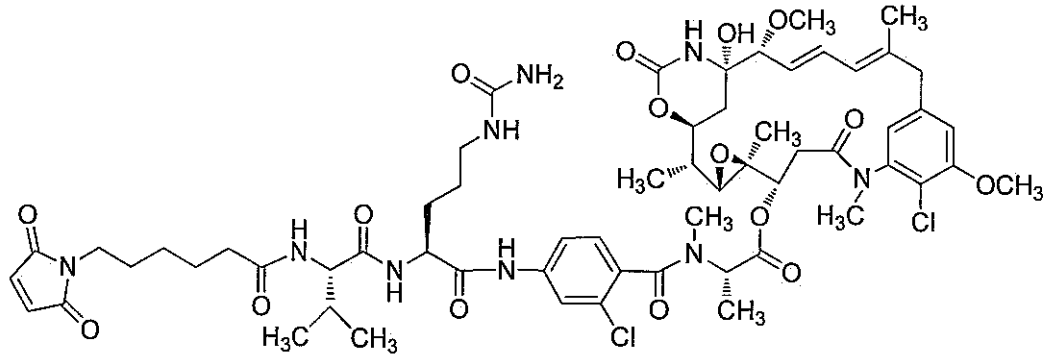
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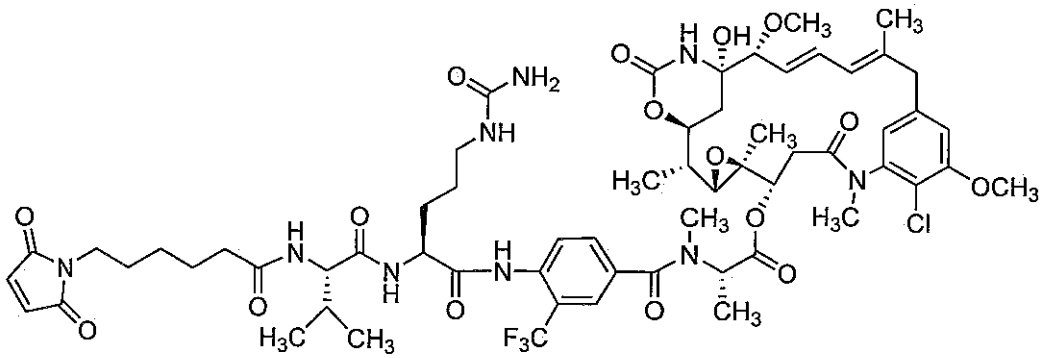
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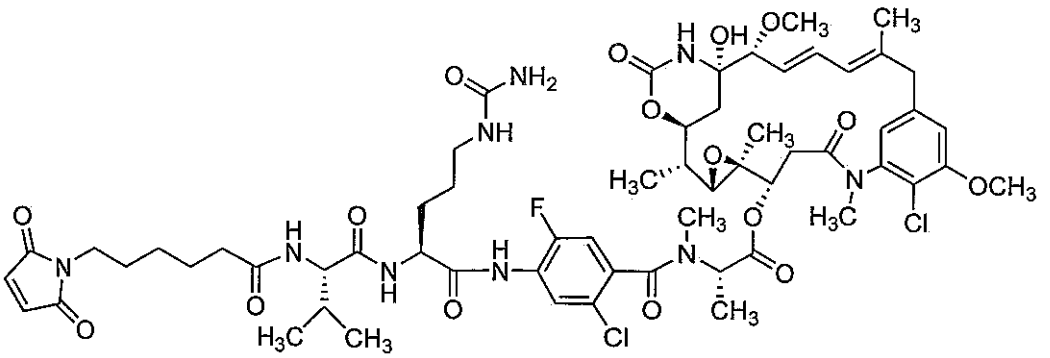
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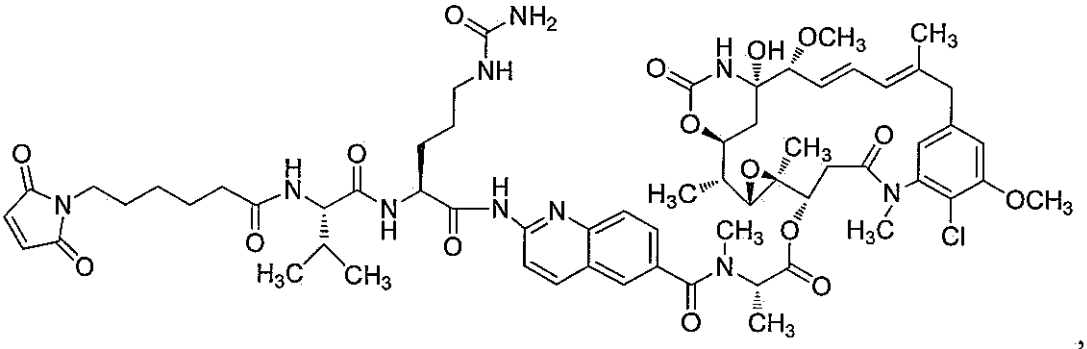
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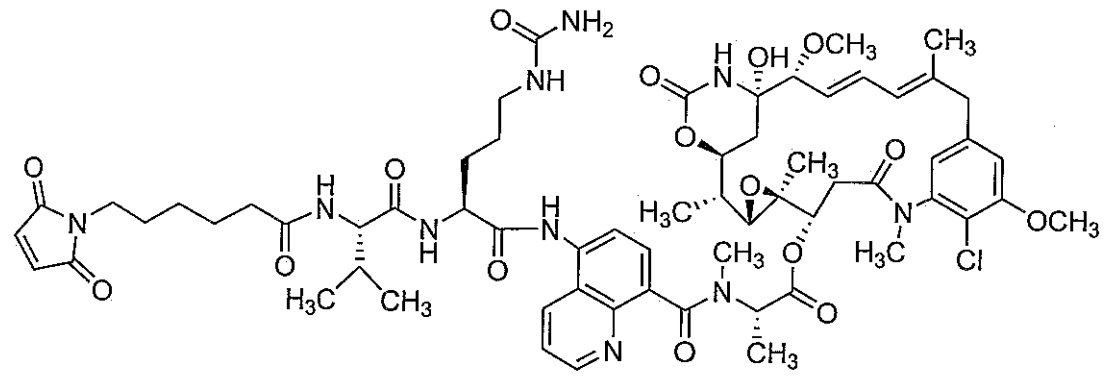
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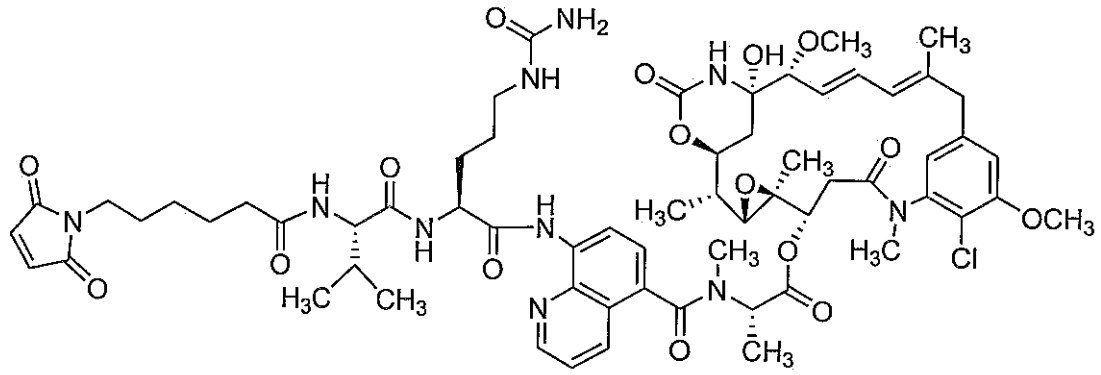
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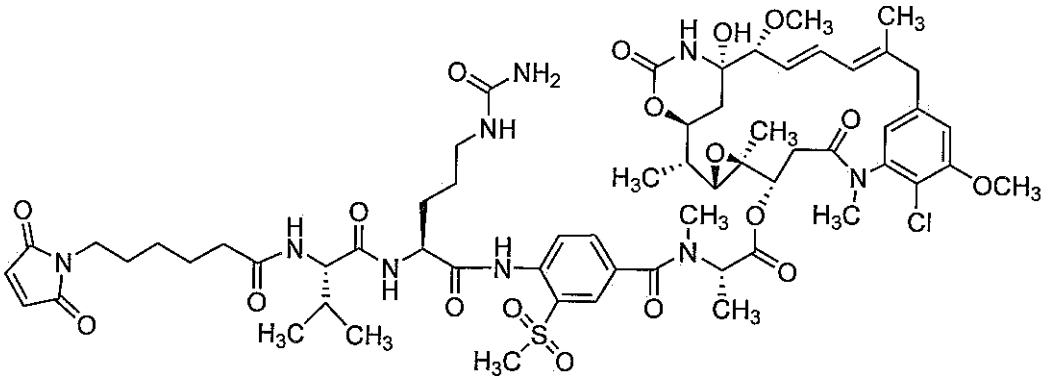
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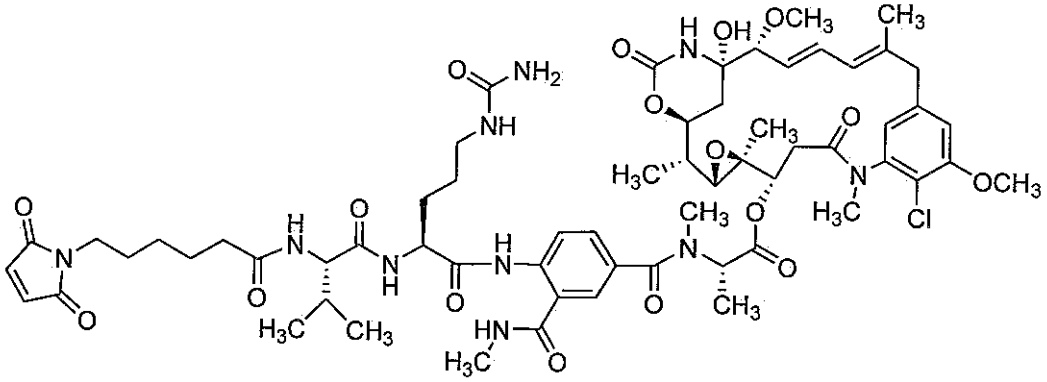
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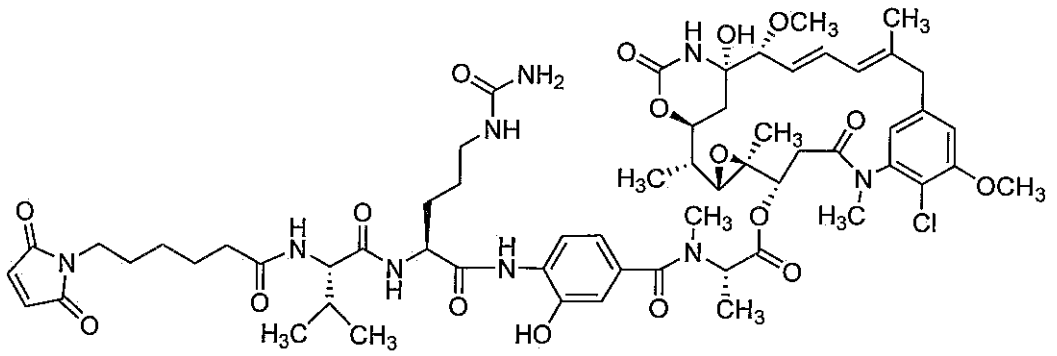
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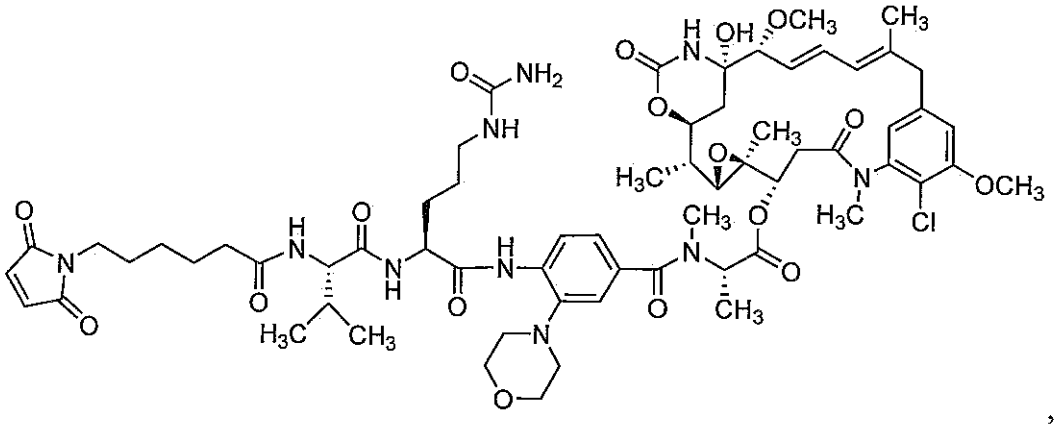


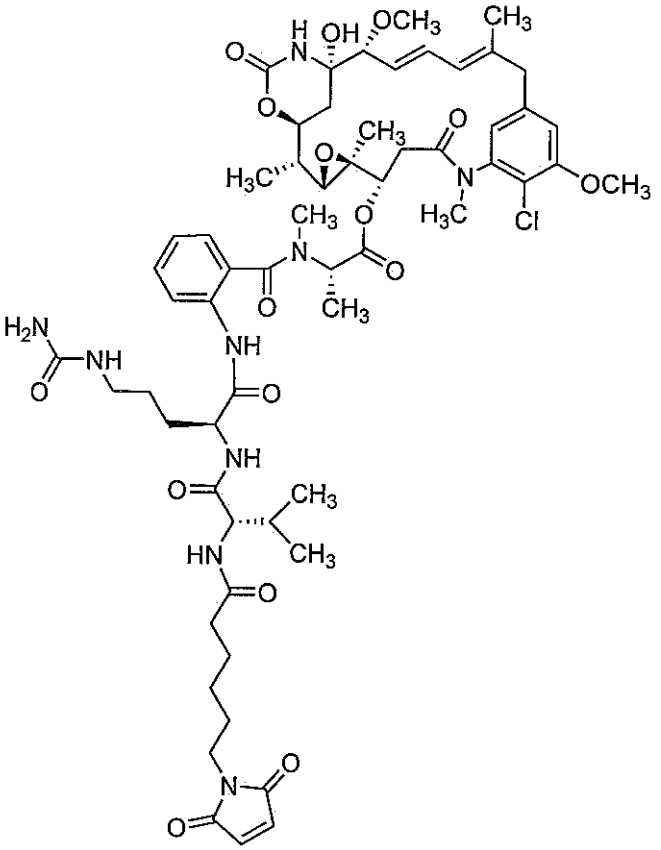
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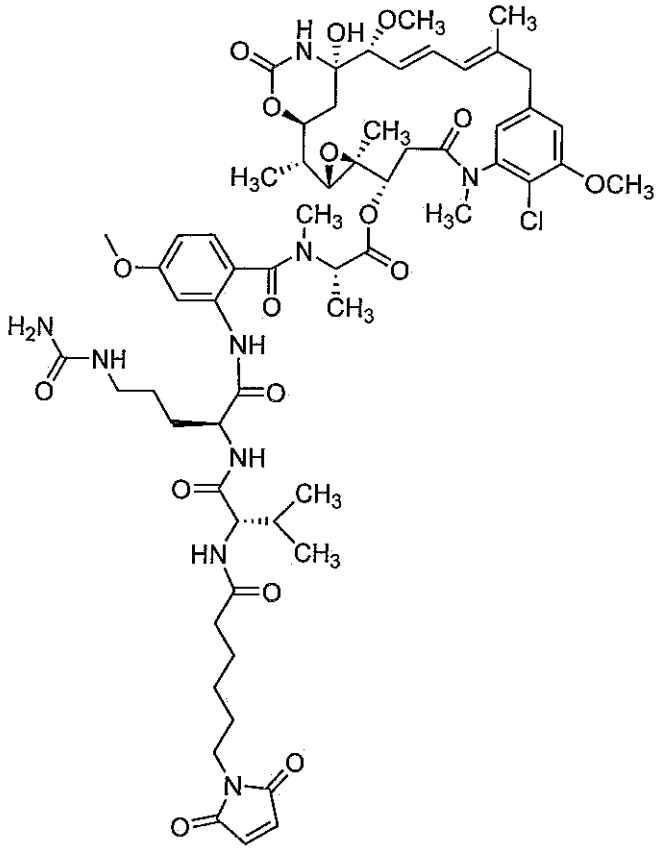
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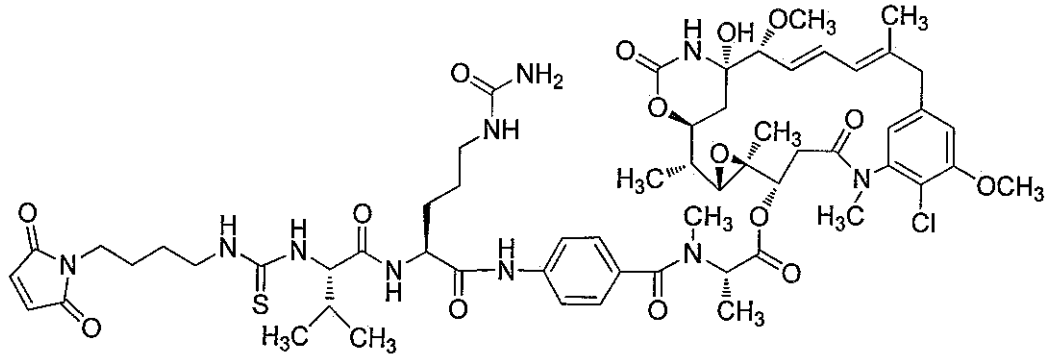



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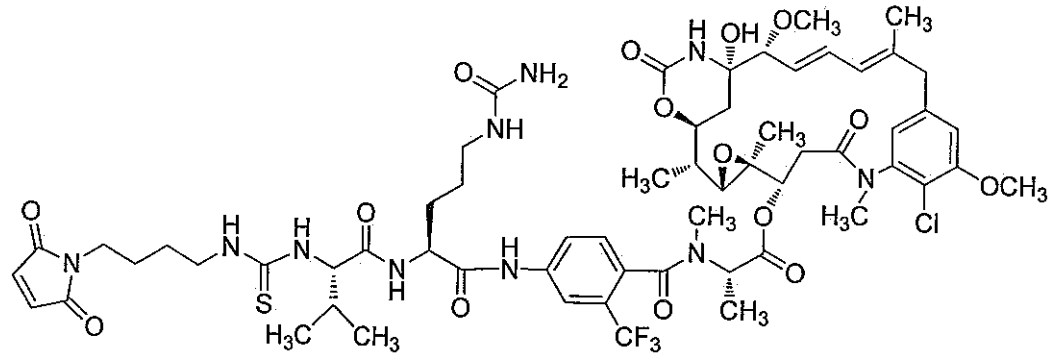
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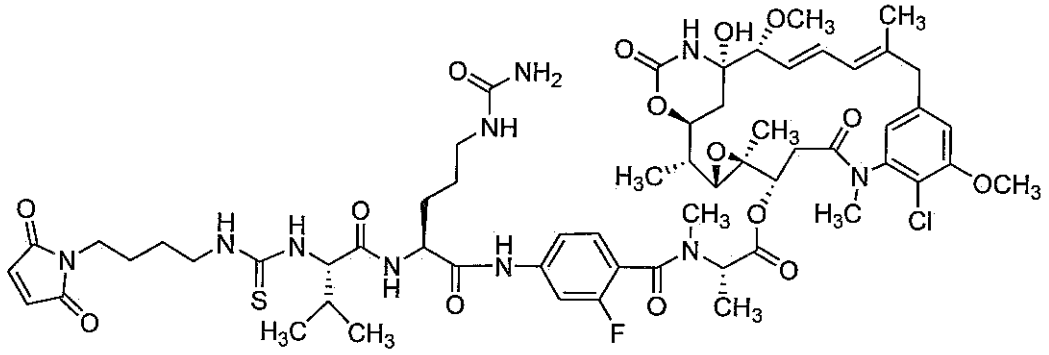
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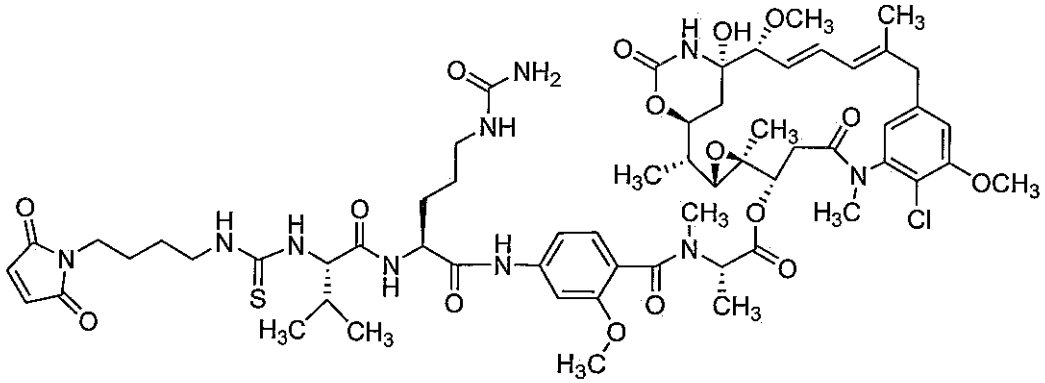
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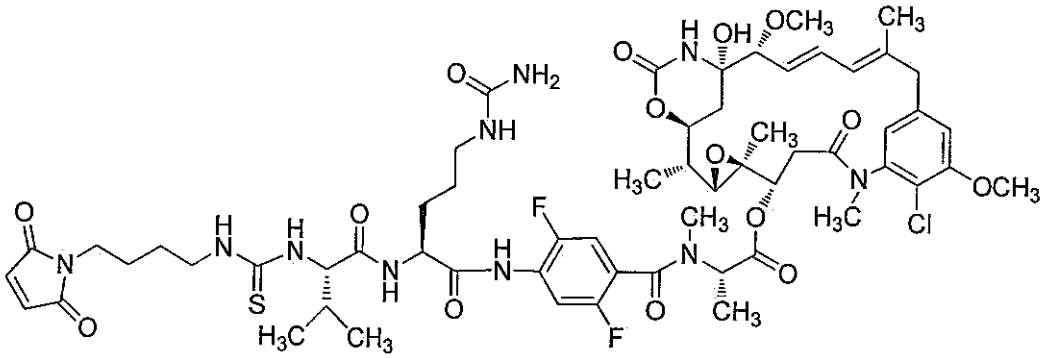
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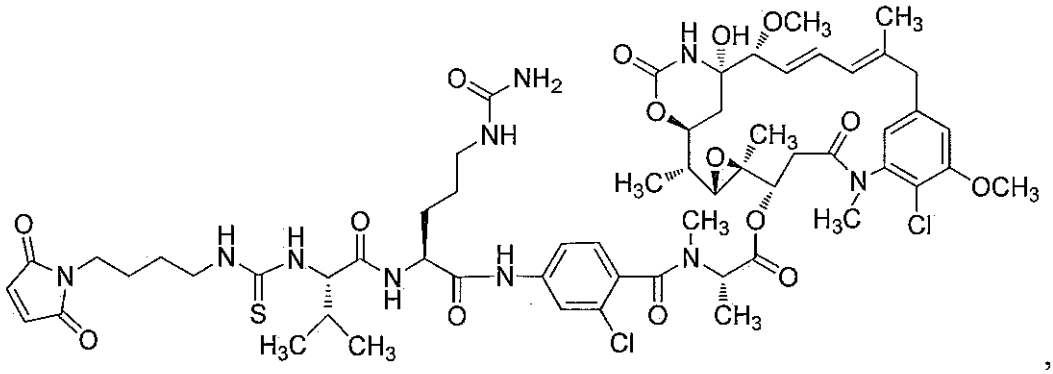
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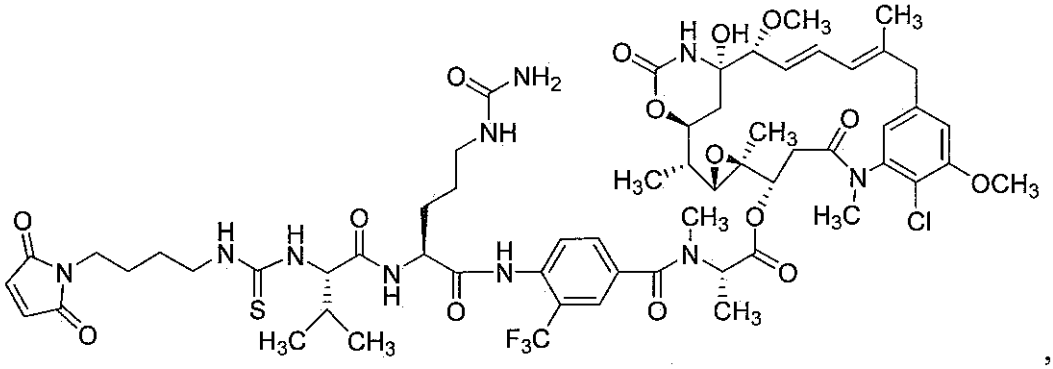
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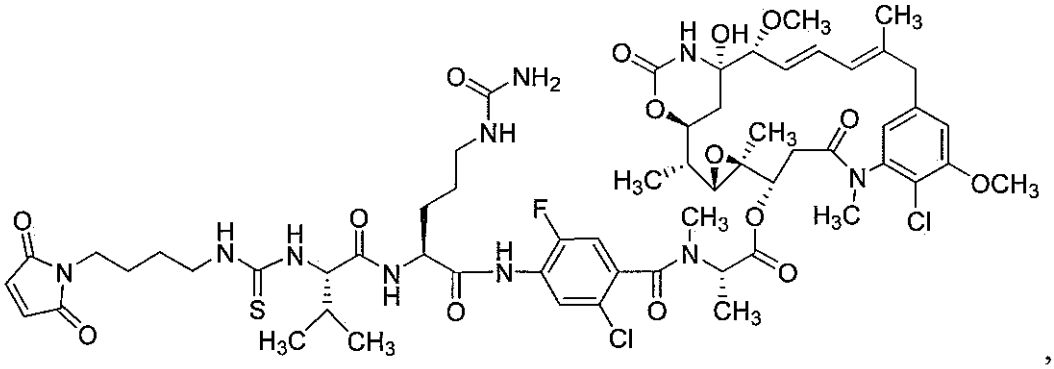
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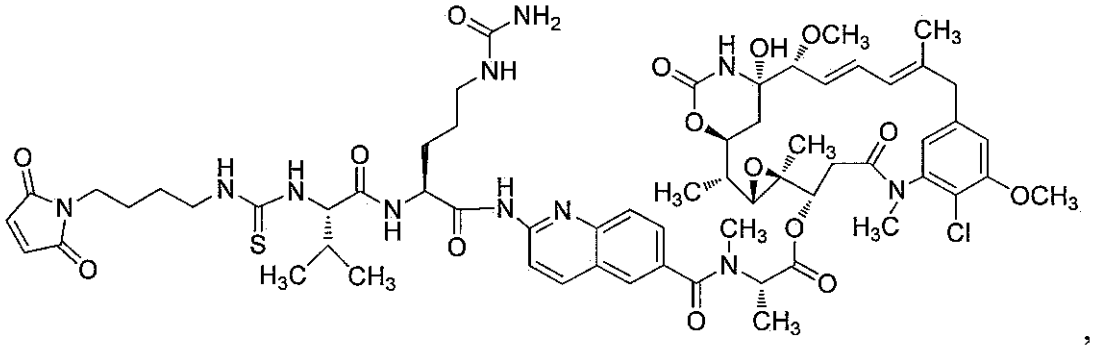
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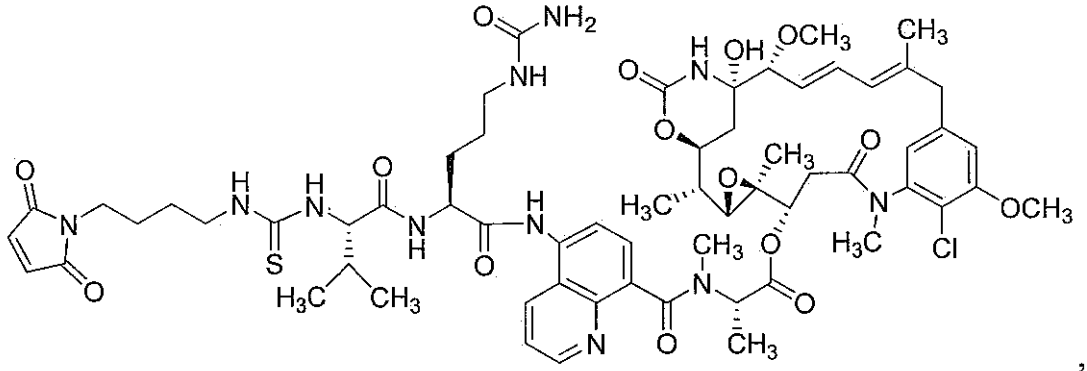
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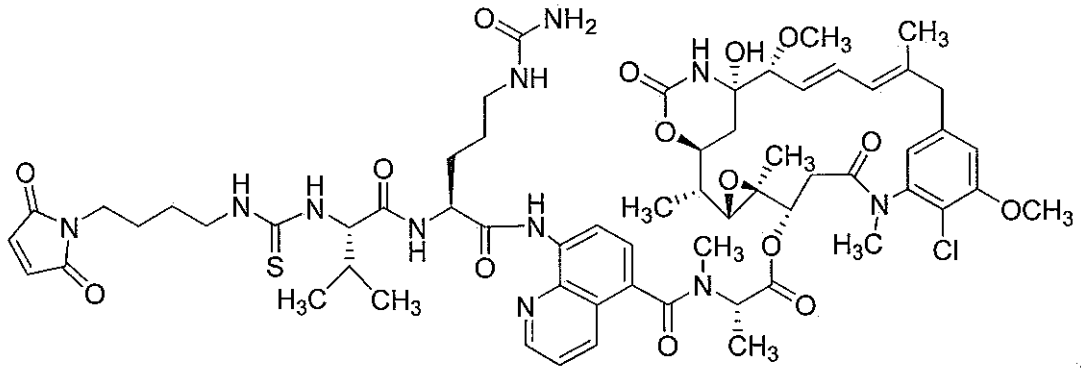
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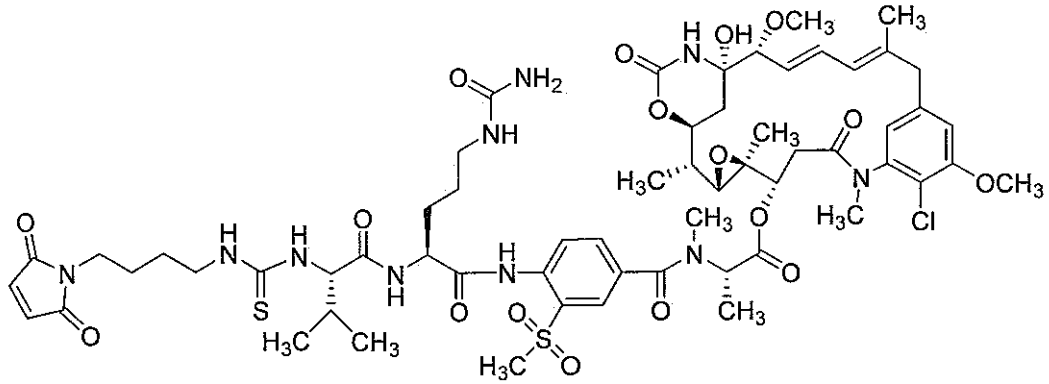
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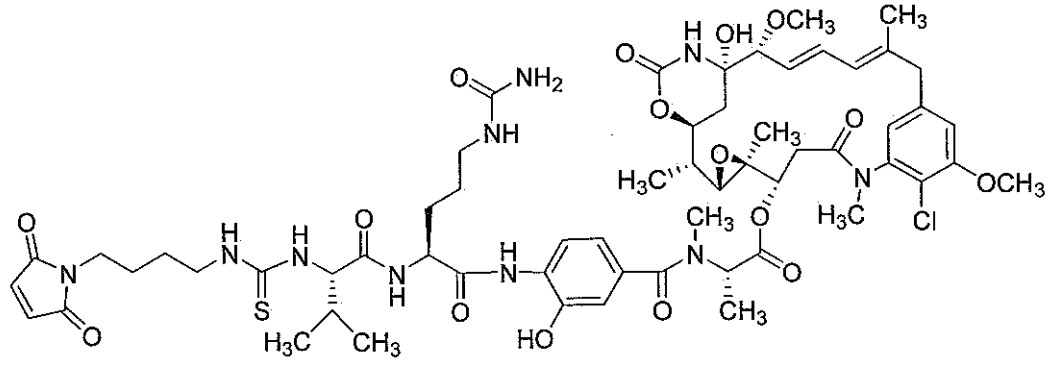
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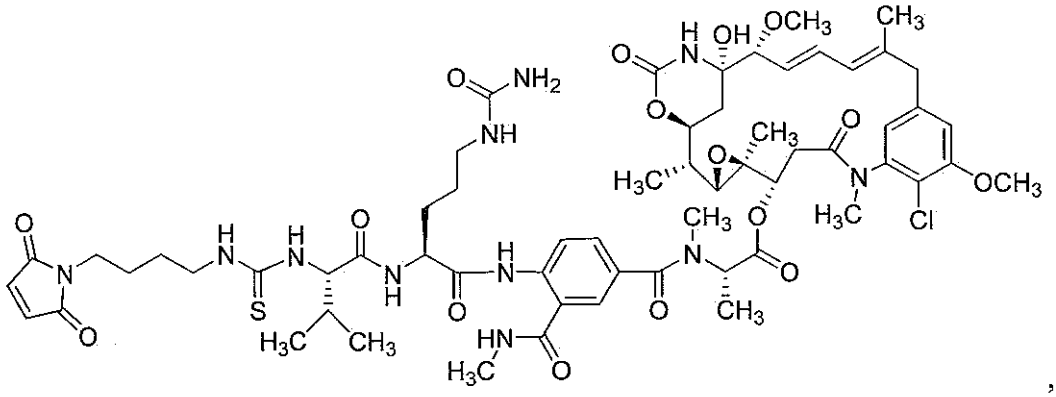
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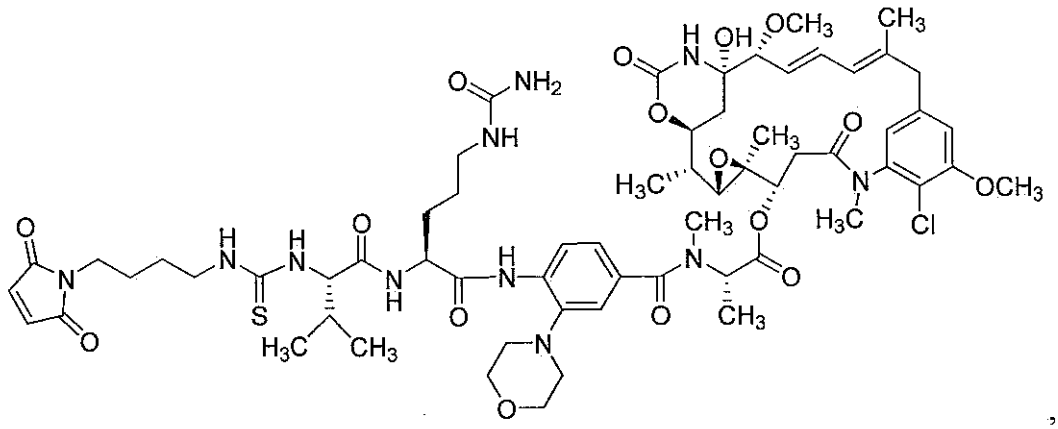
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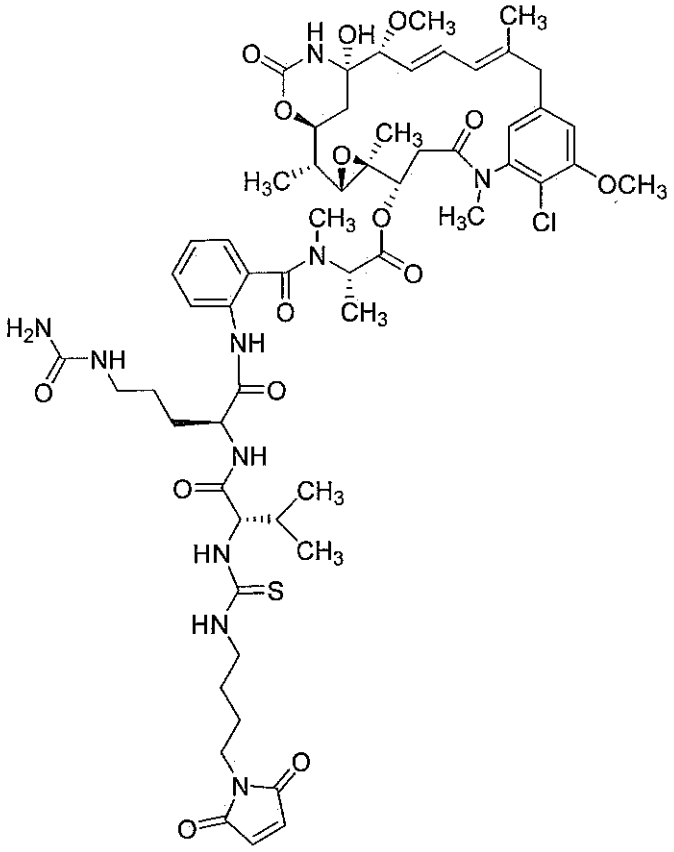
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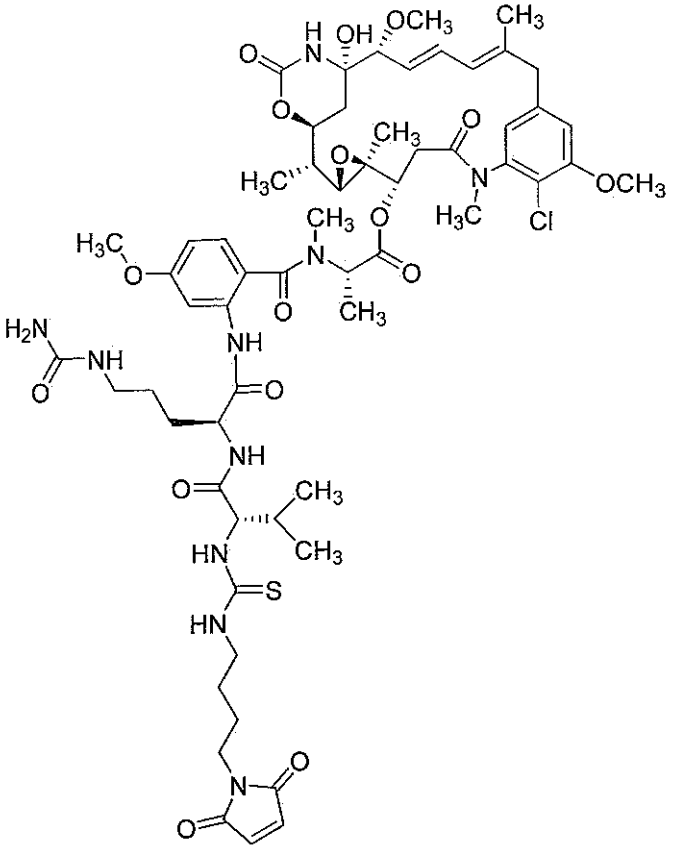
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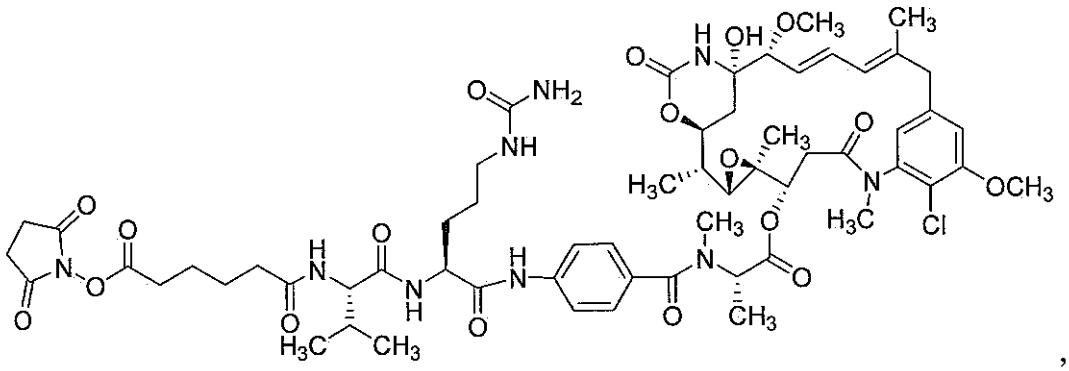
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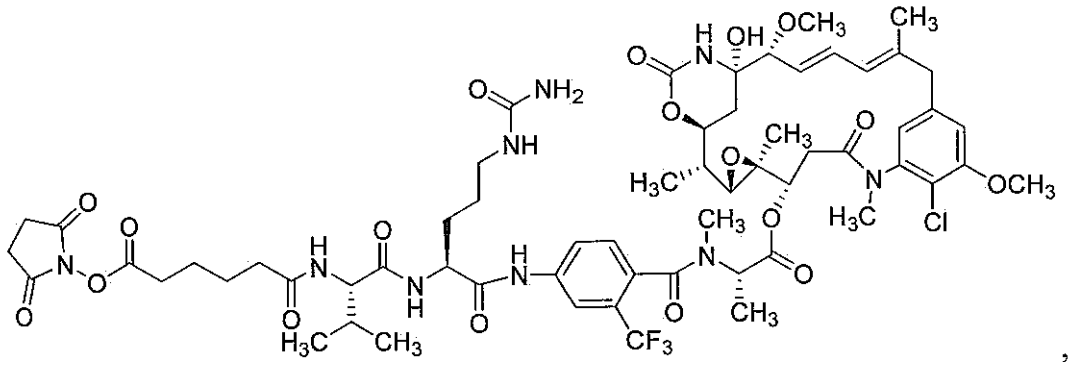
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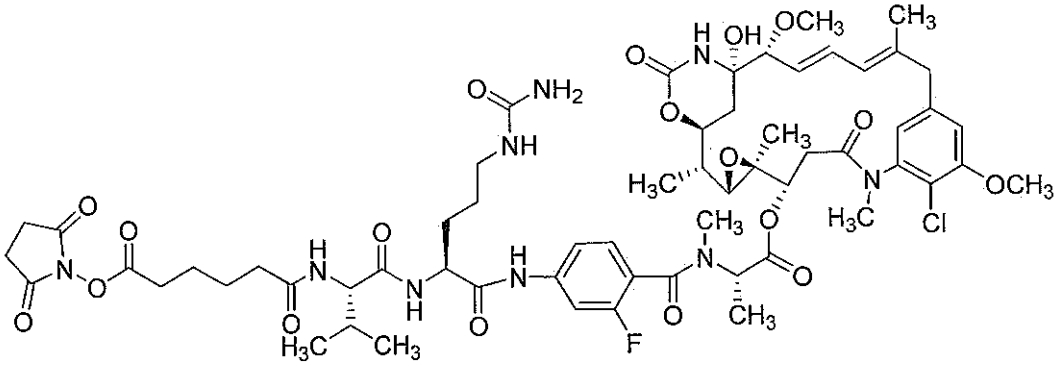
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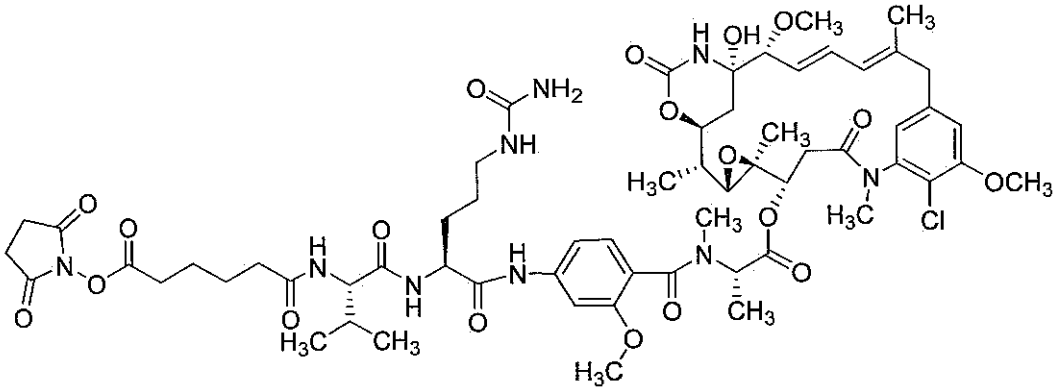
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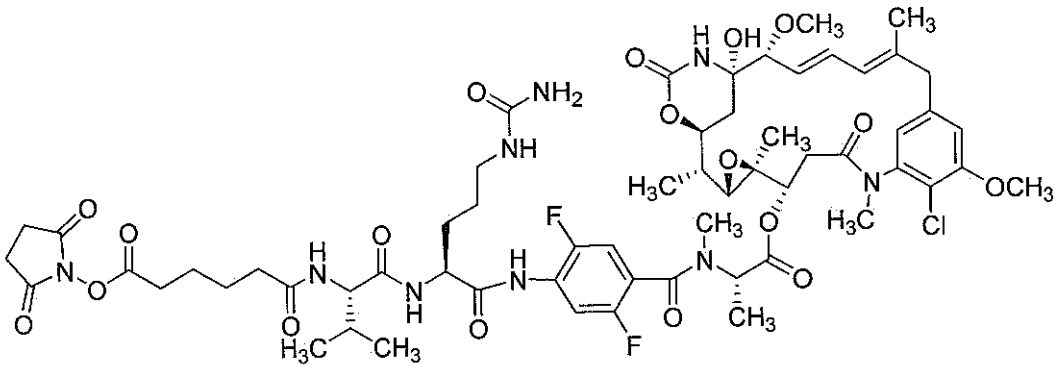
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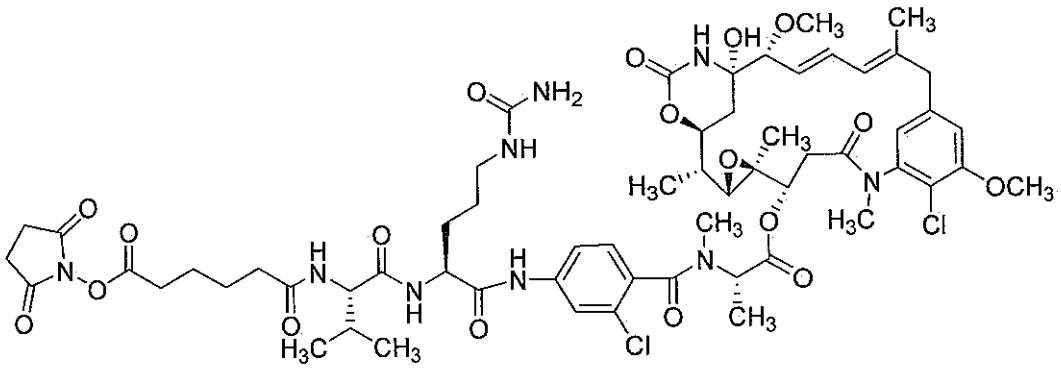
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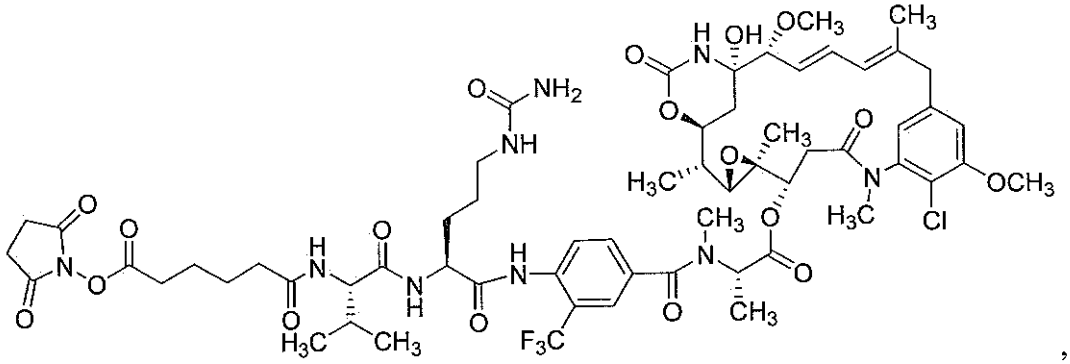
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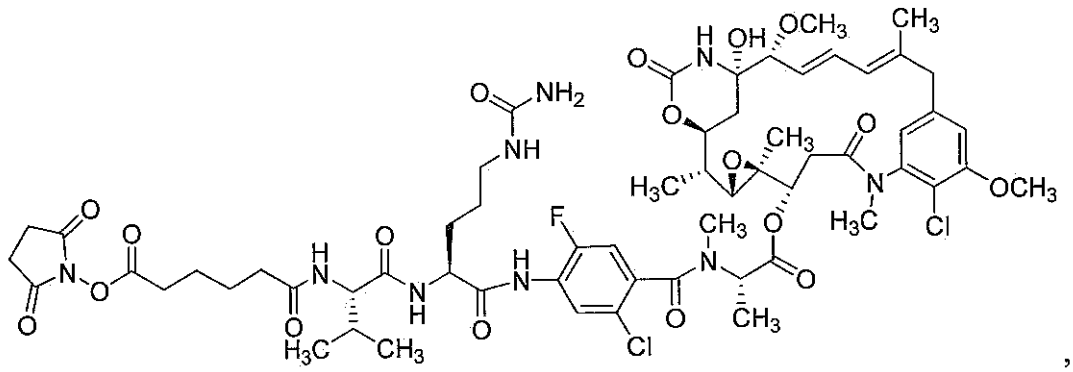
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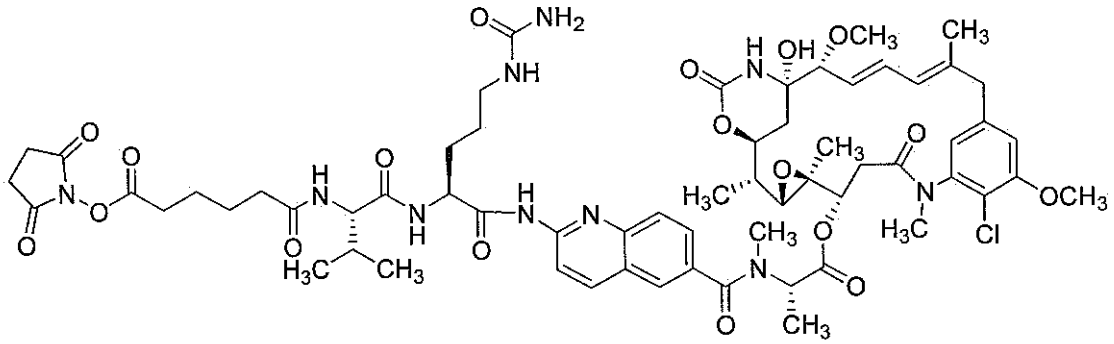
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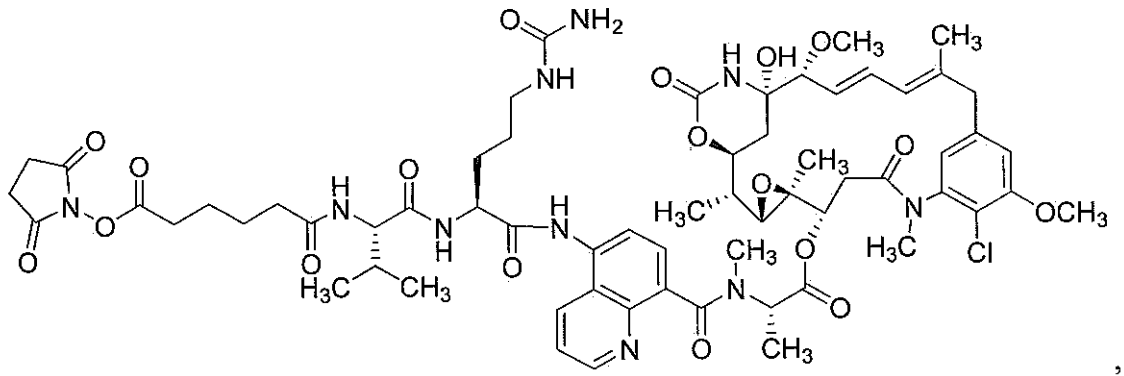
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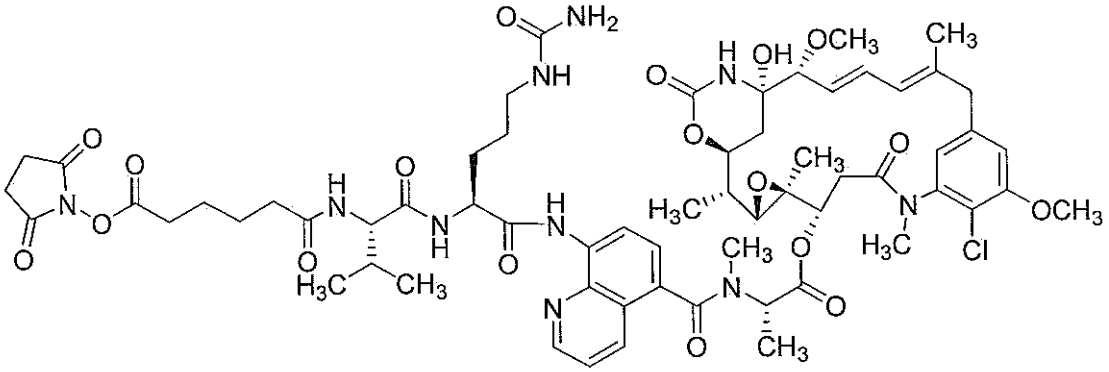
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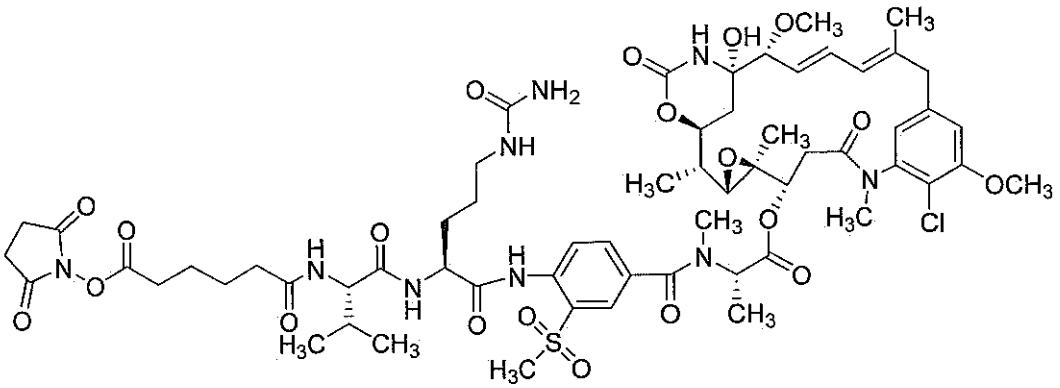
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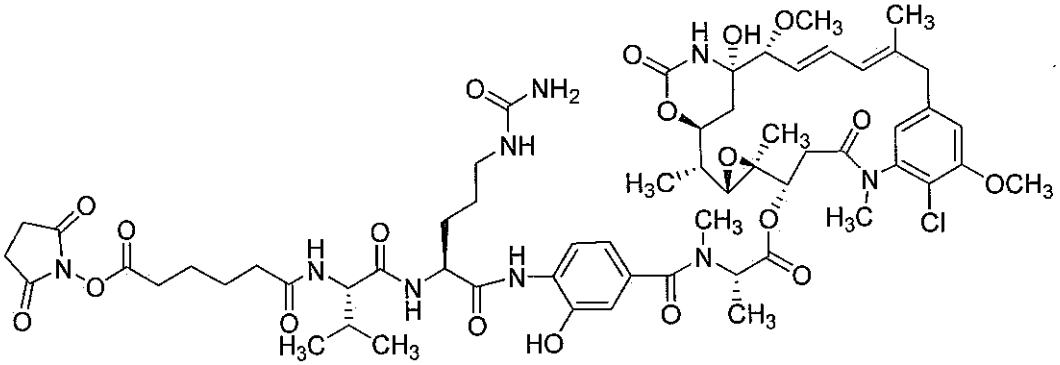
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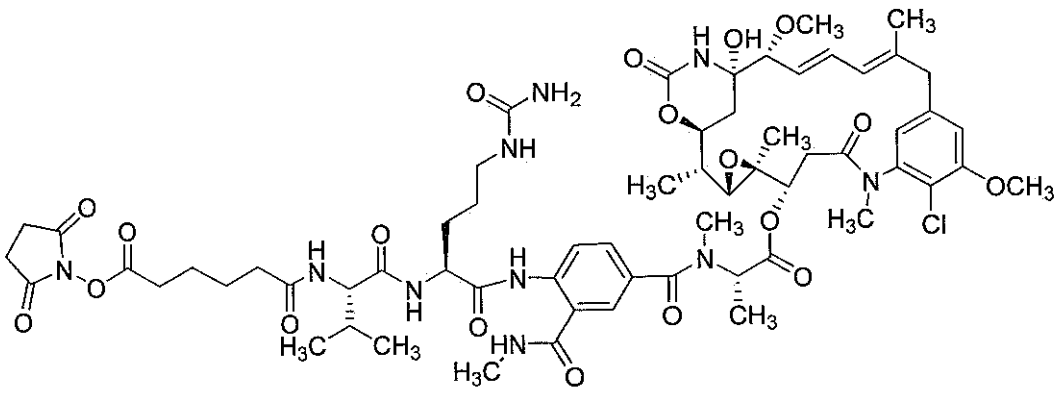
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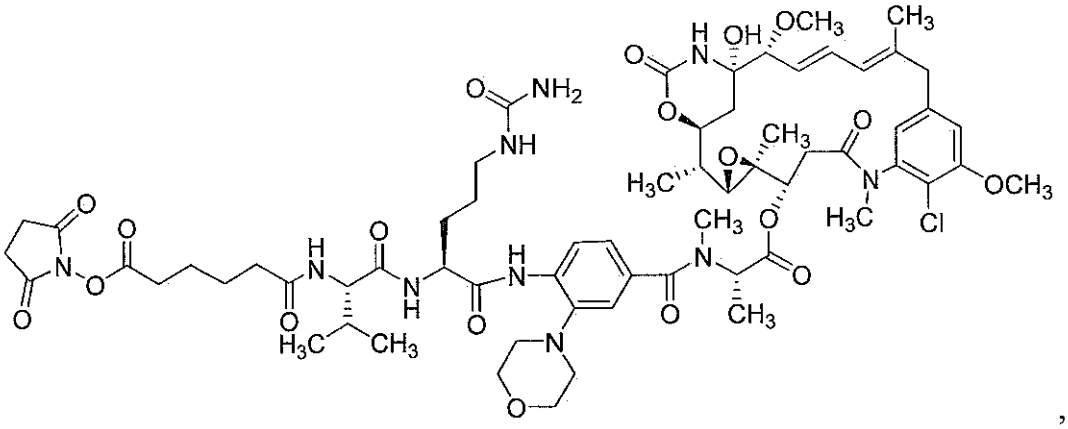
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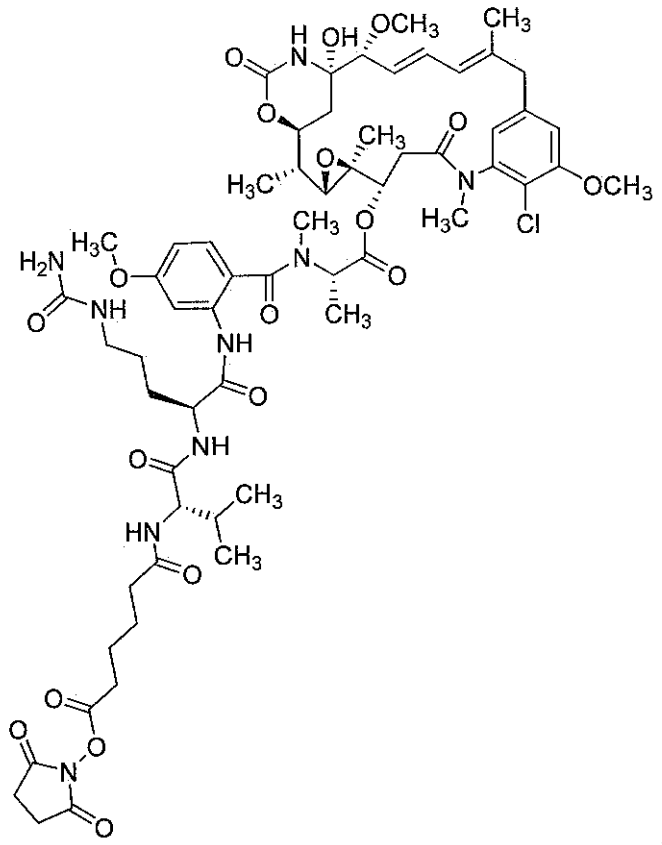
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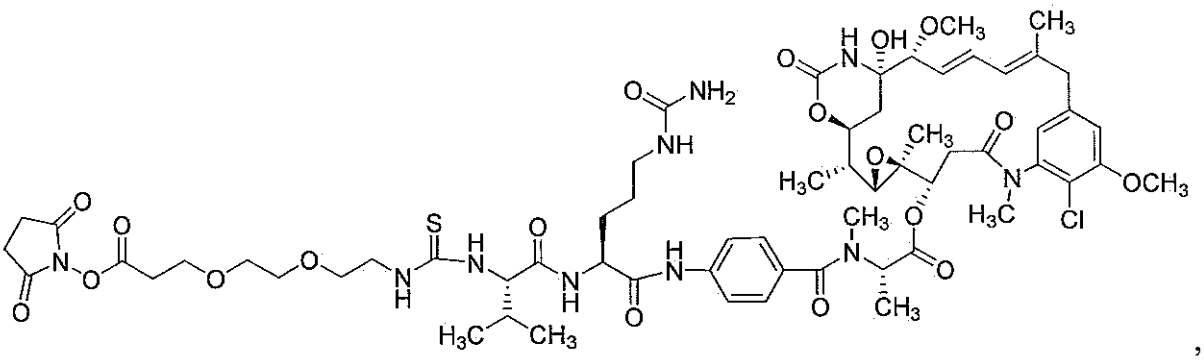
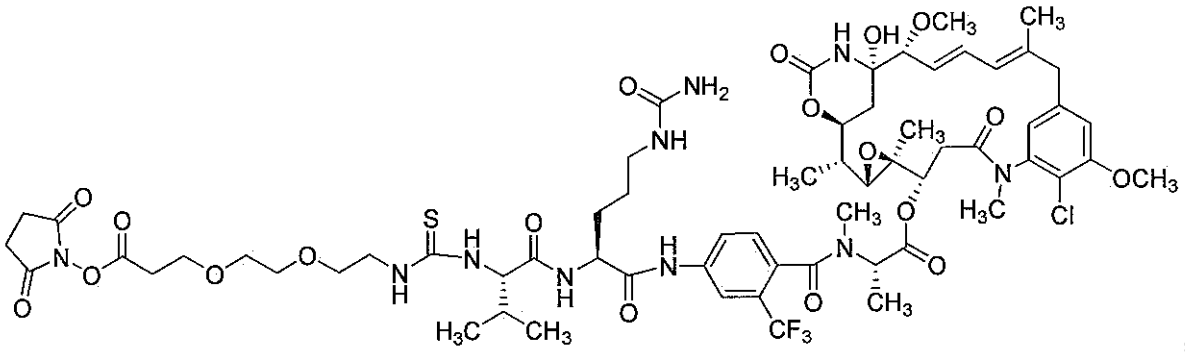
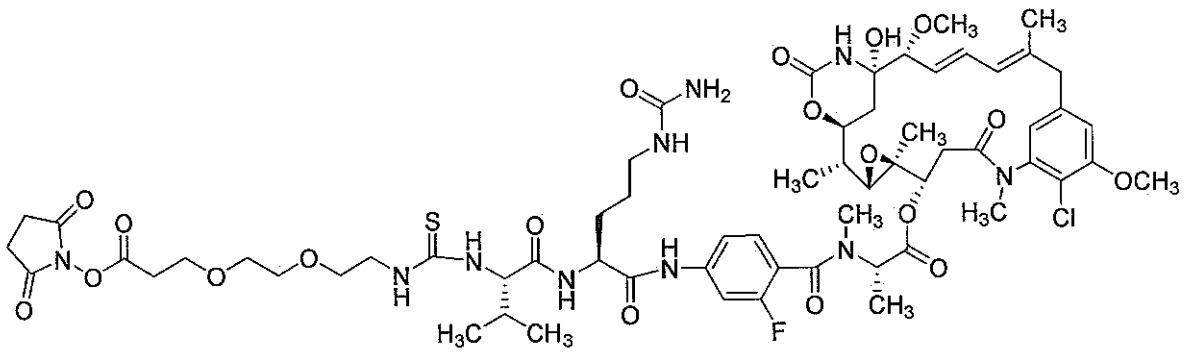
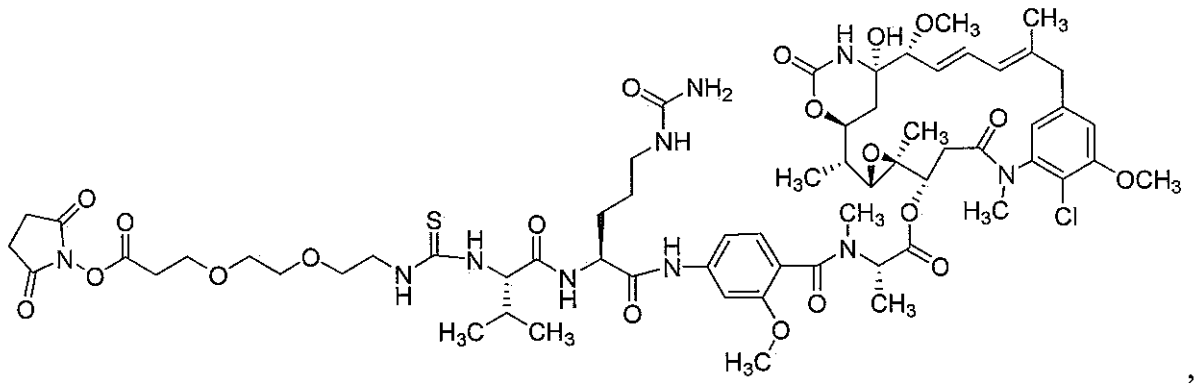
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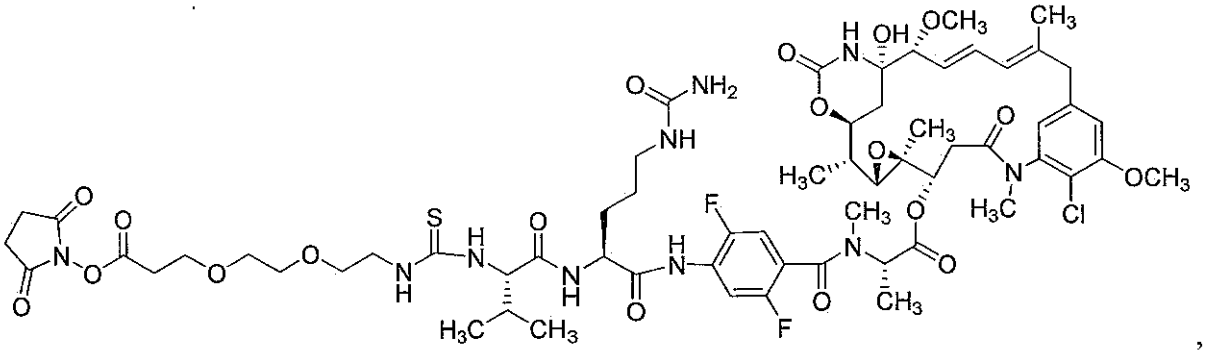


