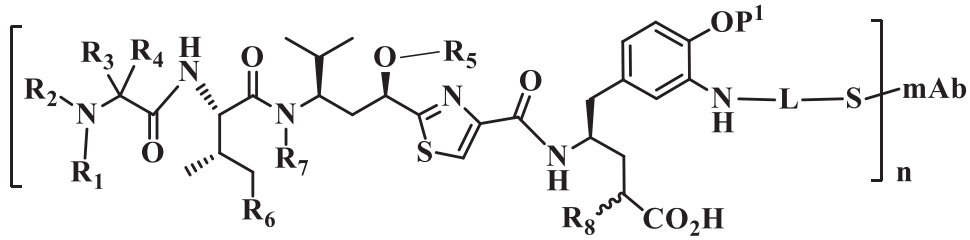
CLAIMS

1. An antibody-Tubulysin B derivative conjugate, wherein the conjugate has a structure of Formula (I):



(I)

or a pharmaceutically acceptable salt, hydrate or hydrated salt thereof; or a polymorphic crystalline structure represented by Formula (I); or an optical isomer of the structure represented by Formula (I); or a derivative thereof with one or more hydrogen (^{1}H) atoms being substituted by one or more deuterium (^{2}H) atoms, or a derivative thereof with one or more ^{12}C atoms being substituted by one or more ^{13}C atoms;

wherein P^1 is H,$COCH_3$,COH,$PO(OH)_2$, $CH_2OPO(OH)_2$, $CONHCH_3$,$CON(CH_3)_2$, $CON(CH_2CH_2)_2NCH_3$, $CON(CH_2CH_3)_2$ or $CON(CH_2CH_2)_2CHN(CH_2CH_2)_2CH_2$;

wherein R_1, R_2, R_3 and R_4 are independently H, C_1-C_6 alkyl group;

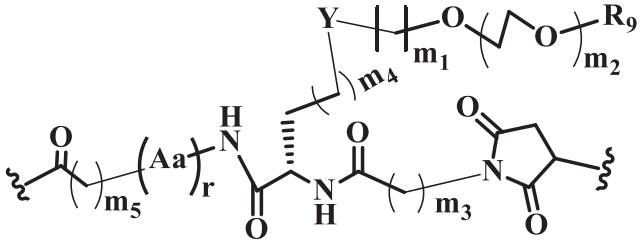
R_5 is H, O-C_1-C_6 alkyl, C(O)-H, C(O)-C_1-C_6 linear or branched alkyl, C(O)-NH-C_1-C_6 linear or branched alkyl or C(O)-N(C_1-C_6 linear or branched alkyl)$_2$;

R_6, R_7 and R_8 are independently H, C_1-C_6 alkyl, C_1-C_6 alkyl ester, C_1-C_6 alkylcarboxy or C_1-C_6 alkylamido group;

mAb is an antibody, monoclonal antibody, polyclonal antibody, nanobody;

n = 1-30.

L is a linker has the structure below (Ia) below:



(Ia),

wherin Aa is a L- or D- natural or non-natural amino acid;

r is an integer between 0 and 12; when R is not 0, (Aa)r is a peptide unit composed of the same or different amino acids;

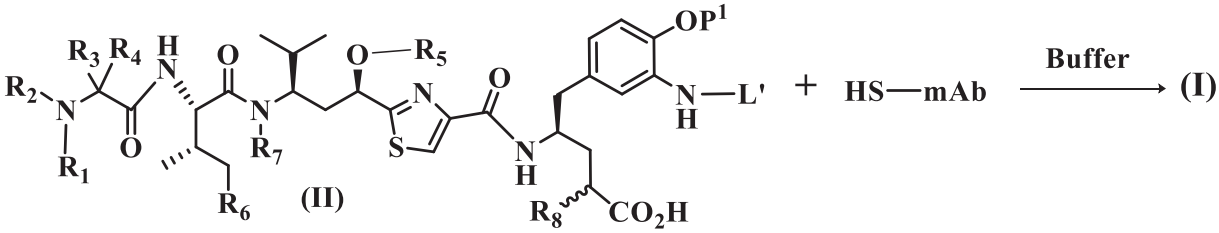
m_1 is an integer between 1 and 18; m_2 is an integer between 1 and 100; m_3 is an integer between 1 and 8; m_4 is an integer between 0 and 8; m_5 is an integer between 1 and 8;

Y is C(O)NH;

R_9 is H, (O=)CR_1, or (O=)CNHR_1; and

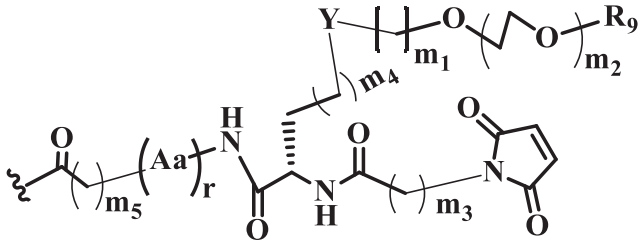
R_1, m_2 and $(Aa)_r$ are defined the same as in **Claim 1**.

2. A method for producing the conjugate according to **Claim 1**, wherein the method comprises synthesis of the conjugate by the following step:



wherein P^1, "〰", R_1, R_2, R_3, R_4, R_5, R_6, R_7 and R_8 in Formula (II) and mAb are defined the same as in **Claim 1**;

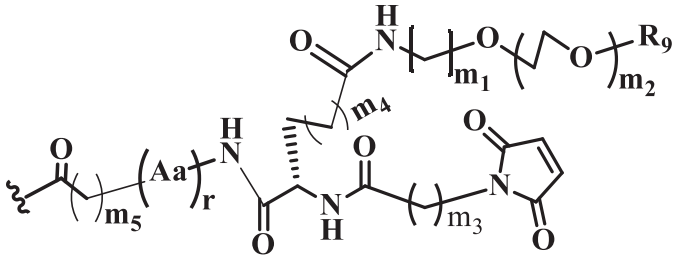
L' has a structure as below:



(II-0)

wherein m_1, m_2, m_3, m_4, m_5, Aa, r and R_9 are defined the same as in **Claim 2**.

3. The method according to **Claim 2**, wherein L' has the structure below:



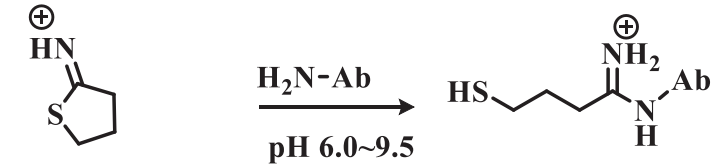
(II-6);

wherein in the above formulae, m_1, m_2, m_3, m_4, m_5, Aa, r and R_9 are defined the same as in **Claim 1**.

4. The method according to **Claim 2**, wherein the method further comprising preparation of mAb-SH by any method of the following:

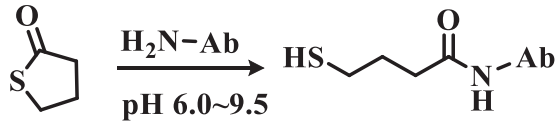
a) Reduction of disulfide bonds between heavy and light chains, heavy and heavy chains or intra-disulfide bonds of an antibody, monocle antibody, polyclonal antibody, nanobody modified by synthetic molecule or protein, by a reducing agent;

b) Generation of a sulfhydryl group by reaction of the amino group of an antibody with Traut's reagent or thiolactone;

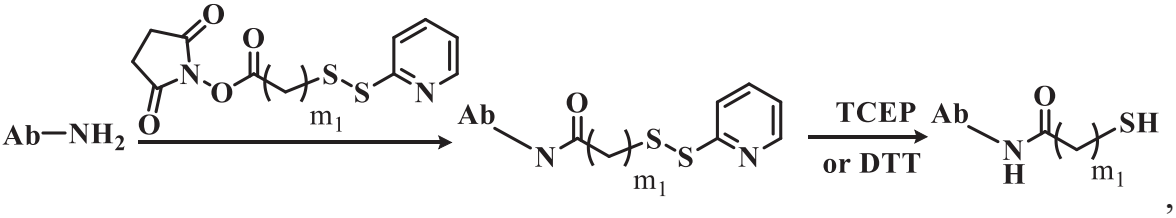


Traut's reagent

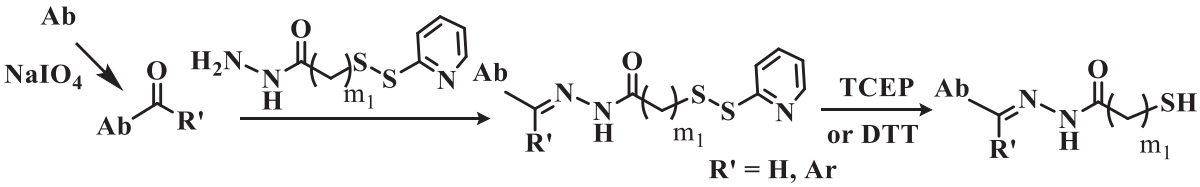
or

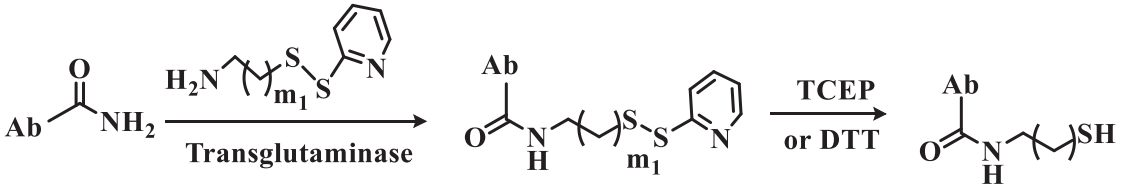


c) Incorporation of an easily reduceable disulfide bond into an antibody by a biochemical reaction in a buffer system, followed by reduction by TCEP, DTT, GSH, β-MEA or β-ME:



,





or

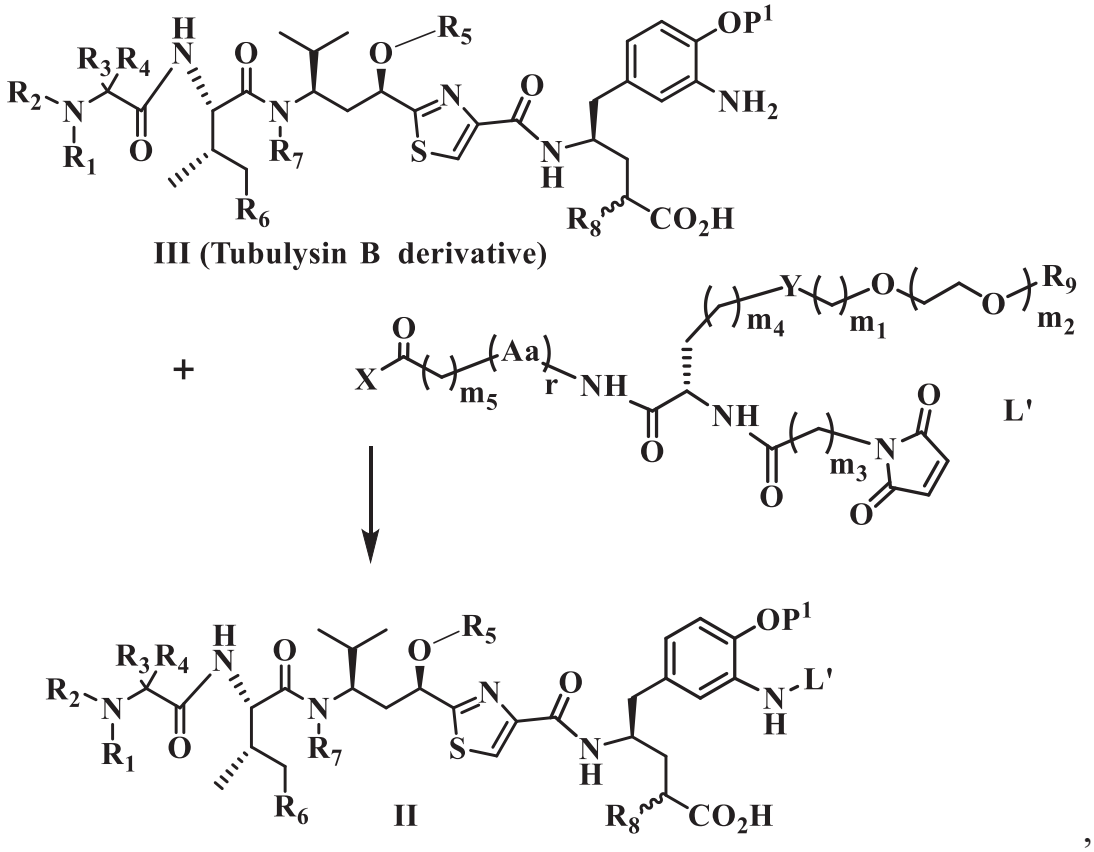
wherein in the above formulae, m_1 is defined the same as in **Claim 2.**

5. The method according to **Claim 2**, wherein the buffer system has a pH of 5.0-9.5, and is a 1 mM ~ 1000 mM phosphoric acid, acetic acid, citric acid, boric acid, carbonic acid, barbituric acid, Tris (trimethylaminomethane), benzoic acid or triethanolamine system, or a mixed buffer solution thereof, and contains 0 to 35% water-soluble organic solvent of methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, acetonitrile, acetone, DMF, DMA or DMSO; conjugation reaction is conducted at a reaction temperature of 0 °C to 45 °C, and a reaction time of 5 minutes to 96 hours.

6. The method according to **Claim 2**, further comprising, after conjugation reaction, ultrafiltration or column chromatography purification to obtain the conjugate of Formula (I).

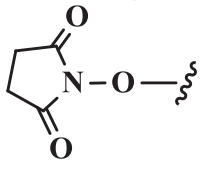
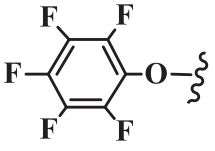
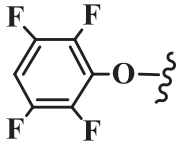
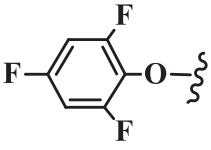
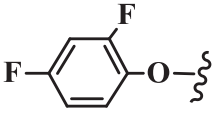
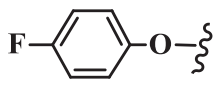
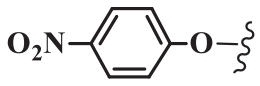
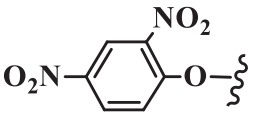
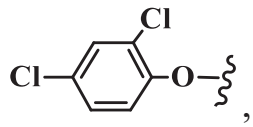
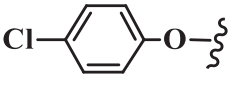
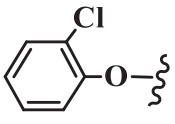
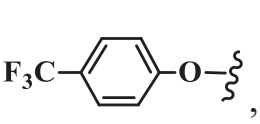
7. The method according to **Claim 6**, wherein the purification column comprises a molecular sieve column, a cationic column, an anionic column, a hydrophobic (HIC) column, a reverse phase column or a protein A or G affinity column.

8. The method according to **Claim 2**, wherein the method further comprises obtaining the structure of Formula (II) by the condensation reaction of a Tubulysin B derivative of Formula (III) with a compound of Formula (L'):



,

wherein in the above formulae, P^1, "〰", R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, m_1, m_2, m_3, m_4, m_5, Aa, and r are defined the same as in **Claim 2**,

wherein X is OH, halogen, phenoxy, pentachlorophenoxy, trifluoromethanesulfonyl, imidazole, dichlorophenoxy, tetrachlorophenoxy, 1-hydroxybenzotriazole, p-toluenesulfonyl, methanesulfonyl, 2-ethyl-5-phenyl isoxazole -3'- sulfonyl group,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , , , an anhydride formed by an acid itself or with another anhydride of acetyl anhydride or formic anhydride;

or a peptide coupling reaction intermediate or a Mitsunobu reaction intermediate;

wherein the condensation reaction is carried out in dichloroethane, DMF, DMA, tetrahydrofuran (THF), DMSO, acetone, isopropanol, n-butanol or acetonitrile, or mixed solvents of two or three of the above, containing 1 to 100% pyridine, triethylamine or diisopropylethylamine; with or without an inert gas, at -20 to 150 °C, for 5 minutes to 120 hours;

or the condensation reaction is conducted in following buffer system and under following conditions: a buffer system has a pH of 5.0 - 9.5, is 1 mM - 1000 mM phosphoric acid, acetic acid, citric acid, boric acid, carbonic acid, barbituric acid, Tris (Tris-hydroxymethyl aminomethane), benzoic acid or triethanolamine system, or a mixture thereof, containing 0 to 35% a miscible organic solvent of methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, acetonitrile, acetone, DMF, DMA or DMSO: a reaction temperature is 0 to 45 °C and reaction time is from 5 minutes to 96 hours.

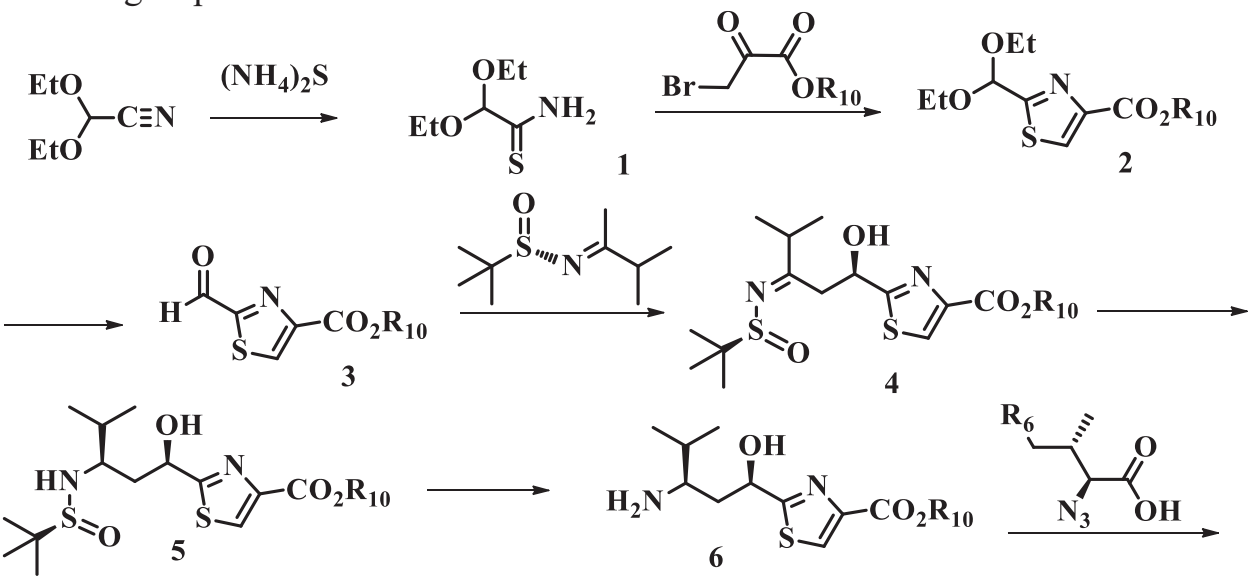
9. The method according to **Claim 8**, wherein the NH_2 group of formula (III) participates in the conjugation reaction in a form of salt, with trifluoroacetic acid, hydrochloride acid, formic acid, acetatic acid, sulfuric acid, phosphoric acid, nitric acid, citric acid, succinic acid, benzoic acid or sulfonic acid.

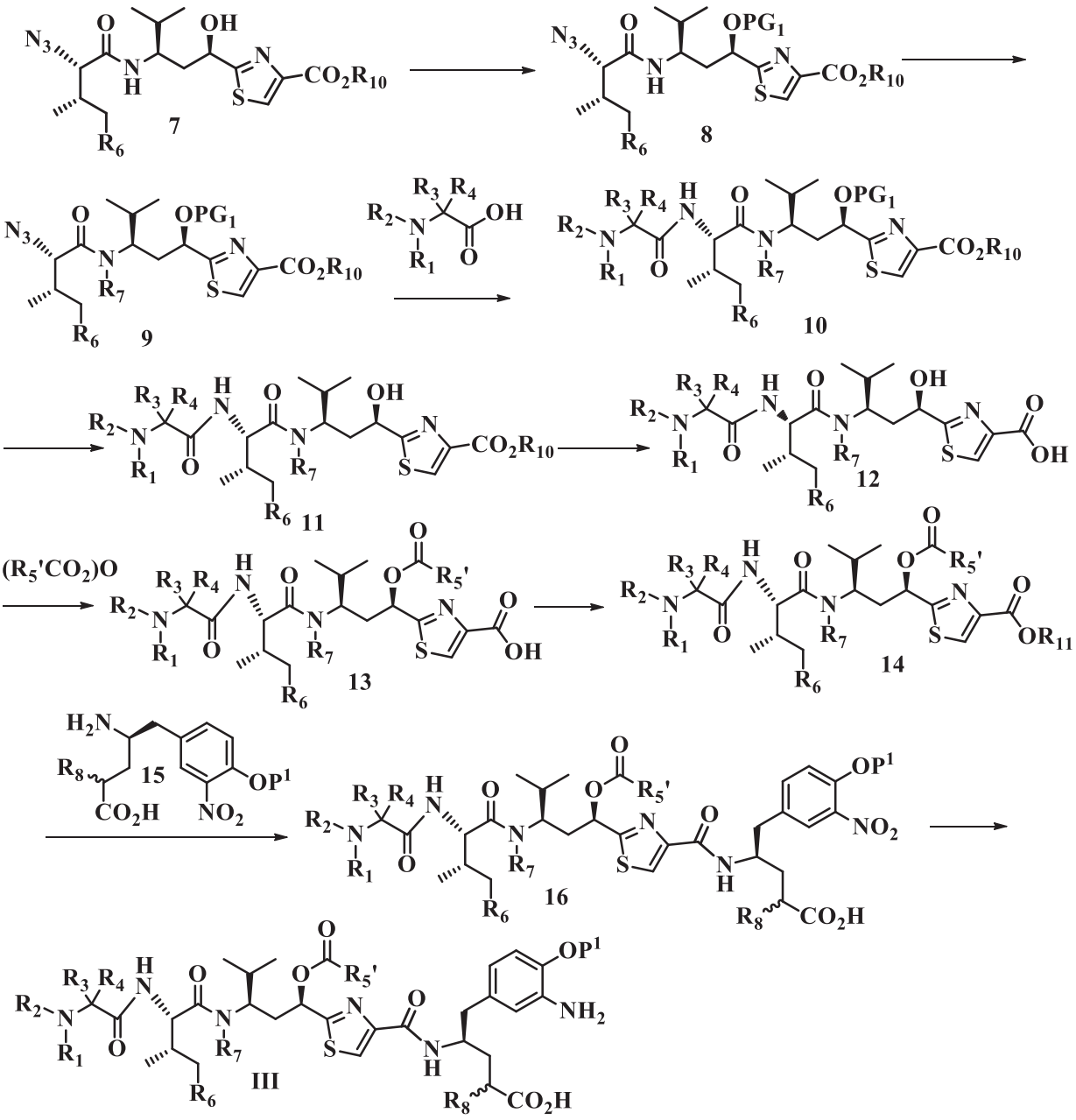
10. The method according to **Claim 8**, when X is OH, the condensation reaction is conducted in the presence of a condensation reagent selected from the group consisting of (N-(3-Dimethylaminopropyl)-N′-ethylcarbodiimide) (EDC), dicyclohexylcarbodiimide (DCC), N, N'-diisopropylcarbodiimide (DIC), N-Cyclohexyl-N′-(2-morpholino-ethyl)carbodiimide metho-p-toluenesulfonate (CMC or CME-CDI), carbonyldiimidazole (CDI), O-benzotriazole-N, N, N′, N′-tetramethyl urea tetrafluoroborate (TBTU), O-