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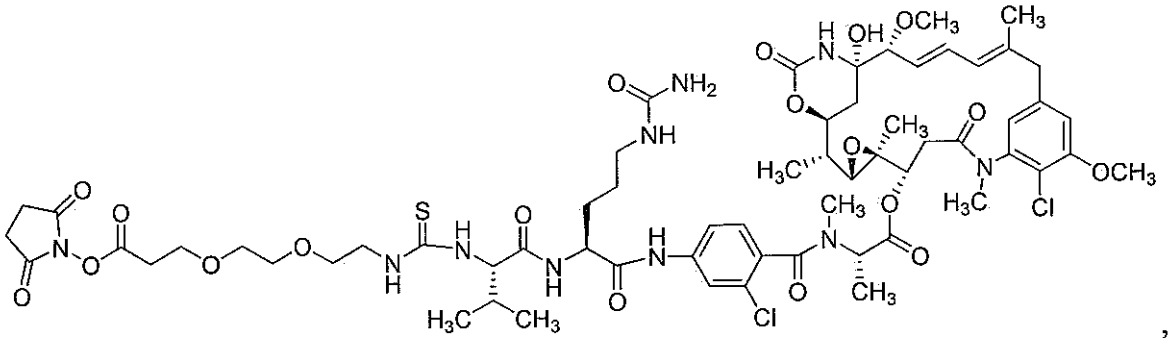


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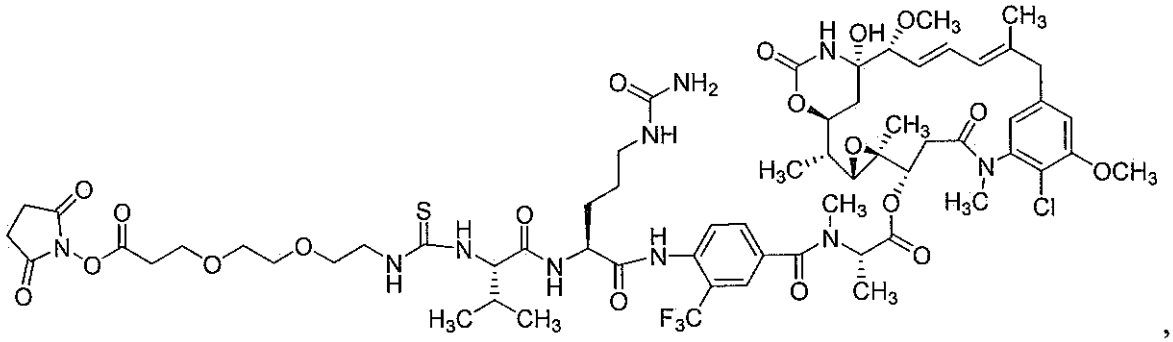

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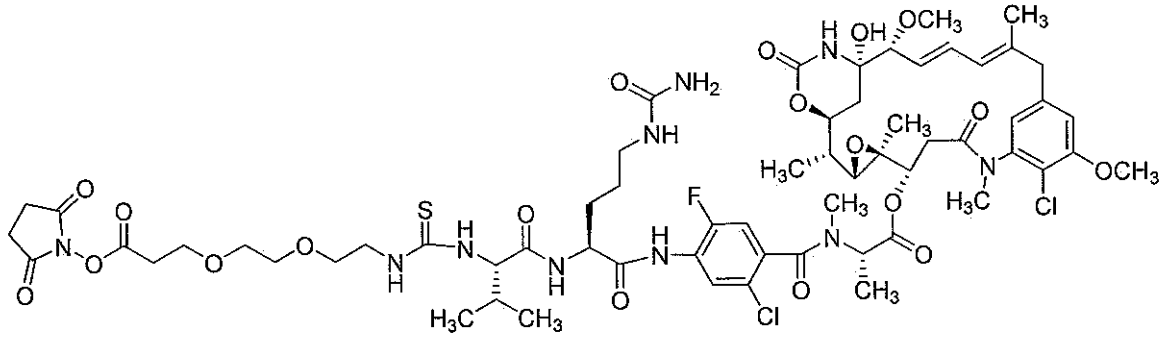
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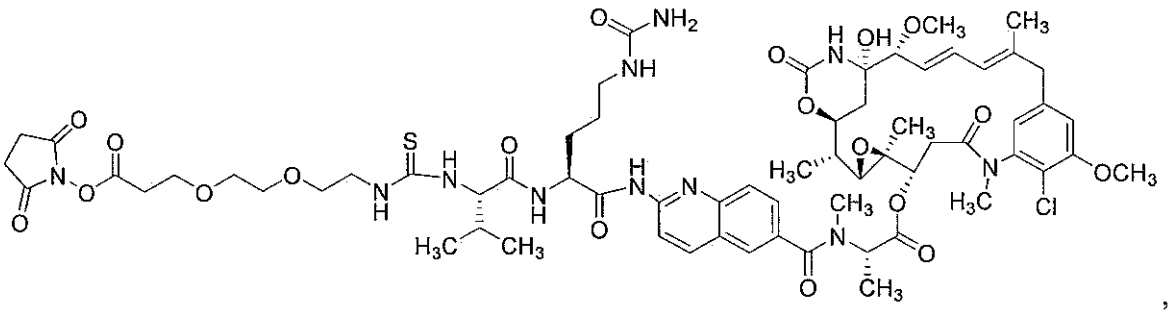
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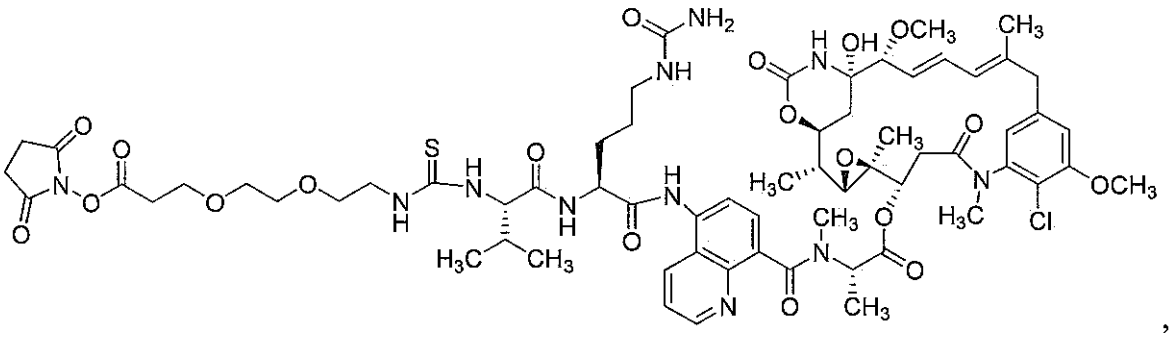
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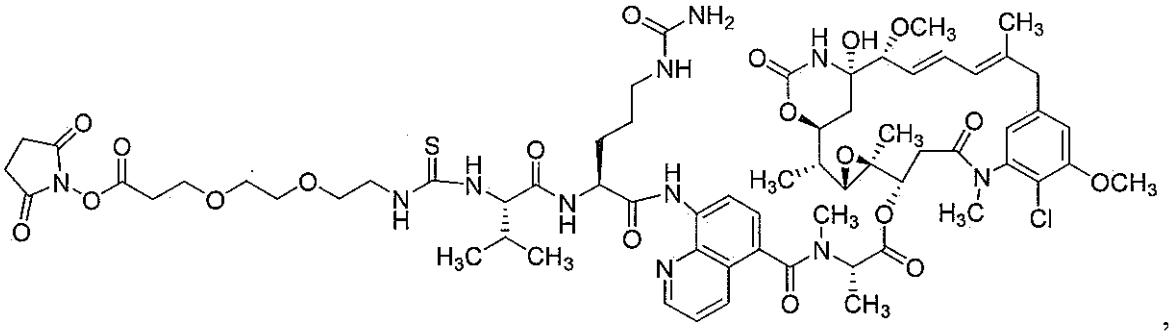
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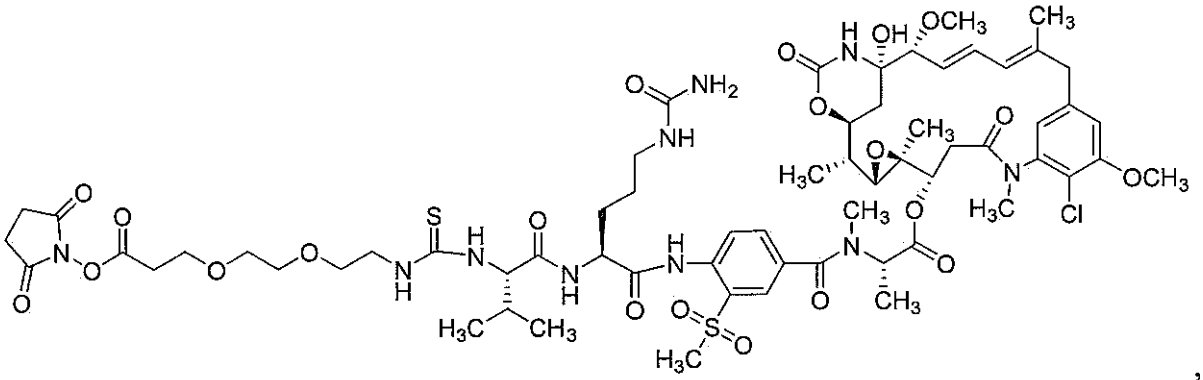
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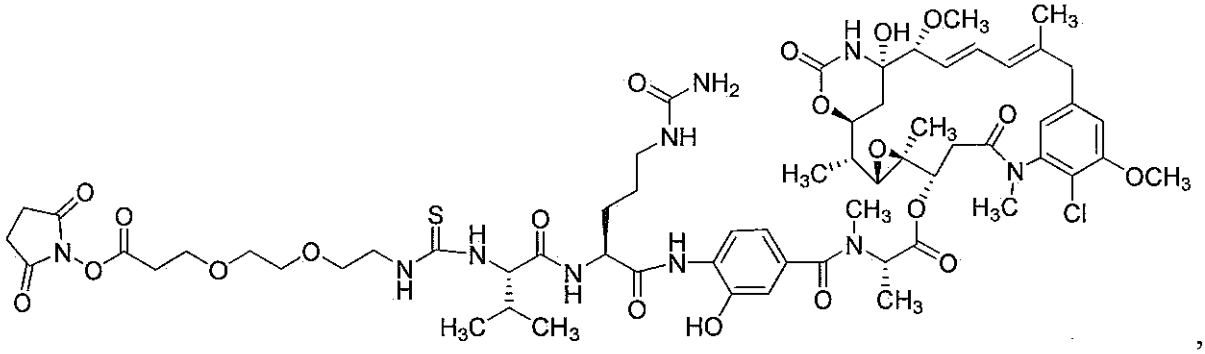
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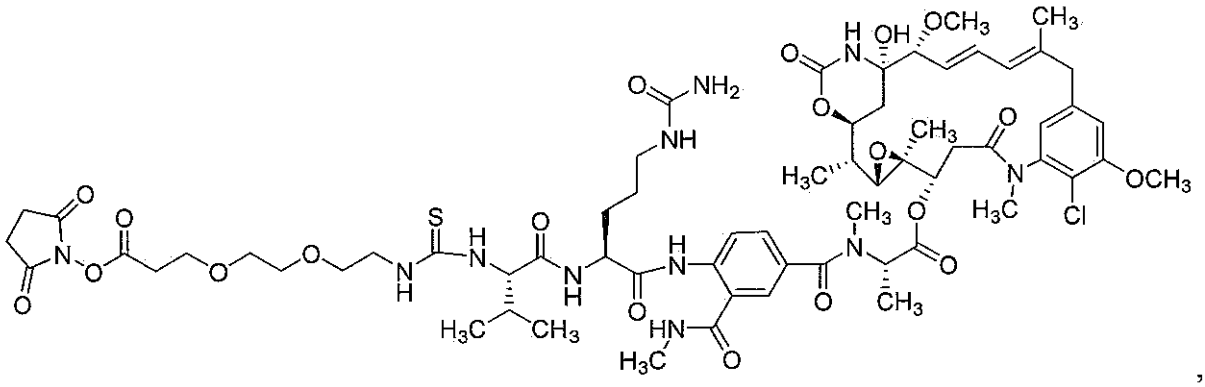
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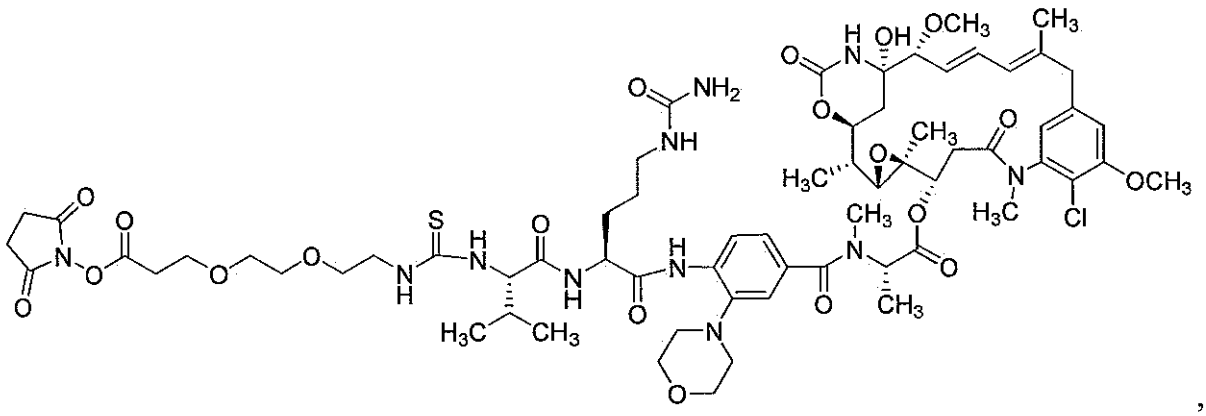
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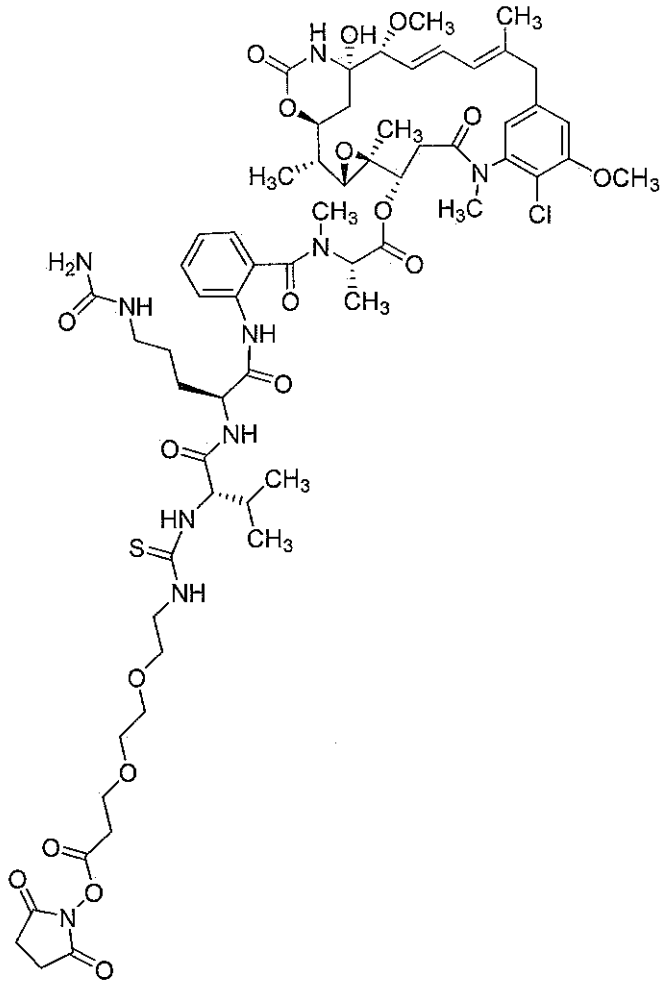
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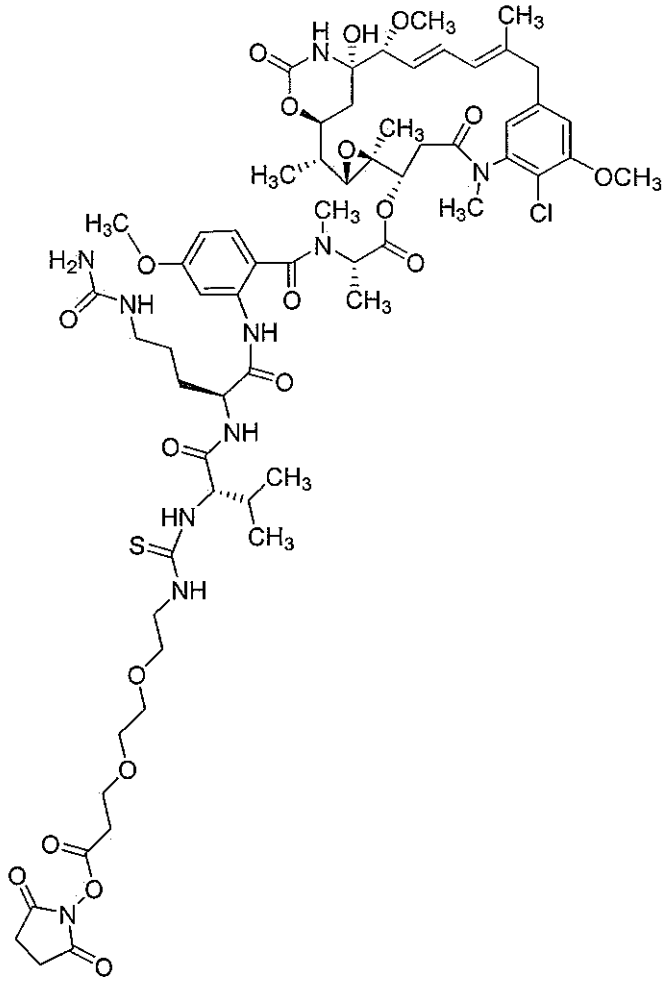
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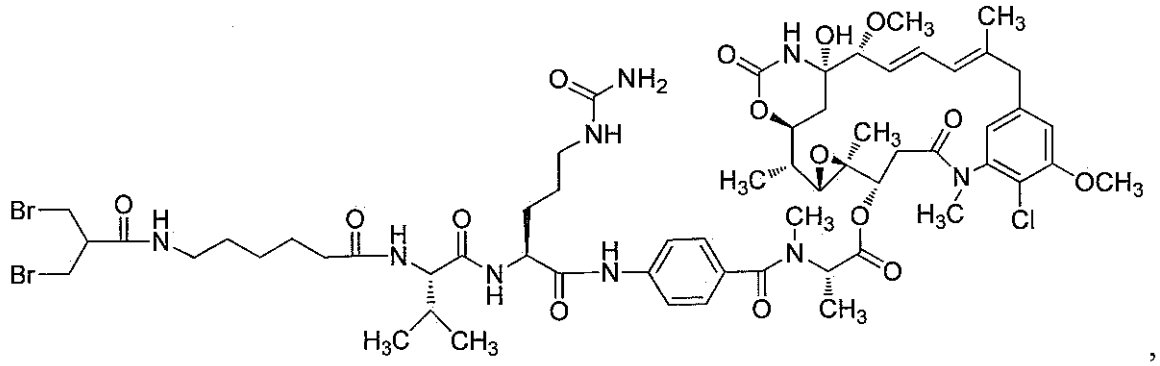
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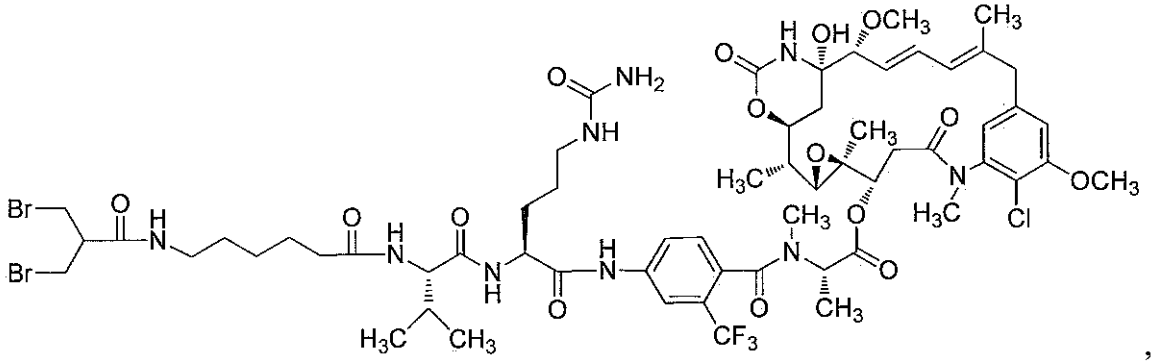
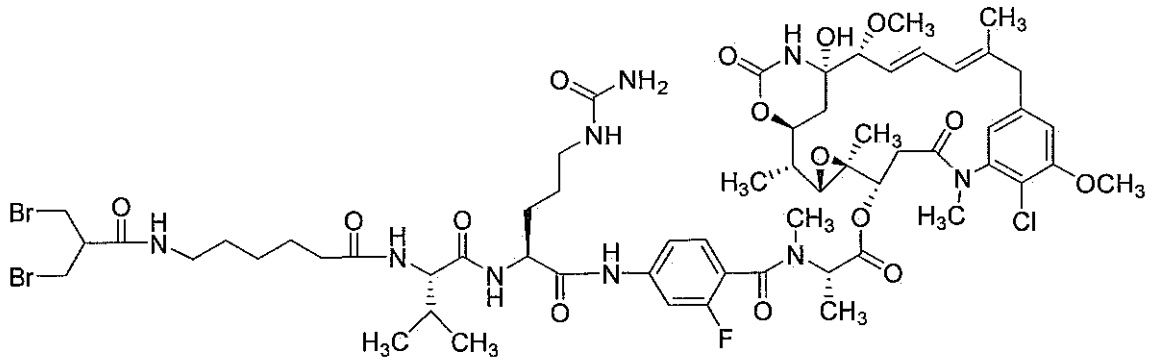
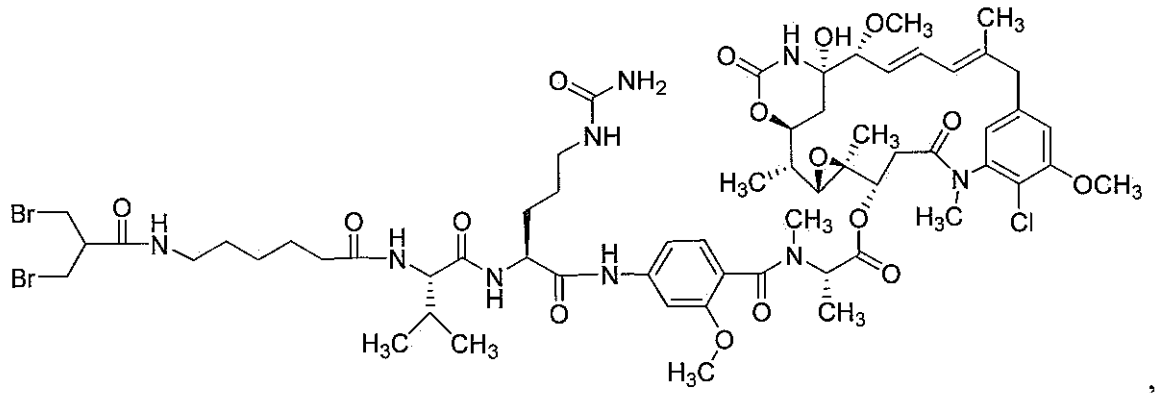
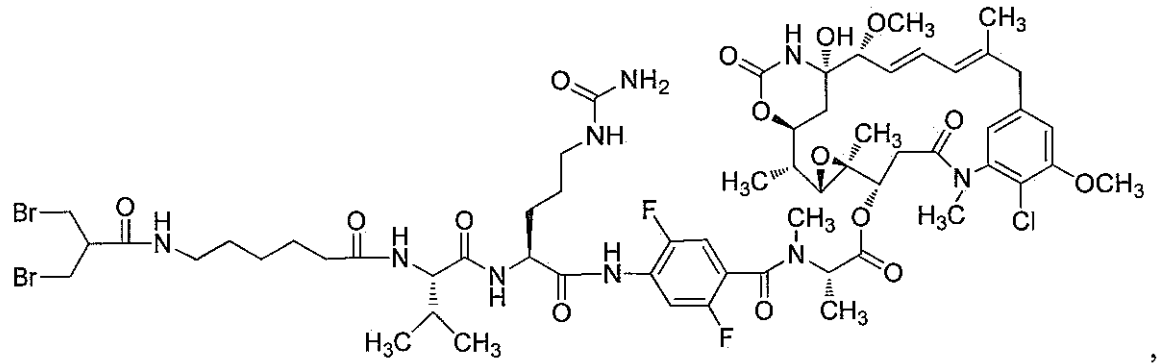
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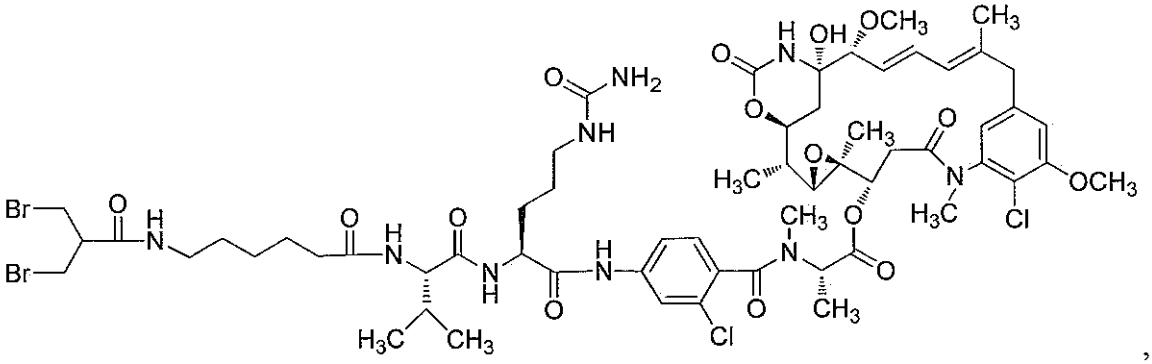


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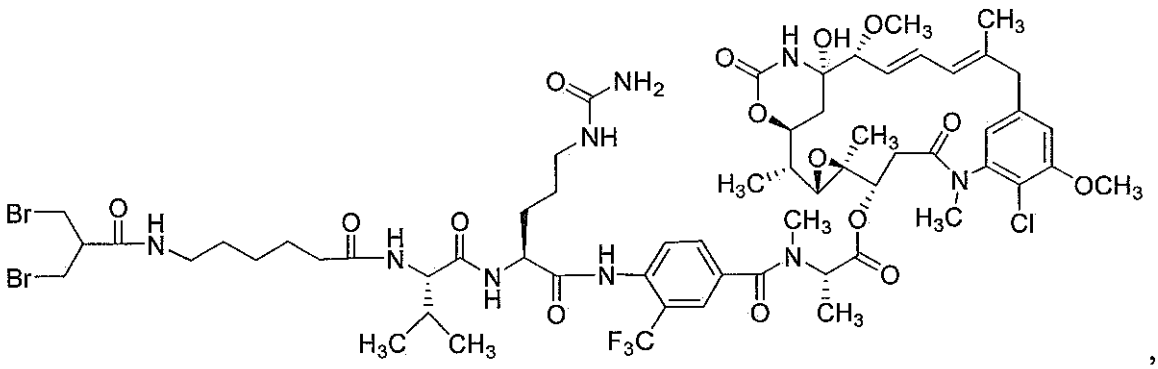


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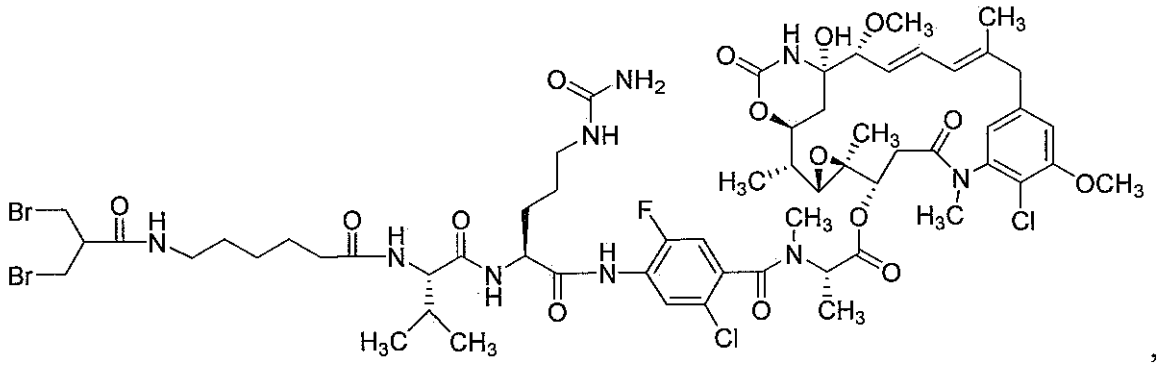

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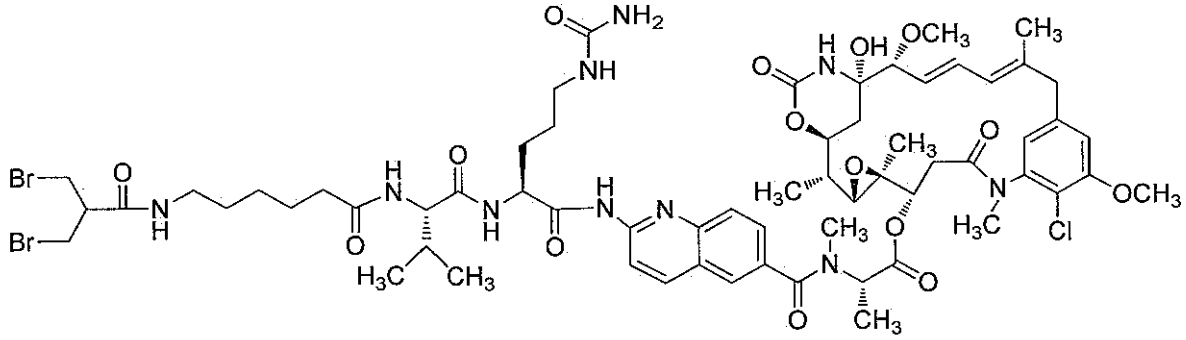
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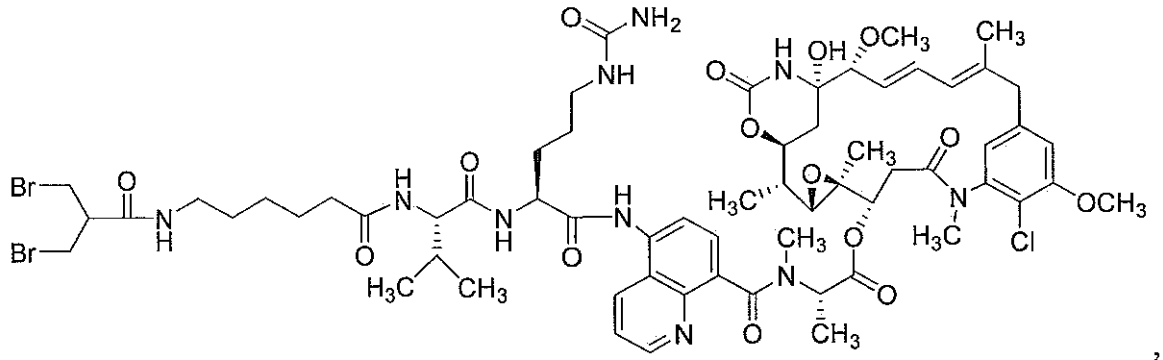
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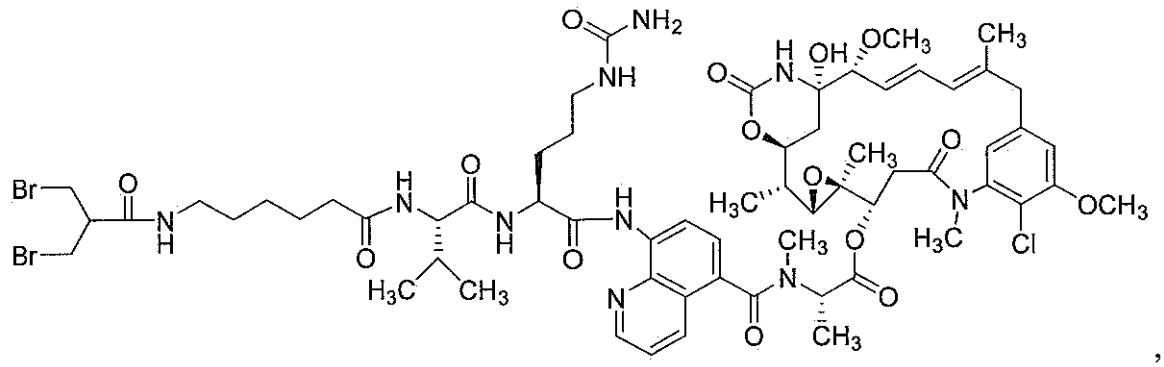
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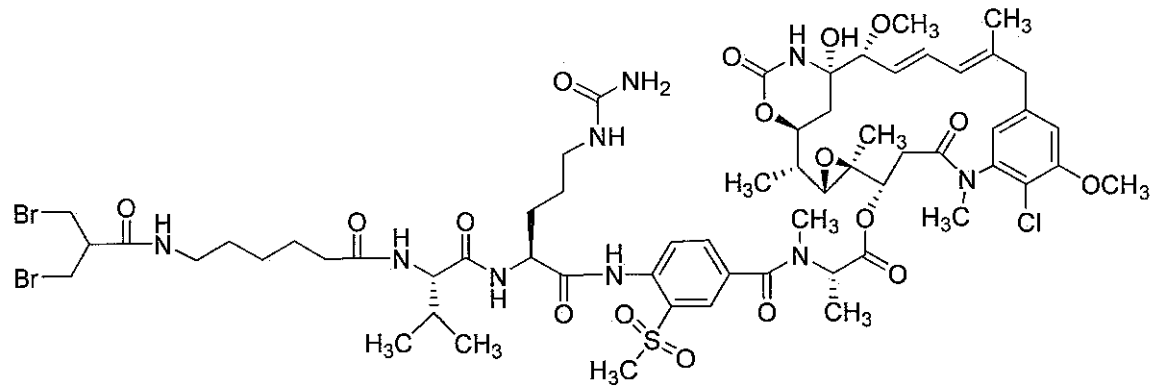
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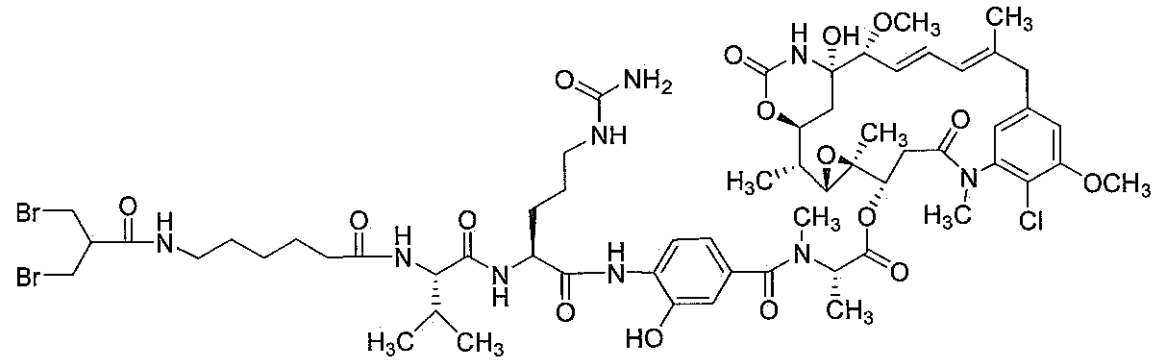
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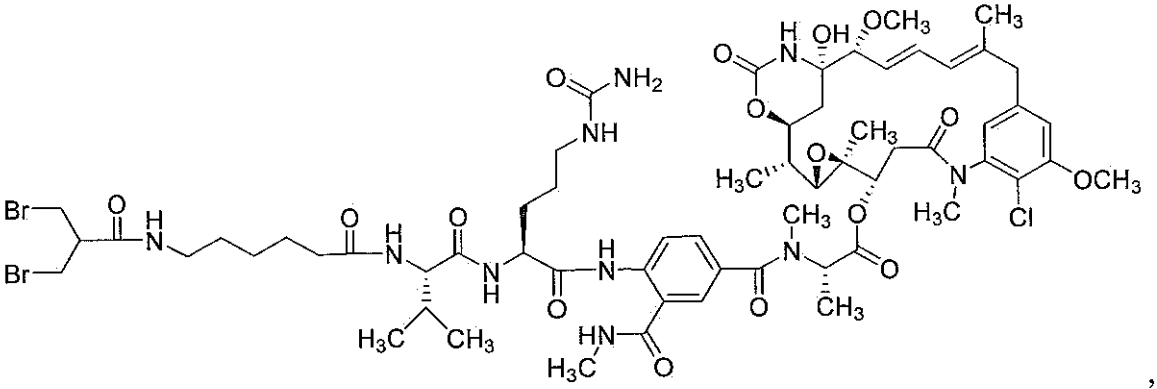
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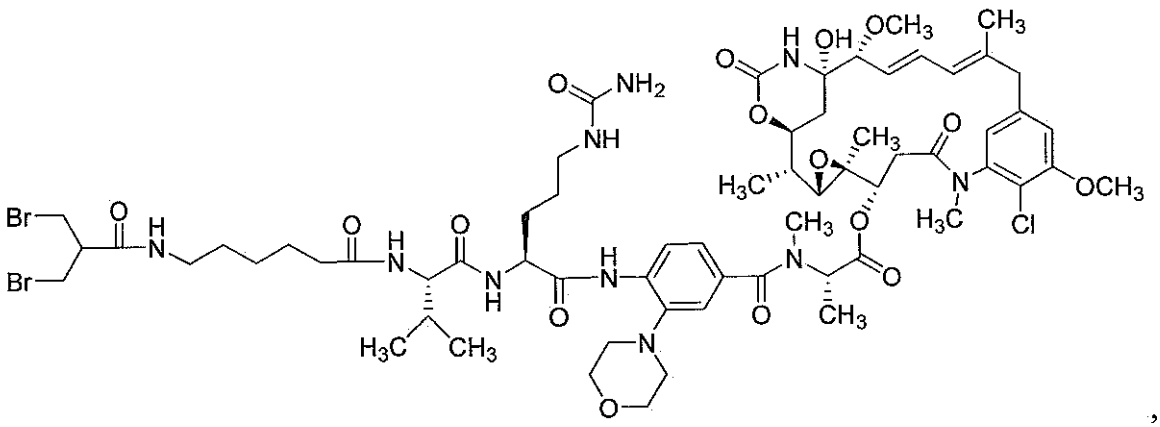
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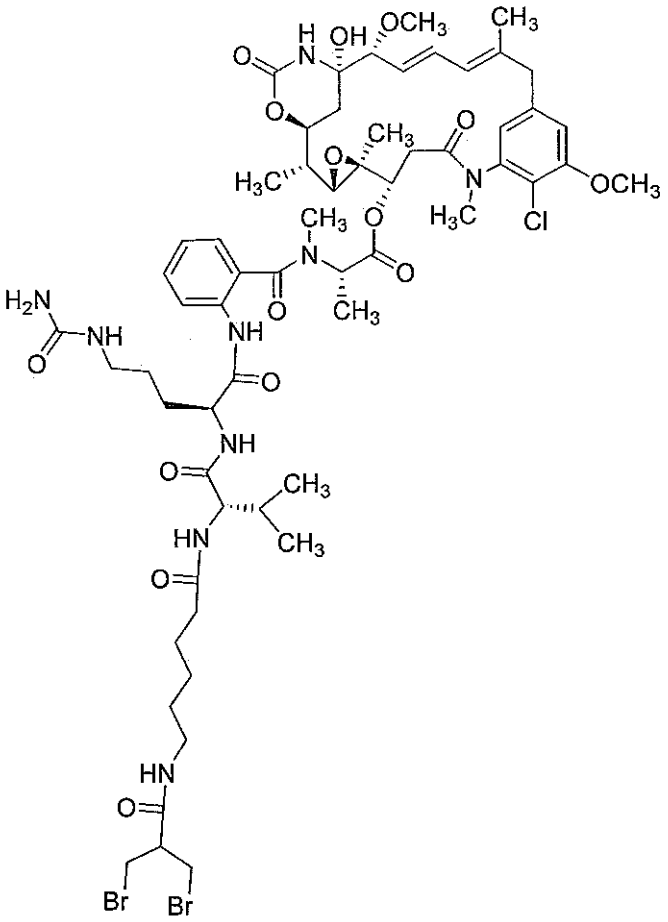
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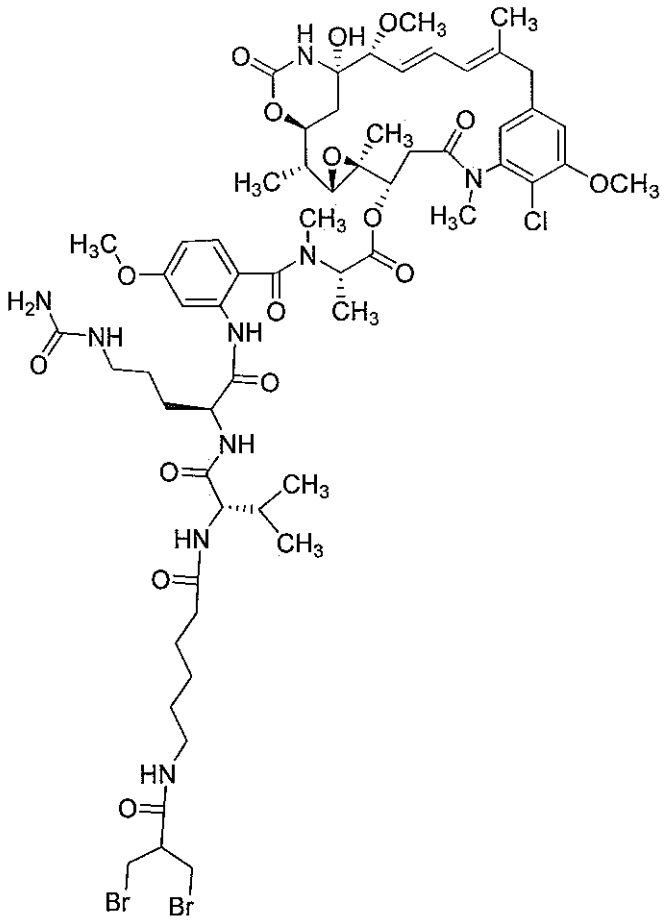

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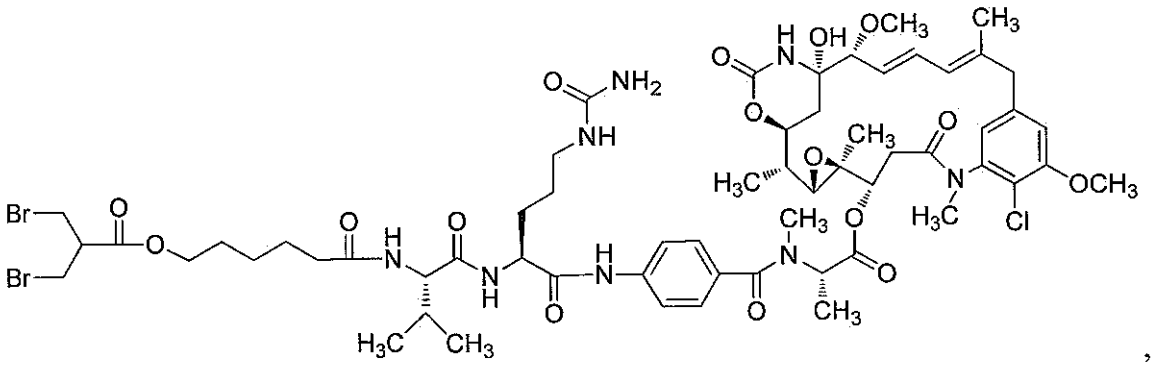

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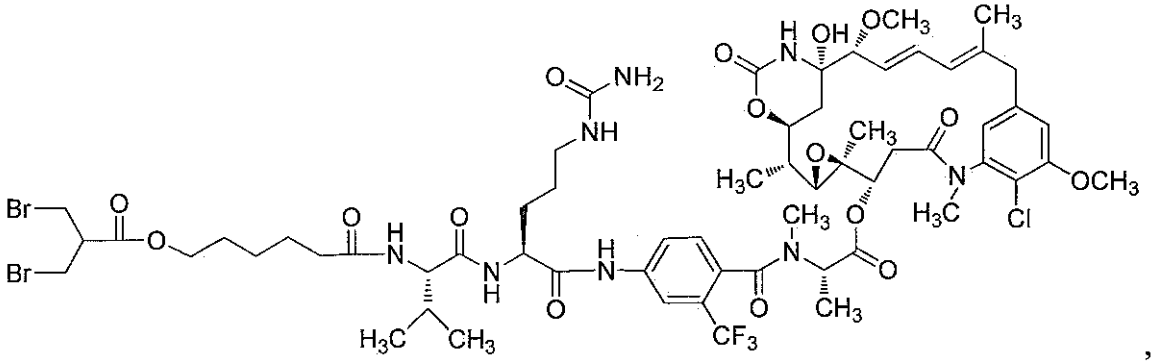

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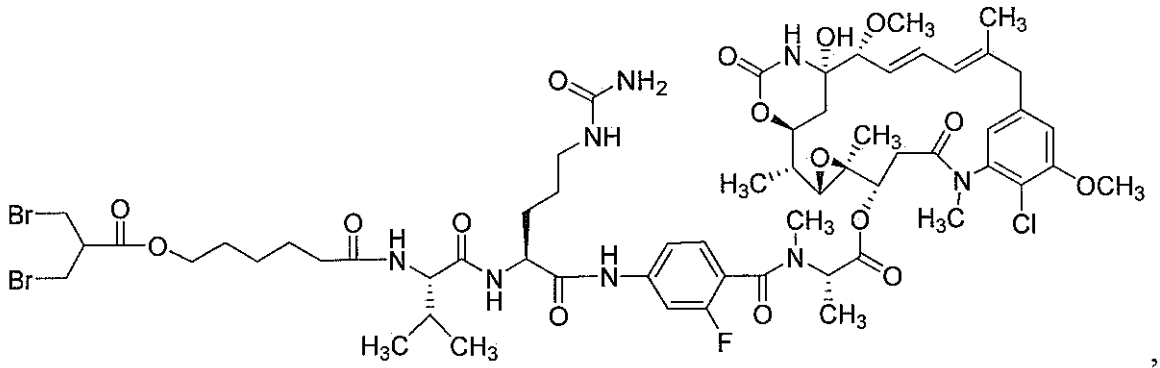
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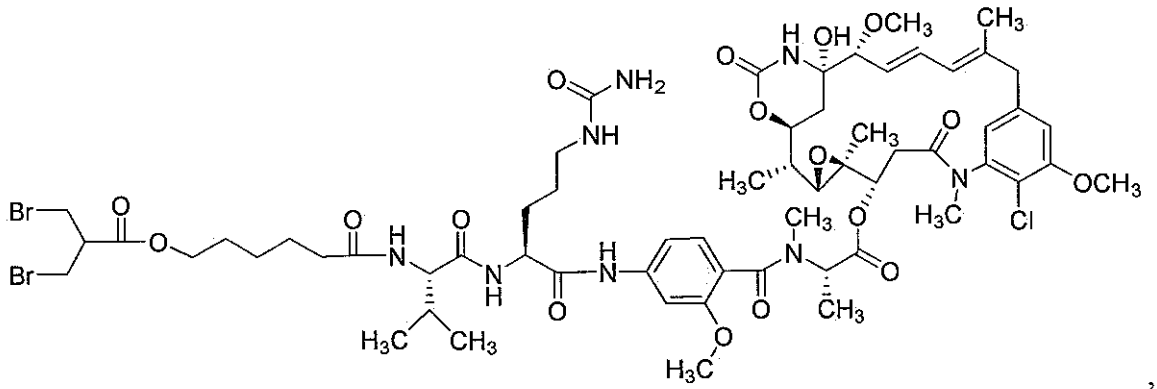
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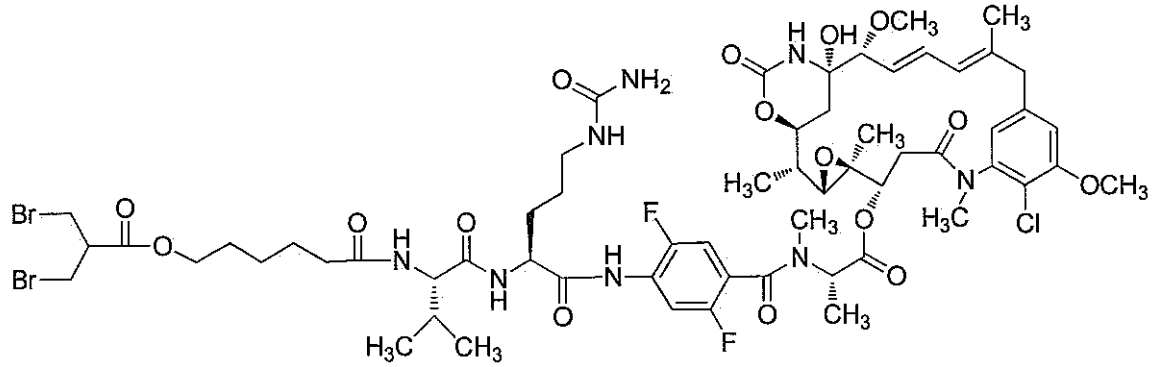
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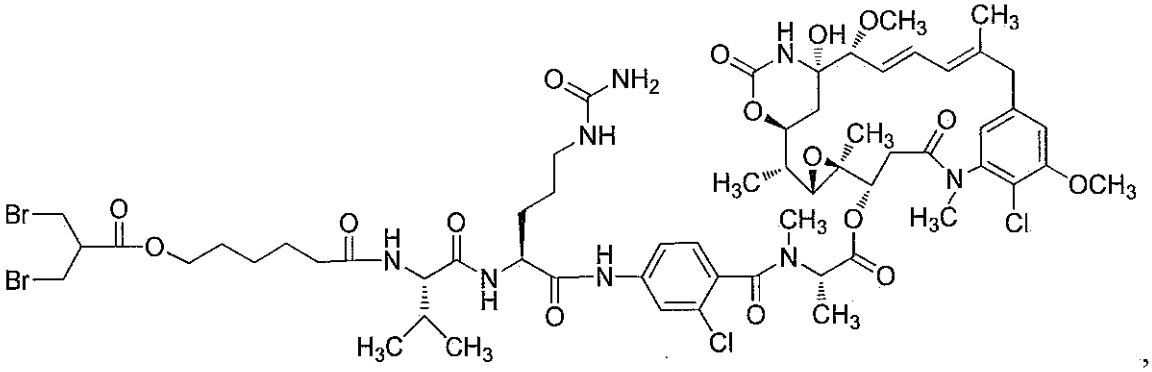
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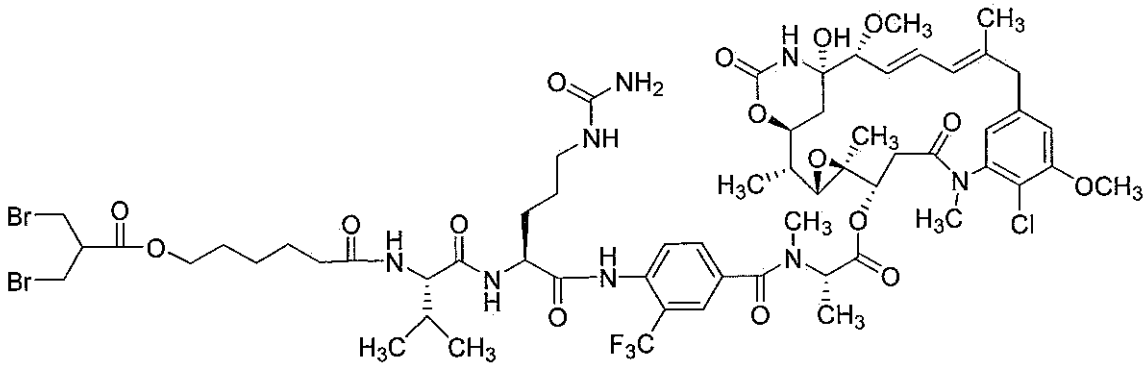
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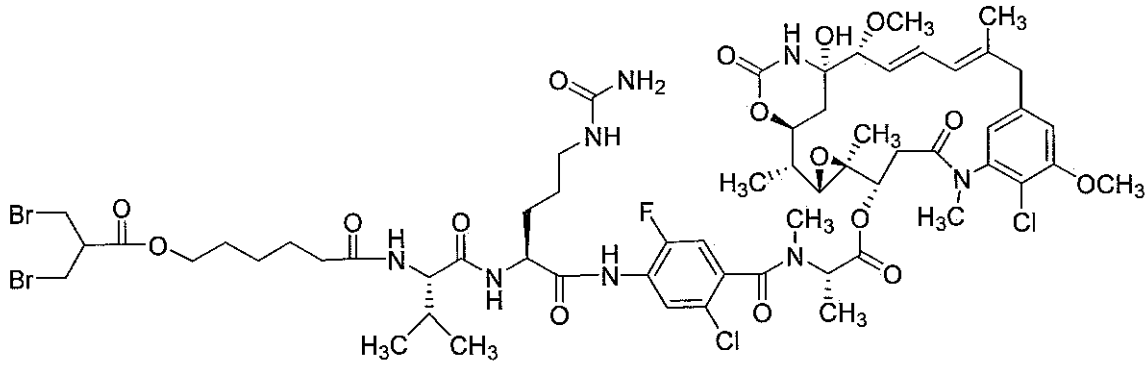
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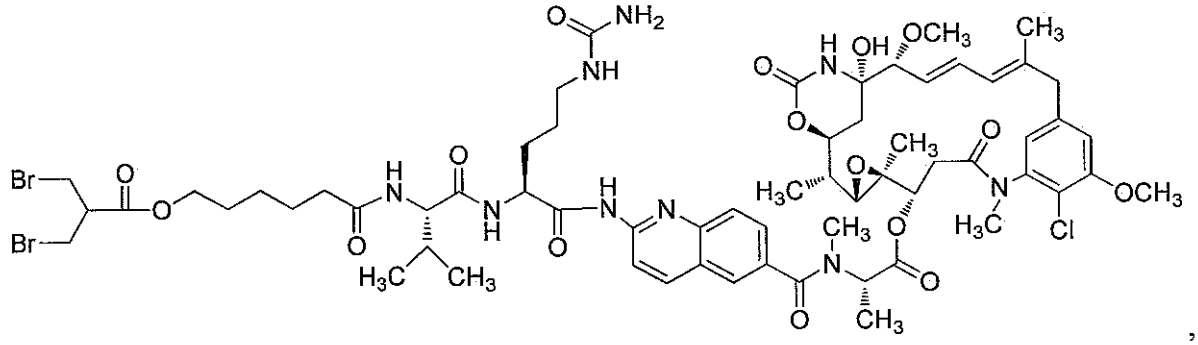
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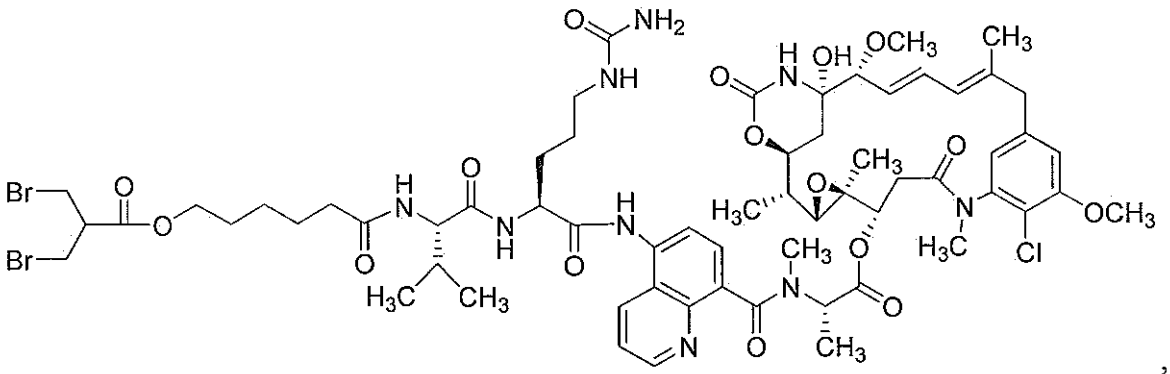
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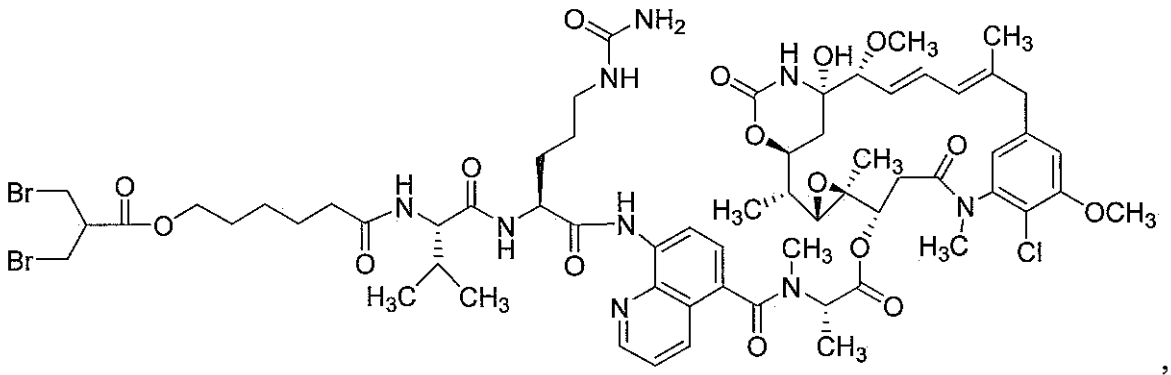
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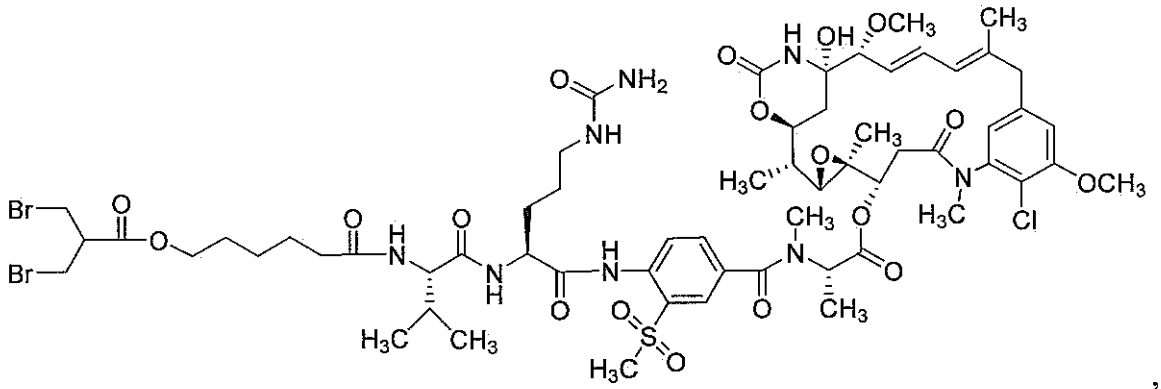
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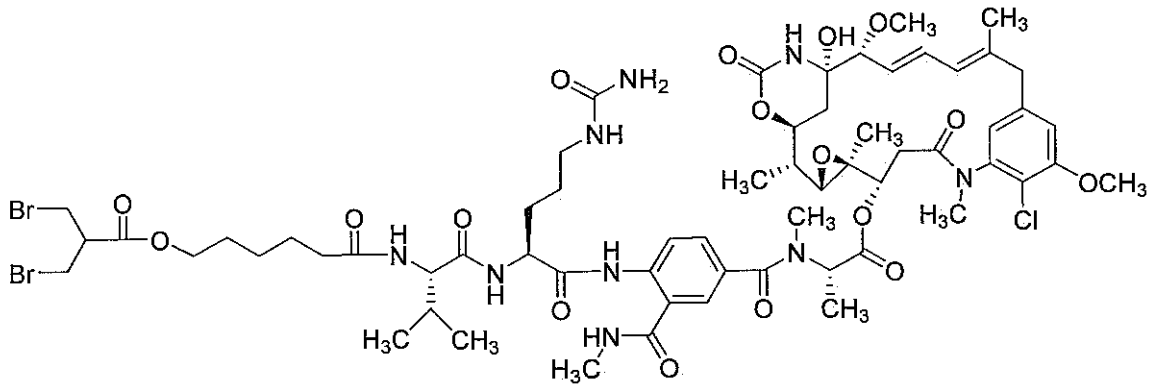
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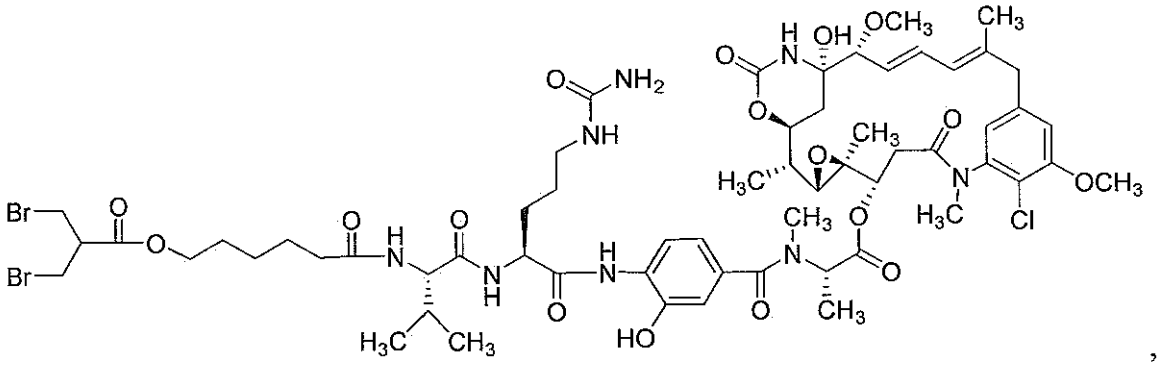
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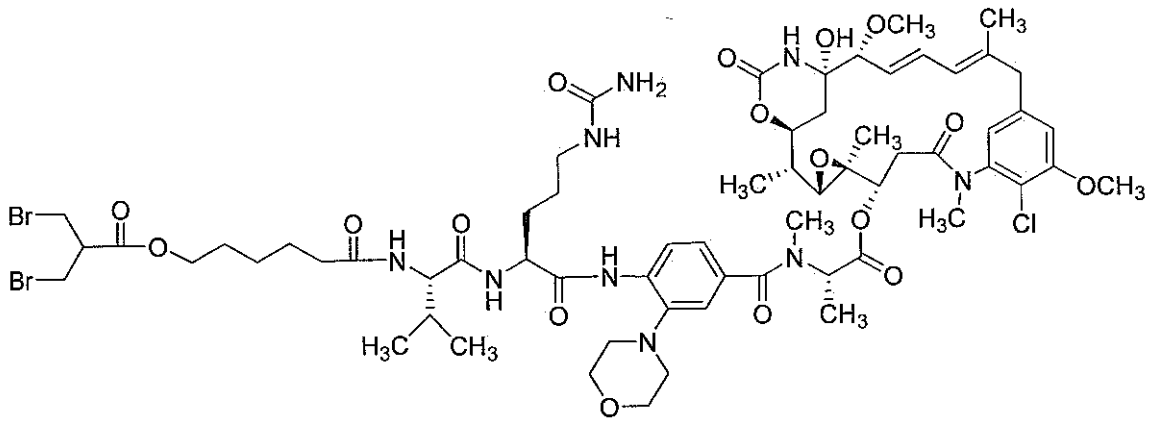
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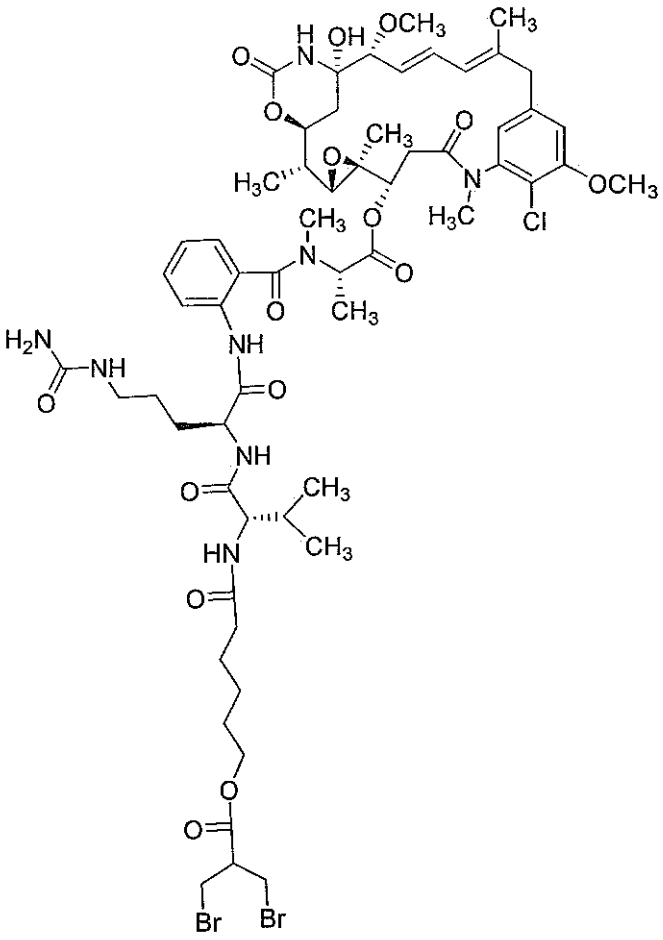
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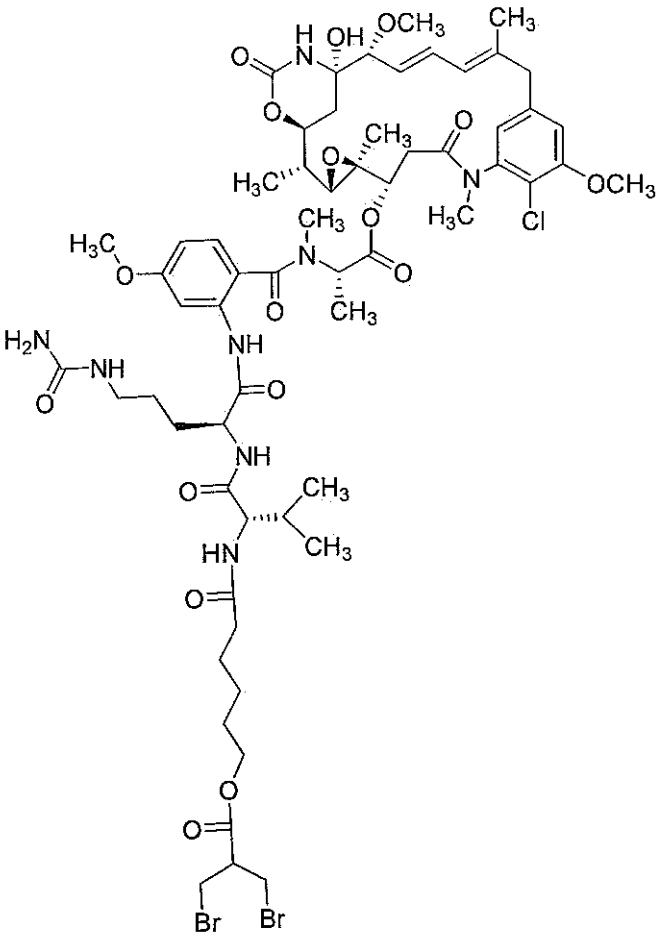