benzotriazole-tetramethyl urea hexafluorophosphate (HBTU), (Benzotriazol-1-yloxy)tris(dimethylamino)- phosphonium hexafluorophosphate (BOP), (Benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (PyBOP), diethyl pyrocarbonate (DEPC), N, N, N′, N′-tetramethylchlorobenzamidine hexafluorophosphate, 2-(7-oxobenztriazole)-N, N, N′, N′-tetramethyluronium hexafluorophosphate (HATU), 1-[(dimethylamino) (morpholinyl) methylene] -1 [1,2,3] triazolo [4,5-b] 1-pyridin-3-oxyhexafluorophosphate (HDMA), 2-chloro-1,3-dimethylimidazolium hexafluorophosphate (CIP), chlorotripyrrolidinylphosphonium hexafluorophosphate Bis (tetramethylene) fluoroformamide (BTFFH), N, N, N′, N′-tetramethyl-sulfur-(1-oxo-2-pyridinyl) thiuronium hexafluorophosphate, 2-(2-pyridone-1-yl) -1,1,3,3-tetramethyl urea tetrafluoroborate (TPTU), sulfur-(1-oxo-2-pyridinyl)-N, N, N′, N′-tetramethylthiourea hexafluorophosphate, O-[(ethoxycarbonyl) cyanamide]-N, N, N′, N′-tetramethylthiourea hexafluorophosphate (HOTU), (1-cyano-2-ethoxy-2-oxoiminoyloxy) dimethylamino-morpholine-carbenium hexafluorophosphate (COMU), N-benzyl- N′-cyclohexylcarbodiimide (or on solid support), N-benzyl- N′-cyclohexyl carbodiimide (or on solid support), di-pyrrolidinyl (N-succinimido-methyl) pyrrolidine hexafluorophosphate (CIB), 2-chloro -1,3-dimethylimidazolium tetrafluoroborate (CIB), (benzotriazol-1-yloxy) dipiperidinyl carbon hexafluorophosphate (TCTU), tris (dimethylamino) phosphine hexafluorophosphate (RRHA), 1-n-propylphosphorus anhydride (PPACA, T3P®) , 2-isocyanoethylmorpholine (MEI), N,N,N',N'-tetramethylurea-oxy-(N-succinimidyl) hexafluorophosphate (HSTU), 2-bromo -1-Ethylpyridine tetrafluoroborate (BEP), oxygen-[(ethoxycarbonyl)cyanomethylamine]-N,N,N',N'-tetramethylthiourea tetrafluoroborate (TOTU), 4-(4,6-dimethoxytriazin-2-yl)-4-methylmorpholine

hydrochloride (MMTM, DMTMM), 2-succinimidyl -1,1,3,3-tetramethyl urea tetrafluoroborate (TSTU), N, N, N′, N′-tetramethyl-O-(3,4-dihydro-4-oxo -1, 2) 3-benzotriazine-3-yl) urea tetrafluoroborate (TDBTU), azodicarbonyldipiperidinyl (ADD), bis (4-chlorobenzyl) azodicarboxylate (DCAD), di-tert-butyl azodicarboxylate (DBAD), diisopropyl azodicarboxylate (DIAD) and diethyl azodicarboxylate (DEAD).

11. The method according to **Claim 8**, wherein the method further comprises synthesis of the Tubulysin B derivatives of formula (III) by one or more of the following steps:





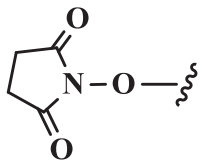
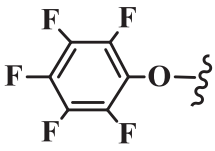
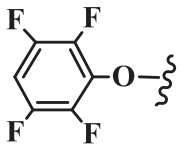
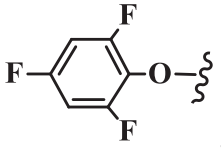
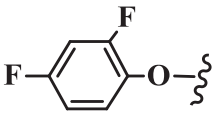
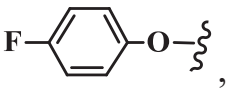
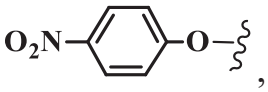
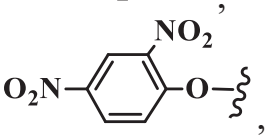
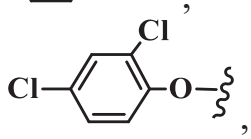
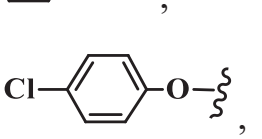
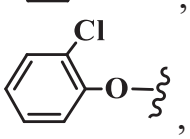
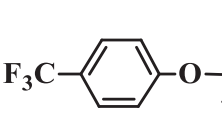
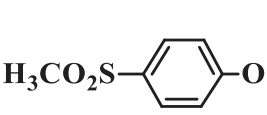
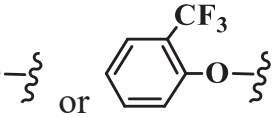
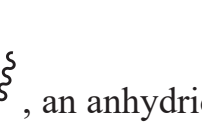
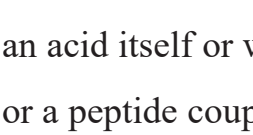
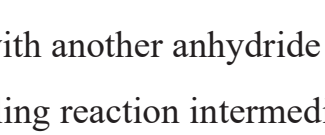
wherein in the above formulae,

R_5' is H, C_1-C_6 alkyl group, C_1-C_6 alkenyl group, or C_1-C_6 linear or branched aminoalkyl group,

R_9 is H, (O=)CR_1, or (O=)$CNHR_1$;

PG_1 is a protecting group;

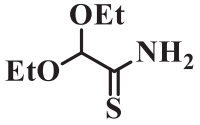
R_{10}, and $R_{11}$are independently halogen, phenoxy, pentachlorophenoxy, trifluoromethanesulfonyl, imidazole, dichlorophenoxy, tetrachlorophenoxy, 1-hydroxybenzotriazole, p-toluenesulfonyl, methanesulfonyl, 2-ethyl-5-phenyl

isoxazole-3'-sulfonyl group,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  or , an anhydride formed by an acid itself or with another anhydride of acetyl anhydride or formic anhydride; or a peptide coupling reaction intermediate or a Mitsunobu reaction intermediate;

P^1, "〰", R_1, R_2, R_3, R_4, R_6, R_7, and R_8 in the above formulae are defined the same as in **Claim 8**.

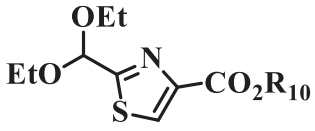
12. The method according to **Claim 11**, wherein the synthesis of the Tubulysin B derivatives of formula (III) comprises one or more of the following steps:

Step 1: Diethoxyacetonitrile and aqueous ammonium sulfide are mixed and stirred at room temperature to yield compound **1**, 2,2-diethoxythioacetamide;



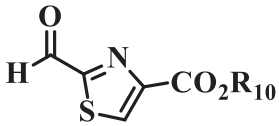
1

Step 2: Compound **1** and bromopyruvate in an anhydrous solvent are heated and condensed to yield compound **2**;



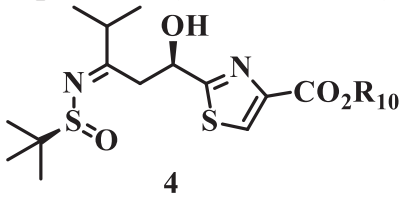
2

Step 3: Compound **2** is dissolved in a solvent and hydrolyzed in the presence of a Lewis acid or protonic acid, to yield compound **3**;



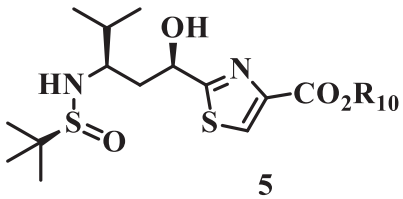
3

Step 4: The sulfinamide is deprotonated by n-butyllithium under a temperature of -45 to -78℃, and then condensed with compound **3** in the presence of a Lewis acid, to yield compound **4** (Adol reaction);



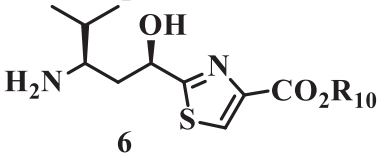
4

Step 5: Compound **4** is selectively reduced at a temperature of -45 to -78℃ by a reducing reagent, to yield compound **5**, wherein a Lewis acid is added to control a stereochemistry outcome;



5

Step 6: Compound **5** is dissolved in a solvent, and tert-butylsulfinyl group is removed by an acid, to yield compound **6**;

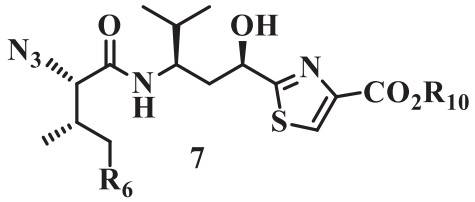


6

Step 7: In the presence of a condensation reagent, compound **6** and azido acid in a solvent is condensed, to yield compound **7**;

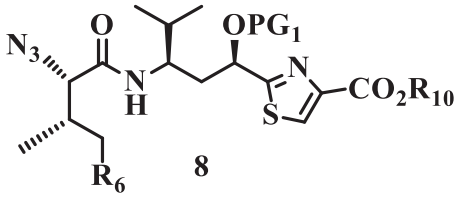
or azido acid reacts with isobutyl chloroformate in THF, in the presence of an organic base, to yield a mixed anhydride, which condenses with the hydrochloride salt of compound **6** to afford **7**;

or azido acid in a solvent reacts with oxalyl chloride, in presence of triethylamine and DMF (catalytic amount), to produce acyl chloride, which then condenses with the hydrochloride salt of compound **6** to afford **7**.