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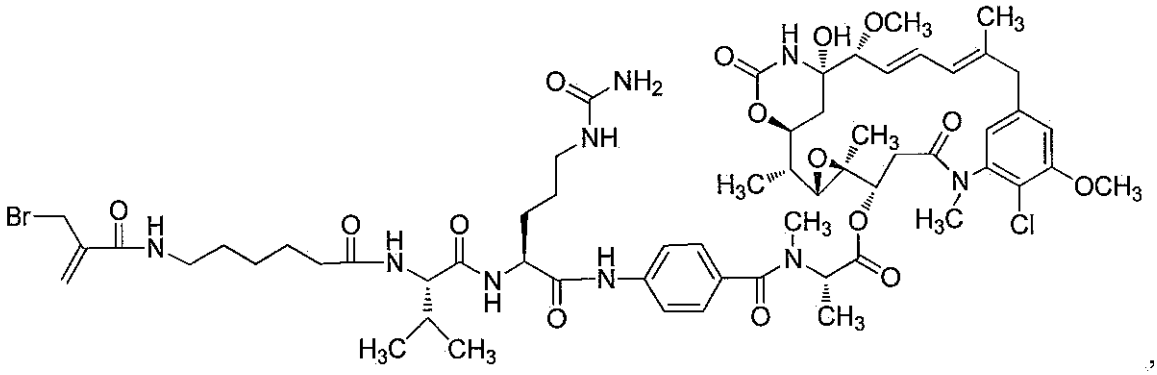


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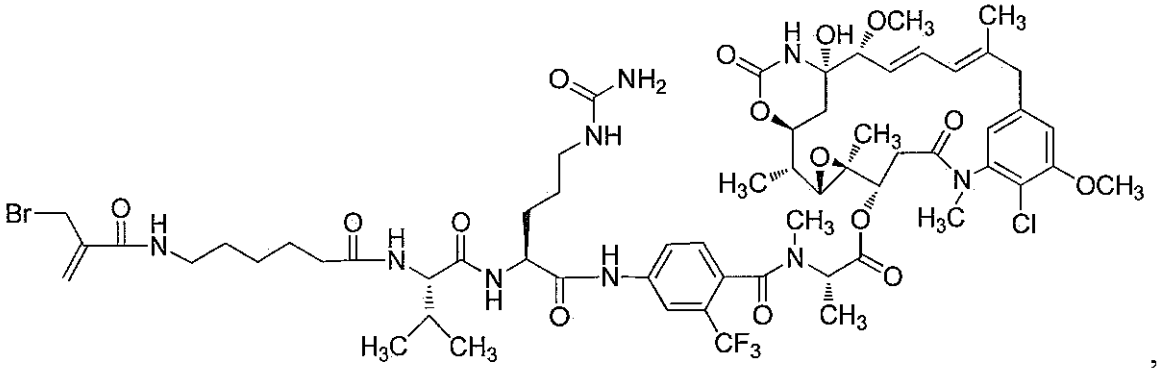




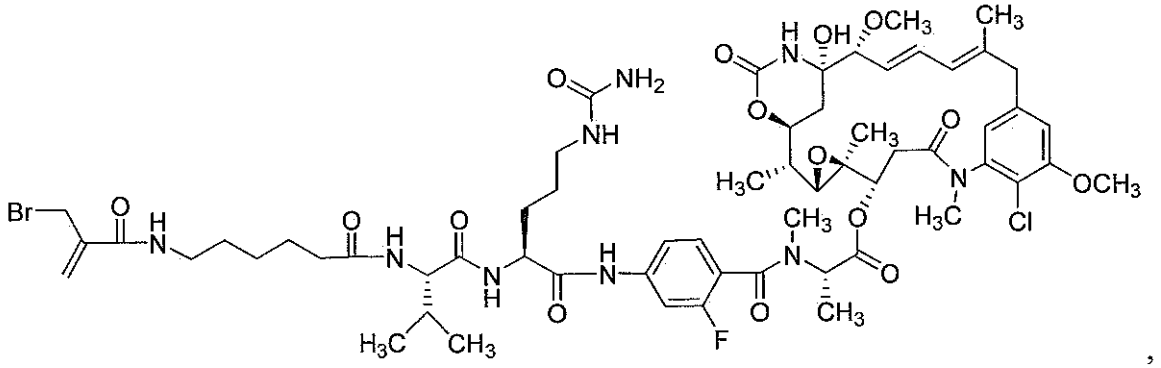
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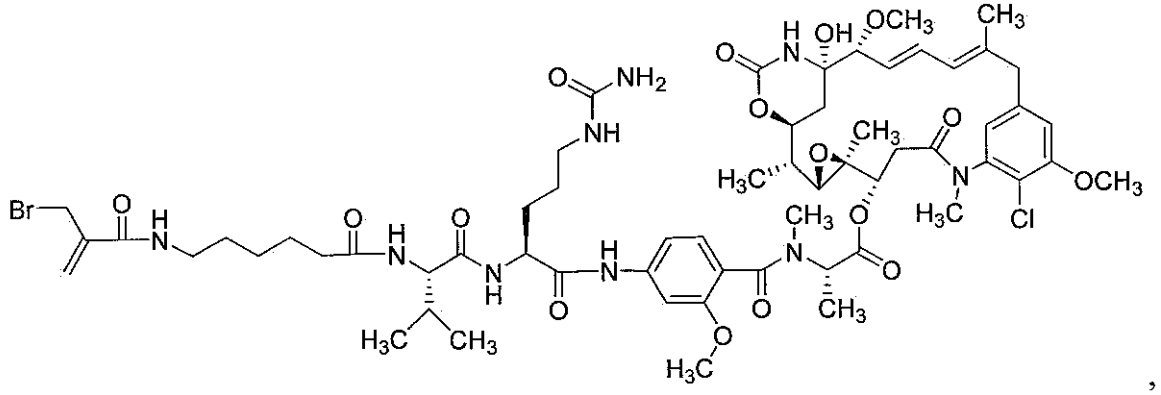
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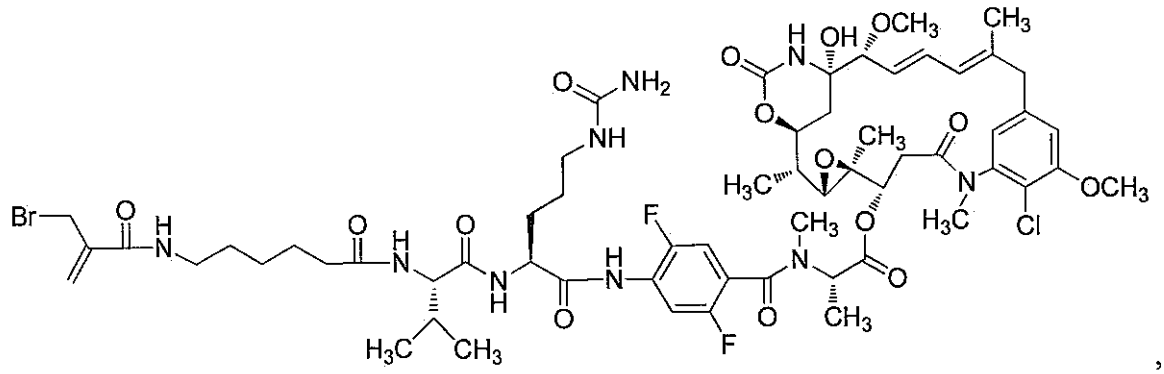
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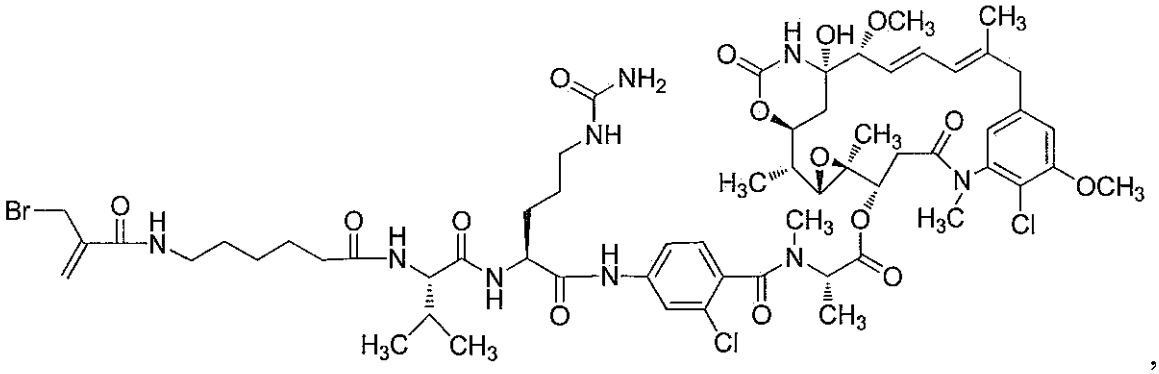
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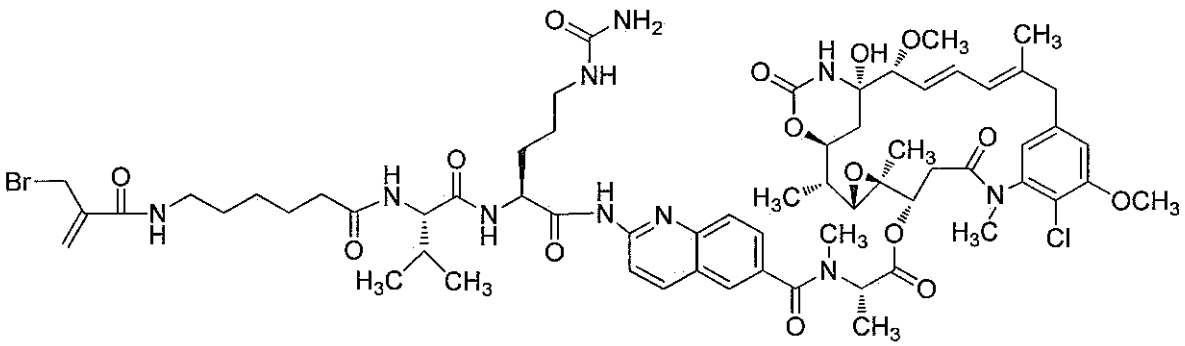
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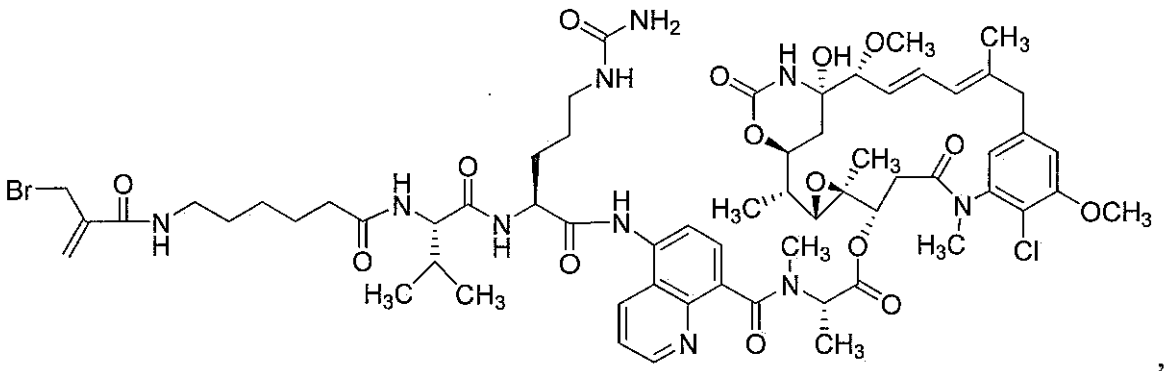
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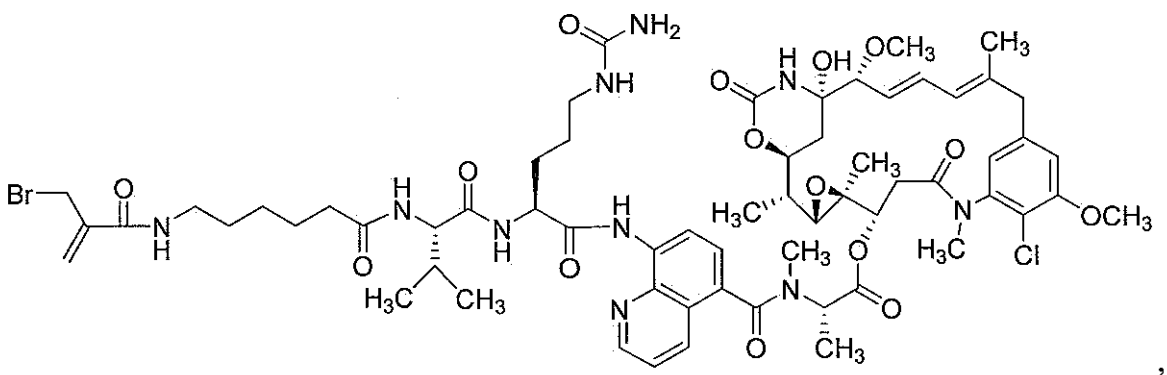
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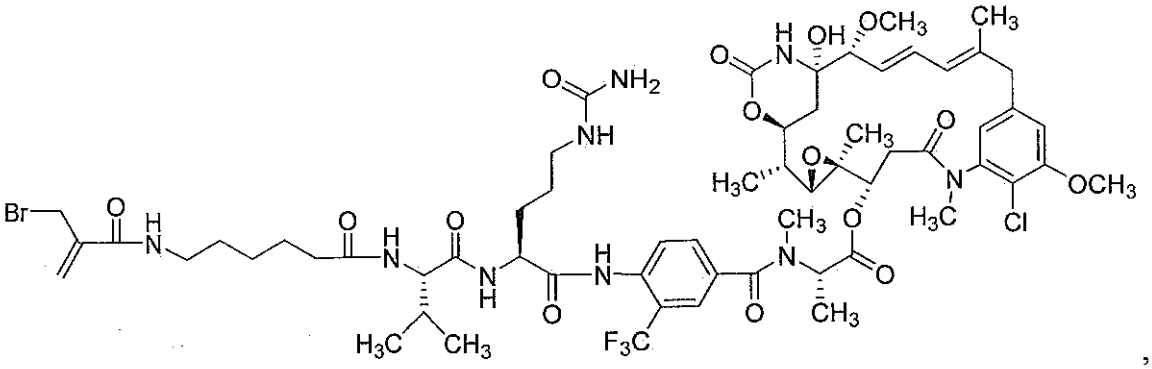
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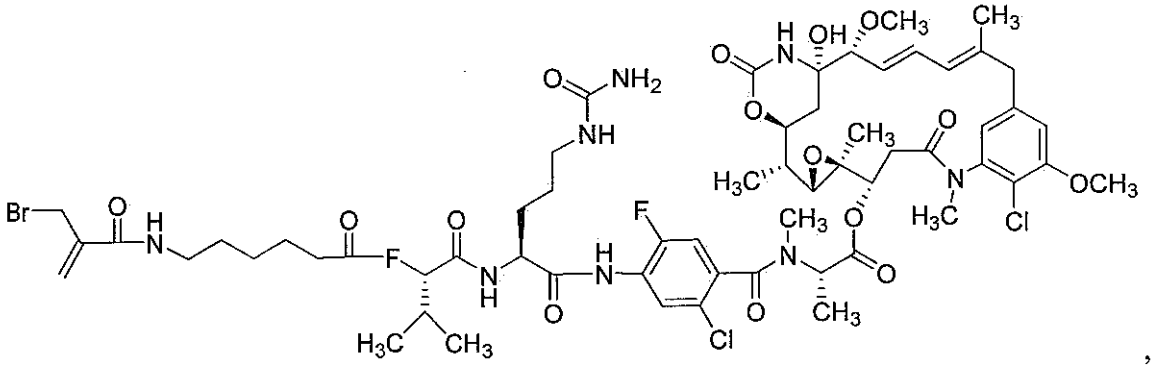
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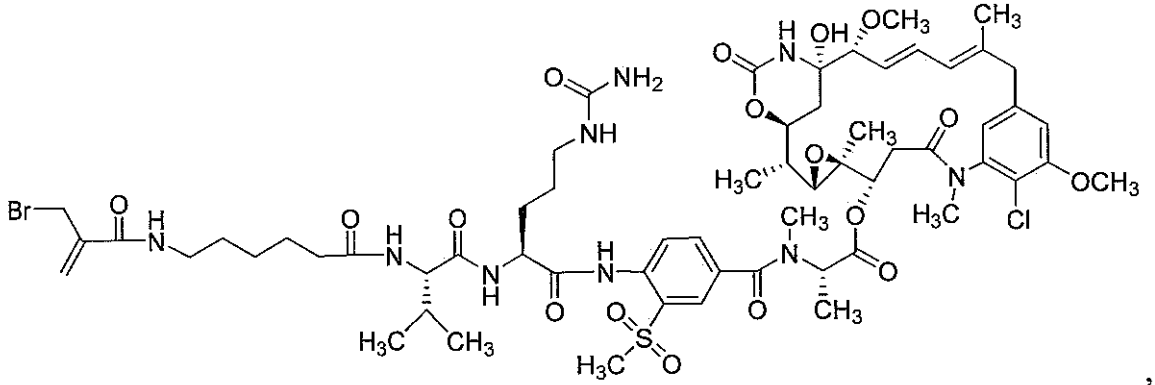
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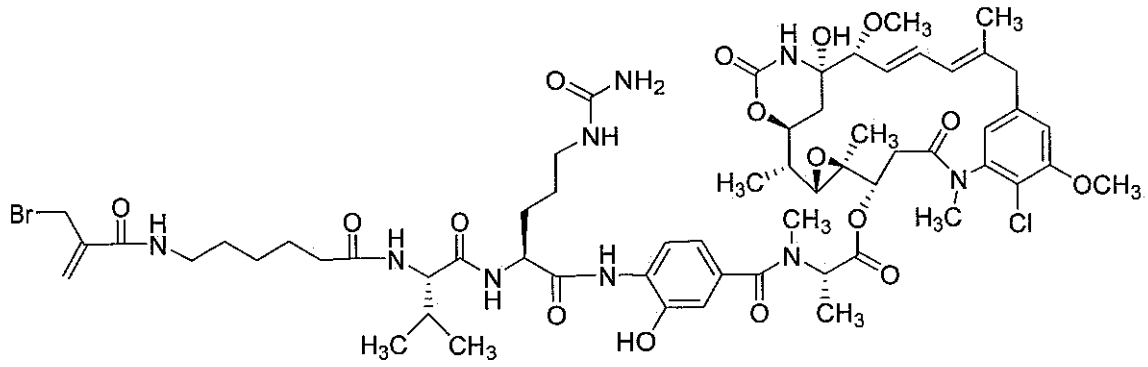
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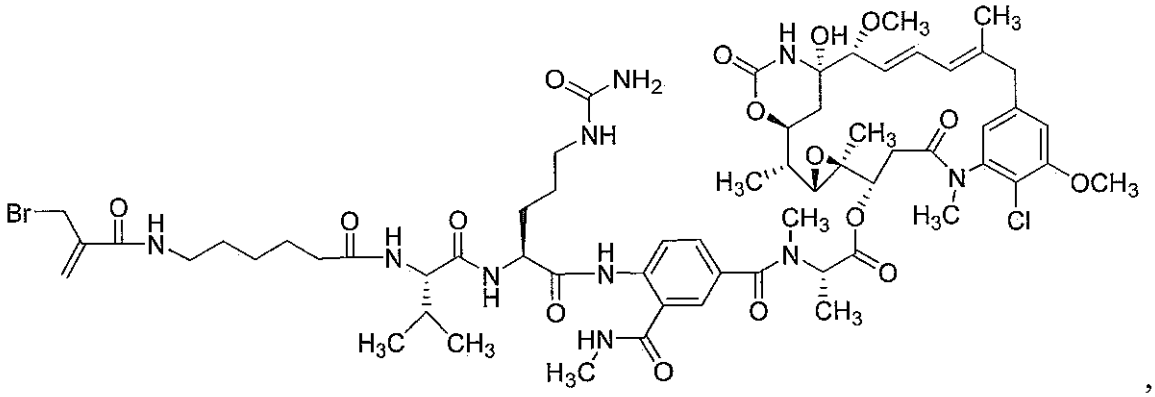
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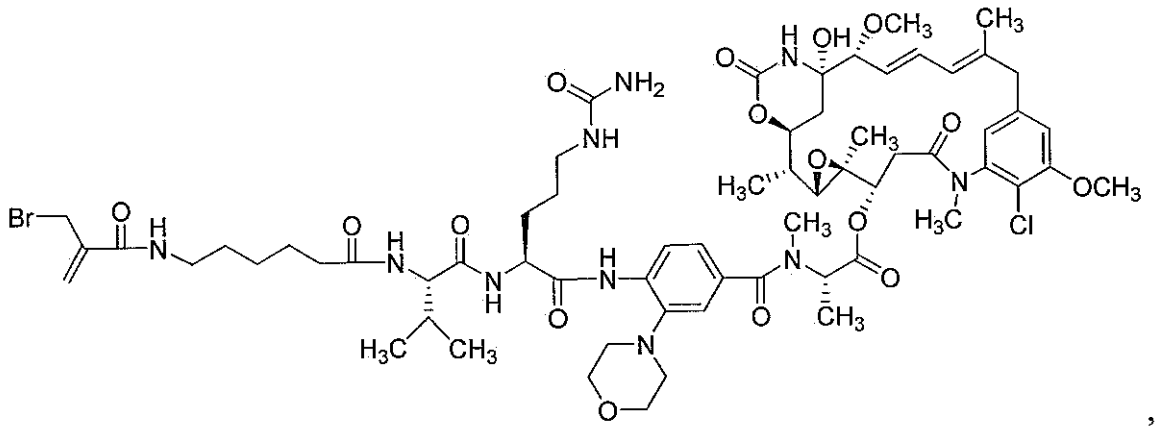
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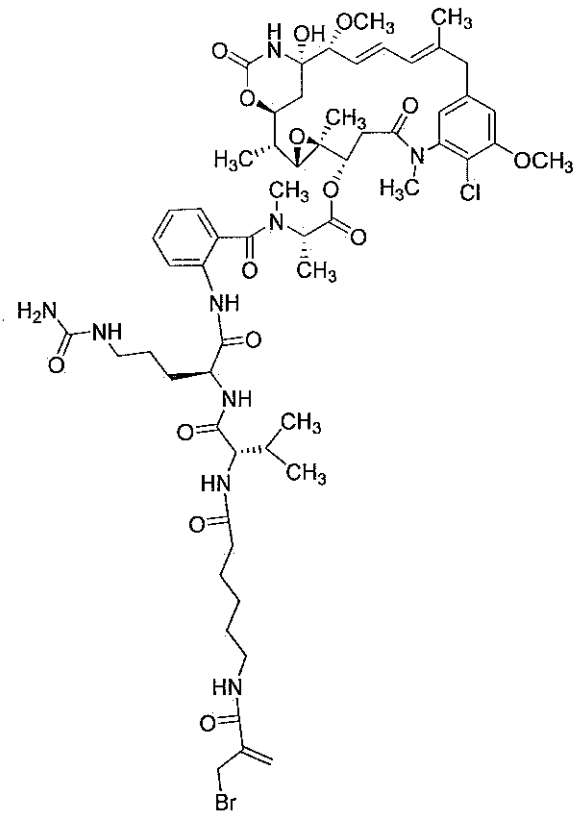
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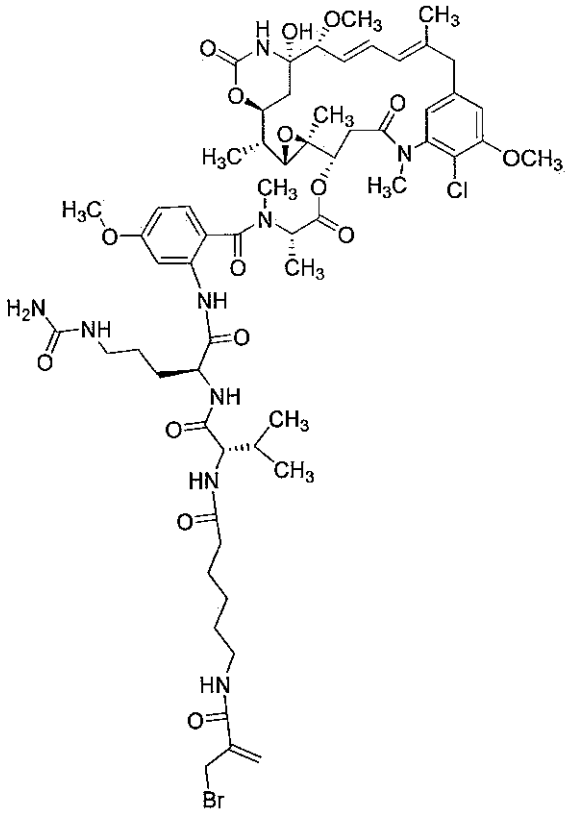


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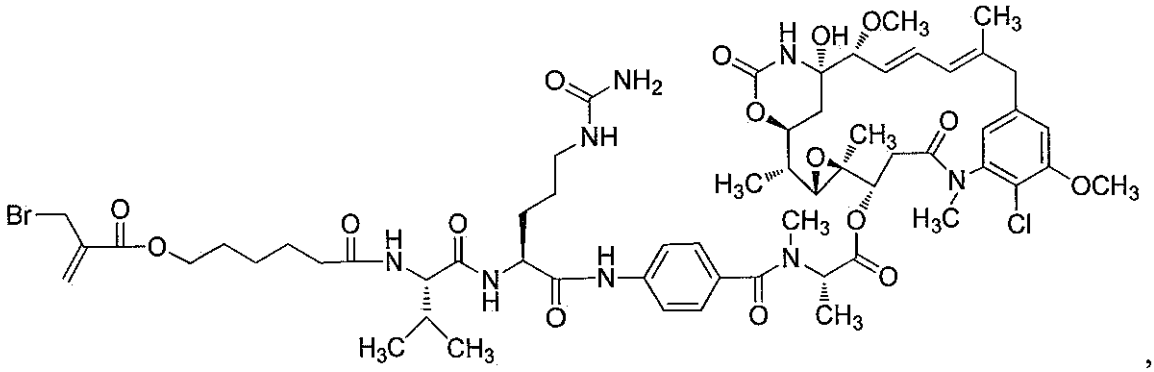


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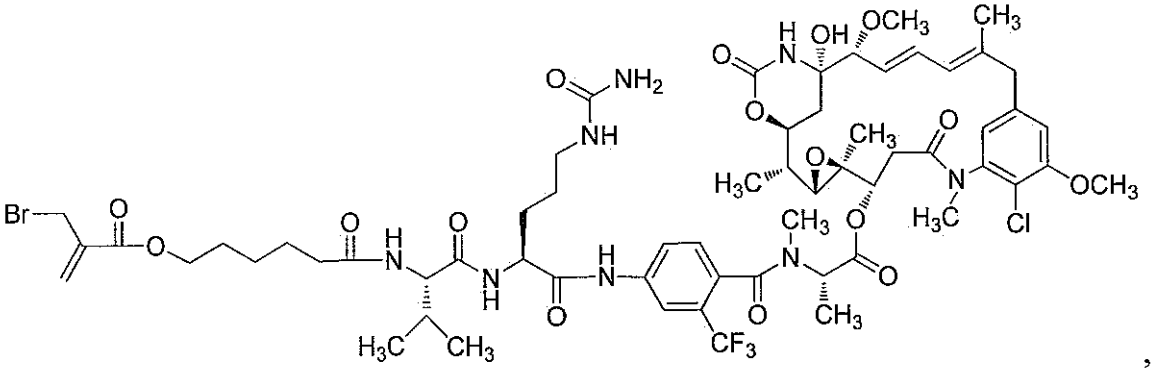




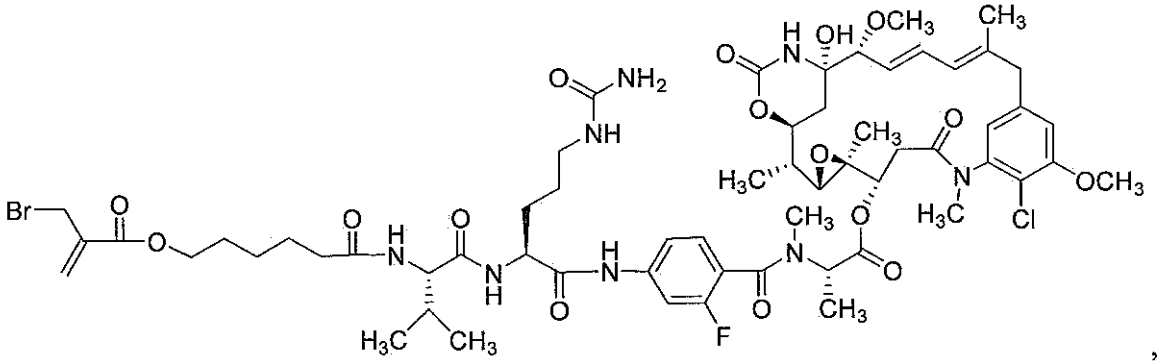
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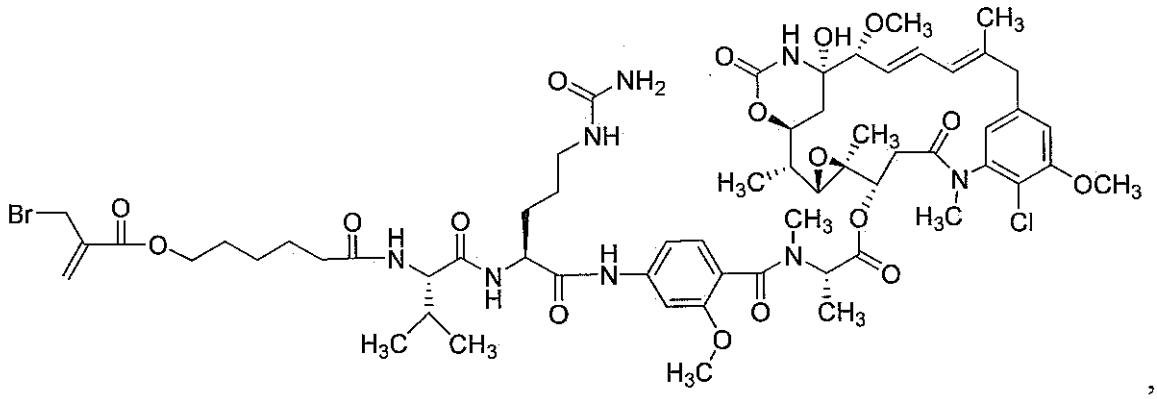
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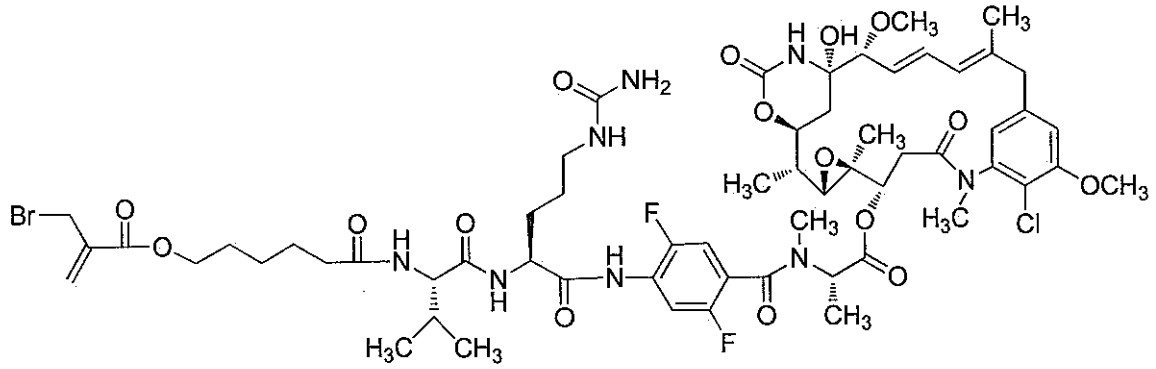
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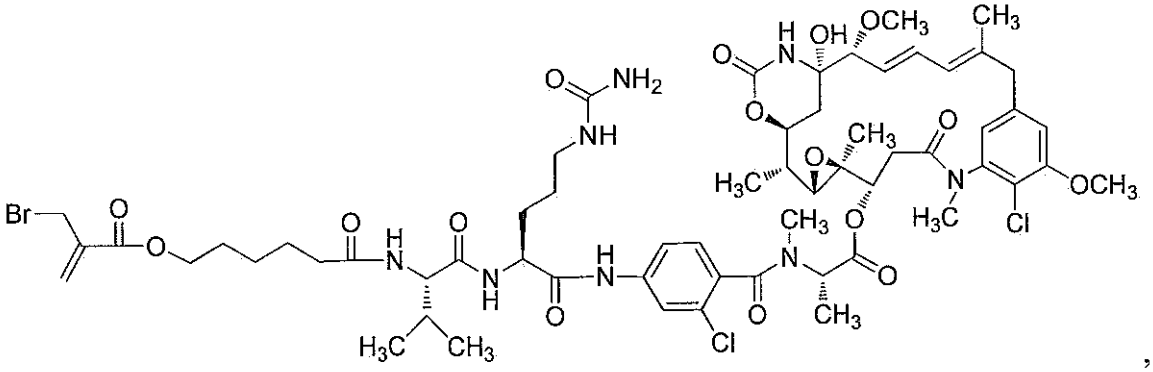
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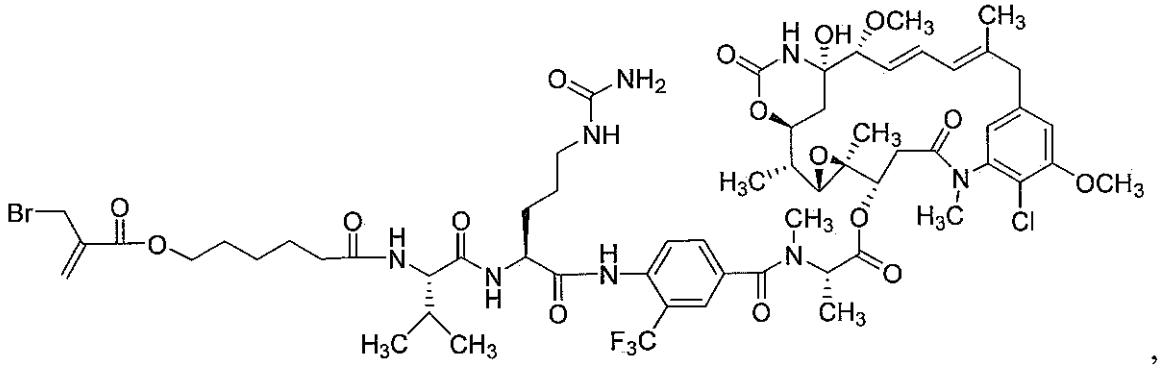
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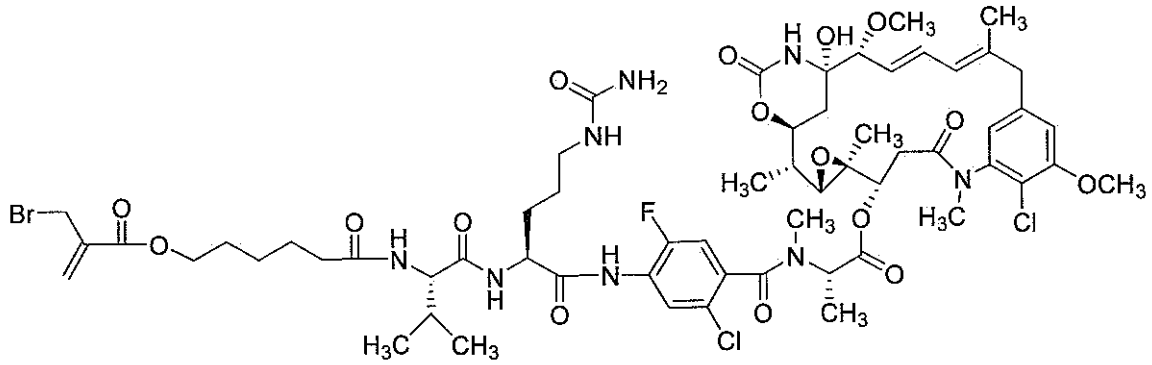
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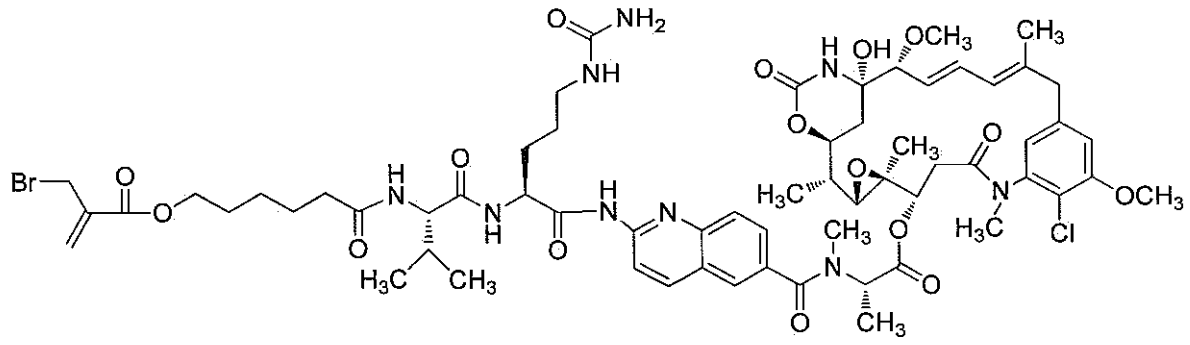
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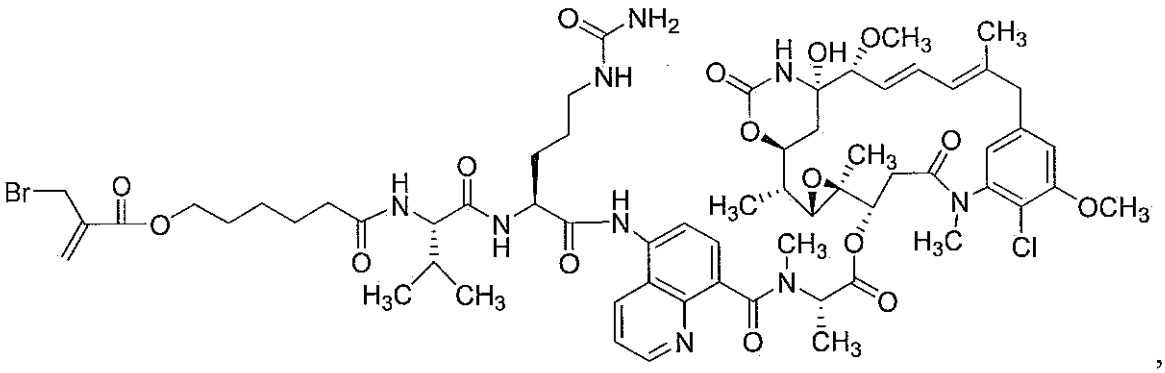
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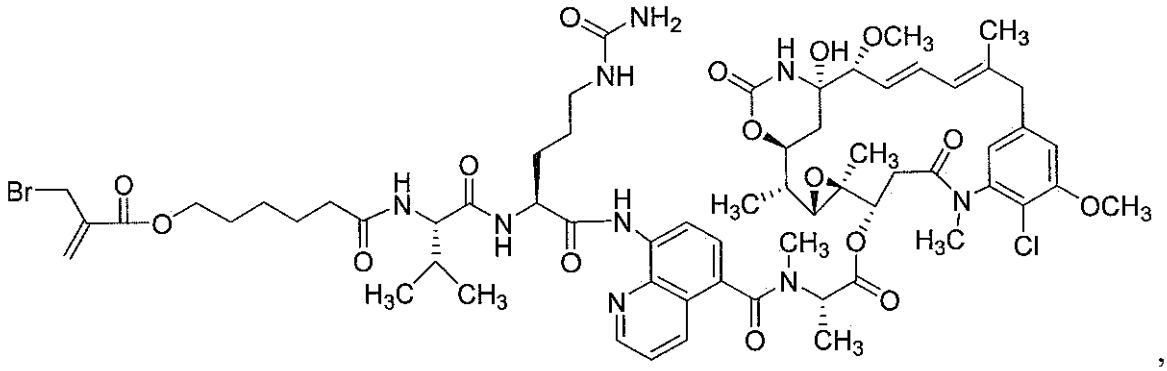
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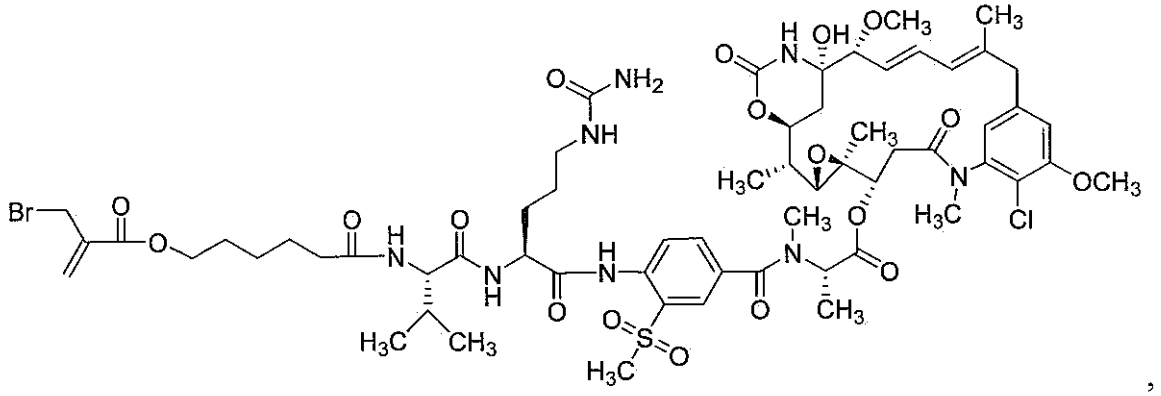
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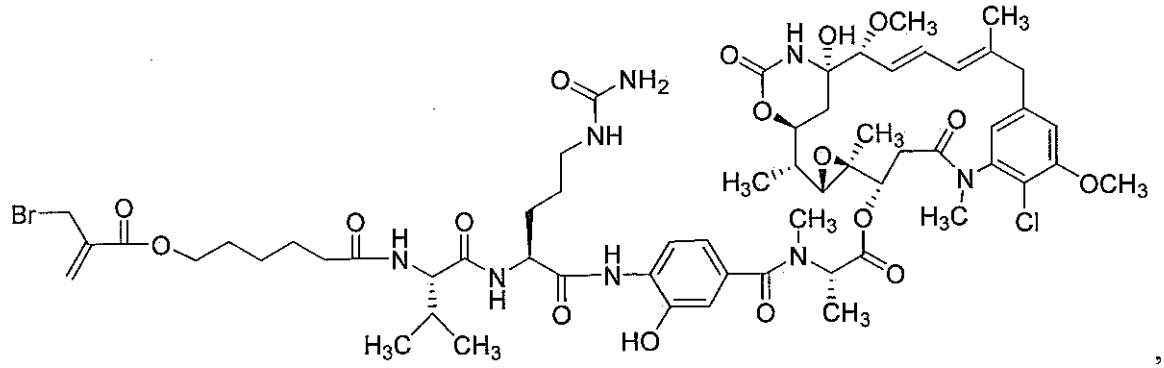
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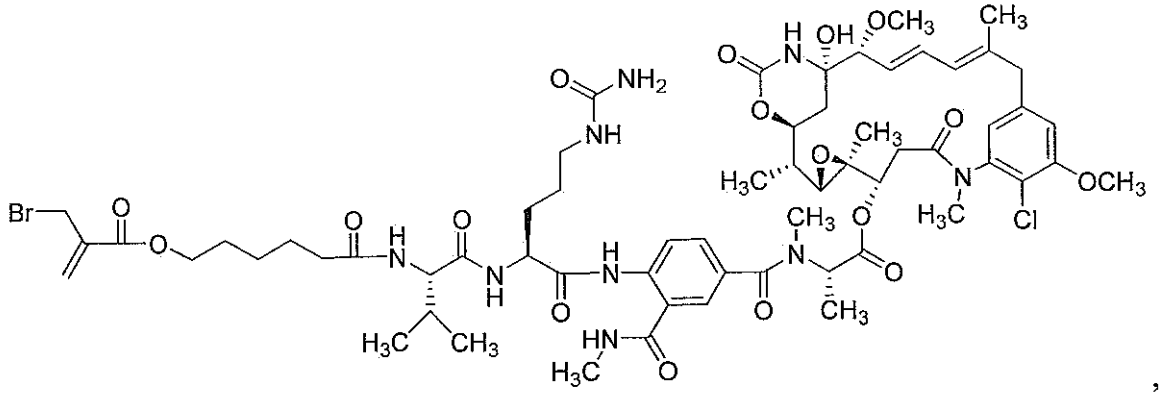
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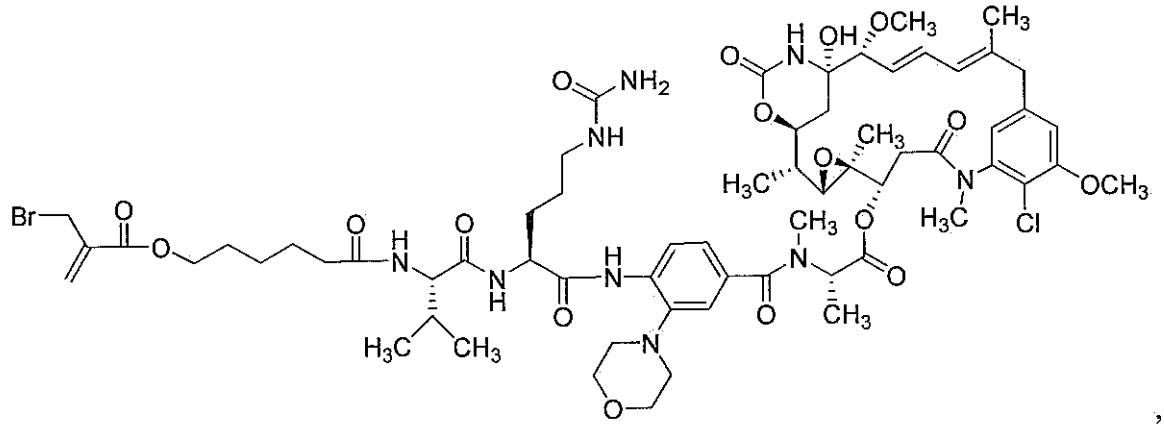
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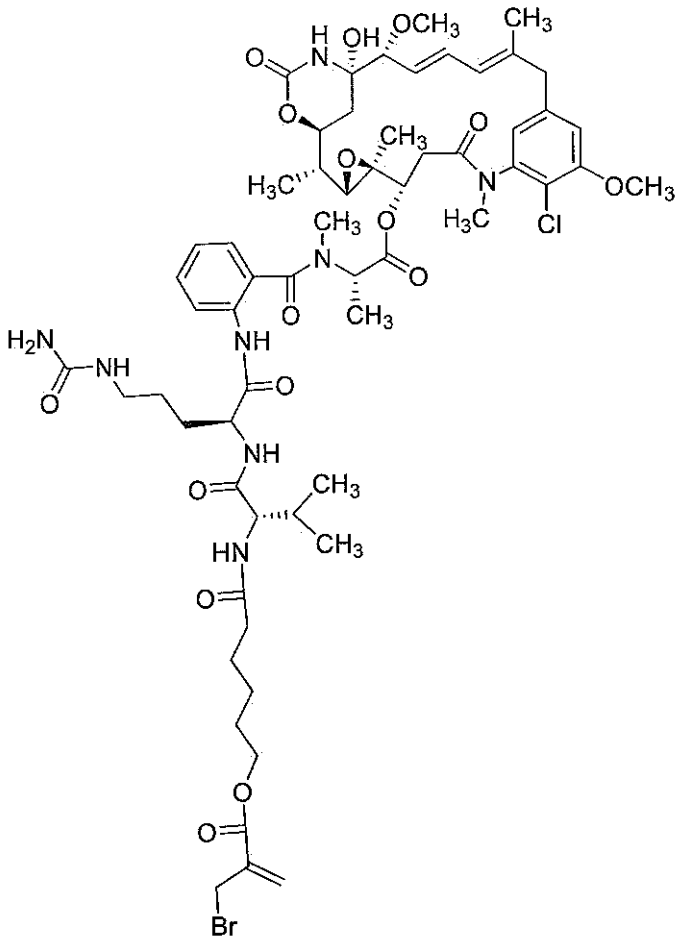
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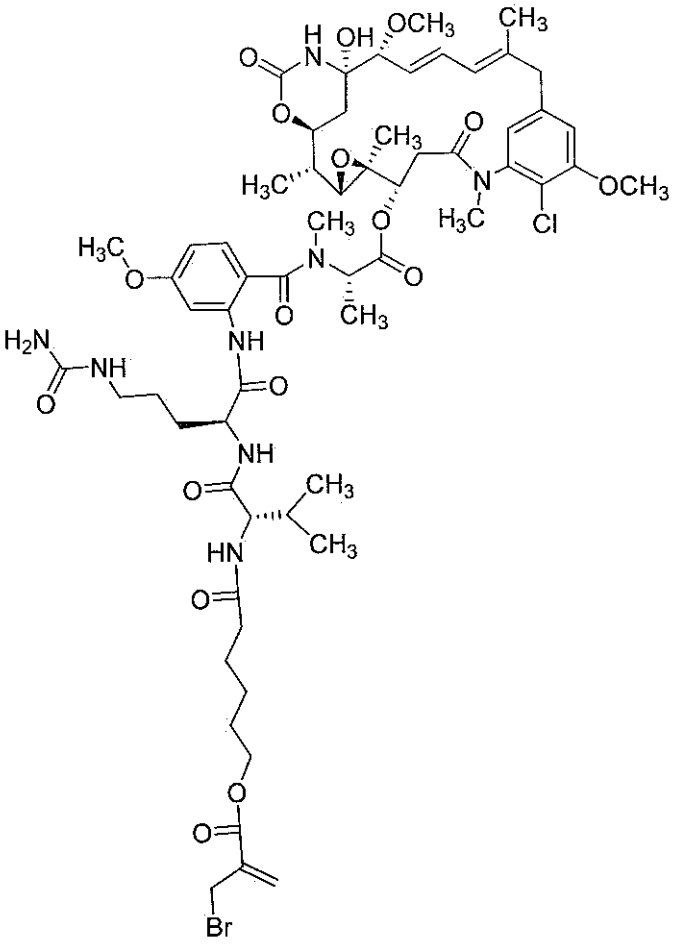
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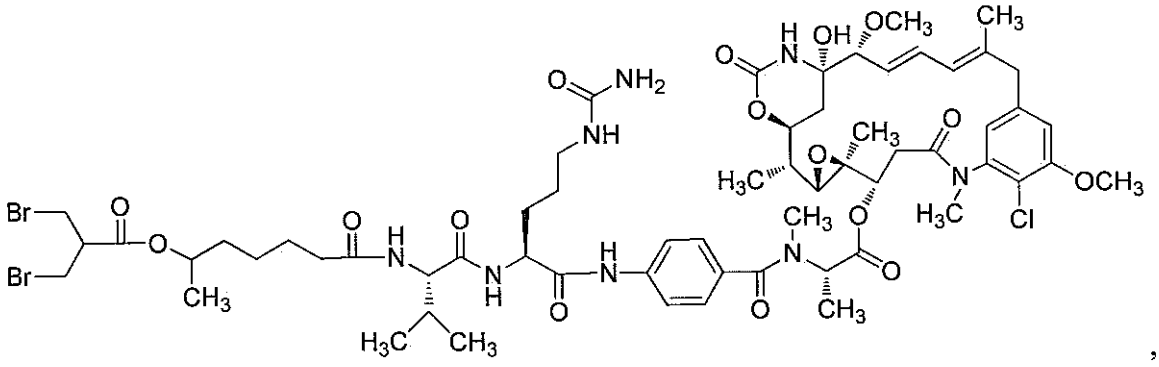
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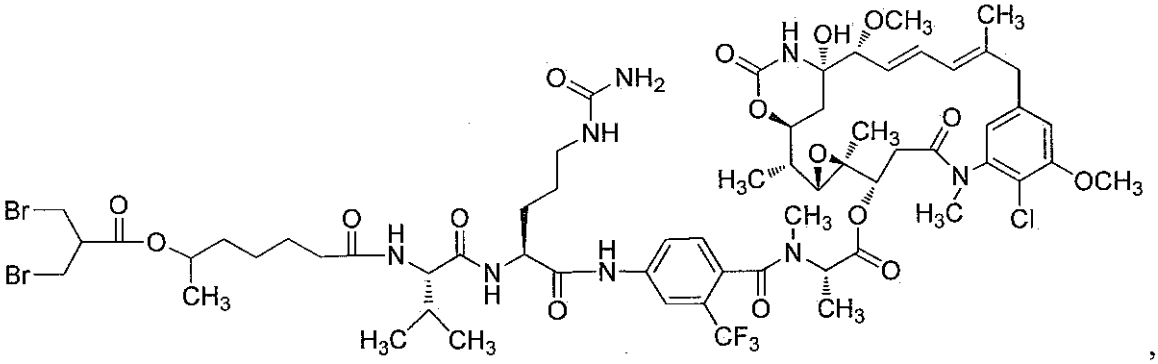
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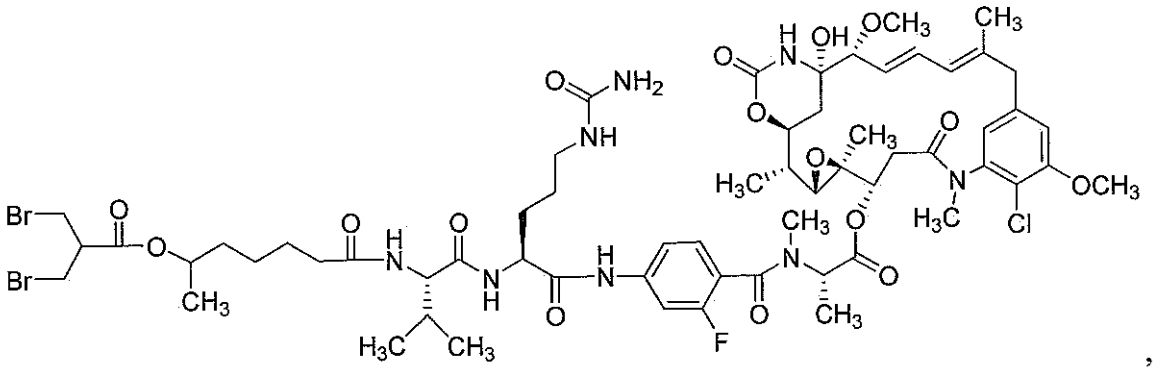


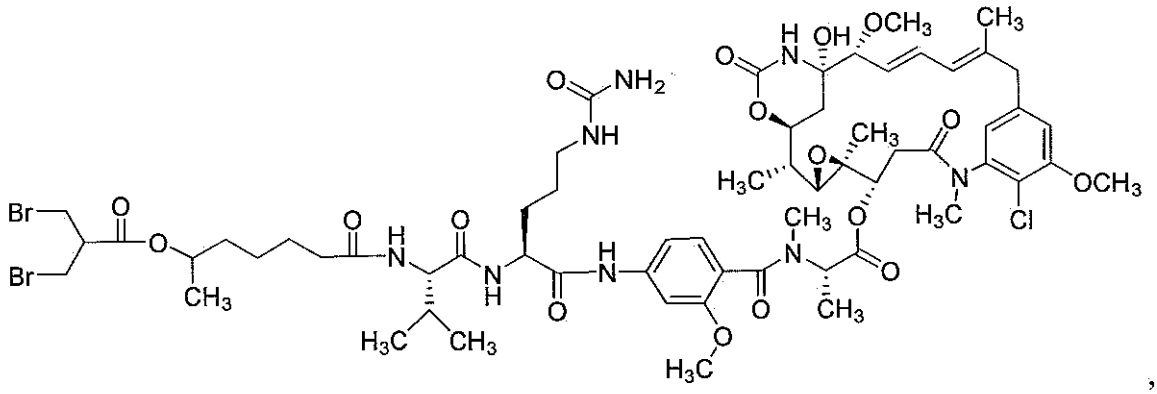
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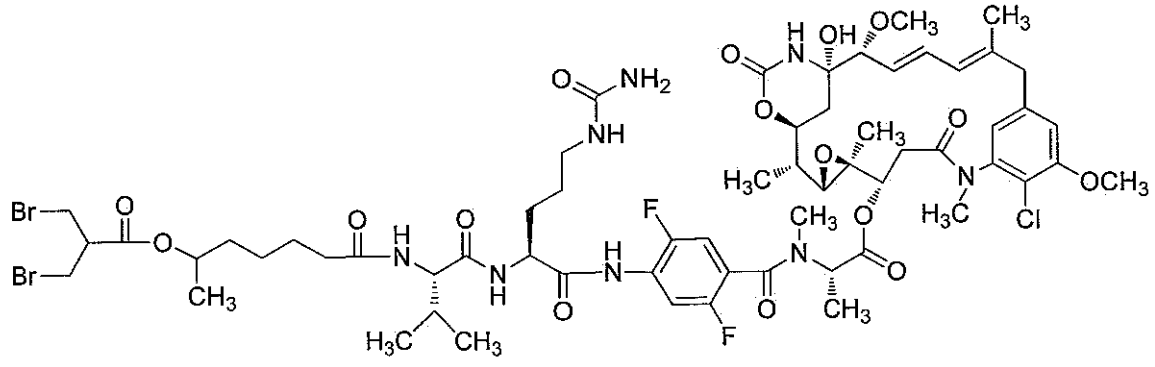


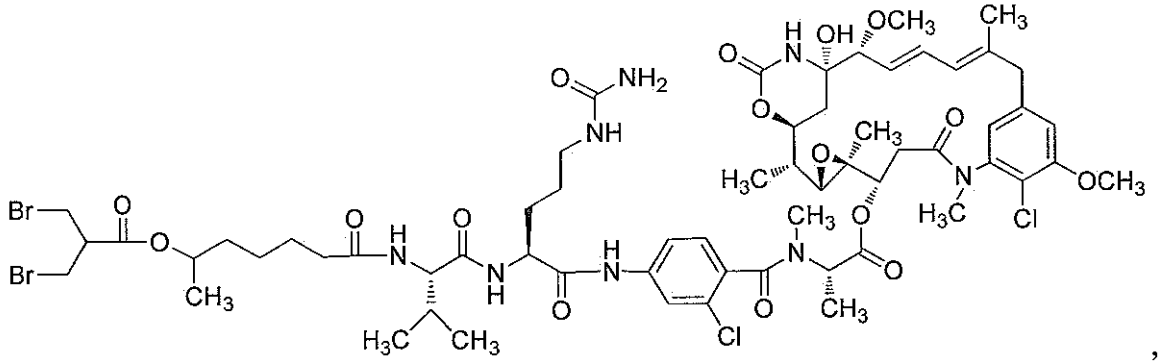
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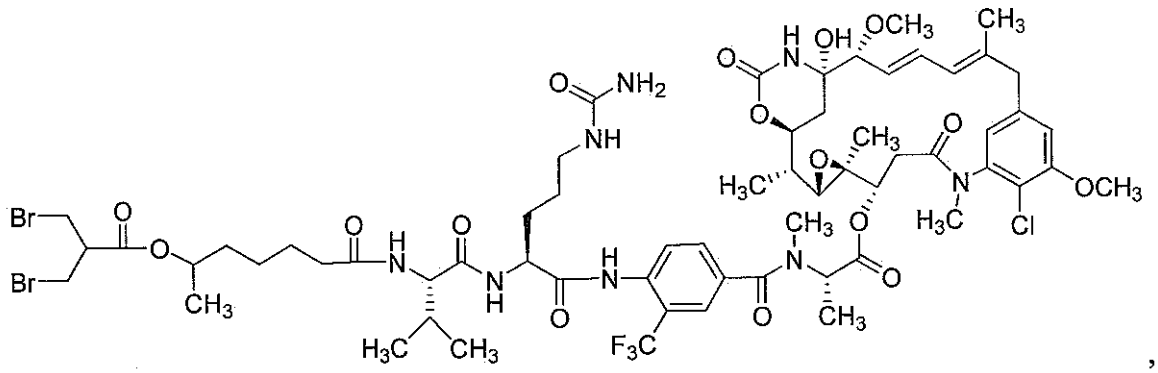

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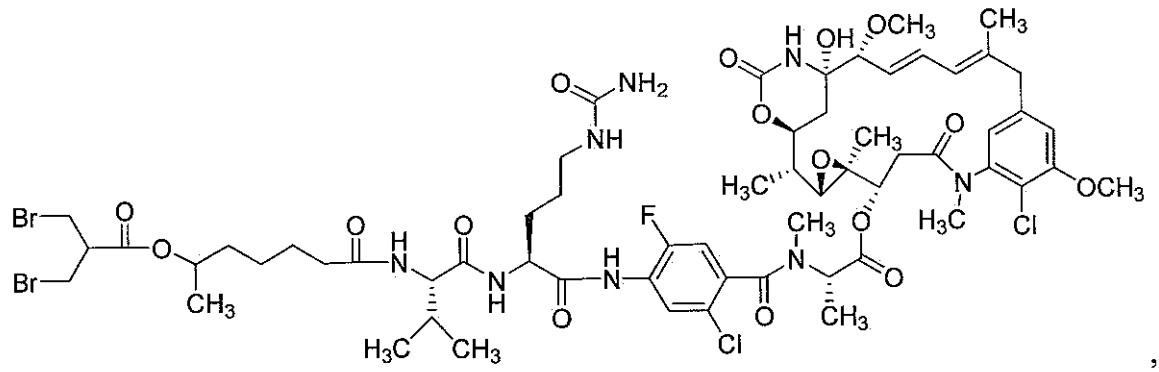

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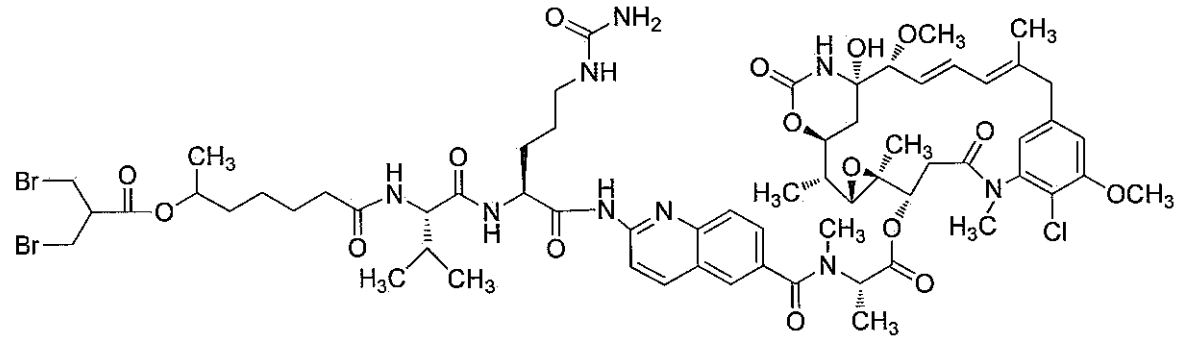

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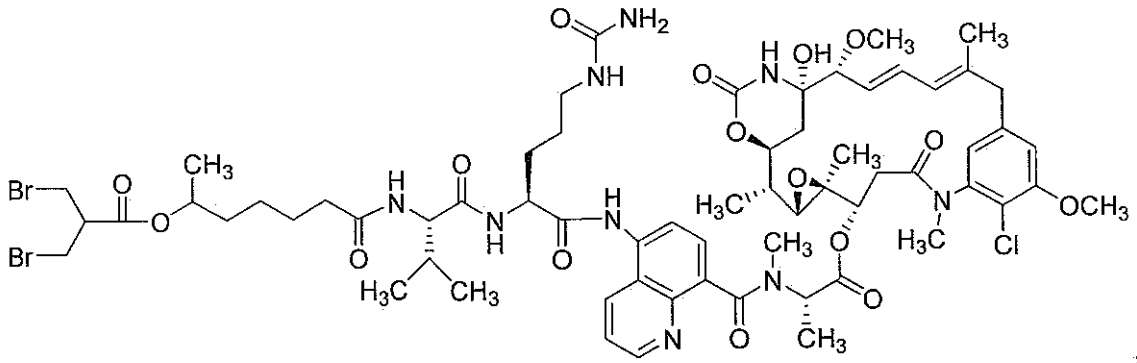

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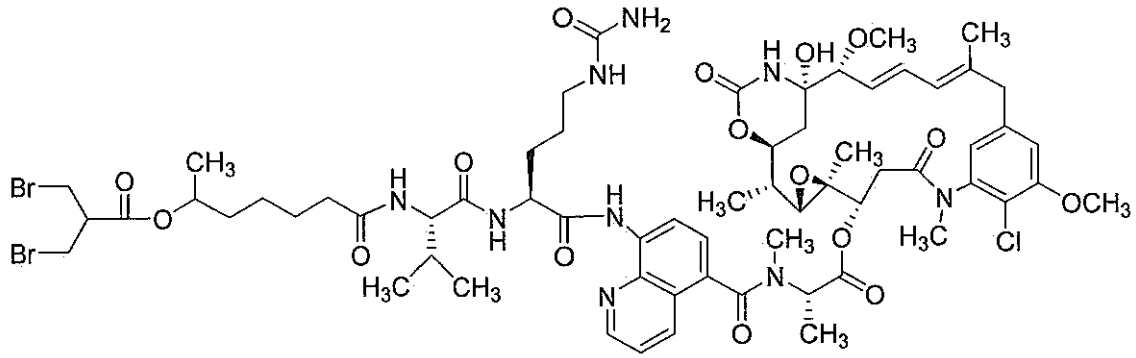

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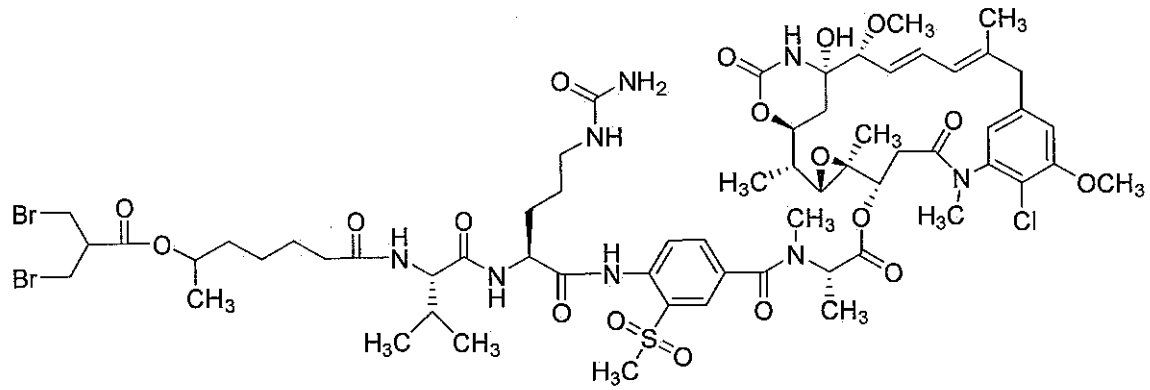

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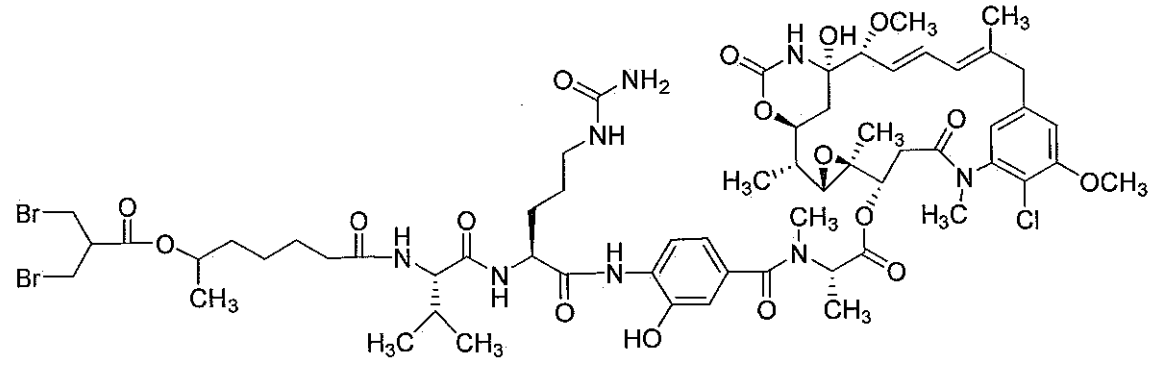
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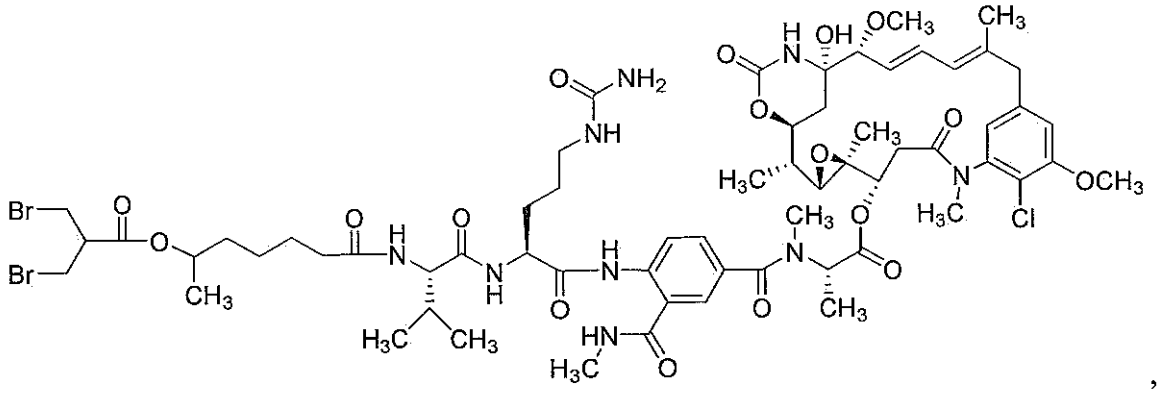
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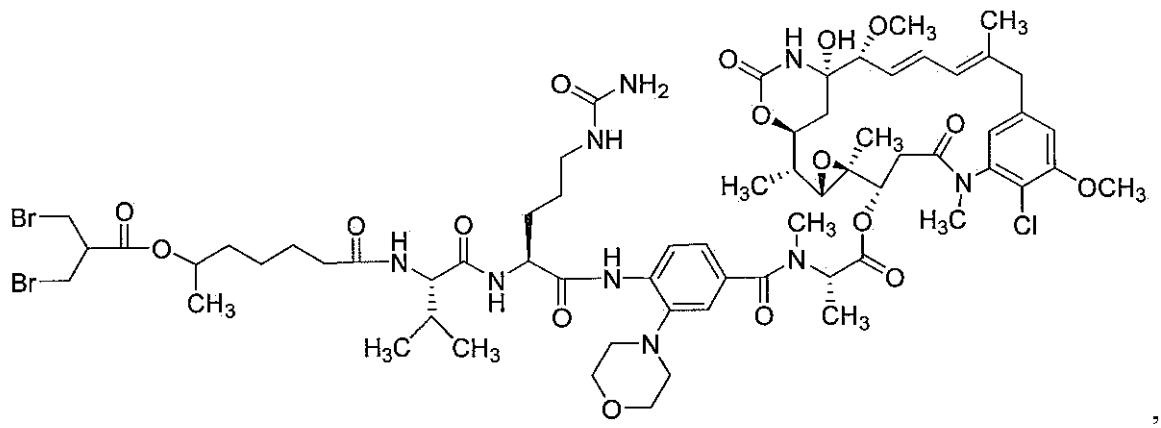
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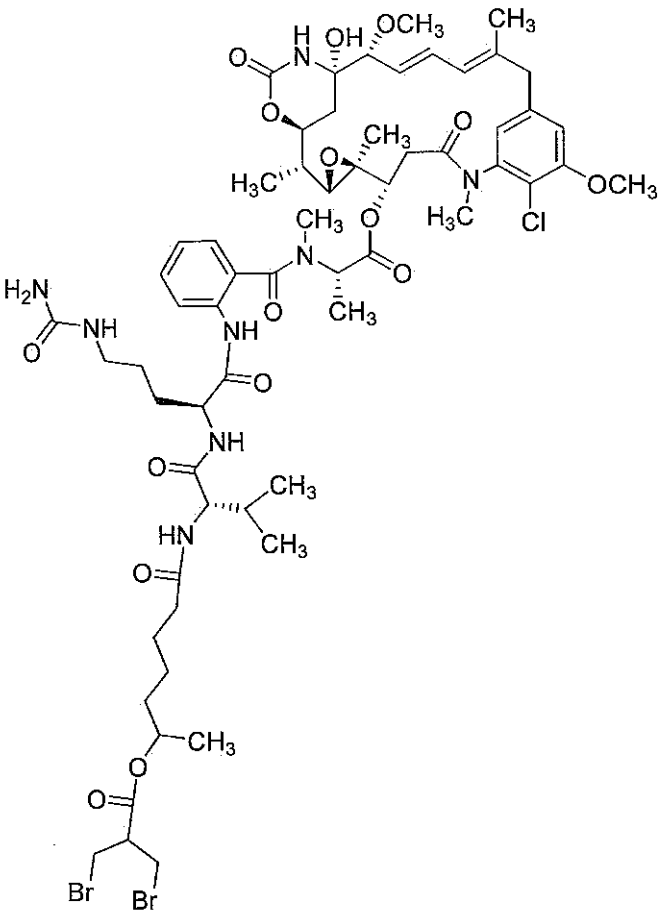
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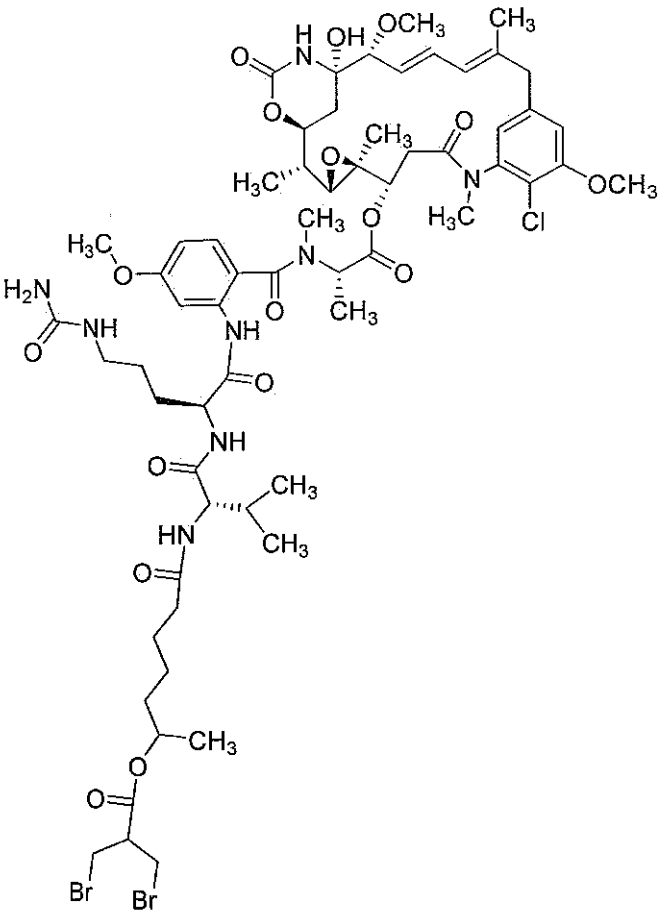


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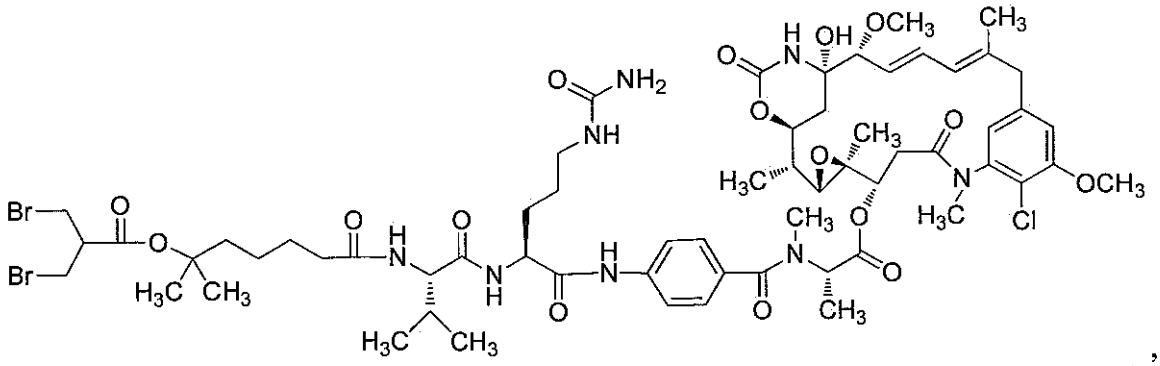


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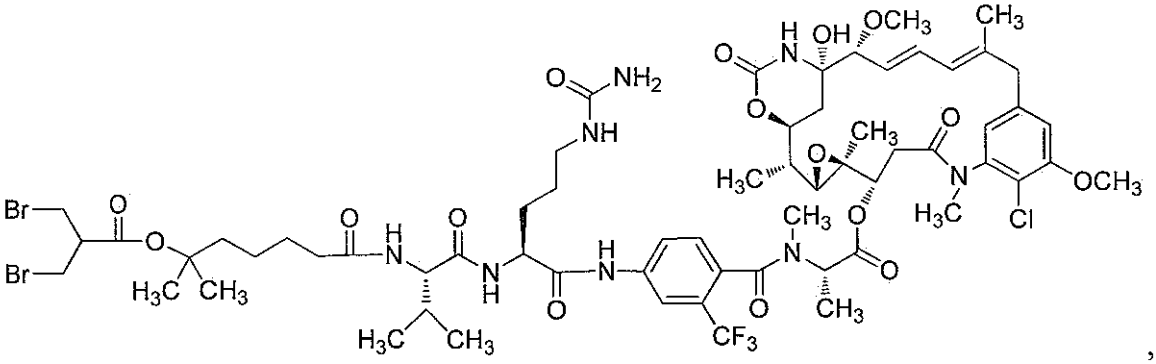


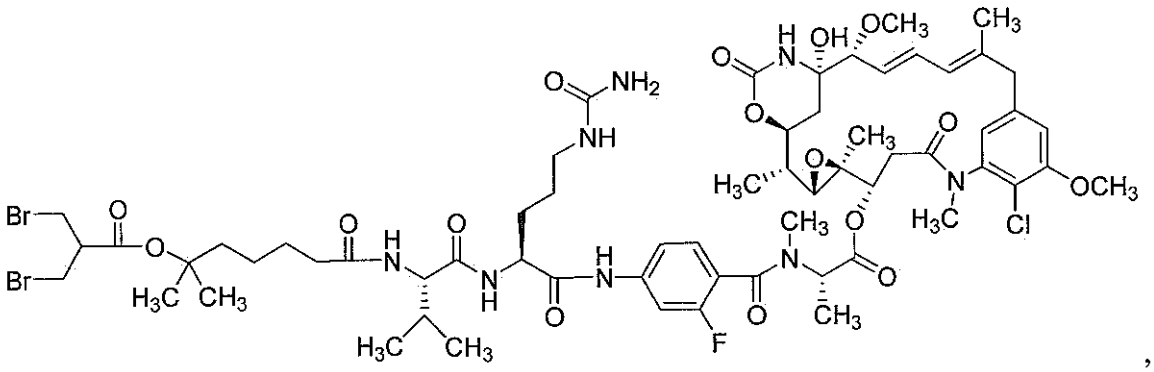


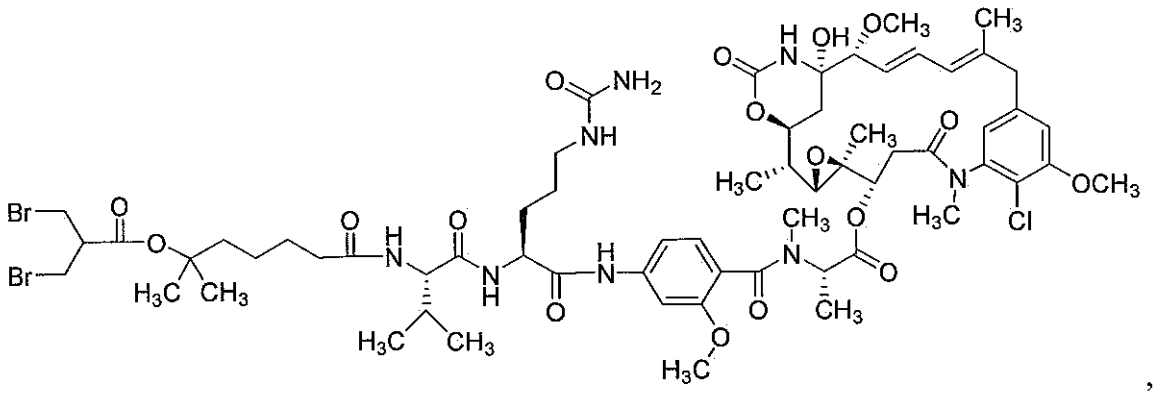
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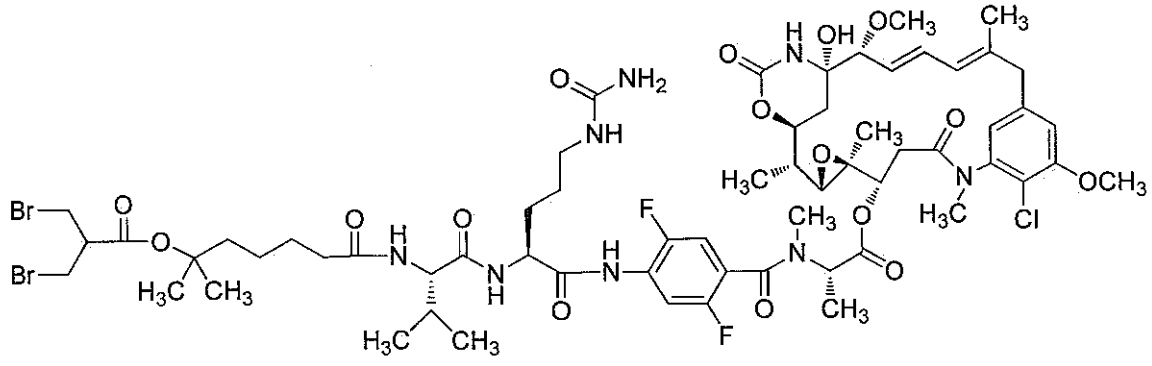


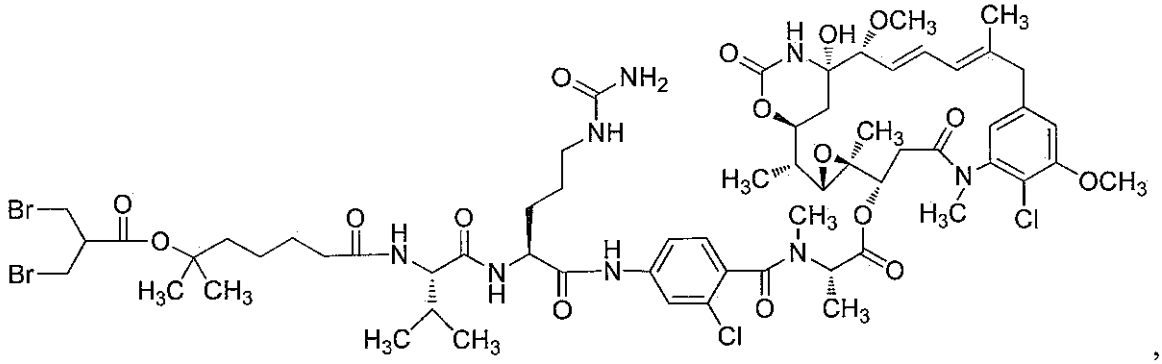
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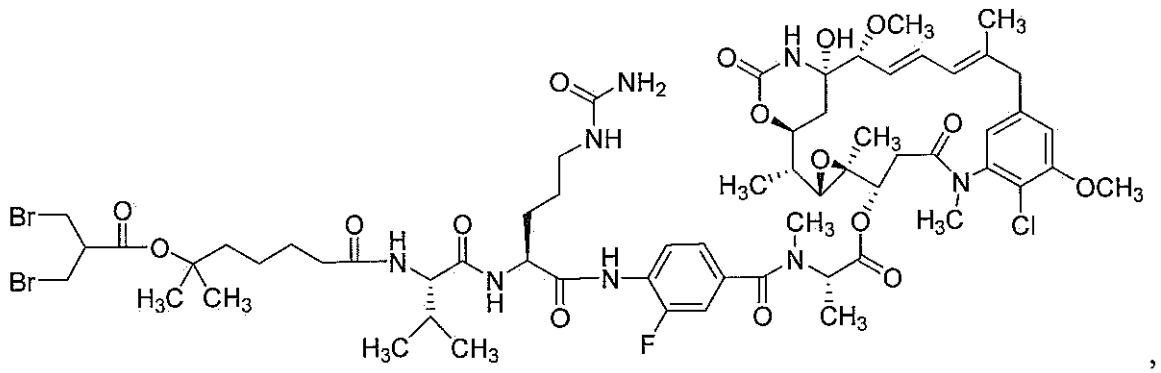

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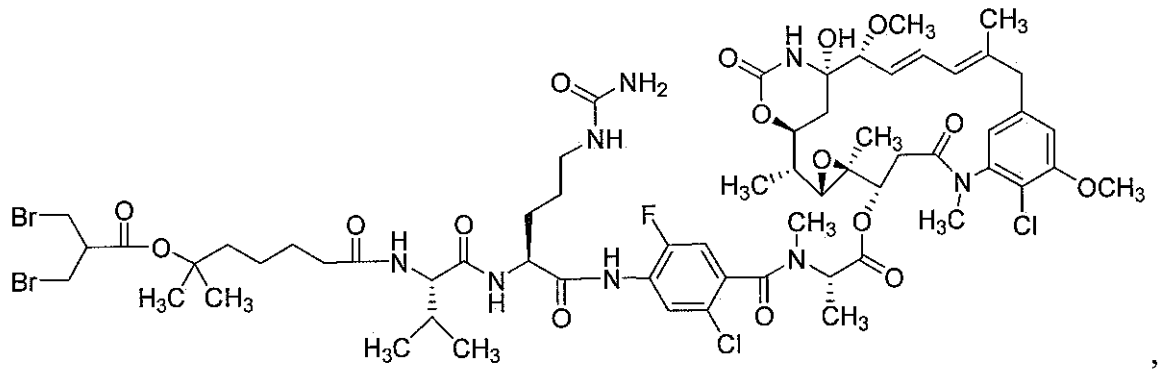

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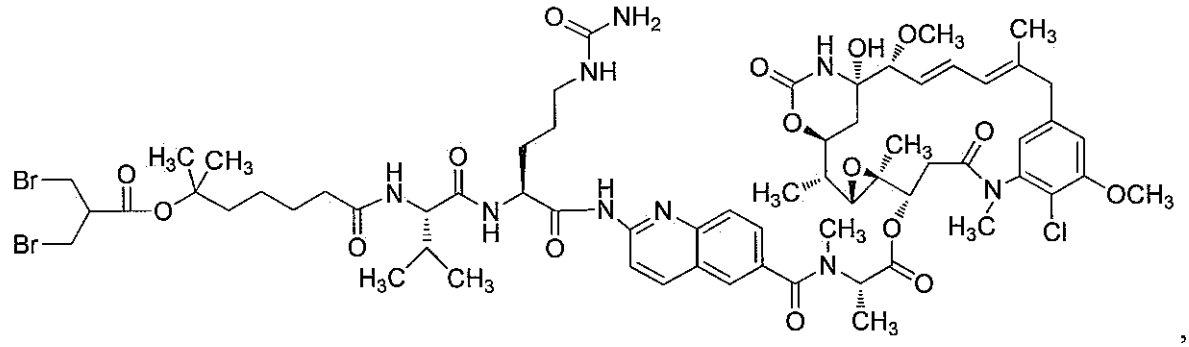
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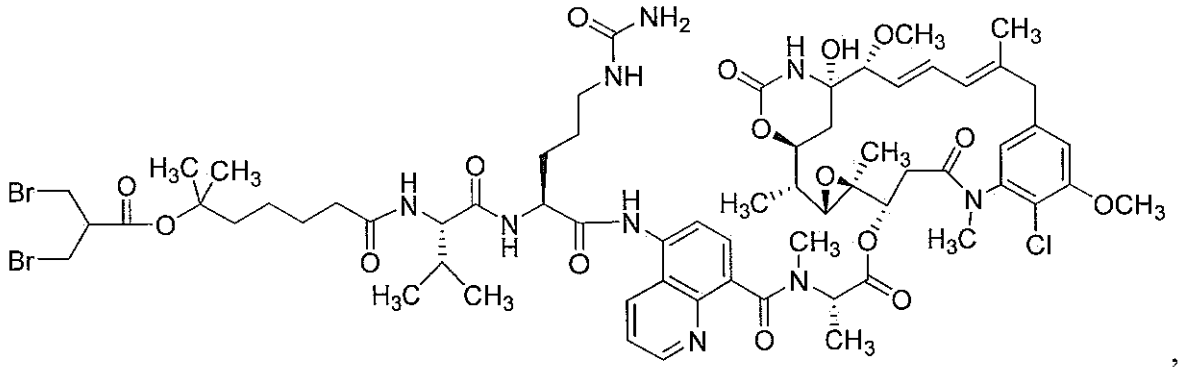
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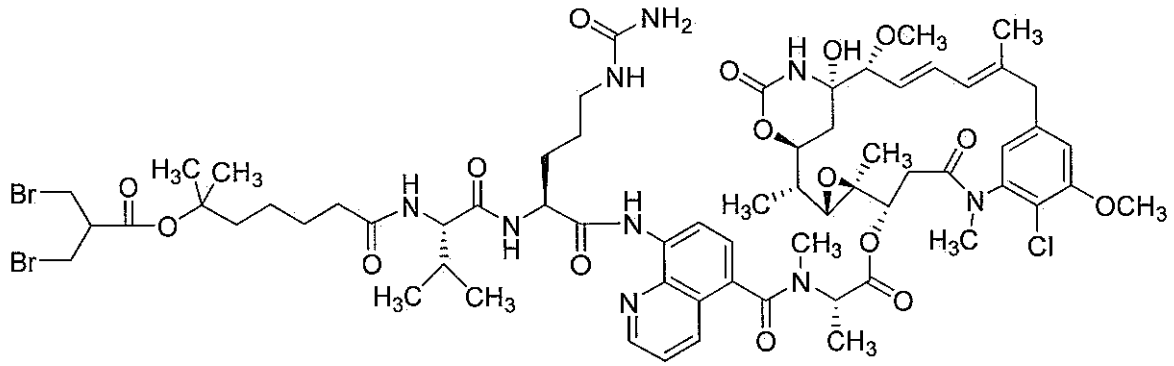