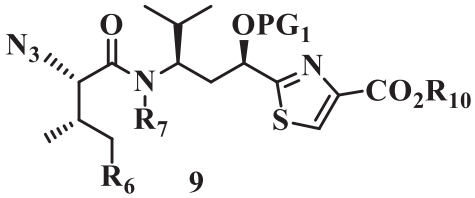
7

Step 8: In a solvent, the hydroxyl group of compound **7** reacts with a hydroxyl protection reagent, in the presence of an organic base, to yield a protected compound **8**;



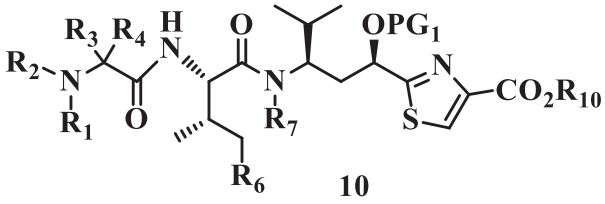
8

Step 9: Compound **8** in a solvent is deprotonated with added base, and then alkylated with iodomethane, bromomethane, dimethyl sulfate, methyl trifluoromethanesulfonate, or iodoethane, to yield compound **9**;



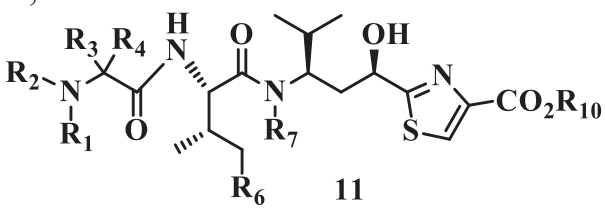
9

Step 10: Compound **9** is dissolved in a solvent, wherein the azido group is reduced to an amino group under conditions of H_2 and Pd/C, triphenylphosphine and water (Staudinger reaction) and then condensed with an acid or an acid derivative having similar reactivity, to afford compound **10**;



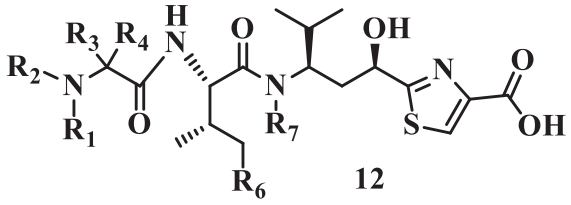
10

Step 11: The hydroxyl protecting group PG_1 of compound **10** is deprotected to yield compound 11;



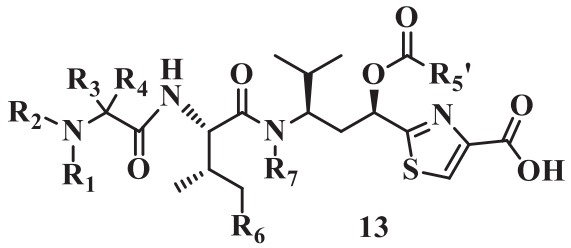
11

Step 12: The ester compound **11** is converted to acid **12**, by being subjected to a base;



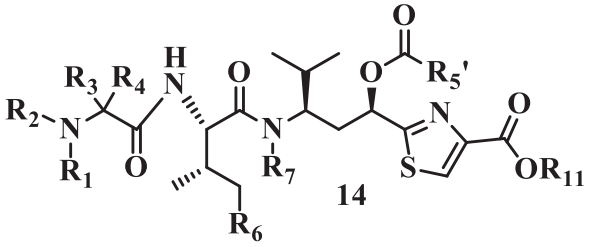
12

Step 13: In the presence or absence of a base and a catalyst, compound **12** reacts with an anhydride, or acyl halide, at a temperature of 0℃ to 23℃, to yield compound **13**;



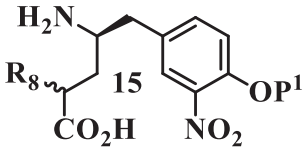
13

Step 14: Compound **13** condenses with a hydroxyl-containing compound in the presence of a condensation reagent, to yield a reactive ester compound **14**;

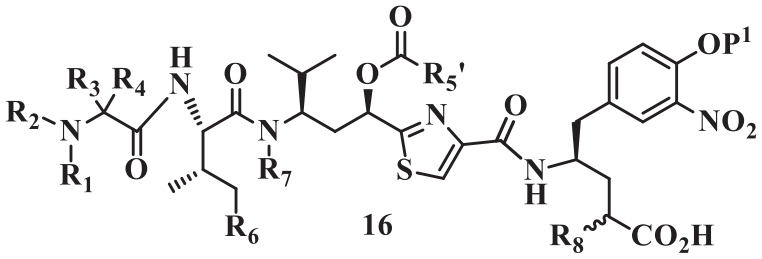


14

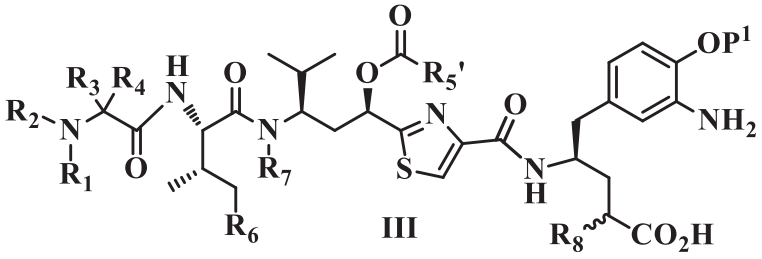
Step 15: Compound **15** and compound **14** condense in an aqueous solution having a pH of 5.0-8.0, or an organic solution, and (i) in the presence of an organic base or an inorganic base, or (ii) in the absence of a base, at a reaction temperature from 0℃ to 23℃ and reaction time from 30 minutes to 18 hours, to yield compound **16**;



15

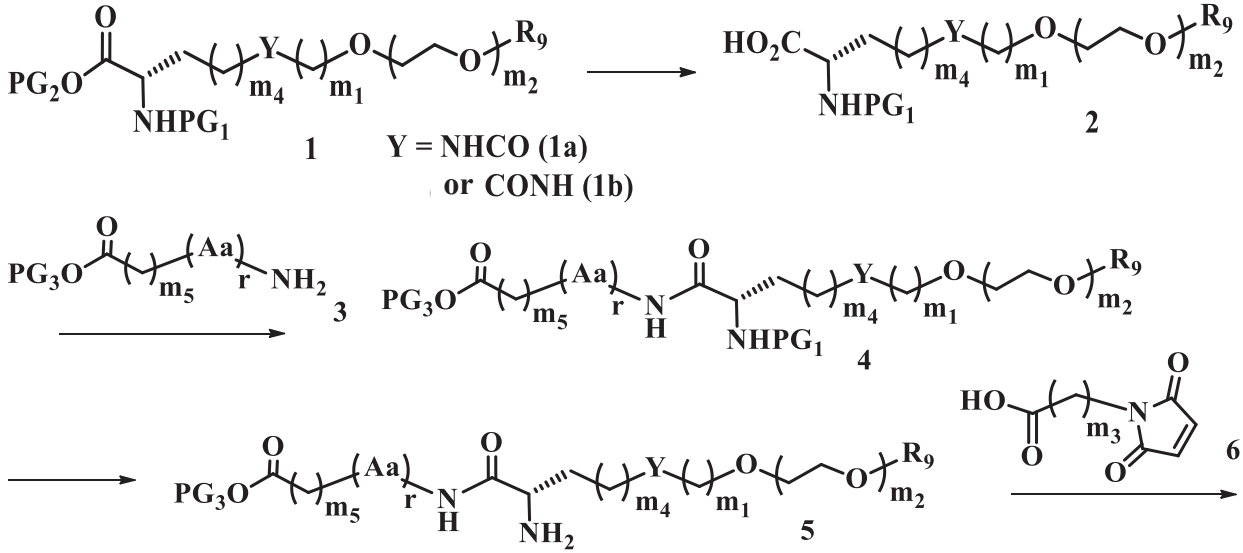


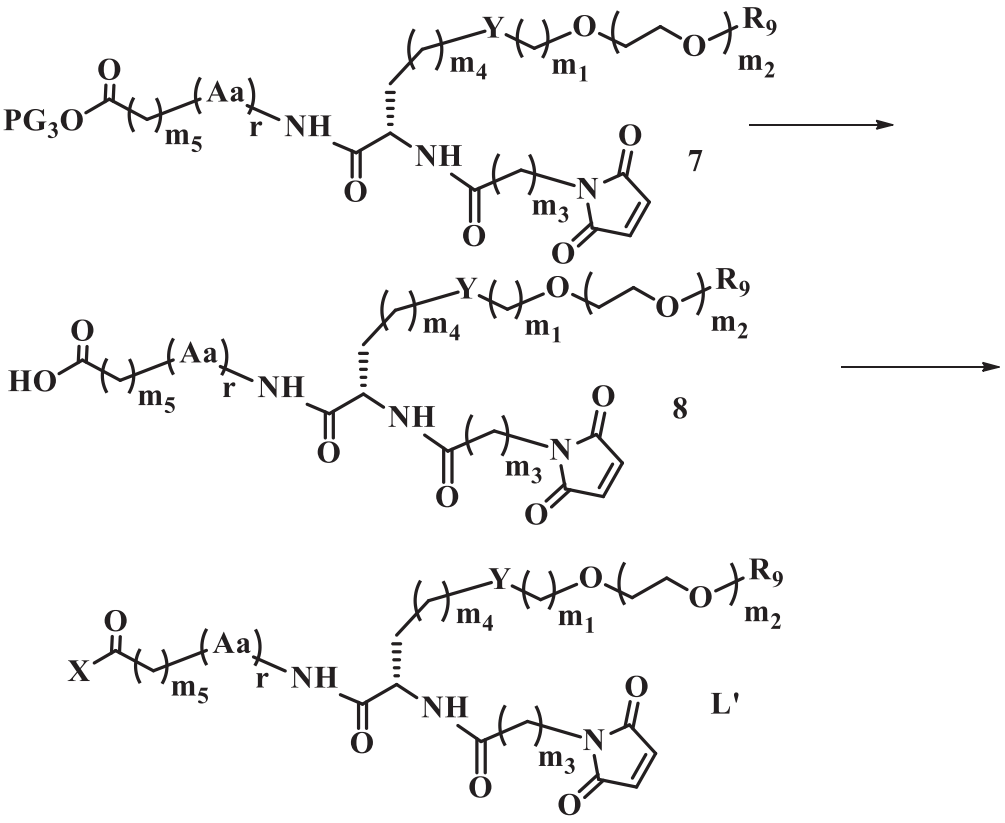
Step 16: The nitro group of compound **16** is reduced to an amino group under reduction conditions of hydrogen and Pd/C catalyst, hydrazine hydrate and $FeCl_3$, or iron powder and acetic acid, to yield compound III.



wherein in the above formulae, PG_1, P^1, "〰", R_1, R_2, R_3, R_4, R_5', R_6, R_7, R_8, R_{10}, and R_{11} are defined the same as in **Claim 11**.

13. The method according to **Claim 8**, wherein the method further comprises synthesis of the compounds of Formula (L') by one or more of the following steps:





wherein in the above formulae,

R_9 is H, (O=)CR_1, or (O=)$CNHR_1$;

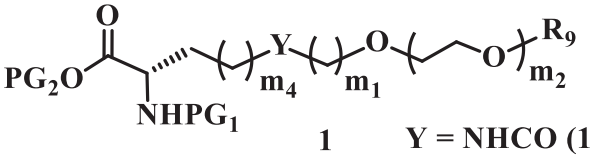
PG_1, PG_2 and PG_3 are independently a protecting group;

X, m_1, m_2, m_3, m_4, m_5, Aa, and r are defined the same as in **Claim 8**.