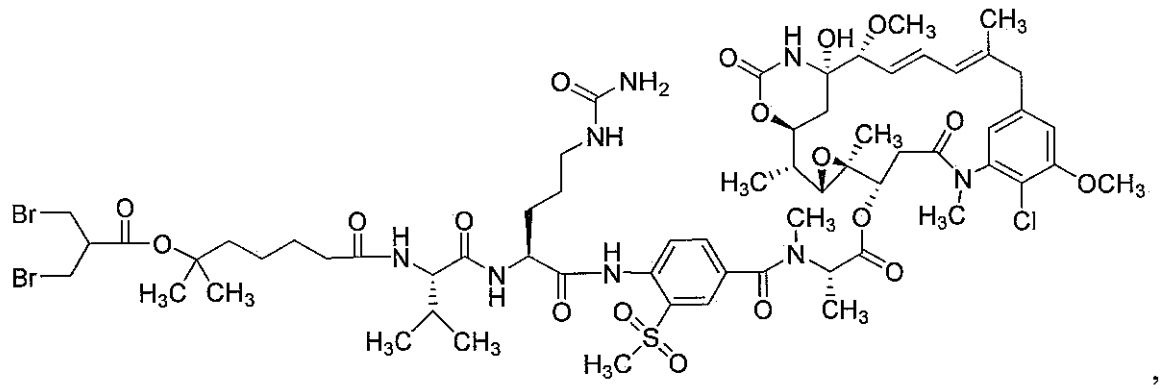
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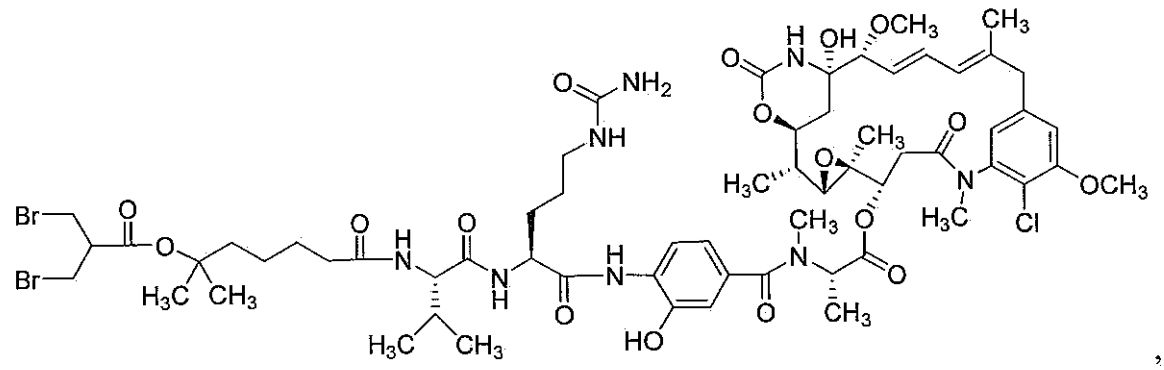


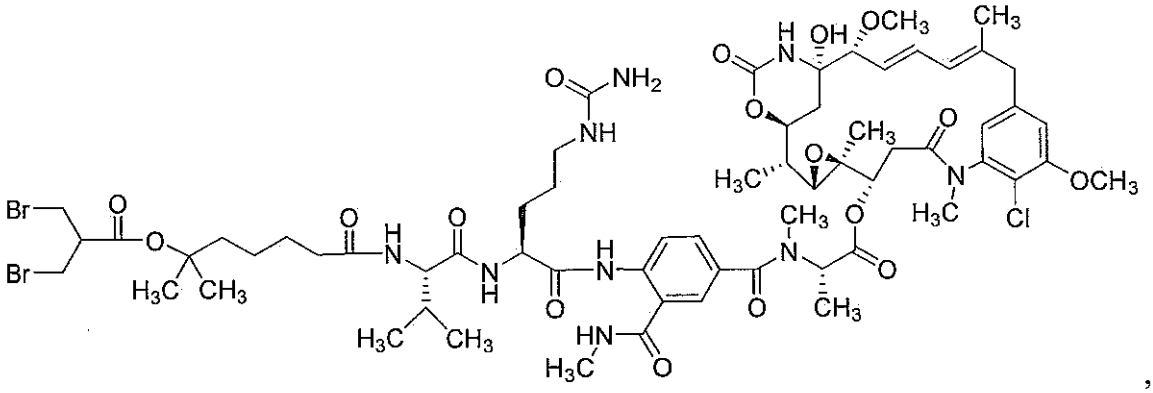
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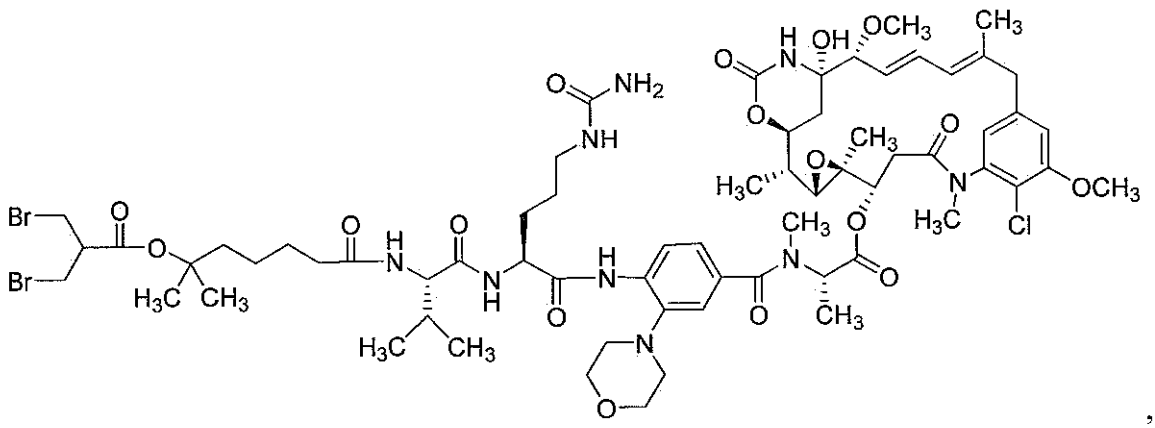




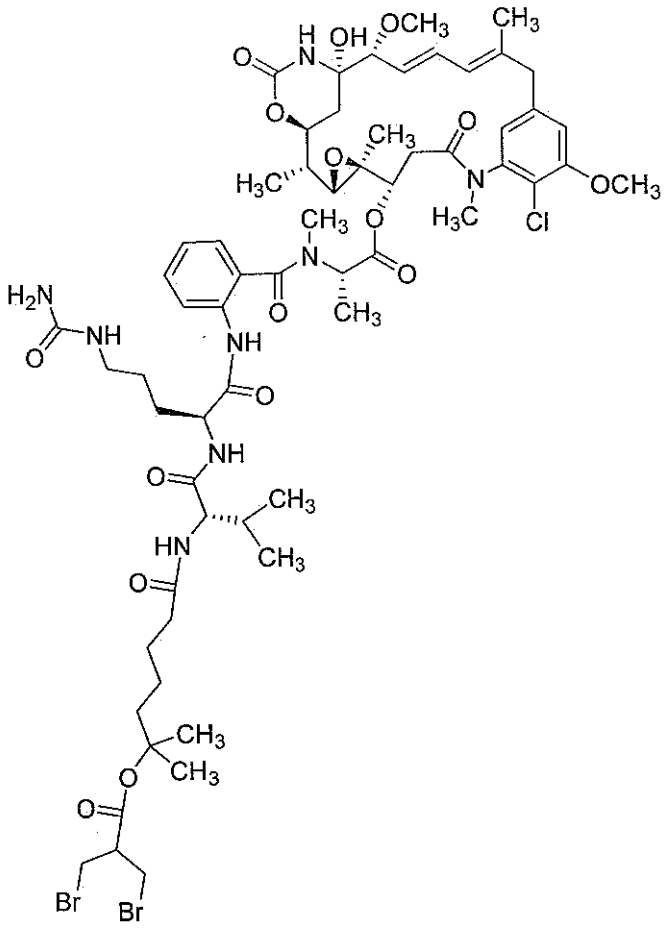


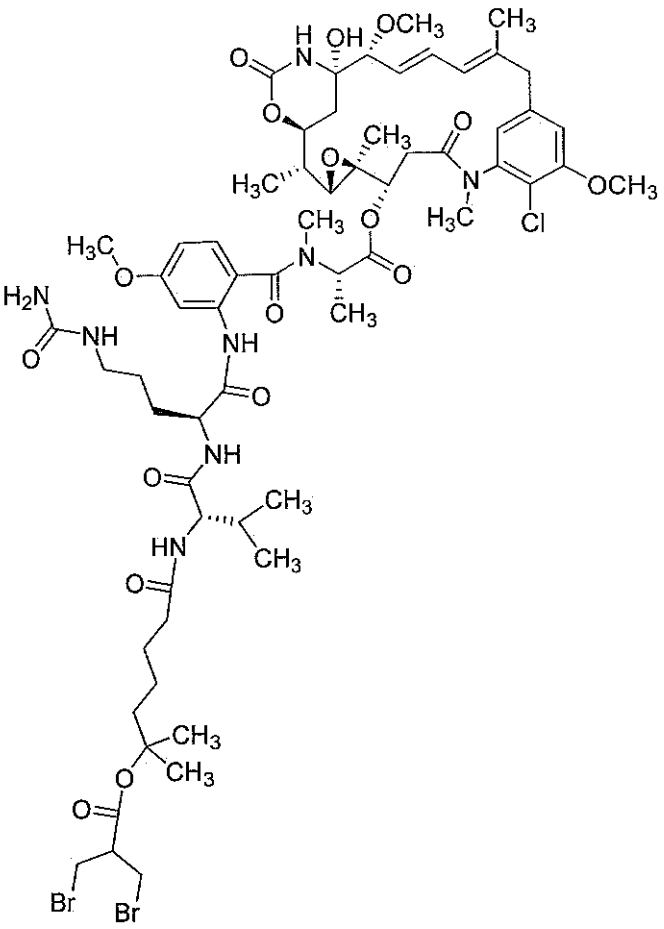


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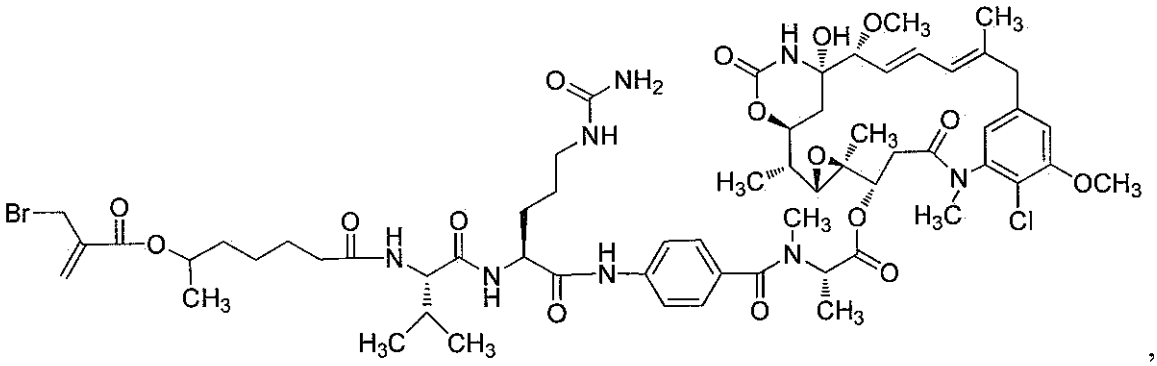


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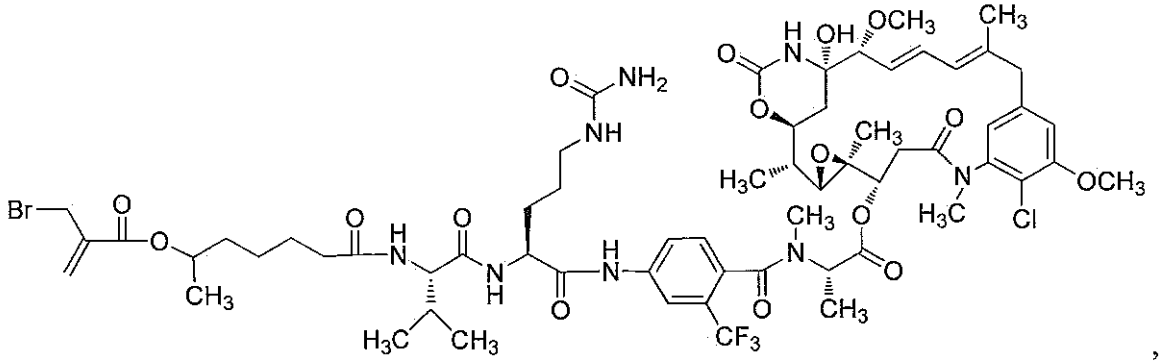




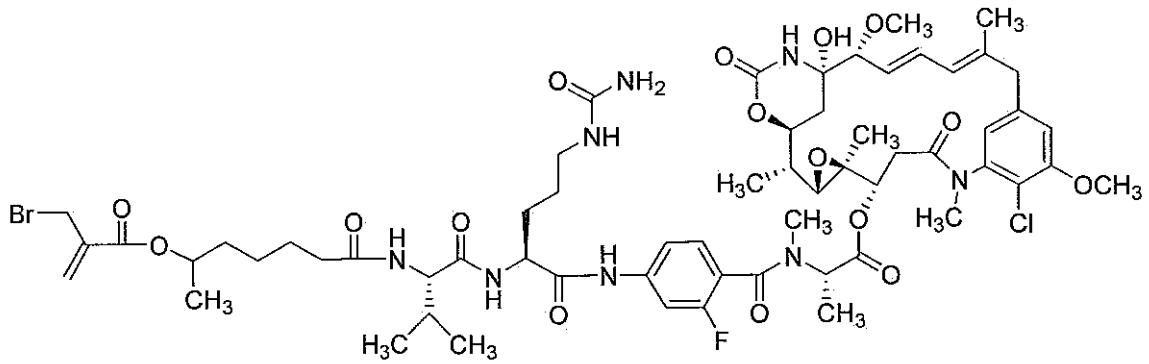
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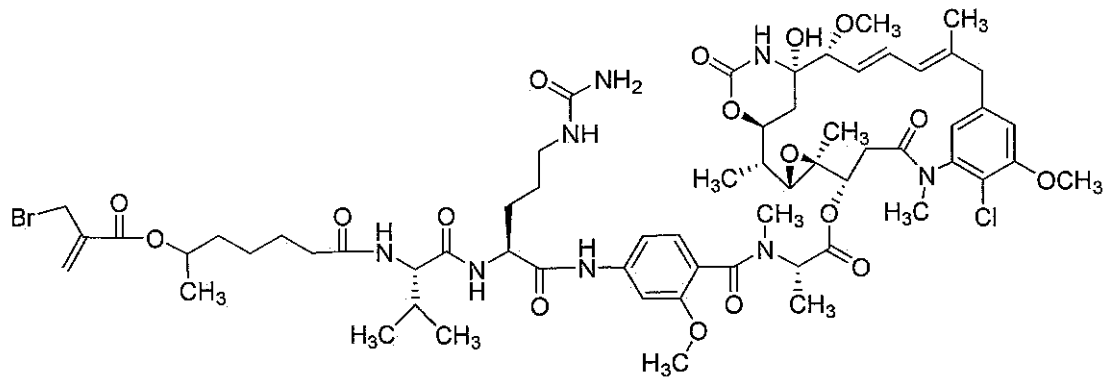
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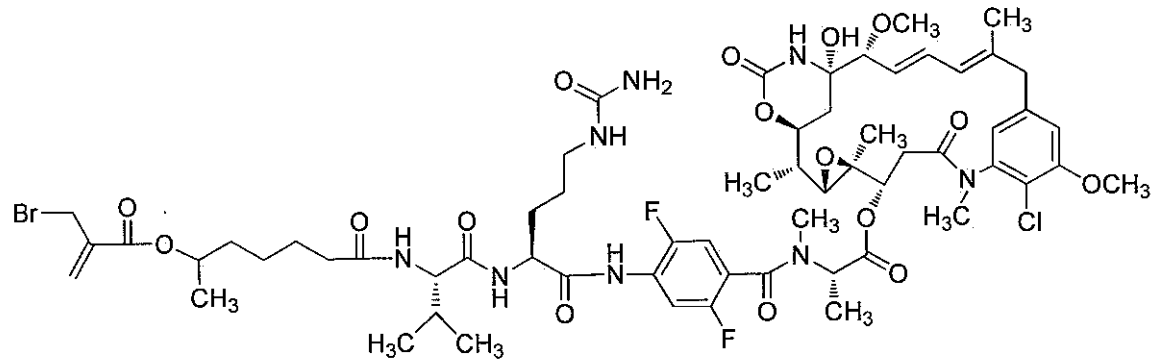
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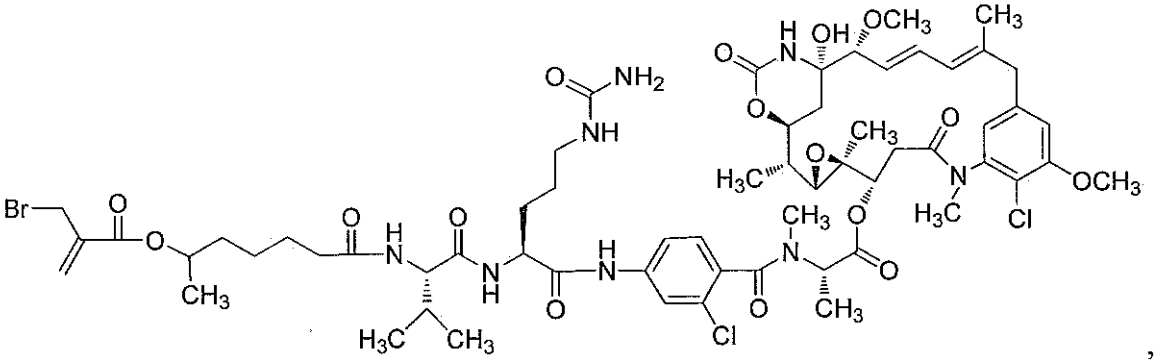
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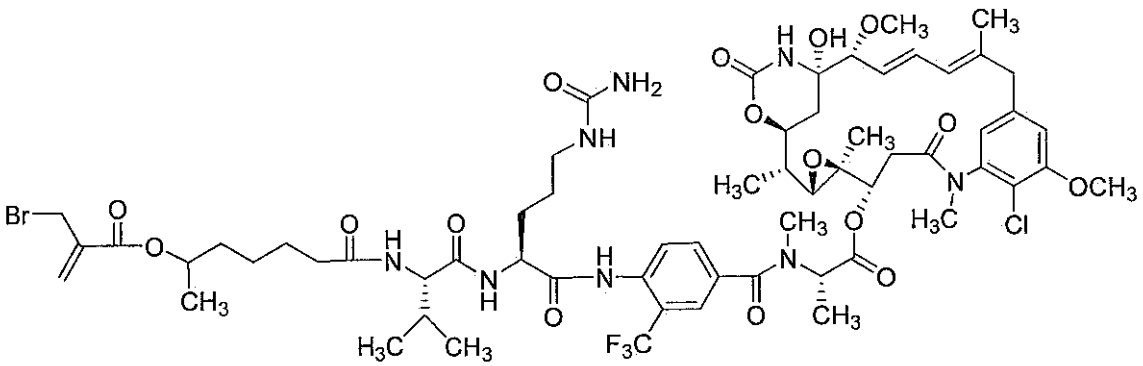
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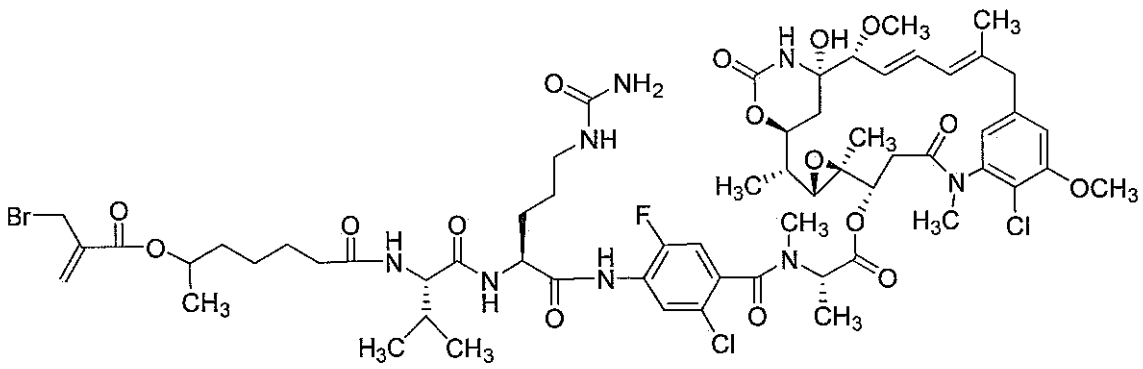
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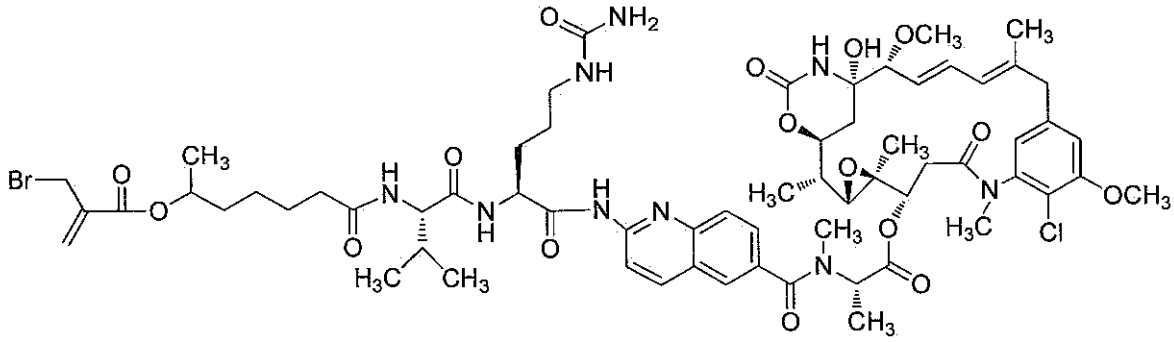
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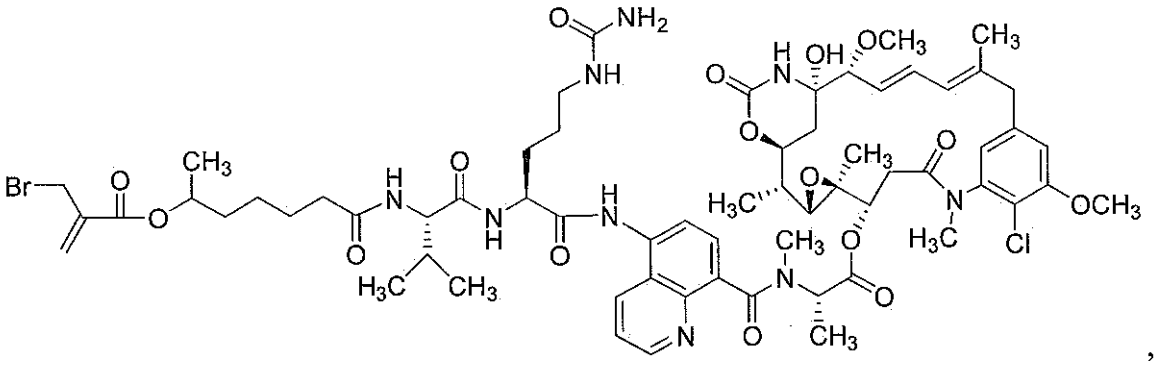
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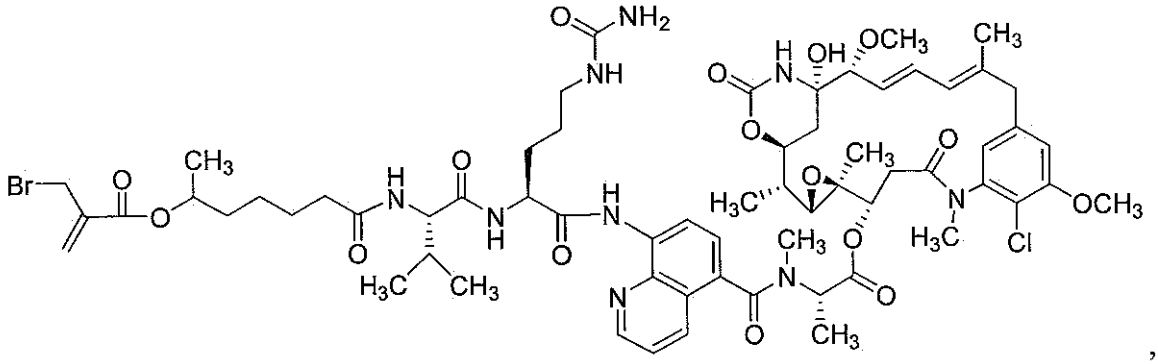
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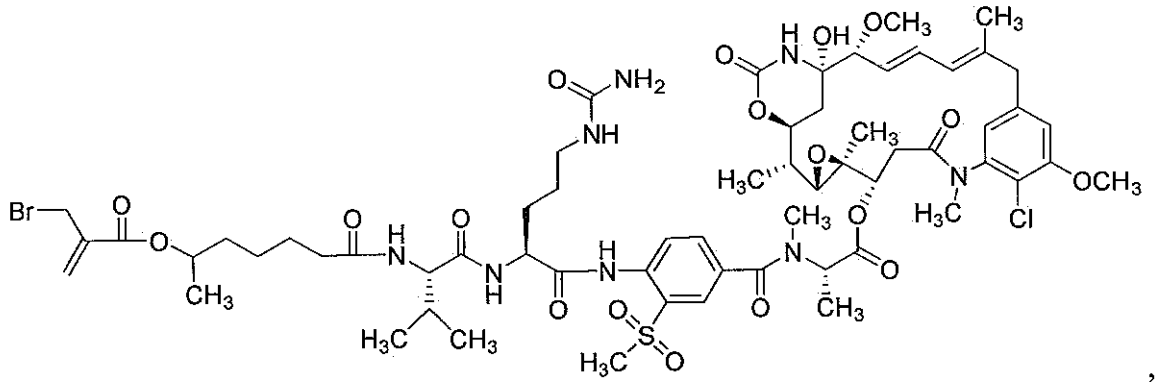
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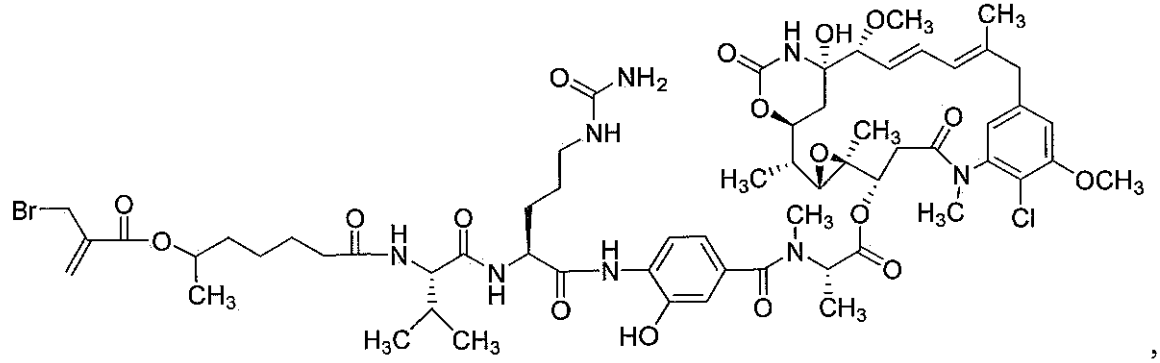
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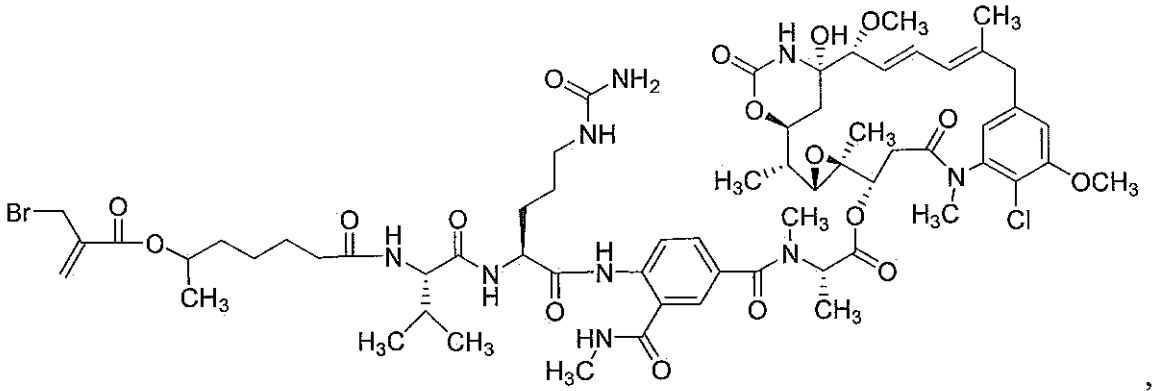
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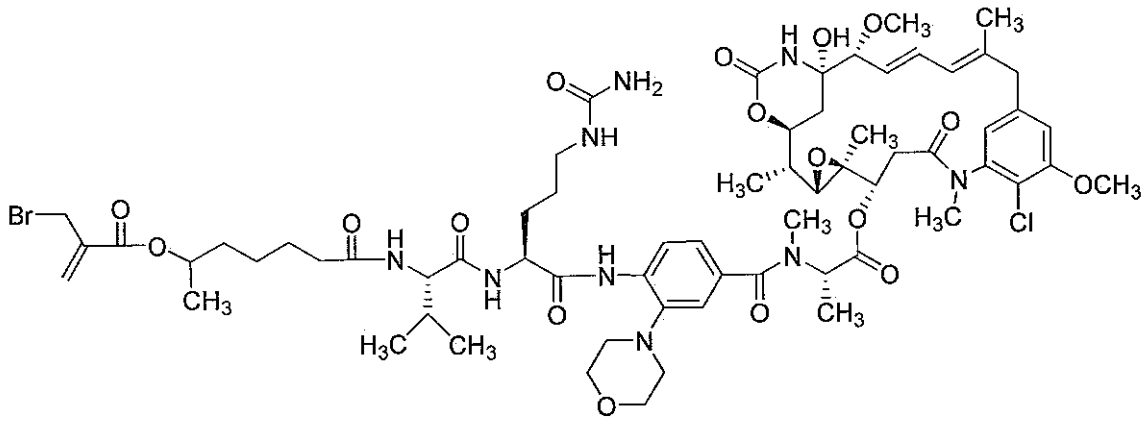
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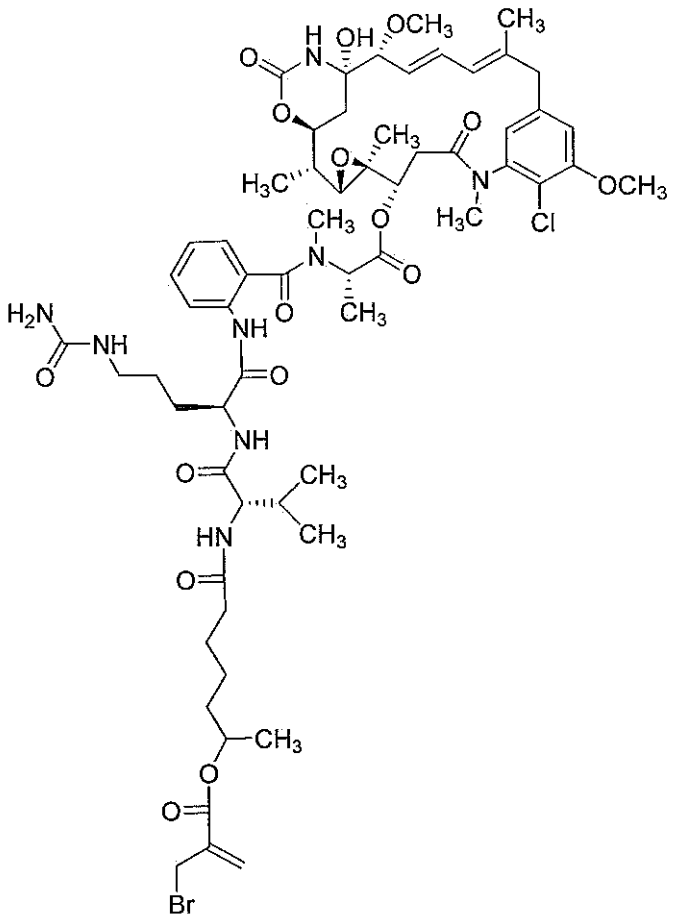
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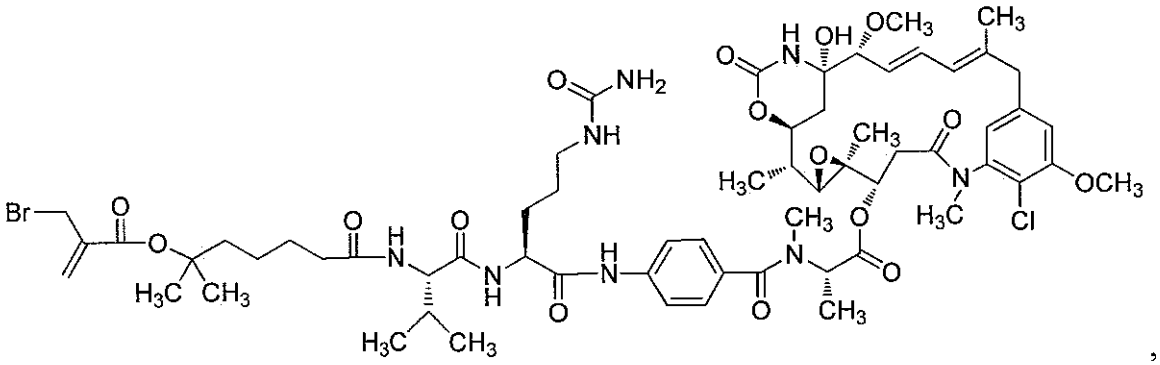
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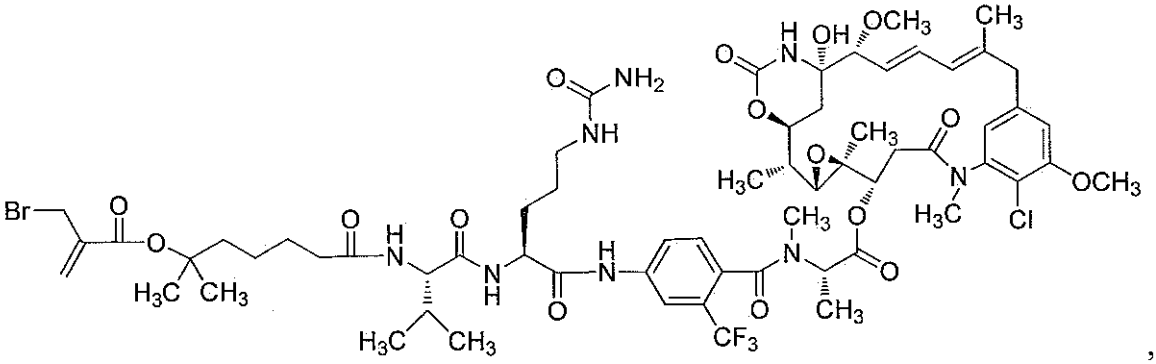
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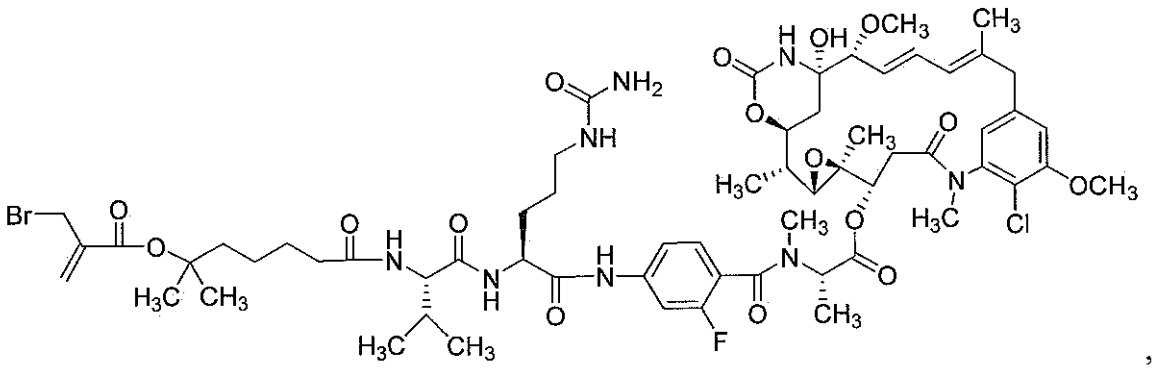
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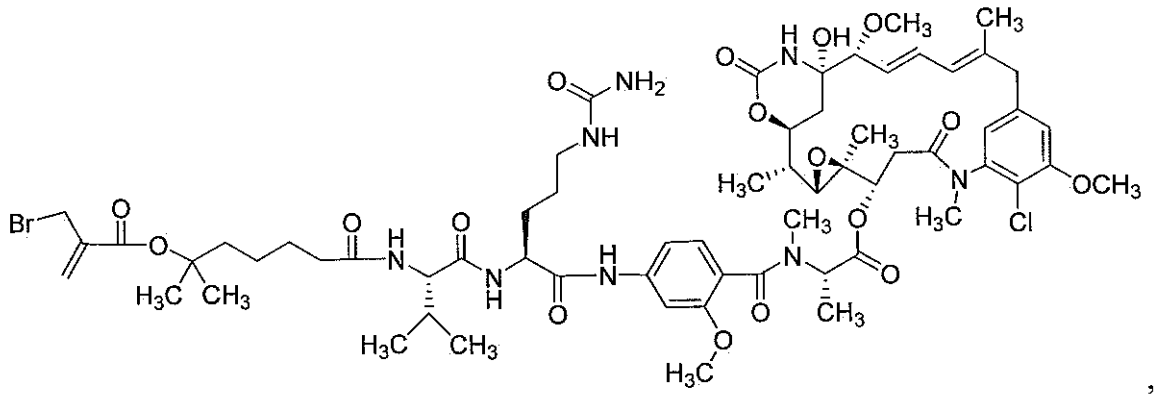
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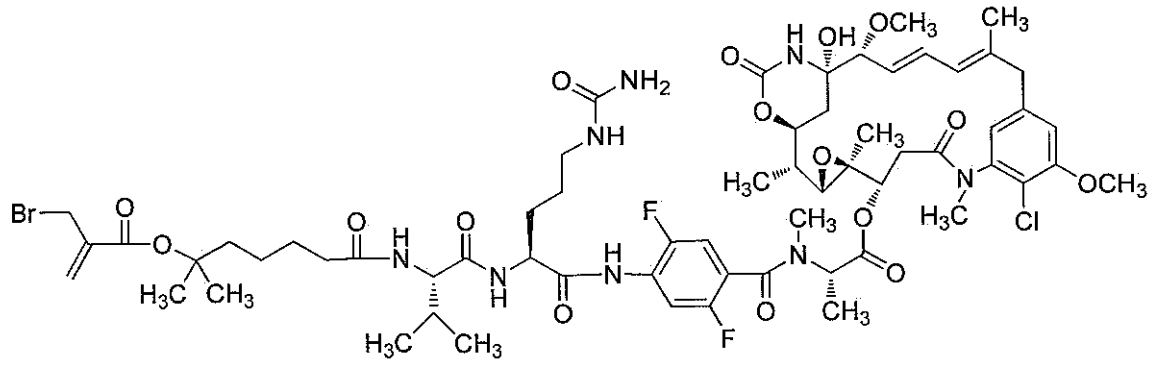
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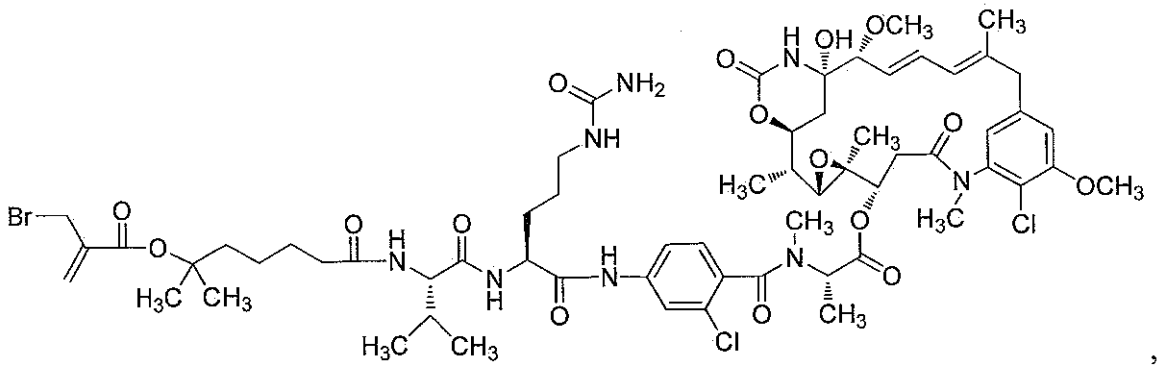
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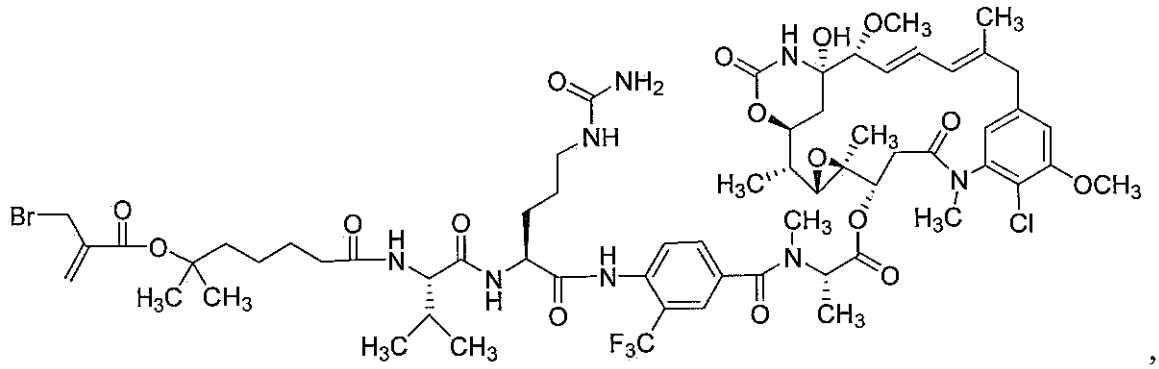
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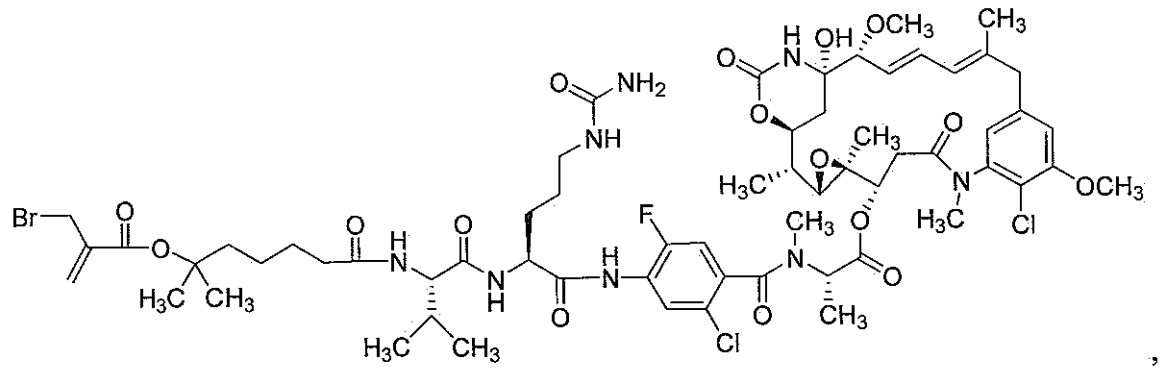
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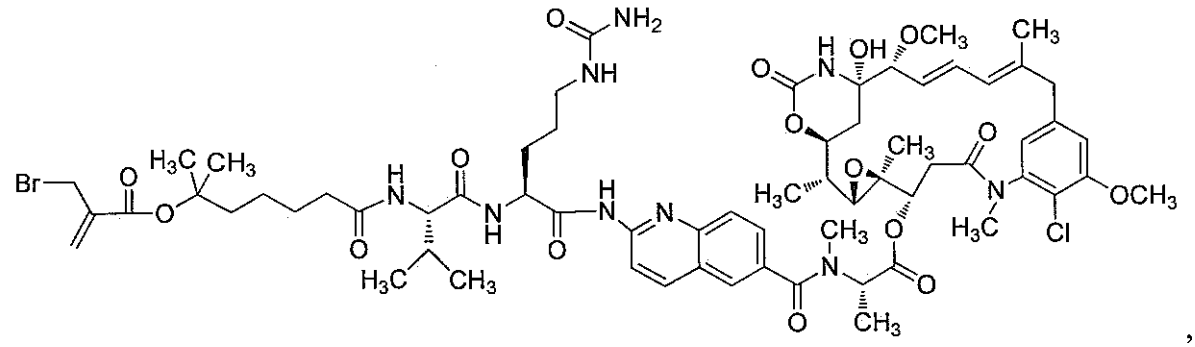
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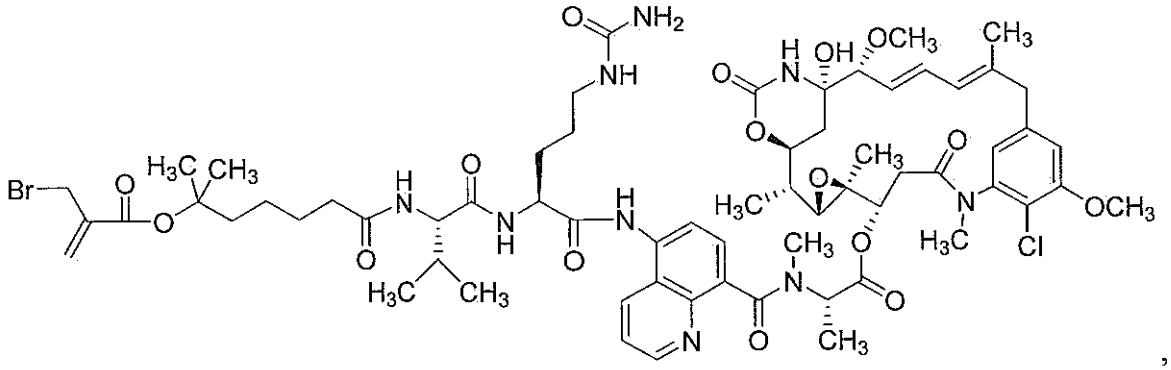
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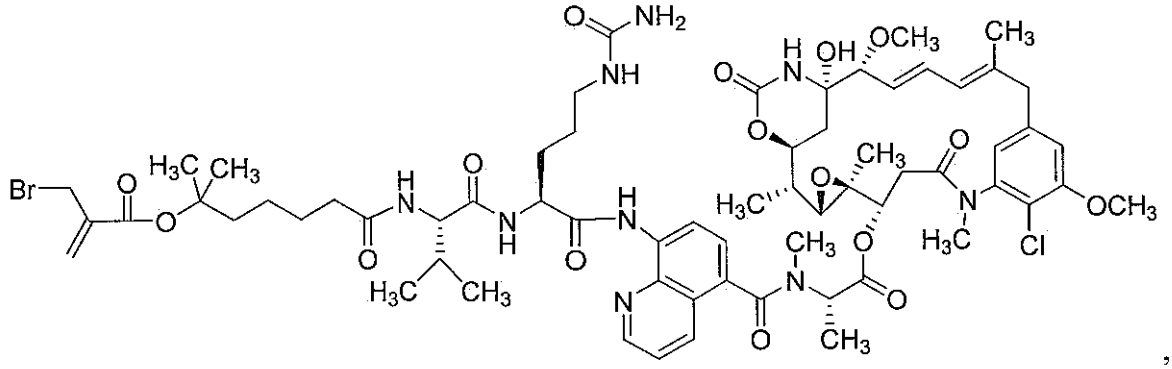
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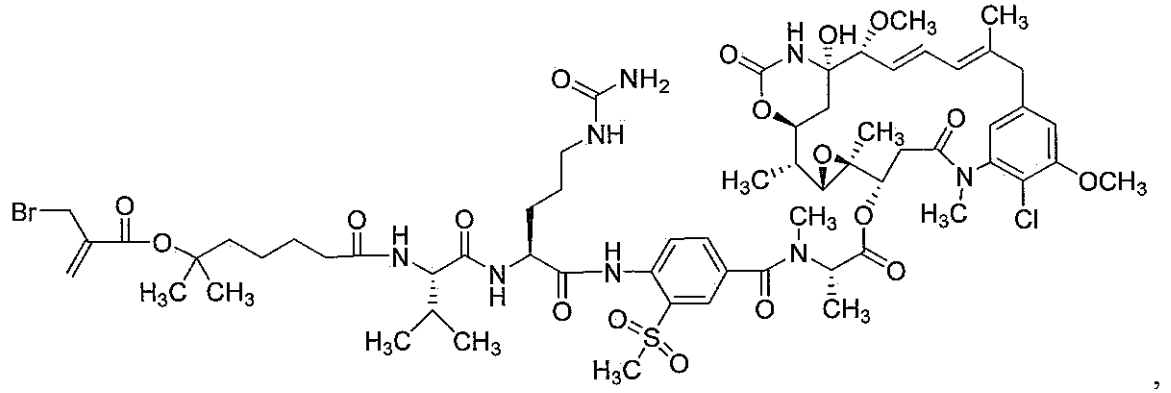
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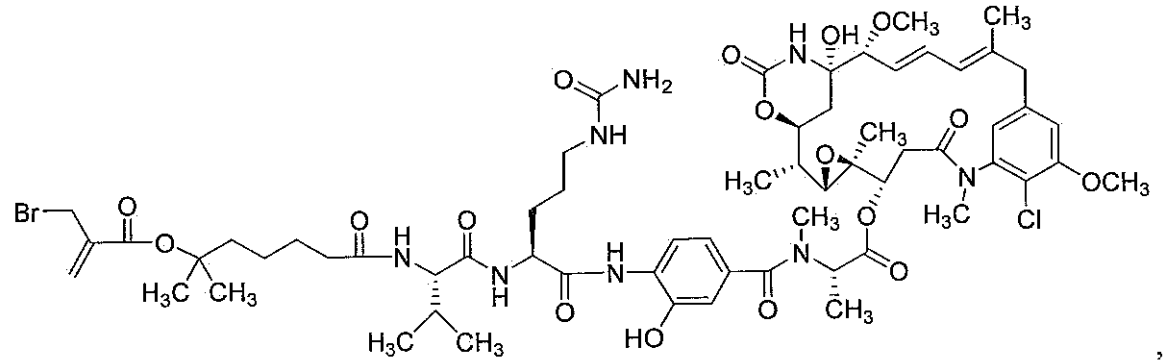
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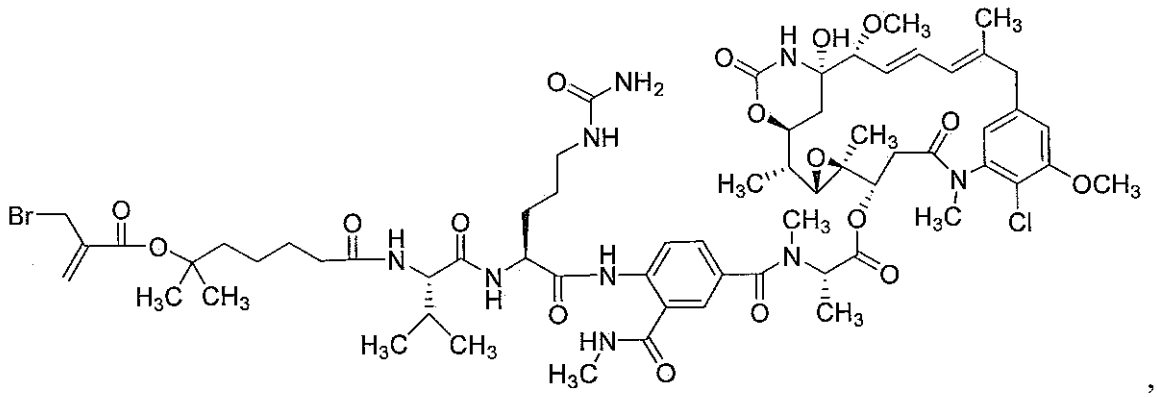
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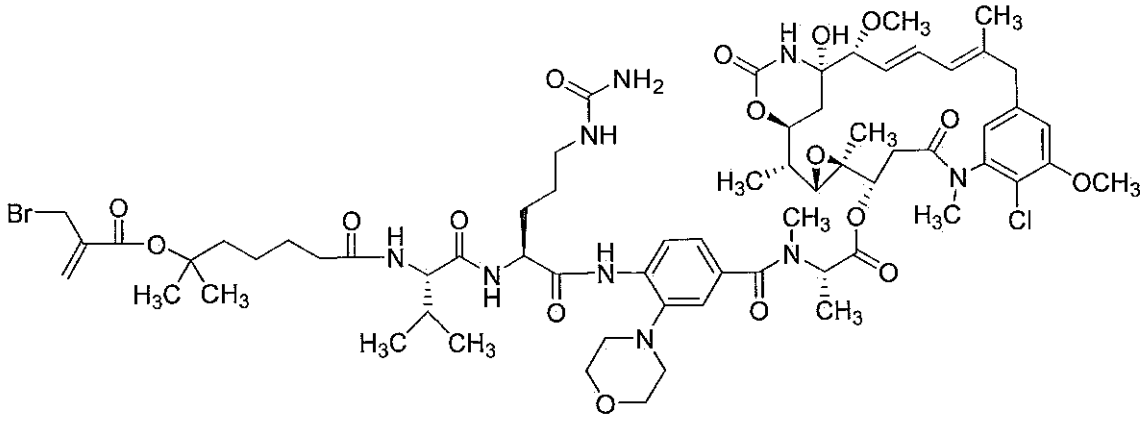
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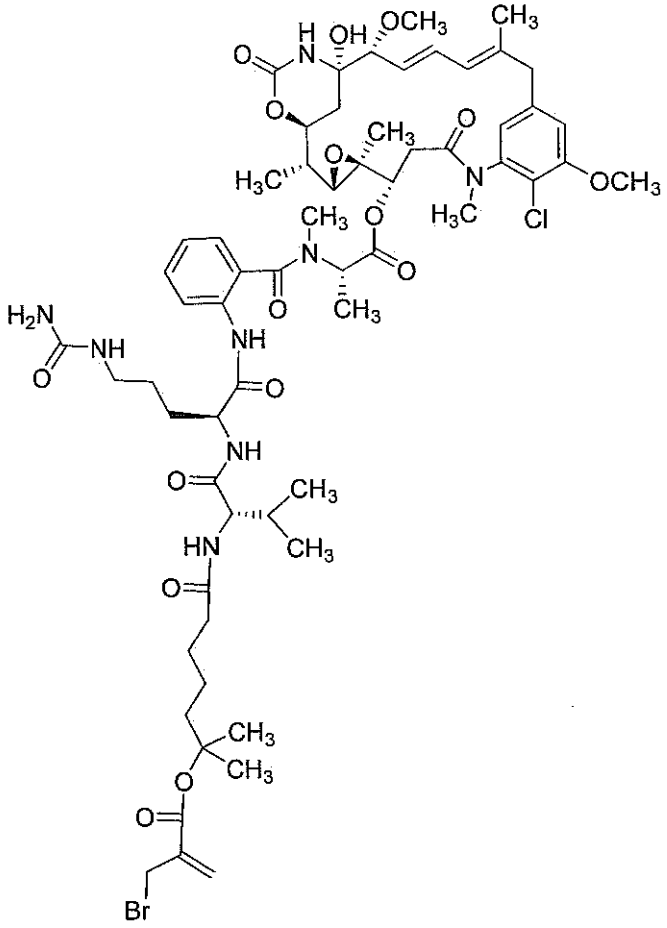
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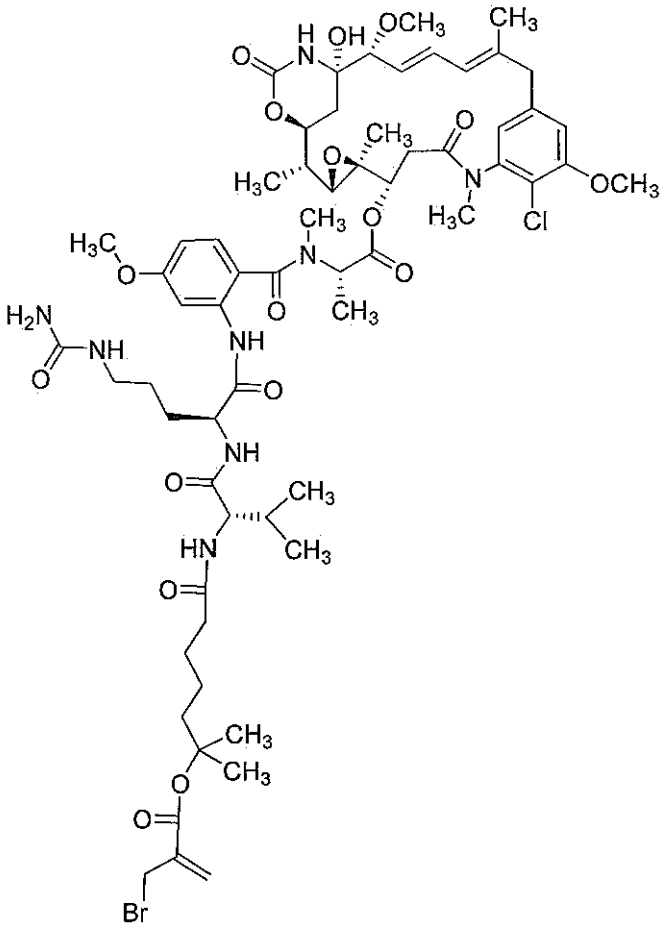
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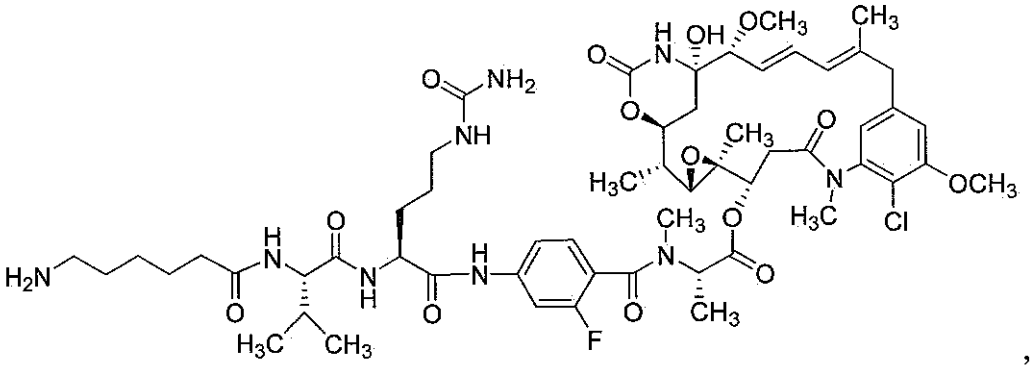
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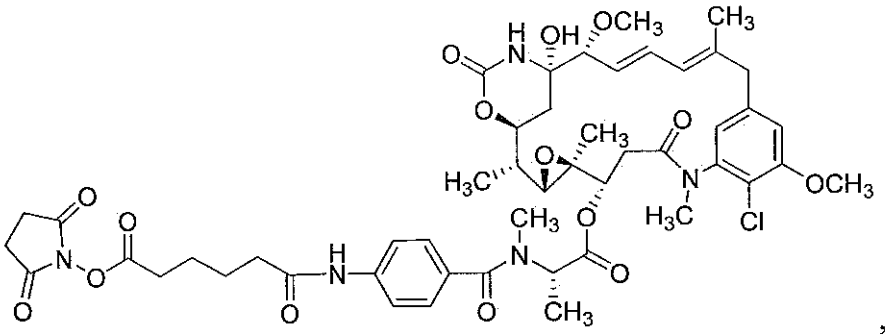
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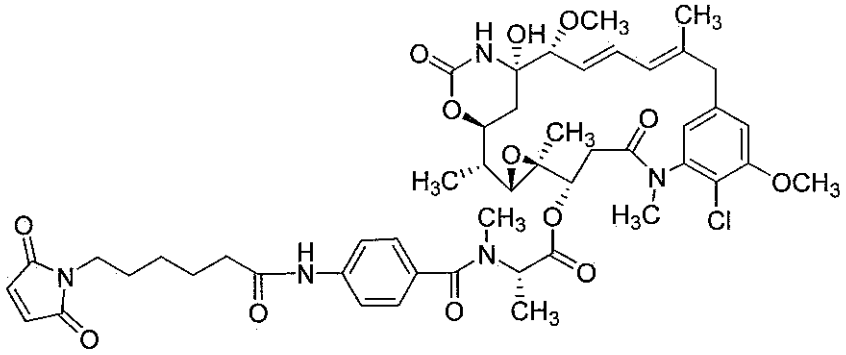
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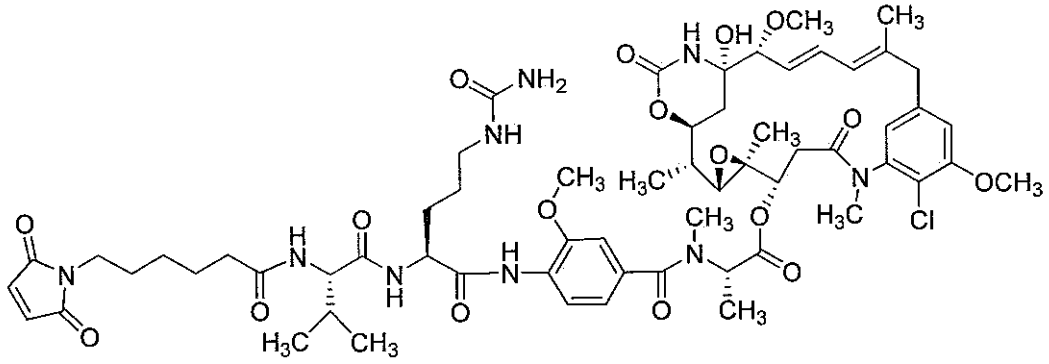


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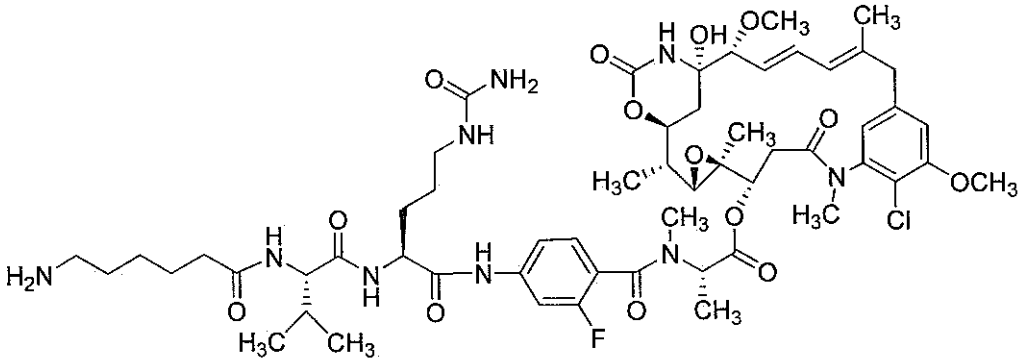


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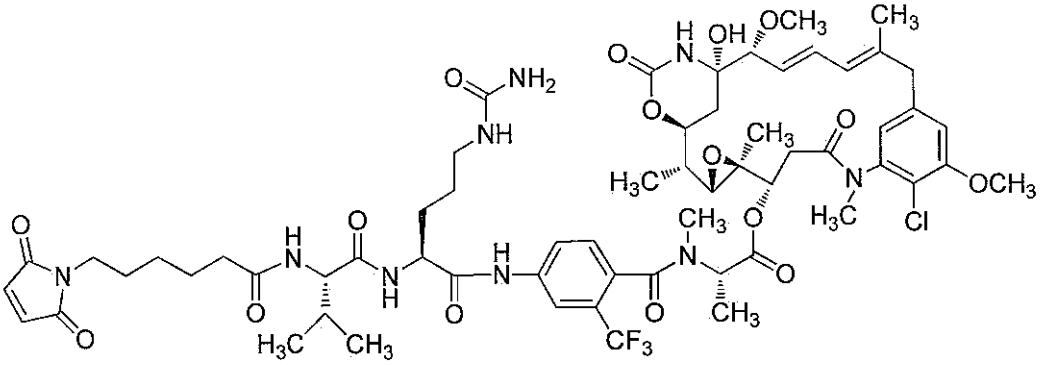
30. The compound of claim 26, wherein the compound is selected from



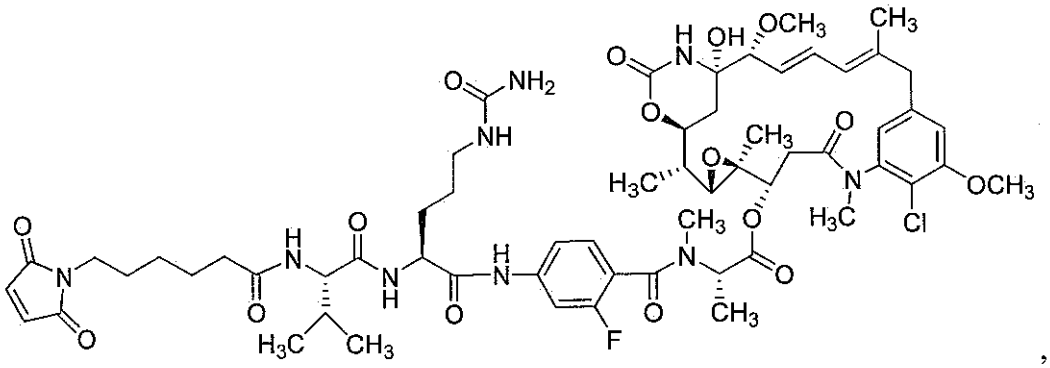
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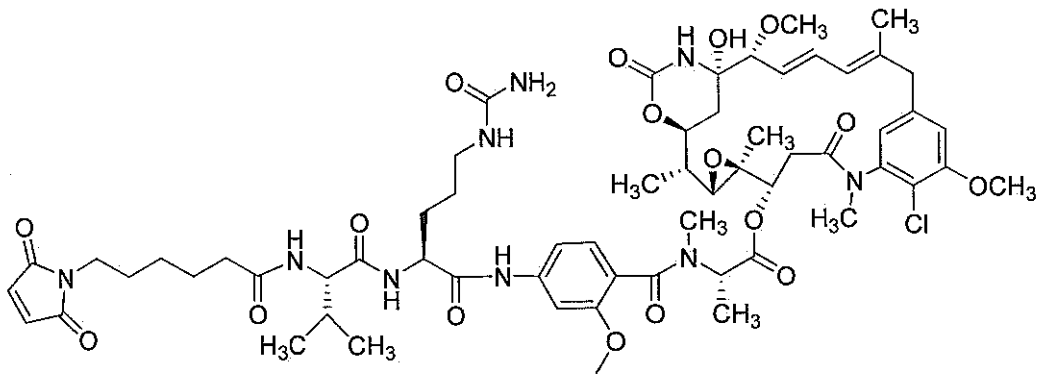
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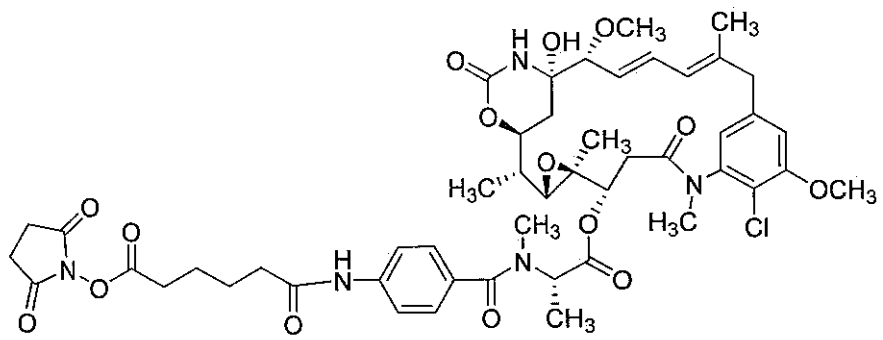


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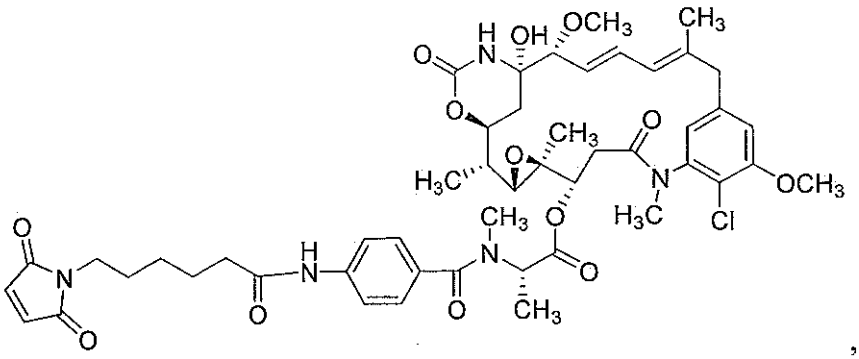


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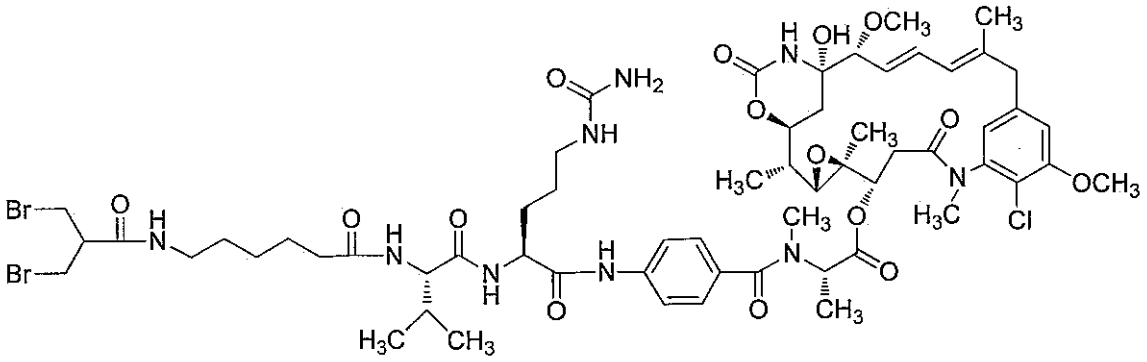




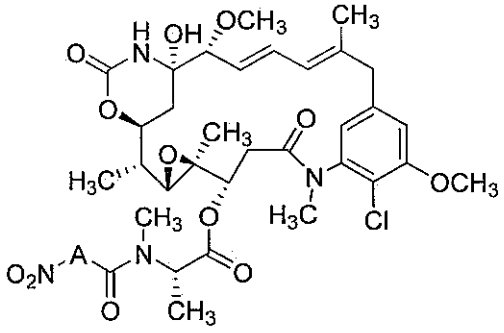
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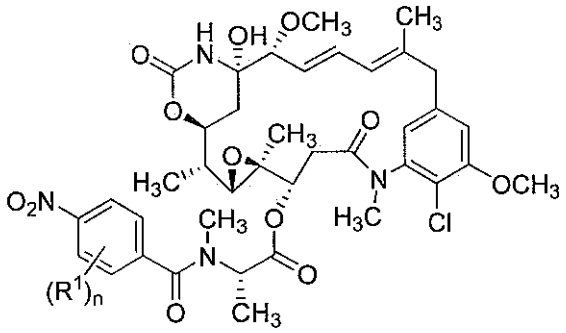
31. A compound of Formula PP5:



PP5

or a salt thereof, wherein A is arylene o r heteroarylene.

32. The compound of claim 31, wherein the compound is a compound of Formula PP5A:



(PP5A)

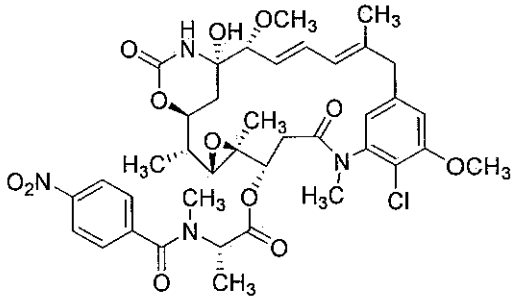
wherein:

R^1, independently at each occurrence, is alkyl, alkenyl, alkynyl, alkoxy, haloalkyl, haloalkoxy, heteroalkyl, aryl, alkaryl, aralkyl, halo, heteroaryl, heterocycloalkyl, cyano, nitro, $-\S-OR^A$, $-\S-SO_2R^A$, $-\S-\overset{O}{\overset{\|}{C}}-R^A$, or azido,

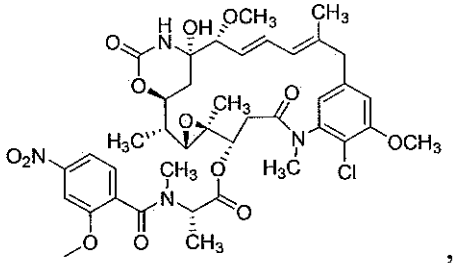
wherein R^A is alkyl;

n is an integer from 0 to 4.

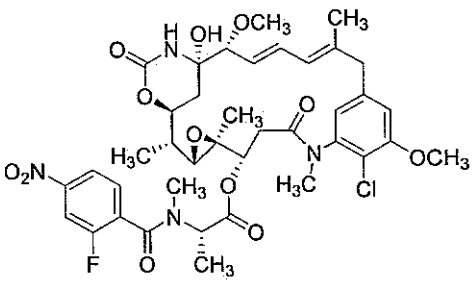
33. The compound of claim 31, wherein the compound is a compound selected from



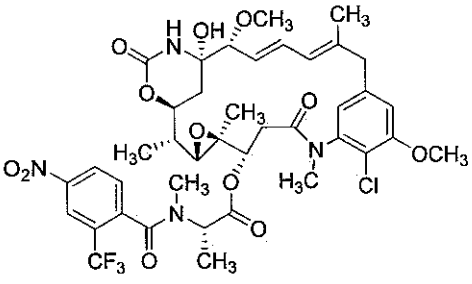
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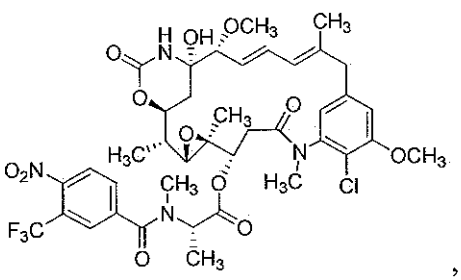
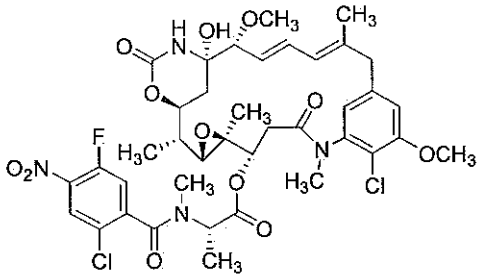
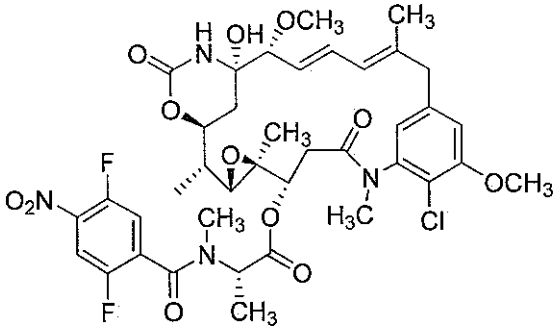
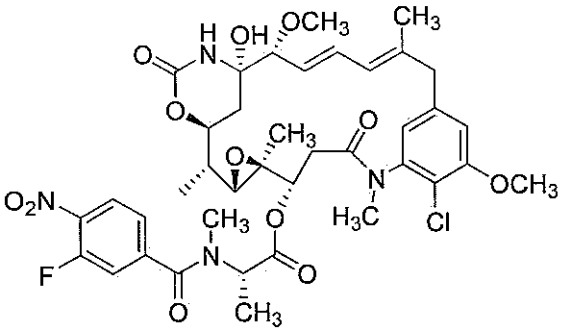
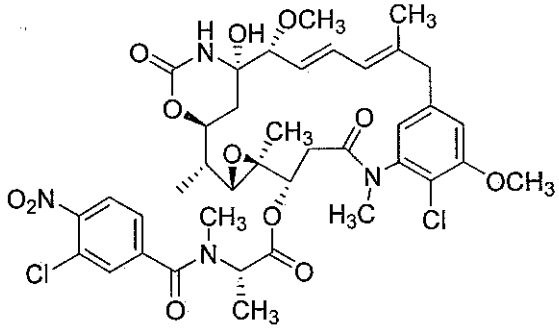
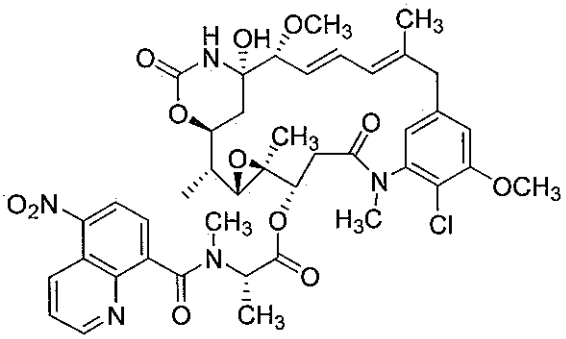
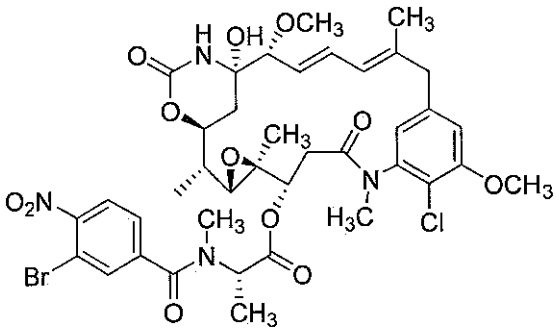
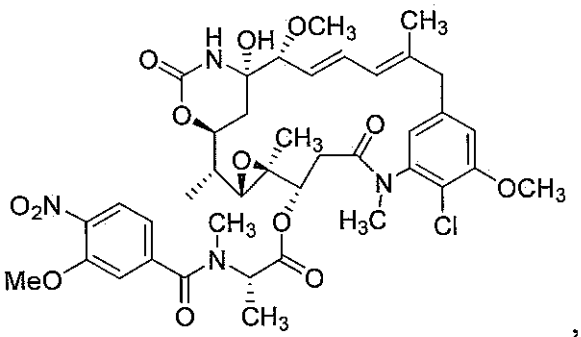
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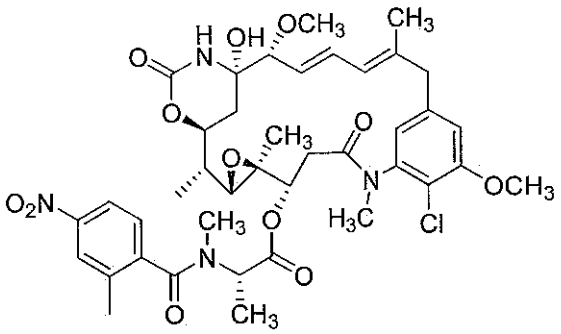
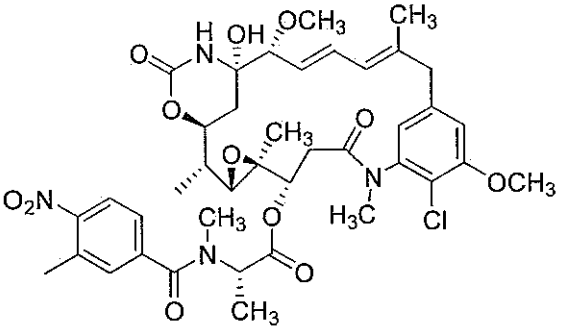
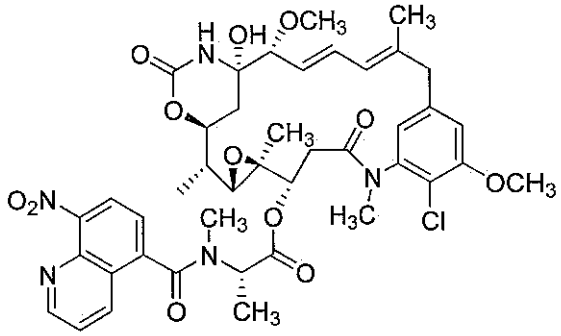
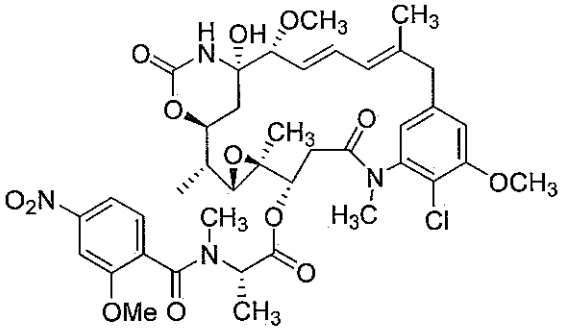
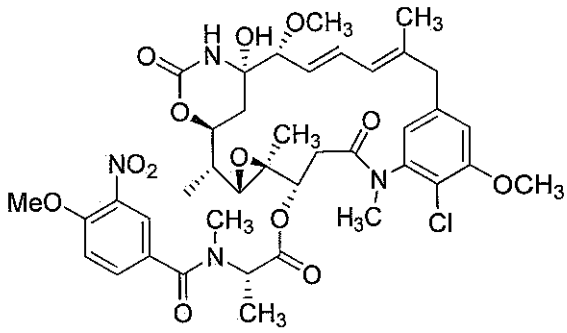
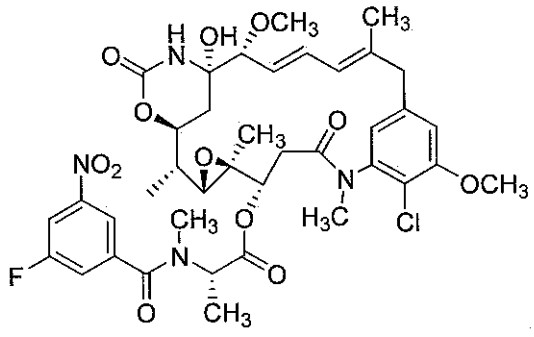
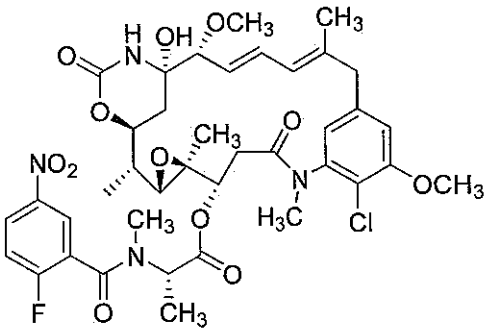
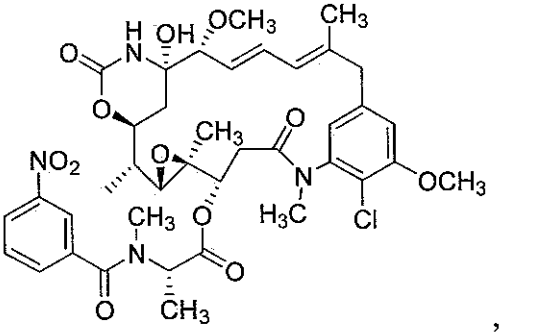


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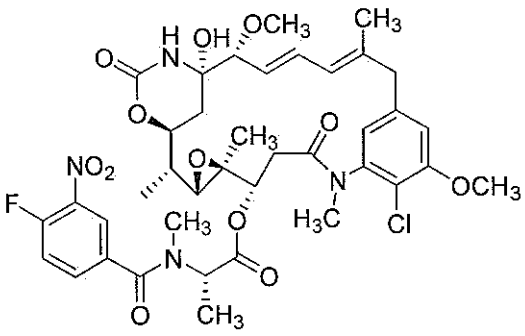
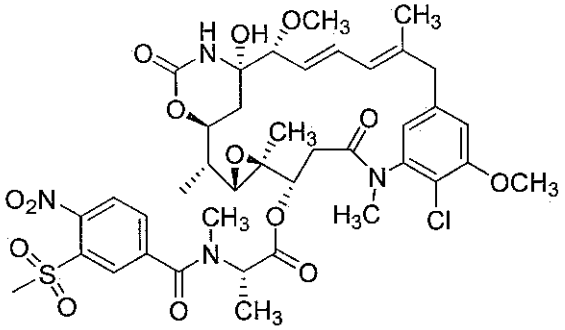
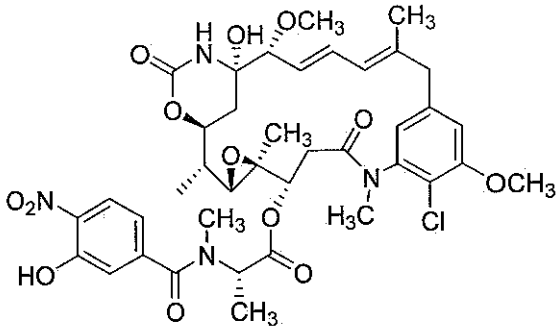
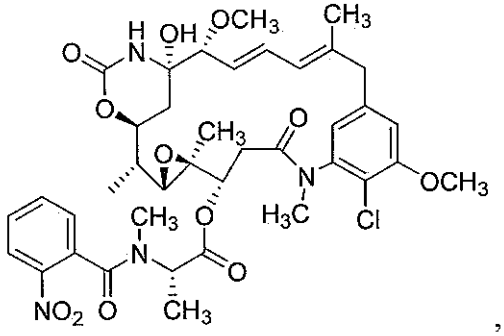
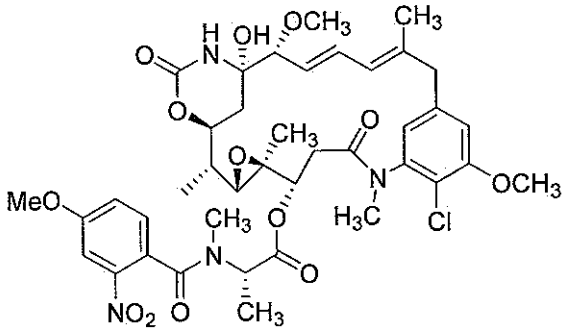
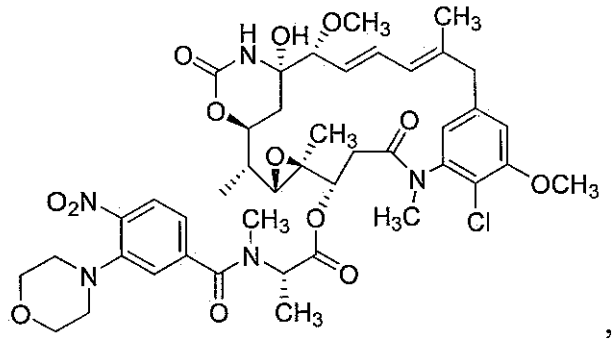
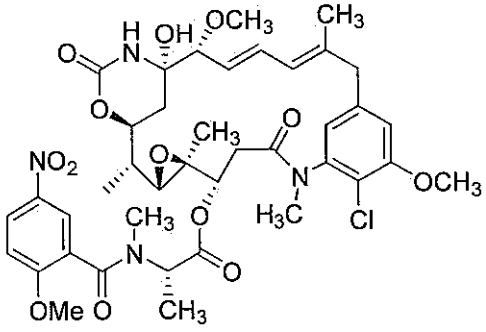
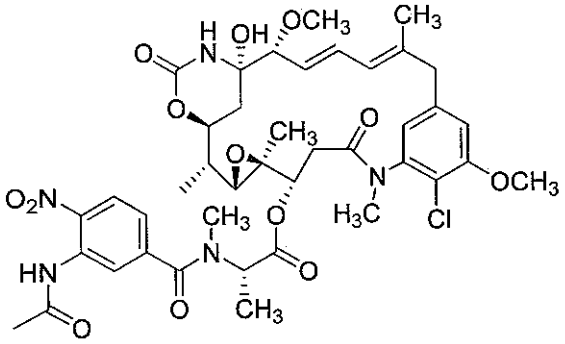
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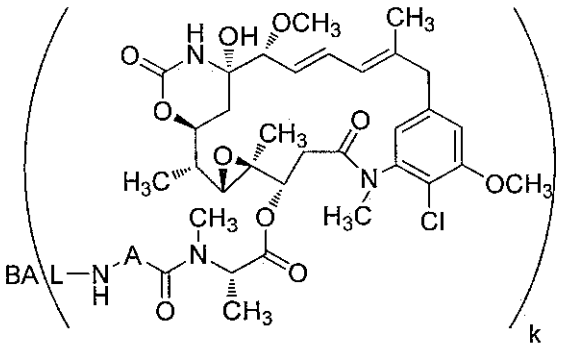

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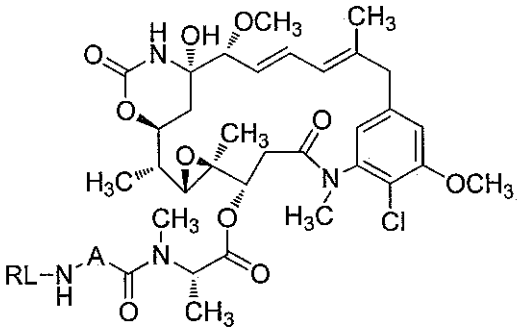

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34. A process of preparing a compound of Formula (I):



I

comprising contacting a compound of Formula P1:



P1

with an antibody or antigen binding fragment thereof under conjugation conditions,

wherein A is arylene or heteroarylene;

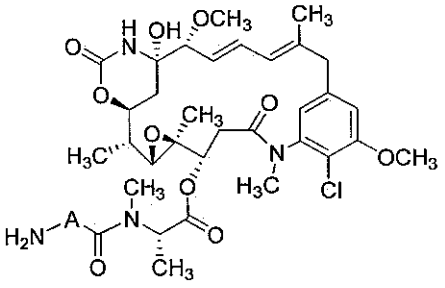
L is a linker;

BA is an antibody or antigen binding fragment thereof;

k is an integer from 1 to 10;

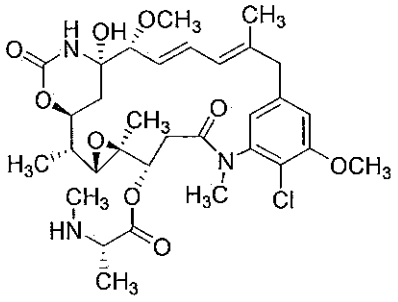
and RL is a reactive linker.