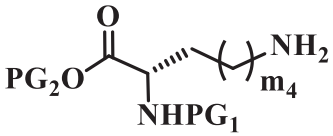
14. The method of **Claim 13**, wherein the synthesis of the compound of Formula (L') comprises one or more of the following steps:

Step 1: Compound **1-1** and compound **1-2** condense directly in the presence of a condensation reagent, or by reacting compound **1-2** with pentafluorophenol, nitrophenol or N-hydroxysuccinimide to yield a corresponding active eater, in the presence of a condensation reagent, and then reacting with compound **1-1**, to yield **1a**;

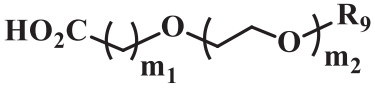
or compound **1-3** and compound **1-4** condense directly, in the presence of a condensation reagent, or by another indirect condensation reaction routes, to yield compound **1b**;



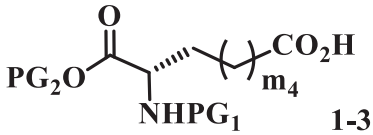
1 Y = NHCO (1a)
或 CONH (1b)



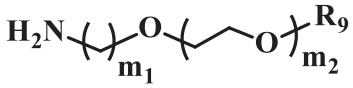
1-1



1-2

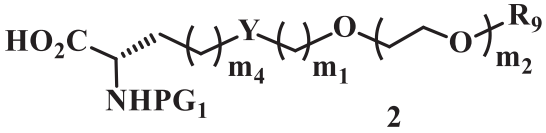


1-3



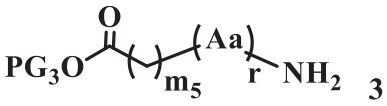
1-4

Step 2: The carboxyl protecting group PG_2 of compound **1** is removed by a deprotection reagent, to yield compound **2**;

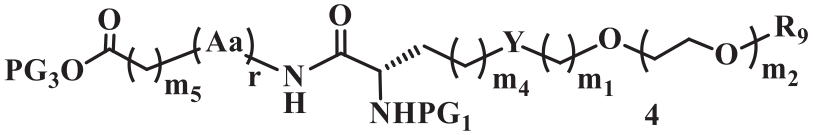


2

Step 3: Compound **2** and compound **3** condense in the presence of a condensation reagent, or by another indirect condensation reaction routes, to yield compound **4**;

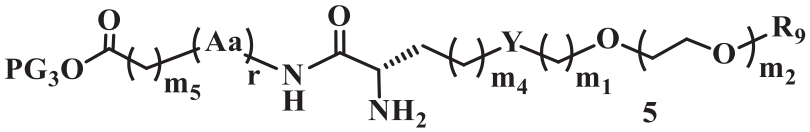


3



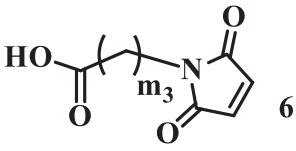
4

Step 4: The amino protecting group PG_1 of compound **4** is removed under deprotection conditions, to yield compound **5**;

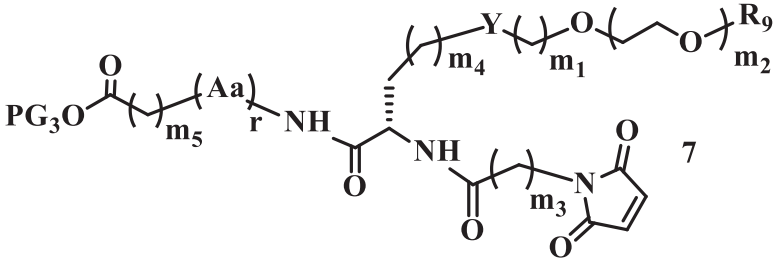


5

Step 5: Compound **6** and compound **5** condense in the presence of a condensation reagent, or by another indirect condensation reaction routes, to yield compound **7**;

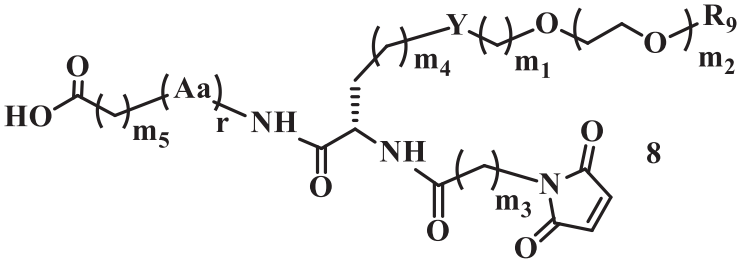


6



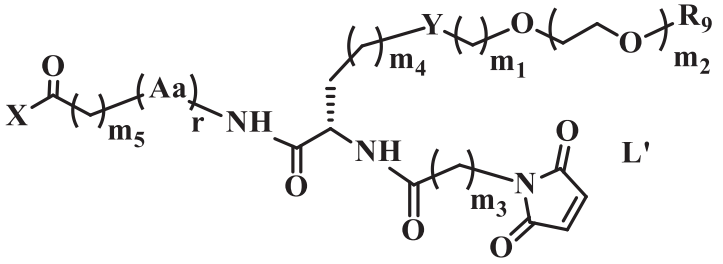
7

Step 6: The carboxyl protecting group PG_3 of compound **7** is removed under deprotection conditions, to yield compound **8**;



8

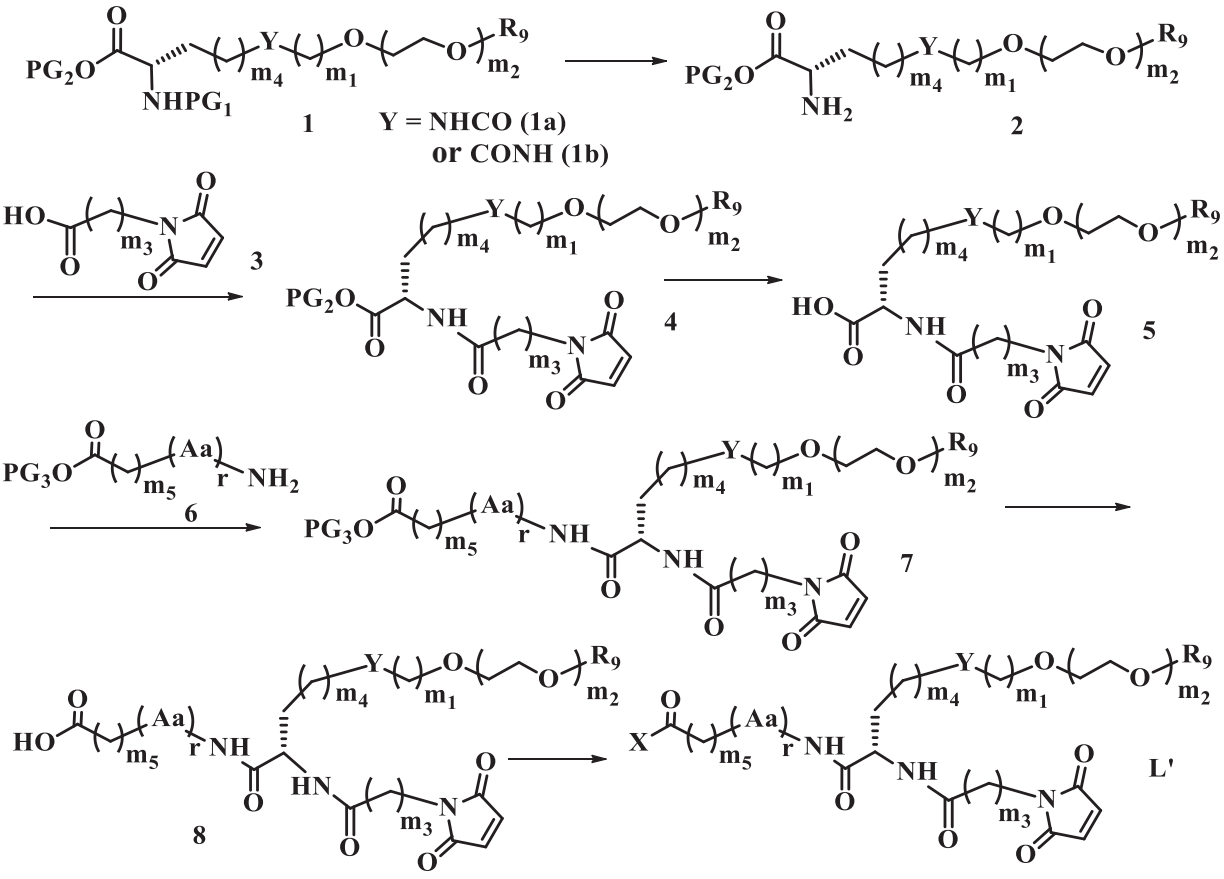
Step 7: Compound **8** reacts with a compound containing a hydroxyl group, in the presence of a condensation reagent, or reacts with another carboxylic acid activating compound, to yield a reactive ester compound L';



L'

wherein in the above formulae, X, R_9, m_1, m_2, m_3, m_4, m_5, Aa, and r are defined the same as in **Claim 13**.

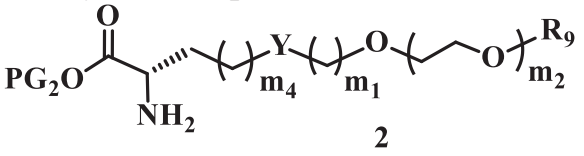
15. The method according to **Claim 8**, wherein the method further comprises synthesis of the compound of Formula (L') by one or more of the following steps:



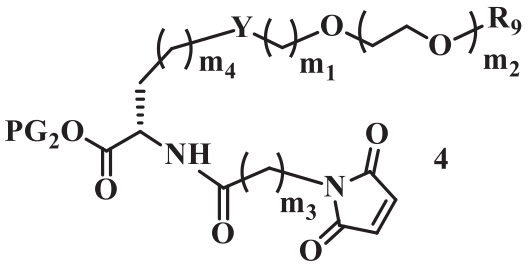
wherein in the above formulae, PG_2 and PG_3 are independently a protecting group; and X, R_9, m_1, m_2, m_3, m_4, m_5, Aa, and r are defined the same as in **Claim 8**.

16. The method according to **Claim 15**, wherein the synthesis of compounds of Formula (L') comprises one or more of the following steps:

Step 1: The amino protecting group PG_1 of compound **1** is removed under deprotection condition, to yield compound **2**;

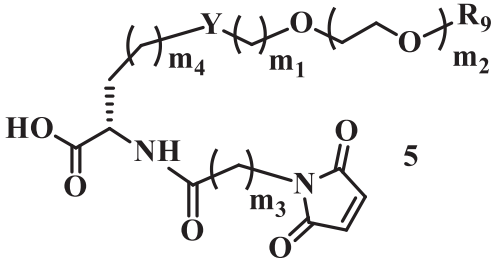


Step 2: Compound **2** and compound **3** condense in the presence of a condensation reagent, or by another indirect condensation reaction route, to yield compound **4**;



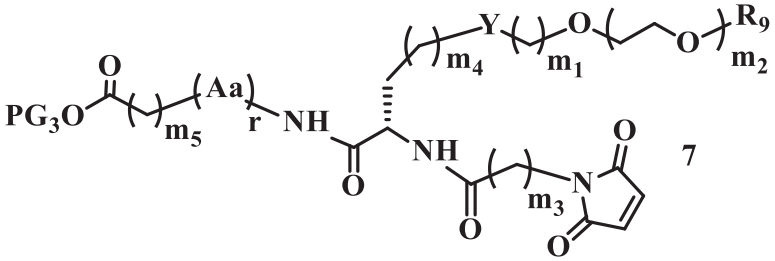
4

Step 3: The carboxyl protecting group PG_2 of compound **4** is removed under deprotection conditions, to yield compound **5**;



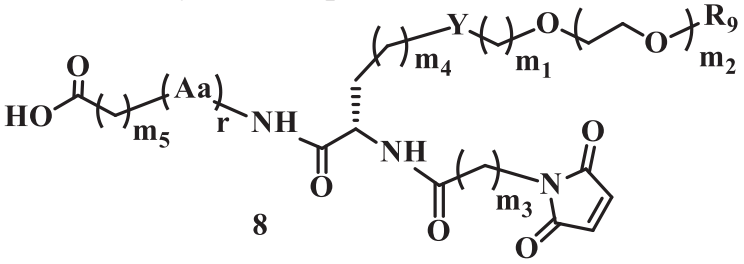
5

Step 4: Compound **5** and compound **6** condense in the presence of a condensation reagent, or by another indirect condensation reaction route, to yield compound **7**;



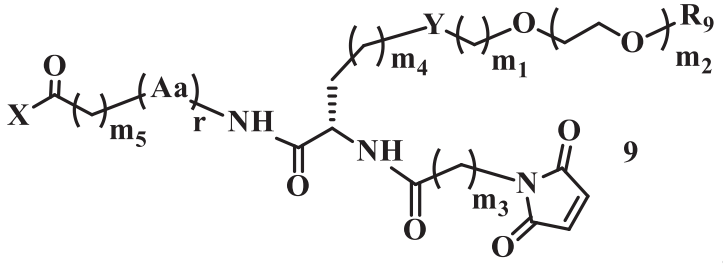
7

Step 5: The carboxyl protecting group PG_3 of compound **7** is removed under deprotection conditions, to yield compound **8**;



8

Step 6: Compound **8** reacts with a compound containing a hydroxyl group, in the presence of a condensation reagent, or reacts with another carboxylic acid activating compound, to yield a reactive ester compound **9**;

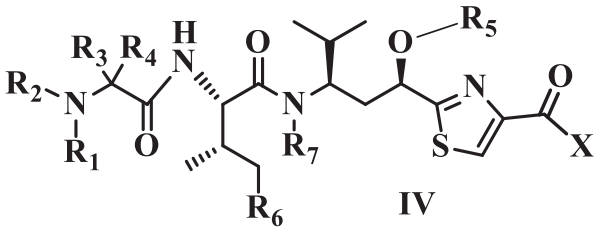


9

.

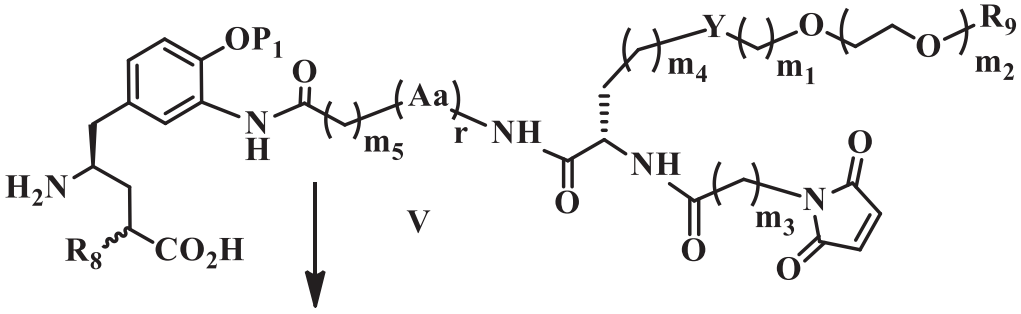
wherein in the above formulae, PG_2, PG_3, X, Y, R_9, m_1, m_2, m_3, m_4, m_5, Aa, and r are defined the same as in **Claim 15**.

17. The method according to **Claim 2**, wherein the method further comprises synthesis of the compounds of Formula (II) by a condensation reaction of compounds of Formula (IV) and Formula (V):

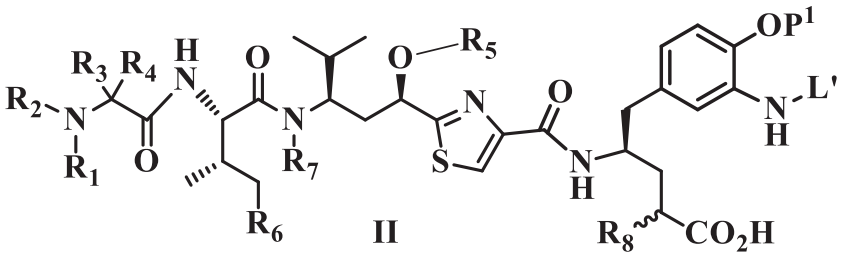


IV

+



V

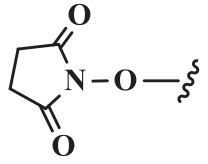
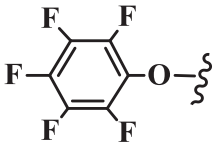
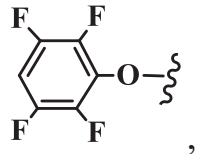
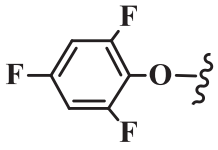
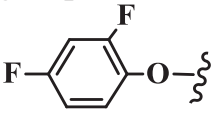
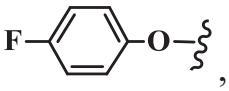
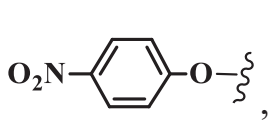
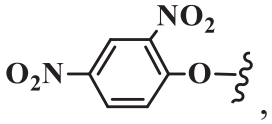
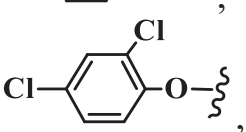
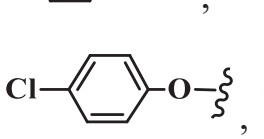
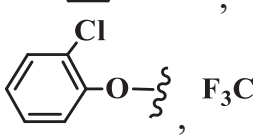
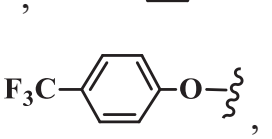
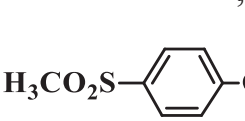
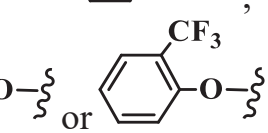
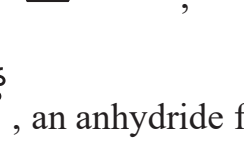
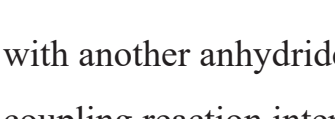
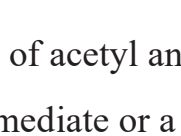


II

wherein in the above formulae,

P^1, "〰", R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, m_1, m_2, m_3, m_4, m_5, Aa, r and Y are defined the same as in **Claim 2**;

X is OH, halogen, phenoxy, pentachlorophenoxy, trifluoromethanesulfonyl, imidazole, dichlorophenoxy, tetrachlorophenoxy, 1-hydroxybenzotriazole, p-

toluenesulfonyl, methanesulfonyl, 2-ethyl-5-phenyl isoxazole -3'- sulfonyl group,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  or  , an anhydride formed by an acid itself or with another anhydride of acetyl anhydride or formic anhydride; or a peptide coupling reaction intermediate or a Mitsunobu reaction intermediate; and

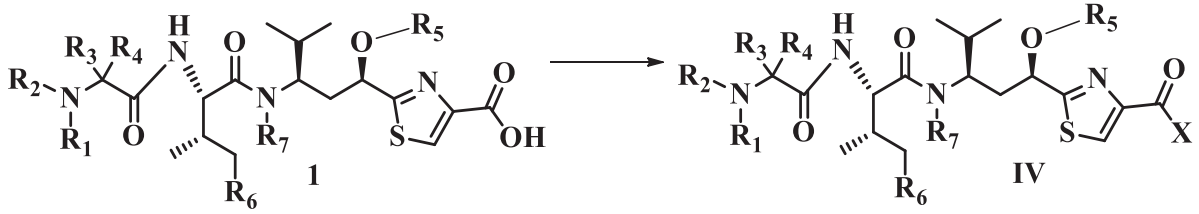
wherein the condensation reaction is carried out in dichloroethane, DMF, DMA, tetrahydrofuran (THF), DMSO, acetone, isopropanol, n-butanol or acetonitrile, or mixed solvents of two or three of the above, containing 1 to 100% pyridine, triethylamine or diisopropylethylamine; with or without an inert gas, at -20 to 150 °C, for 5 minutes to 120 hours;

or the condensation reaction is conducted in following buffer system and under following conditions: a buffer system has a pH of 5.0 - 9.5, is 1 mM - 1000 mM phosphoric acid, acetic acid, citric acid, boric acid, carbonic acid, barbituric acid, Tris (Tris-hydroxymethyl aminomethane), benzoic acid or triethanolamine system, or a mixture thereof, containing 0 to 35% a miscible organic solvent of methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, acetonitrile, acetone, DMF, DMA or DMSO; a reaction temperature is 0 to 45 °C and reaction time is from 5 minutes to 96 hours.

18. The method according to **Claim 17**, wherein the NH_2 group of Formula (V) participates in the conjugation reaction in a form of salt, with trifluoroacetic

acid, hydrochloride acid, formic acid, acetatic acid, sulfuric acid, phosphoric acid, nitric acid, citric acid, succinic acid, benzoic acid or sulfonic acid.

19. The method according to **Claim 17**, wherein the method further comprises synthesis of the compound of Formula (IV) by the following steps:



wherein in the above formulae, R_1, R_2, R_3, R_4, R_5, R_6, R_7, and X are defined the same as in **Claim 17**.

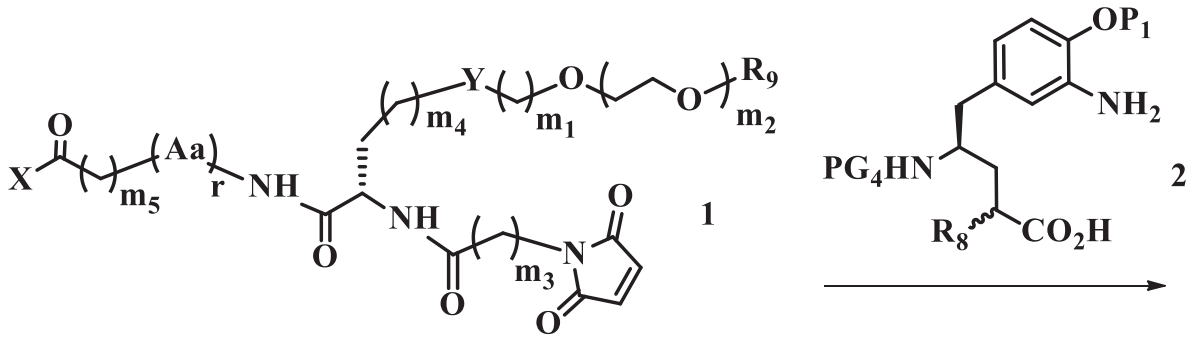
20. The method according to **Claim 19**, wherein the synthesis of the compounds of Formula (IV) comprises the following steps:

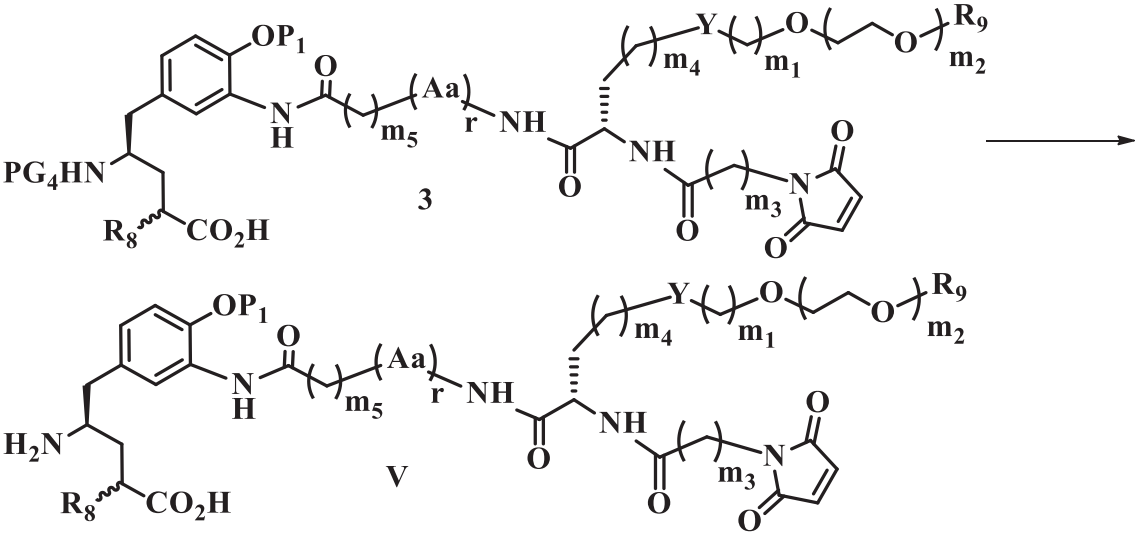
Compound **1** and a compound with a hydroxyl group condense in the presence of a condensation reagent to yield a reactive ester;

or carboxylic acid **1** reacts with ethyl chloroformate, or isobutyl chloroformate, in the presence of an organic base to yield a reactive mixed anhydride;

or carboxylic acid **1** reacts with oxalyl chloride, in the presence of an organic base, and a catalytic amount of DMF to yield an acyl chloride.