35. A process of making a compound of formula PP3:



PP3 , comprising:

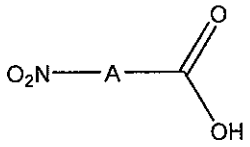
(a) contacting a compound of formula P2



P2

,

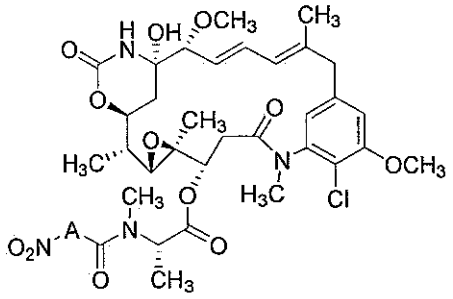
with a compound of formula PP6:



PP6

,

under amide synthesis conditions to form a compound of formula PP5:



PP5

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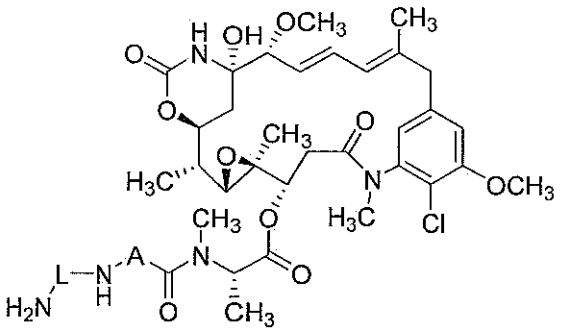
wherein A is arylene or heteroarylene; and

(b) reducing the compound of formula PP5 by contacting the compound of formula PP5 with a reducing agent to form a compound of formula PP3.

36. The process of claim 35, wherein the reducing agent is zinc.

37. A process of preparing an antibody-drug-conjugate compound of Formula (I): comprising

(a) reacting a deglycosylated antibody or aglycosylated antibody with a compound of Formula (PT1) in the presence of transglutaminase:

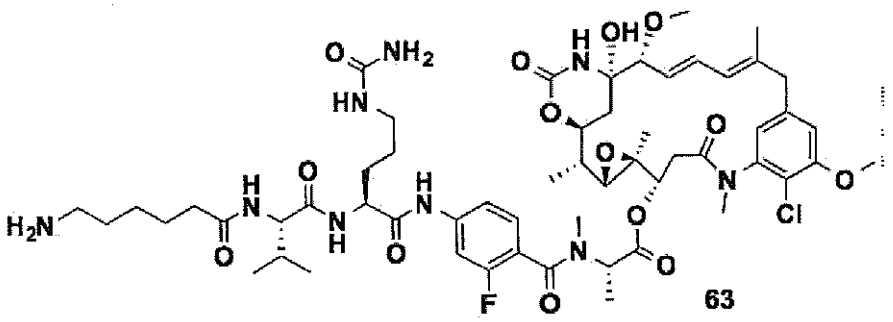


PT1

wherein:

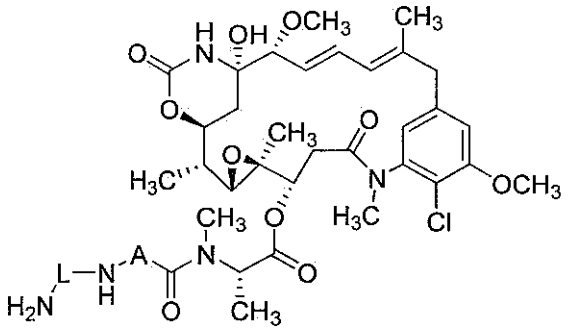
A is arylene or heteroarylene; and L is a linker.

38. The process of claim 37, wherein the compound of Formula (PT1) is



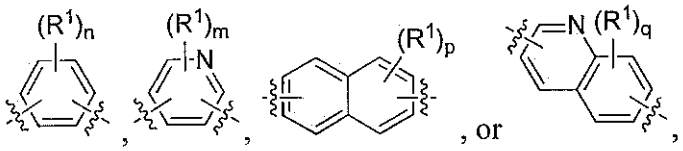
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39. The process of any one of claims 37 or 38, wherein the compound of Formula (PT1) of step (a) is according to the following formula:



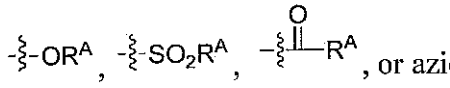
PT1

wherein A is:



wherein:

R^1, independently at each occurrence, is alkyl, alkenyl, alkynyl, alkoxy, aryl, alkaryl, aralkyl, halo, haloalkyl, haloalkoxy, heteroaryl, heterocycloalkyl, hydroxyl, cyano, nitro,



, or azido,

wherein R^A is alkyl or heteroalkyl;

n is an integer from 0 to 4;

m is an integer from 0 to 3;

p is an integer from 0 to 6; and

q is an integer from 0 to 5.

40. The process of any one of claims 37-39, further comprising

(b) reacting the glutaminyl-modified antibody with a reactive payload compound to form an antibody-payload conjugate.

41. The process of any one of claims 37-39, further comprising

(b) reacting the glutaminyl-modified antibody with a reactive linker-payload compound to form an antibody-linker-payload conjugate.

42. The process of any one of claims 37-39, further comprising

(b) reacting the glutaminyl-modified antibody with a reactive linker compound to form an antibody-linker conjugate; and

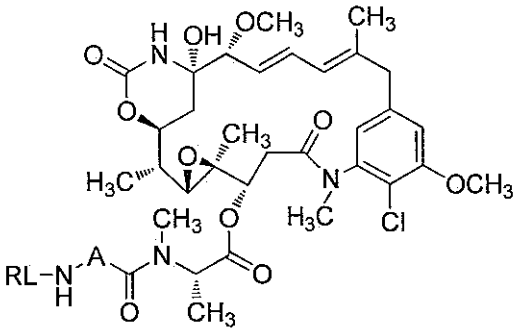
(c) reacting the antibody-linker conjugate with a reactive payload compound to form an antibody-linker-payload conjugate.

43. A glutaminyl-modified antibody produced by the process of any one of claims 37-39..

44. A pharmaceutical composition comprising the antibody of claim 43 and one or more pharmaceutically acceptable diluents, excipients, or carriers.

45. Use of the antibody of claim 43 in the manufacture of a medicament for treating a condition in a subject in need thereof.

46. A compound prepared by the process of contacting a compound of Formula P1 with an antibody or antigen binding fragment thereof under conjugation conditions,



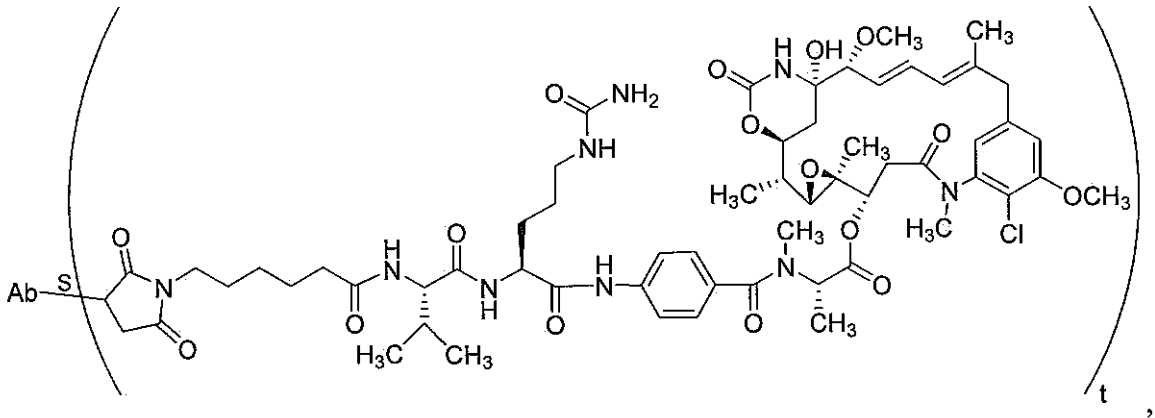
P1

wherein A is arylene or heteroarylene;

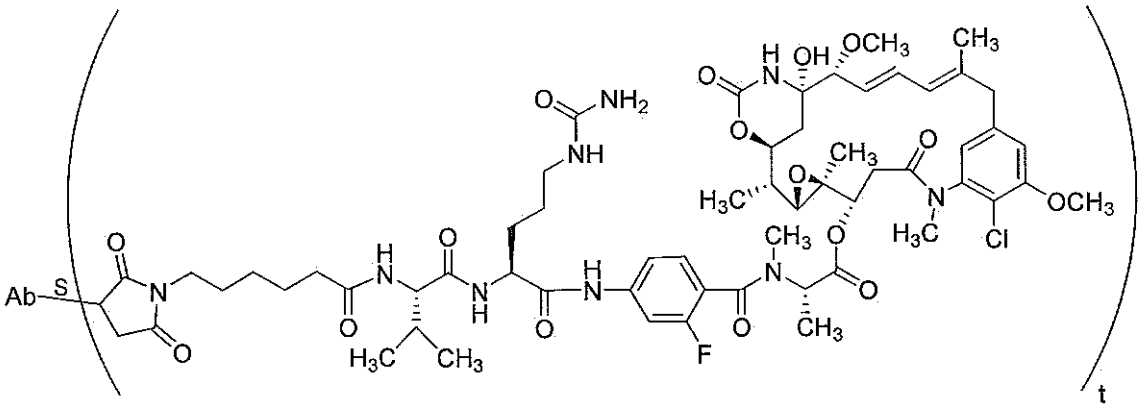
RL is a reactive linker; and

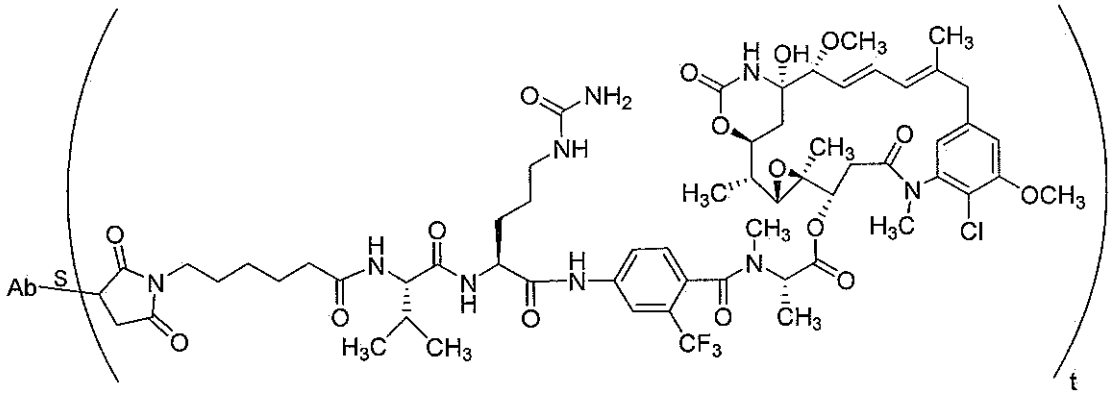
wherein Formula P1 is coupled to one or more cysteine or lysine residues of the antibody or antigen binding fragment thereof.

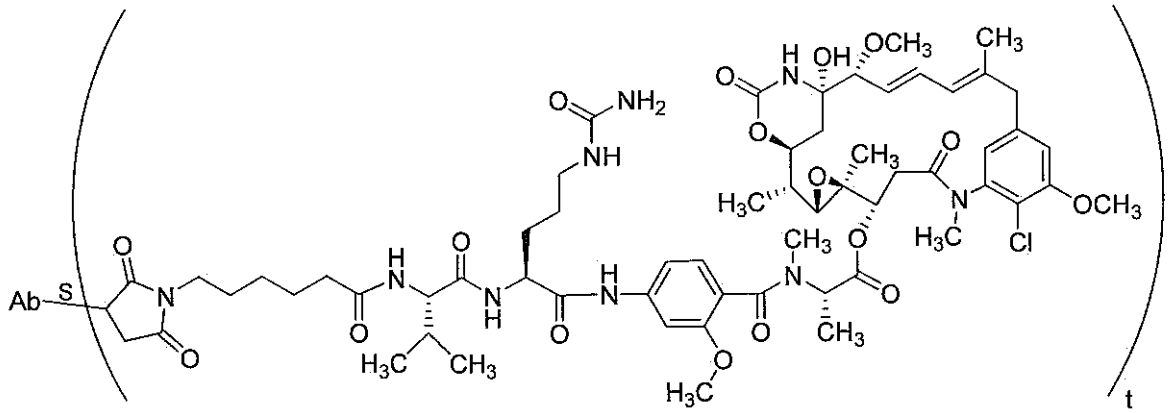
47. The compound of claim 1 selected from the group consisting of

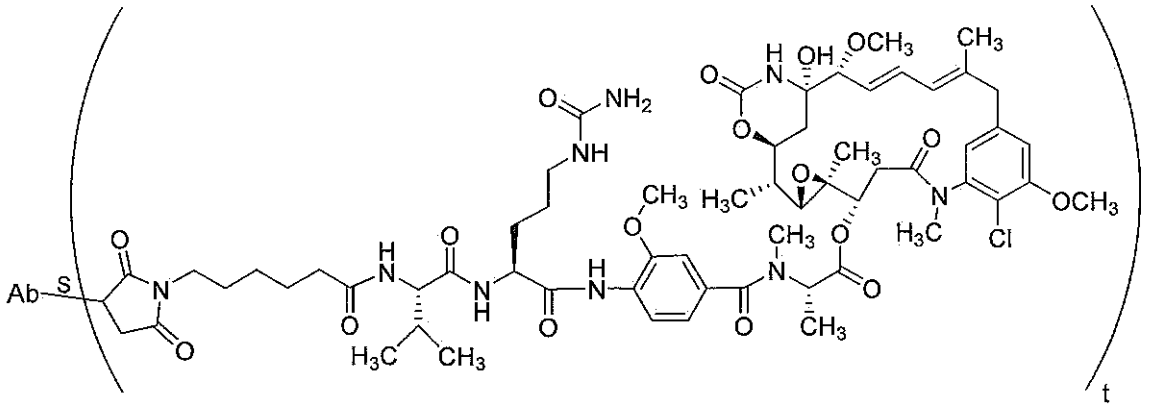


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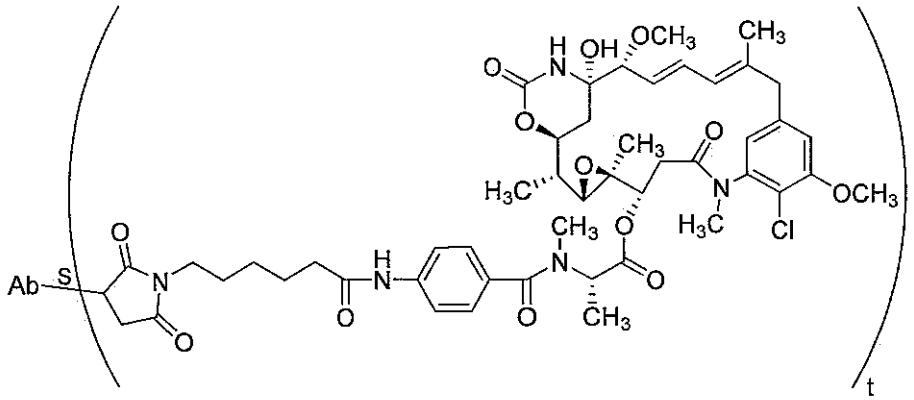




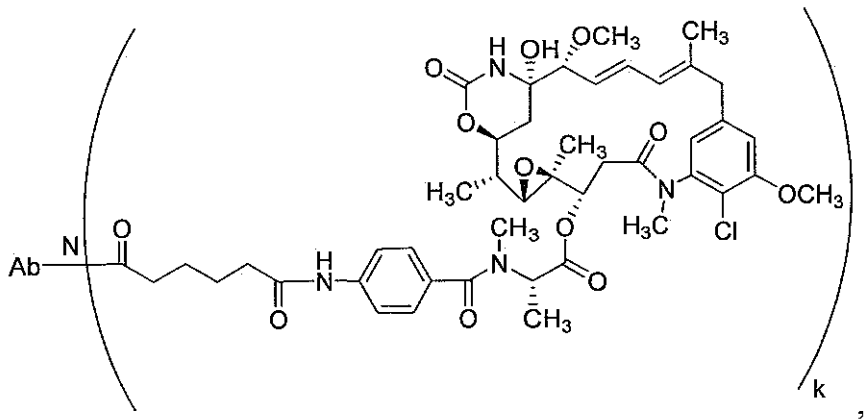



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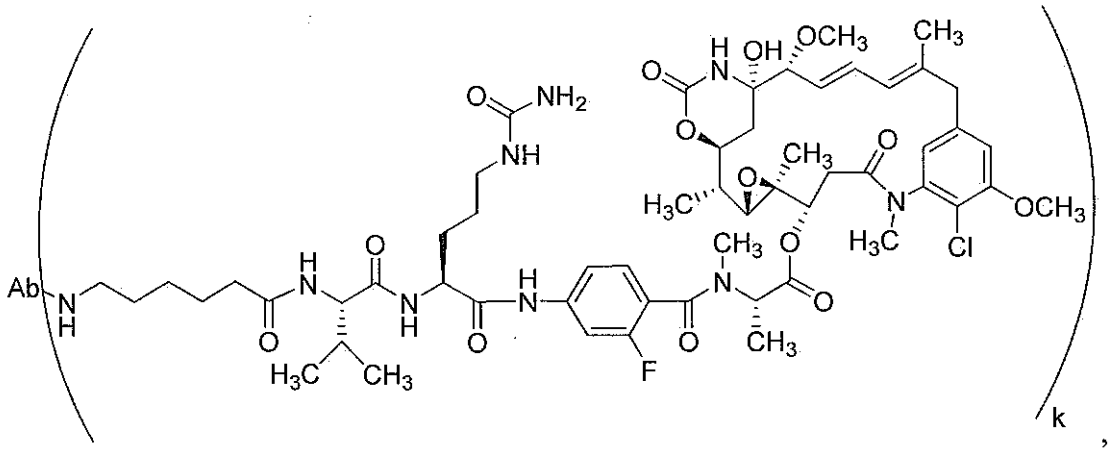
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Ab
S
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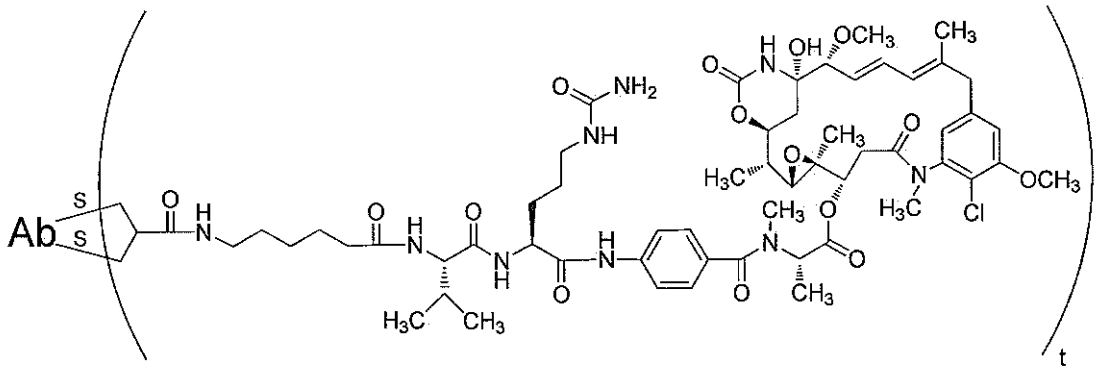
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, and



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wherein:

Ab is an antibody or an antigen binding fragment thereof;

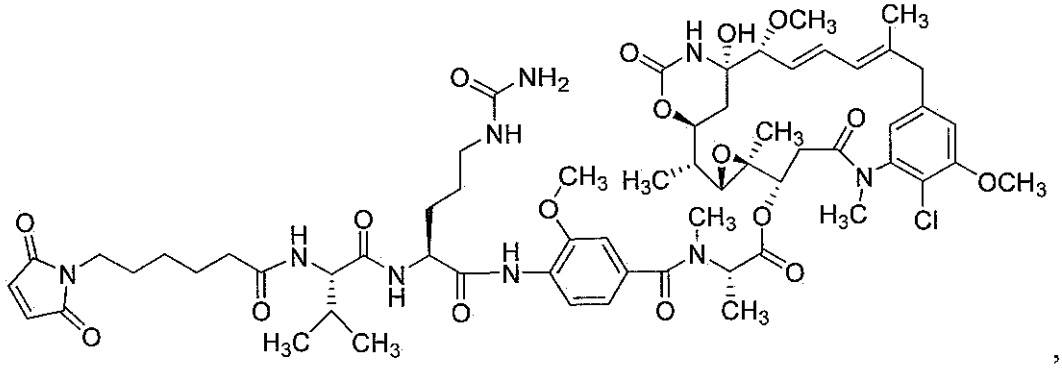
—S— is a bond to a cysteine of the antibody or an antigen binding fragment thereof;

—N— is a bond to a lysine of the antibody or an antigen binding fragment thereof;

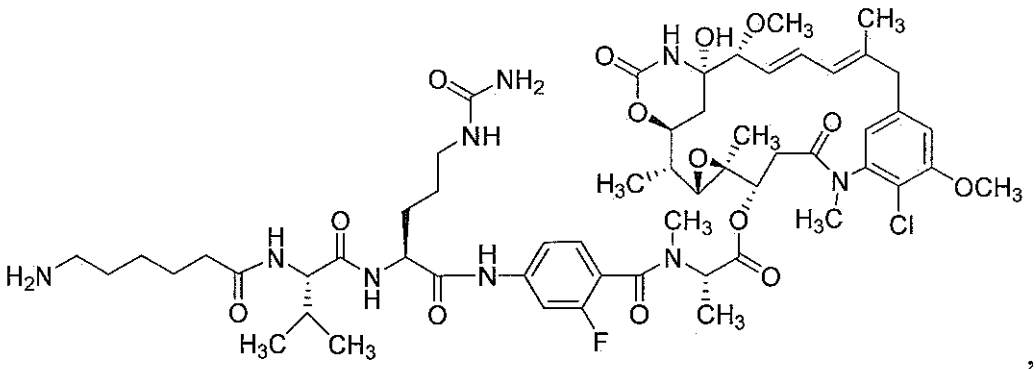
k is 1, 2, 3, or 4; and

t is 1, 2, 3, or 4.

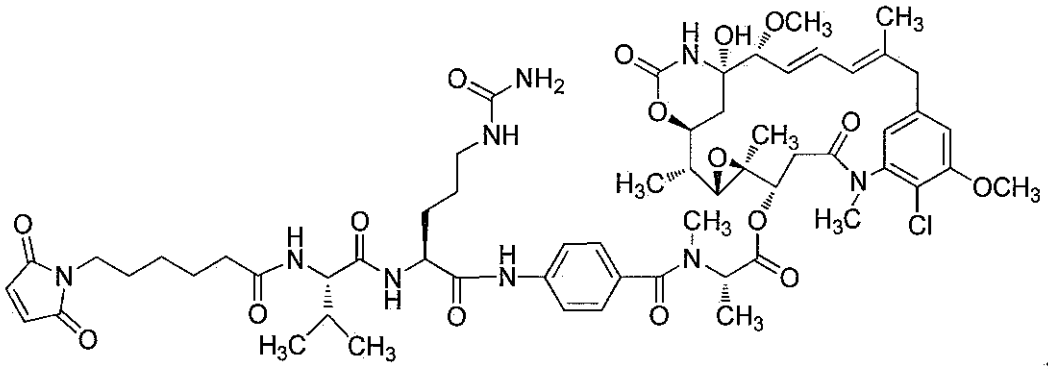
48. The compound of claim 33 selected from the group consisting of



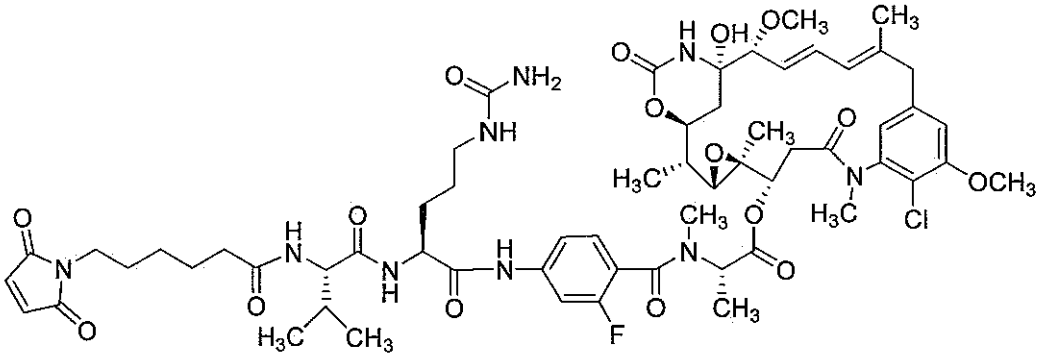
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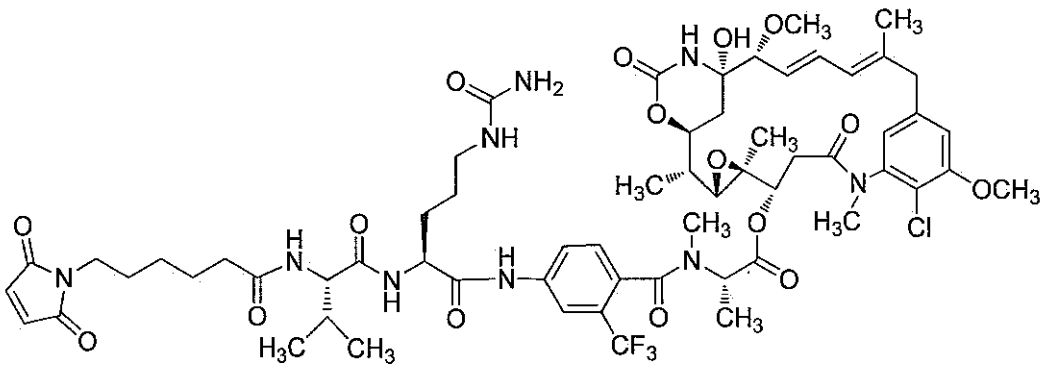
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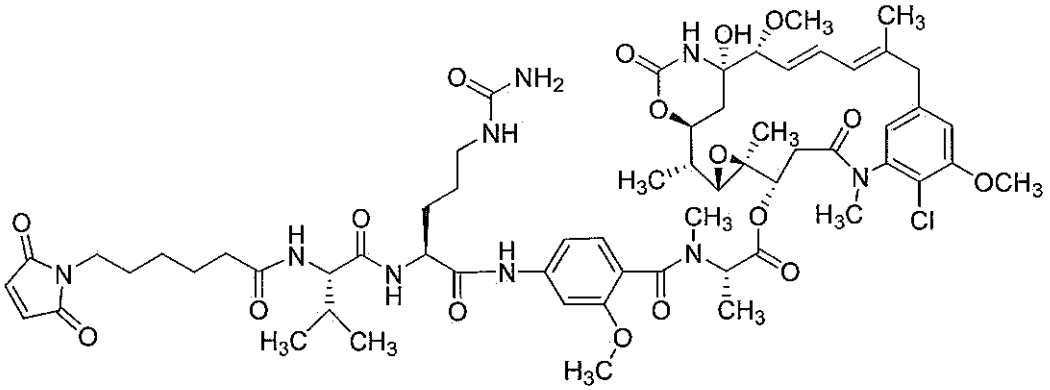
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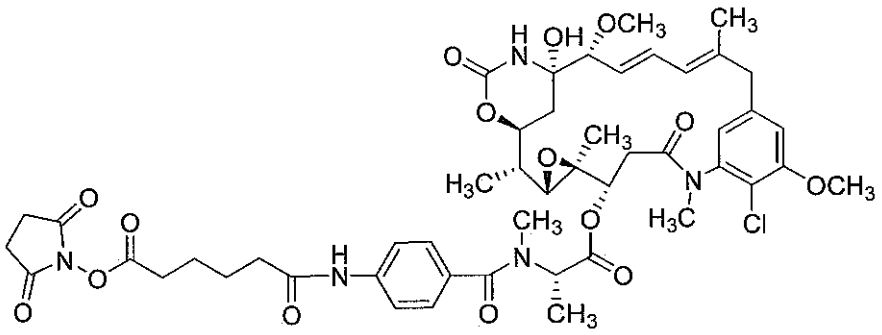
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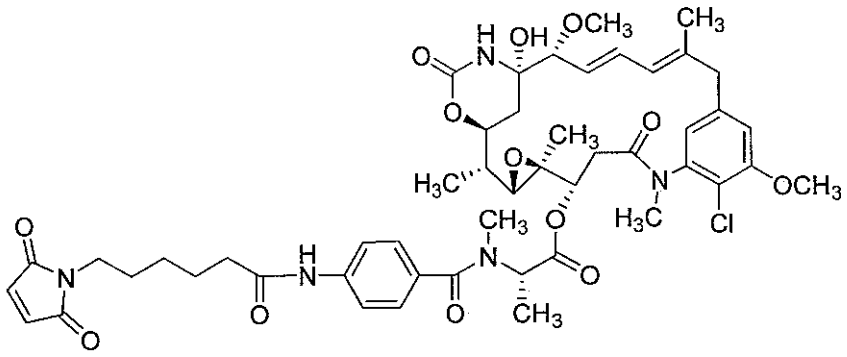
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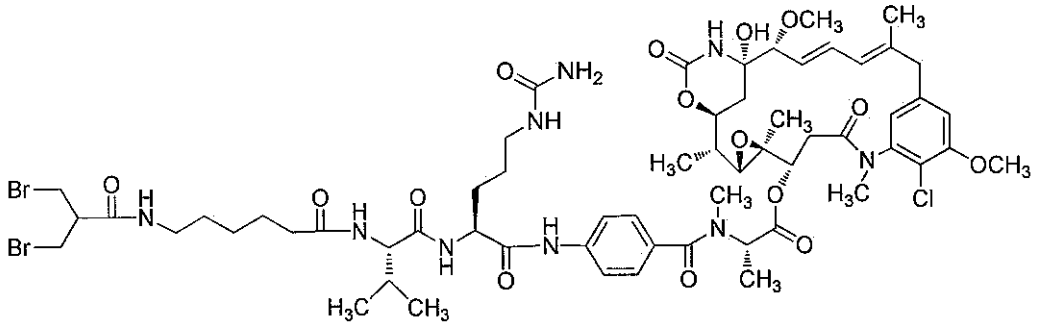
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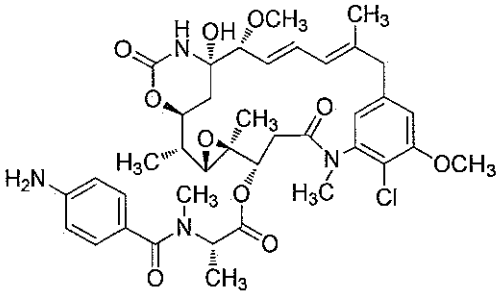
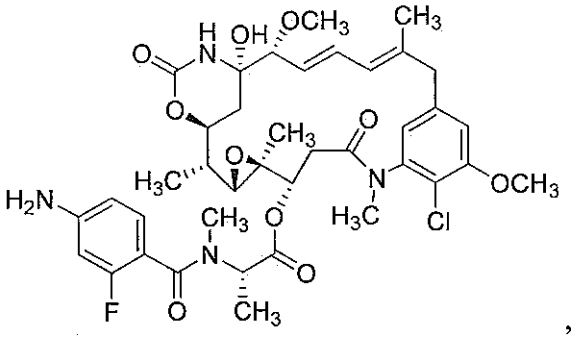
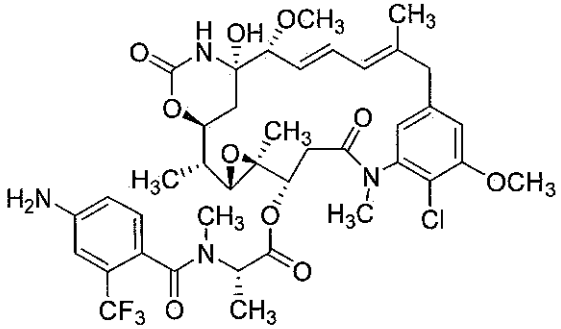
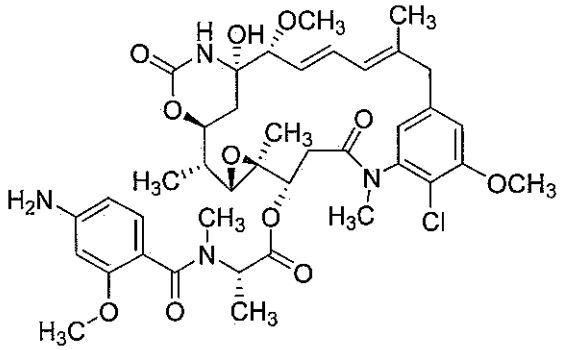
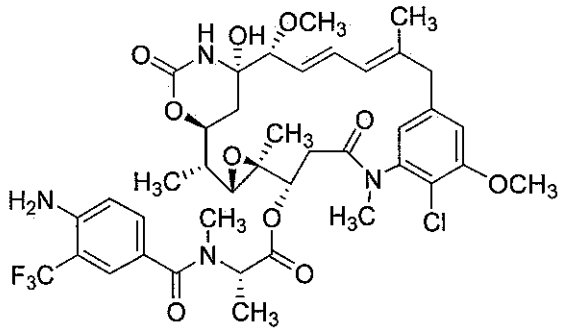


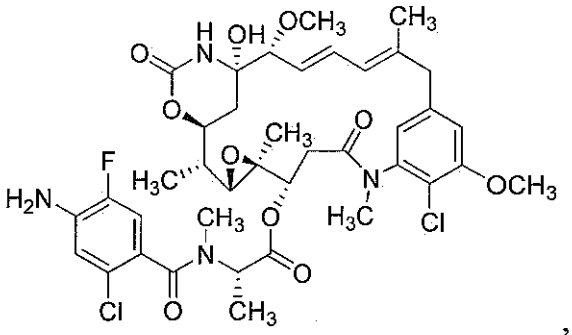
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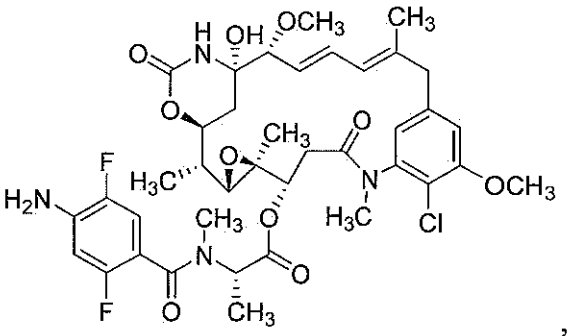


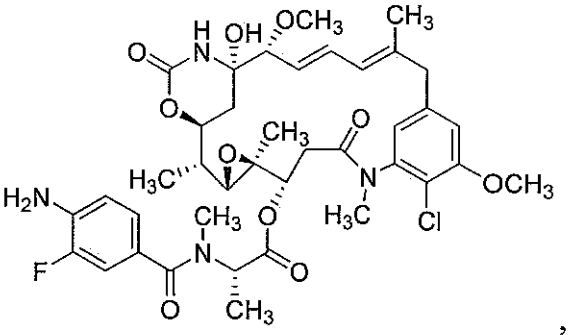
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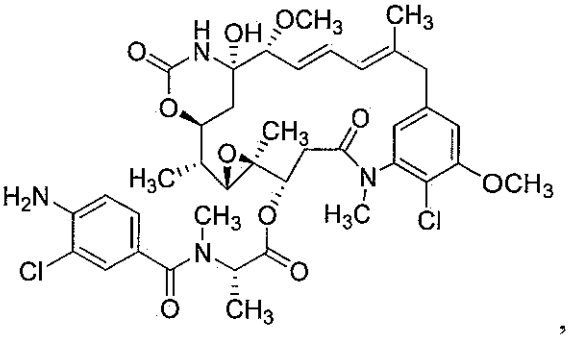
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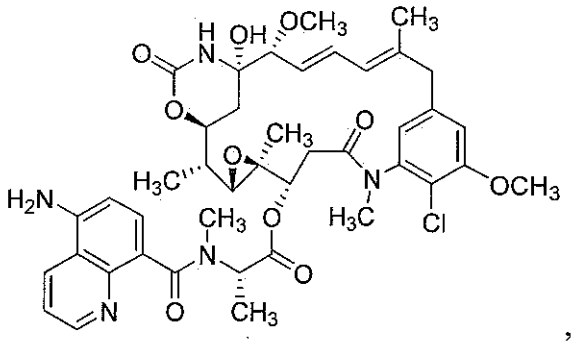

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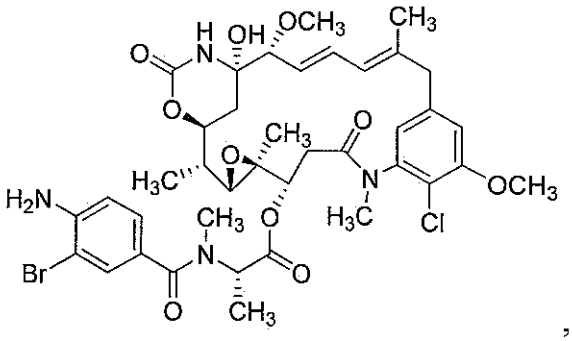

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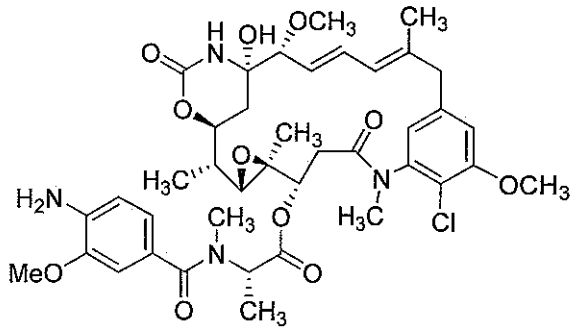

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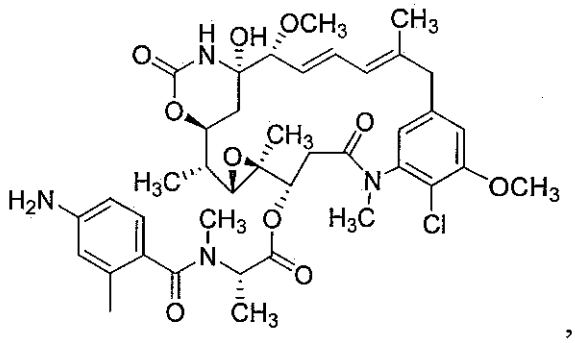
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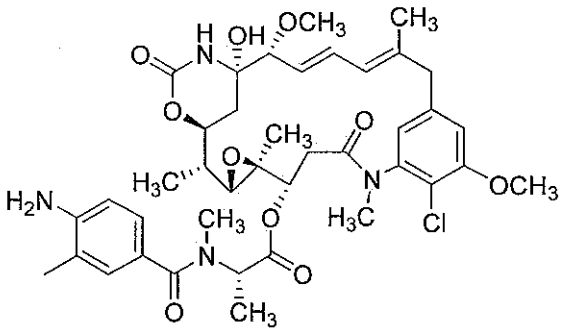
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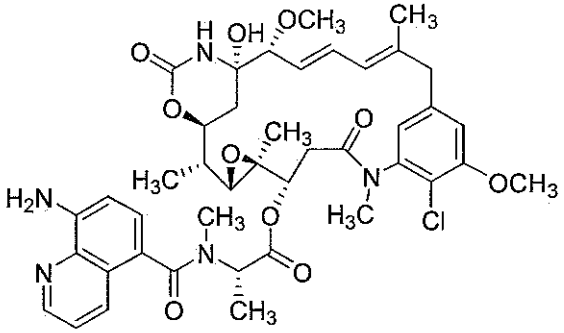
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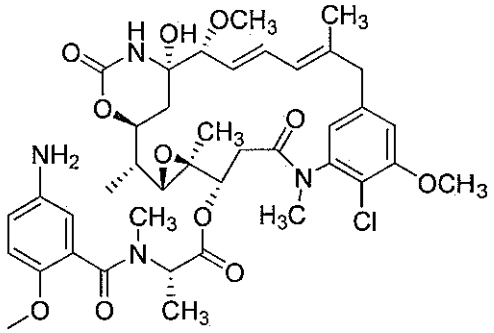
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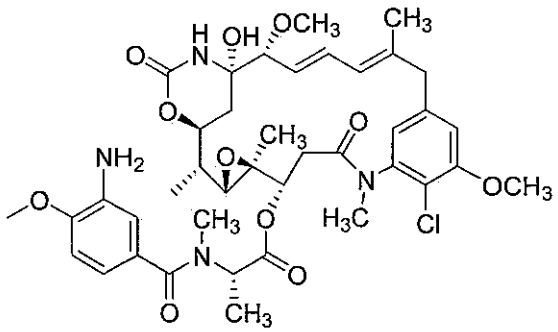
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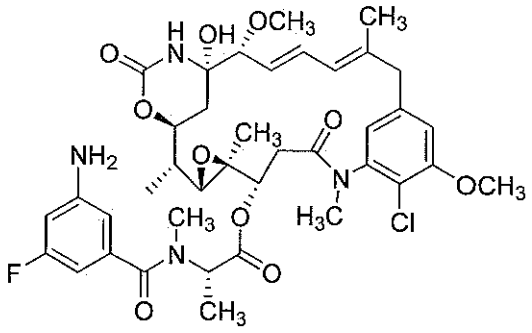
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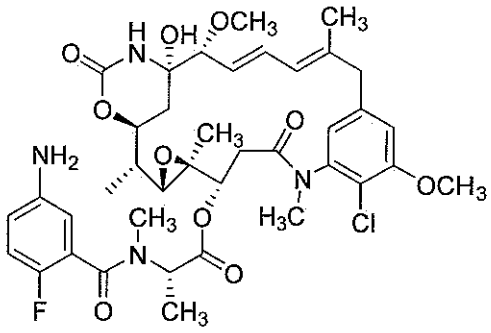


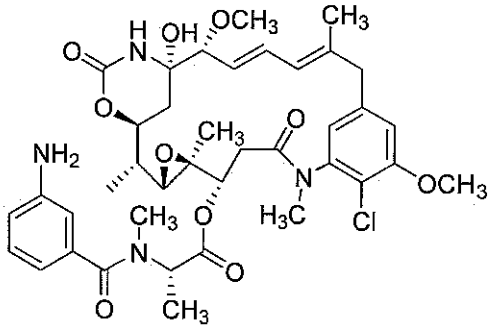
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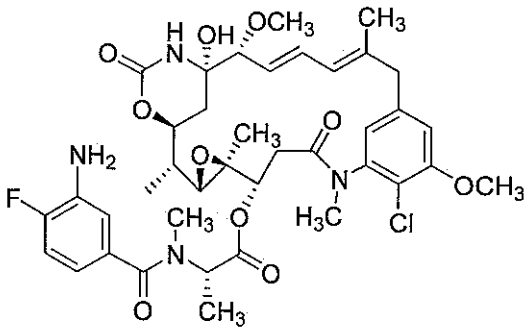


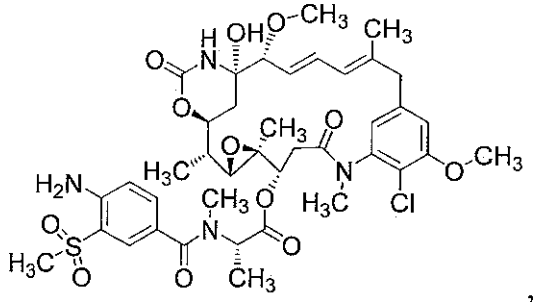
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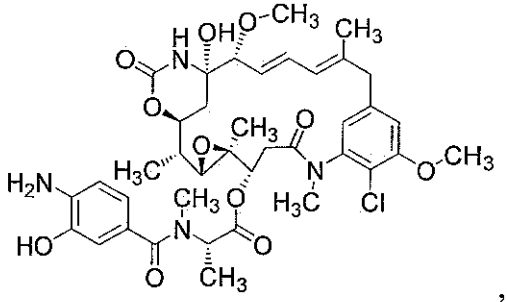

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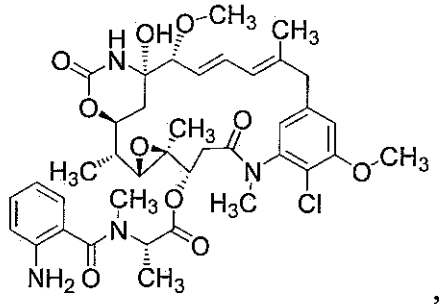

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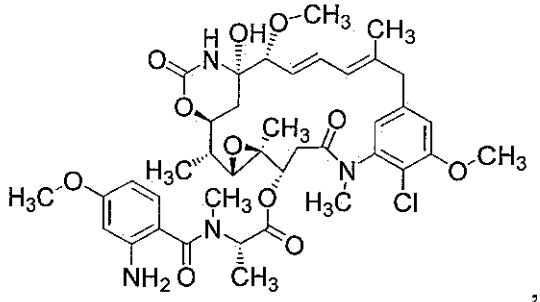
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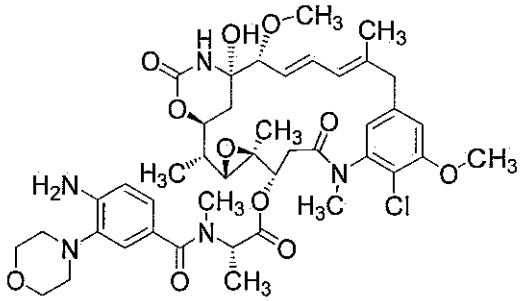
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