21. The method according to **Claim 17**, wherein the method further comprises synthesis of the compound of Formula (V) by one or more of the following steps:





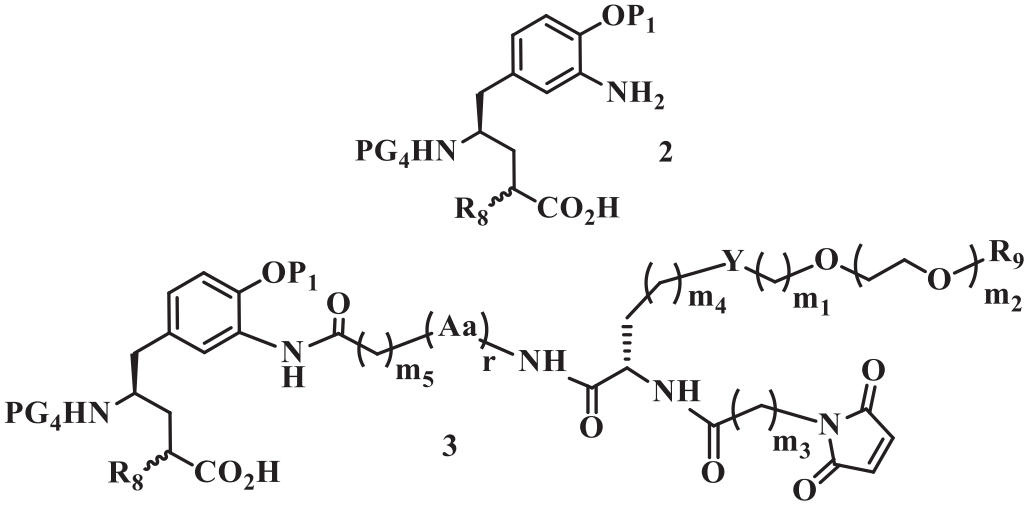
wherein in the above formulae,

PG_4 is a protecting group; and

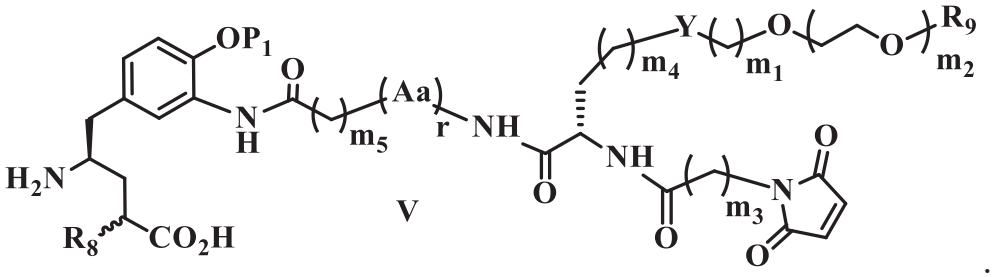
P^1, "〰", R_8, R_9, m_1, m_2, m_3, m_4, m_5, Aa, r, X, and Y are defined the same as in **Claim 17**.

22. The method of **Claim 21**, wherein the synthesis of the compound of Formula (V) comprises one or more of the following steps:

Step 1. Compound **1** and compound **2** condense in an aqueous solution of having a pH of 5.0-8.0, or an organic solution, and (i) in the presence of an organic base or an inorganic base, or (ii) without a base, at a predetermined reaction temperature and reaction time, to yield compound **3;**



Step 2. The amino protecting group PG_4 of compound **3** is removed under deprotection conditions, to yield compound V;

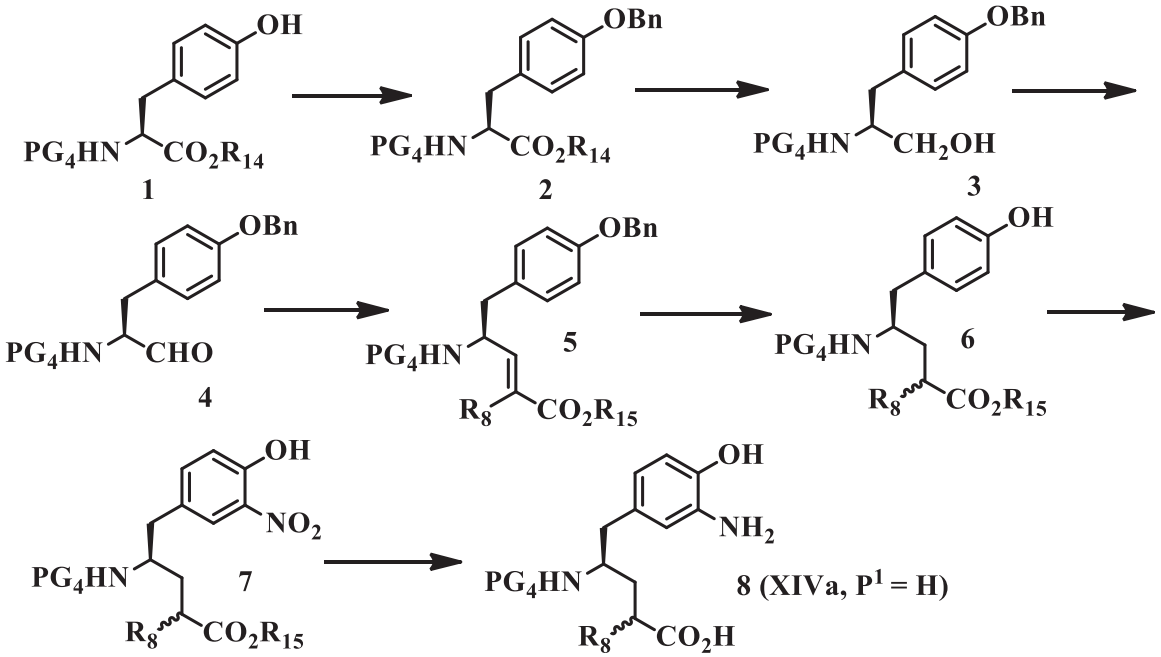


V

.

wherein in the above formulae, P^1, "〰", R_8, R_9, m_1, m_2, m_3, m_4, m_5, Aa, r, PG_4, and Y are defined the same as in **Claim 21**.

23. The method according to **Claim 21**, wherein the method further comprises synthesis of compound **2** by one or more of the following steps:



,

wherein in the above formulae, "〰" and R_8 are defined the same as in **Claim 21**;

R_{14}, and R_{15} are indepensently a C_1-C_6 alkyl group;

wherein compound **8** (compound XIVa) is the same as compound **2**.

24. The method of **Claim 23**, wherein the synthesis of compound 2 comprises one or more of the following steps:

Step 1. To an ester derivative of L-tyrosine (**1**) in a solvent or a solvent mixture of a solvent and water, is added benzyl chloride, benzyl bromide or

other benzyl compound at 0 ~ 60°C, followed by an organic or inorganic base, and optionally an additive, or a phase transfer catalyst, to yield compound **2**;

Step 2. Compound **2** is dissolved in an organic solvent, and then react with a reducing reagent, optionally in the presence of an addctive to tune the activity of the reducing reagent, to yield compound **3**;

Step 3. Alcohol **3** is oxidized, under oxidation conditions, to yield aldehyde **4**;

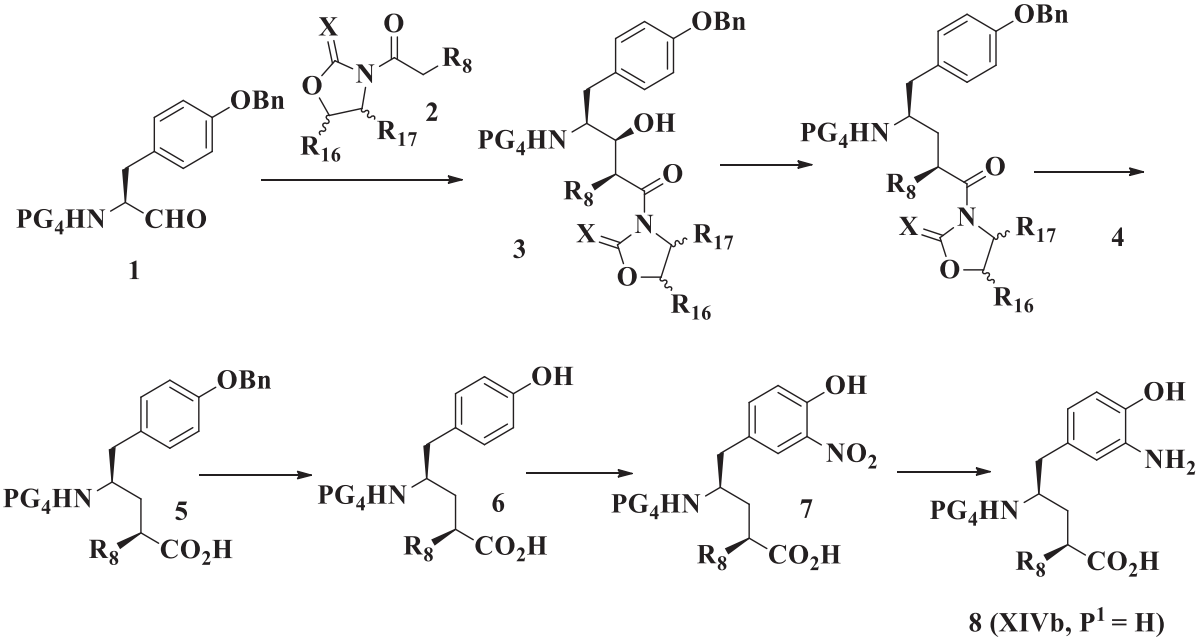
Step 4. Aldehyde **4** reacts with a phosphate ester (Horner-Wadsworth-Emmons reaction) or a phosphorus ylide (Wittig reaction) to elongate the carbon chain and yield compound **5**;

Step 5. The double bond of compound **5** is reduced, in the presence of a homogeneous or heterogeneous catalyst, wherein the benzyl group is also removed, to yield a stereochemically pure compound, or a mixture of two diastereomers; the heterogeneous catalyst includes Pd/C, $Pd(OH)_2/C$, $Pd/BaSO_4$, PtO_2, Pt/Al_2O_3, Ru/C, or Raney Ni, and the homogeneous asymmetric hydrogenation catalyst includes Crabtree catalyst, [Ru (II)-(BINAP)]-type catalyst, or $[(Ph_3P)CuH]_6$,to yield compound **6**;

Step 6. Compound **6** is dissolved in an organic solvent, and undergoes nitration in the presence of a nitration reagent of nitric acid, nitric acid/acetic acid, potassium nitrate/sulfuric acid, tert-butyl nitrite, nitric acid/trifluoroacetic anhydride, NO_2BF_4, or nitropyridine,to yield compound **7**;

Step 7. The nitro group of compound **7** is reduced to an amino group, under H_2/Pd/C, Fe or Zn/HOAc, or $SnCl_2$/HCl.

25. The method according to **Claim 21**, wherein the method further comprises synthesis of compound **2** by one or more of the following steps:



wherein compound **8** (Compound XIVb) is the same as compound **2**;

wherein in the above formulae, "〰", R_8 and PG_4 are defined the same as in **Claim 21**; X = O or S; R_{16} = H, methyl, or phenyl; and R_{17} = H, methyl, isopropyl, phenyl, or benzyl.

26. The method of **Claim 25**, wherein the synthesis of compound **2** comprises one or more of the following steps:

Step 1: Compound **1** undergoes Aldol reaction with Evans' chiral N-acyl oxazolidinone or thioketone **2** at -78 °C to -45°C, to yield a stereochemically pure compound **3**;

Step 2: The hydroxyl group of compound **3** is deoxygenated under Barton–McCombie deoxygenation conditions: the alcohol is first converted to a thiocarbonyl derivative, and then treated with *n*-Bu_3SnH/AIBN, *n*-Bu_3SnH/AIBN/*n*-BuOH/PMHS or $(Bu_4N)_2S_2O_8/HCO_2Na$, to undergo radical cleavage to afford a dehydrogenation product;

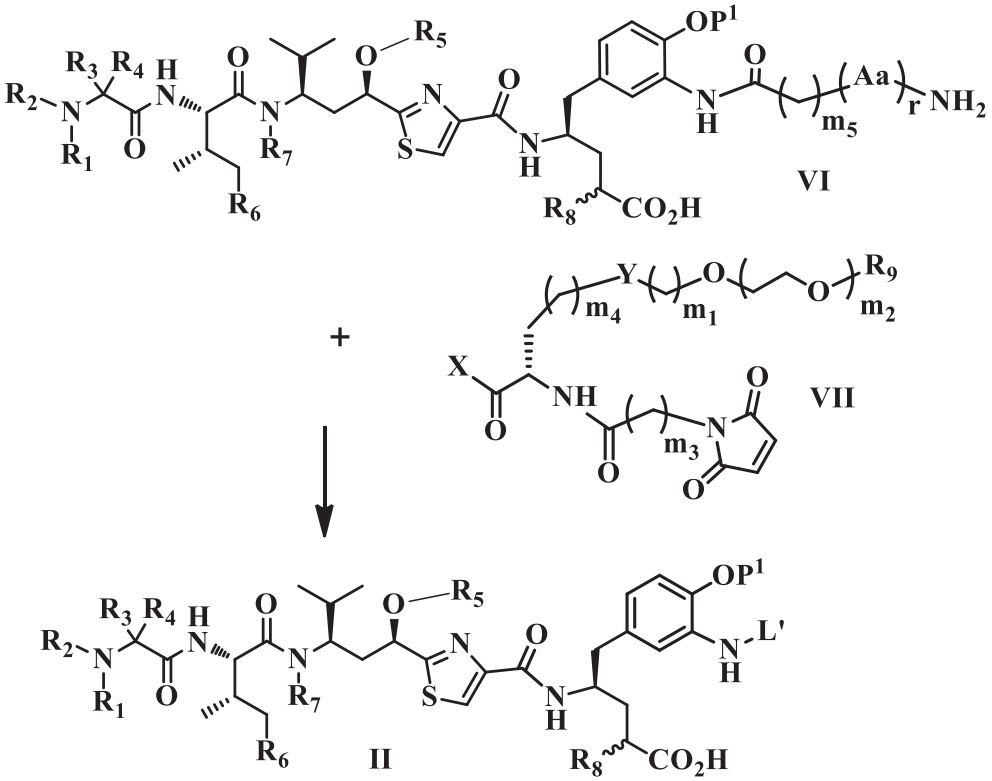
Step 3: Compound **4** is dissolved in tetrahydrofuran and the Evans chiral auxiliary group is cleaved by $LiOH/H_2O_2$, to yield corresponding acid **5**;

Step 4: Compound **5** is dissolved in an organic solvent and hydrogenated in the presence of Pd/C catalyst, wherein the benzyl group is also removed, to yield compound **6**;

Step 5: Compound **6** is dissolved in an organic solvent, and undergoes nitration in the presence of a nitration reagent including nitric acid, nitric acid/acetic acid, potassium nitrate/sulfuric acid, tert-butyl nitrite, nitric acid/trifluoroacetic anhydride, NO_2BF_4, or nitropyridine,to yield compound **7**;

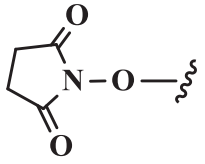
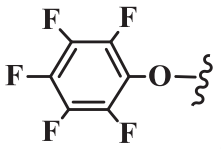
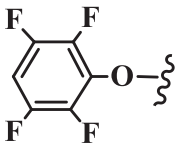
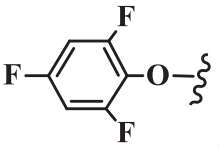
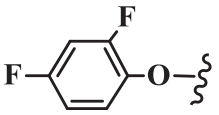
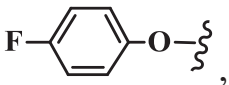
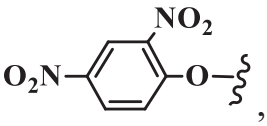
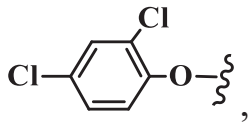
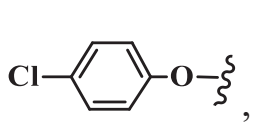
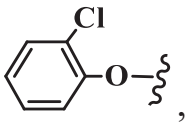
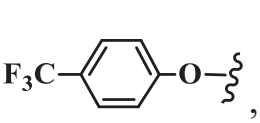
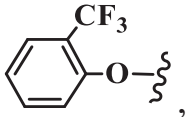
Step 6 : The nitro group of compound **7** is converted to amino group, under condition of H_2/Pd/C, Fe or Zn/HOAc or $SnCl_2$/HCl, to yield stereochemically pure compound **2**.

27. The method according to **Claim 2**, wherein the method further comprises obtaining the compound of formula (II) by a condensation reaction of compounds of Formula (VI) and Formula (VII):



wherein in the above formulae,

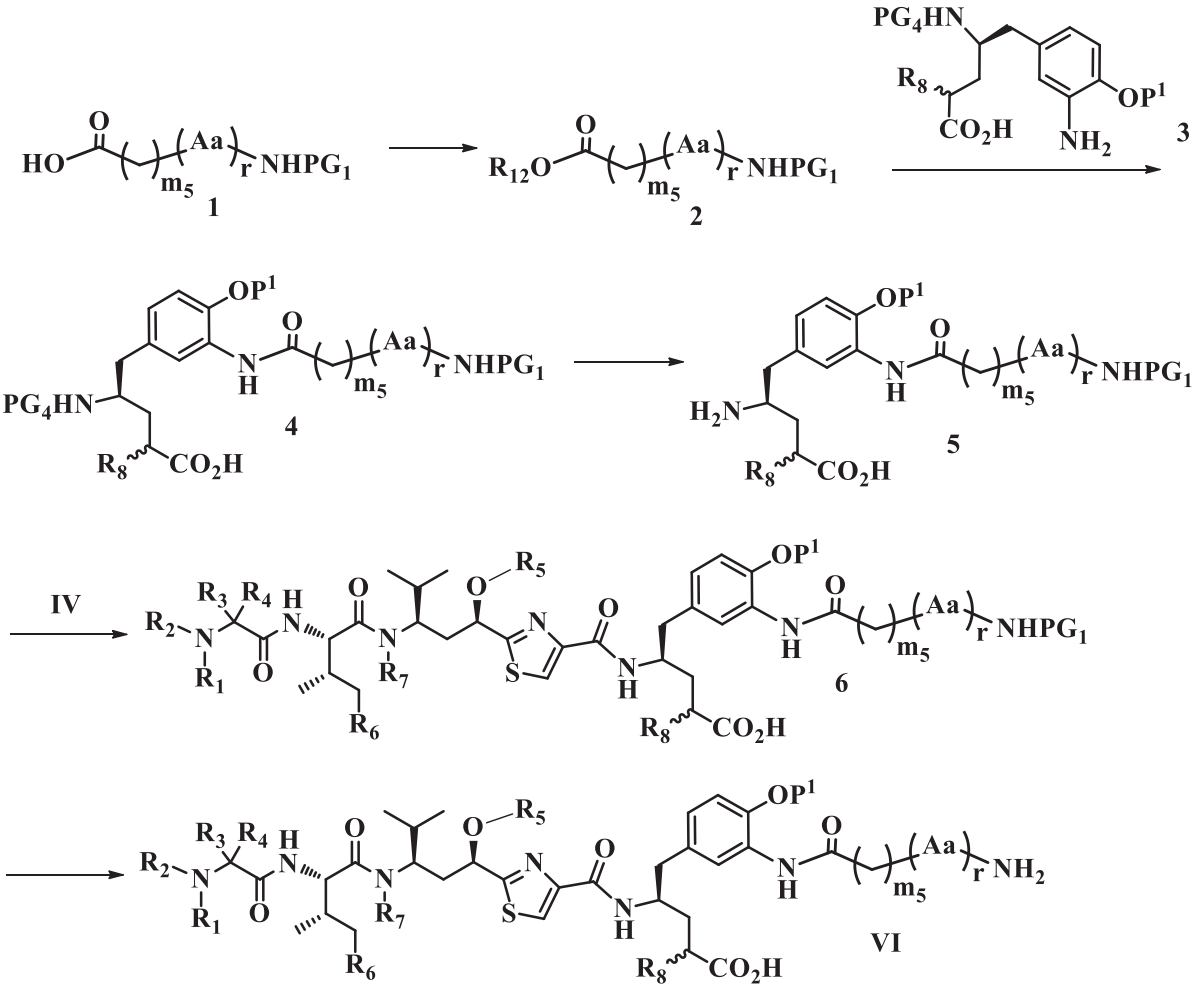
P^1, "〰", R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_9, m_1, m_2, m_3, m_4, m_5, Aa, r and Y are defined the same as in **Claim 2**;

X is OH, halogen, phenoxy, pentachlorophenoxy, trifluoromethanesulfonyl, imidazole, dichlorophenoxy, tetrachlorophenoxy, 1-hydroxybenzotriazole, p-toluenesulfonyl, methanesulfonyl, 2-ethyl-5-phenyl isoxazole -3'- sulfonyl group,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , , or  , an anhydride formed by an acid itself or with another anhydride of acetyl anhydride or formic anhydride; or a peptide coupling reaction intermediate or a Mitsunobu reaction intermediate;

wherein the condensation reaction is carried out in dichloroethane, DMF, DMA, tetrahydrofuran (THF), DMSO, acetone, isopropanol, n-butanol or acetonitrile, or mixed solvents of two or three of the above, containing 1 to 100% pyridine, triethylamine or diisopropylethylamine; with or without an inert gas, at -20 to 150 °C, for 5 minutes to 120 hours;

or the condensation reaction is conducted in following buffer system and under following conditions: a buffer system has a pH of 5.0 - 9.5, is 1 mM - 1000 mM phosphoric acid, acetic acid, citric acid, boric acid, carbonic acid, barbituric acid, Tris (Tris-hydroxymethyl aminomethane), benzoic acid or triethanolamine system, or a mixture thereof, containing 0 to 35% a miscible organic solvent of methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, acetonitrile, acetone, DMF, DMA or DMSO; a reaction temperature is 0 to 45 °C and reaction time is from 5 minutes to 96 hours.

28. The method of **Claim 27**, wherein the method further comprises synthesis of the compounds of formula (VI) by one or more of the following steps:



wherein in the above formulae,

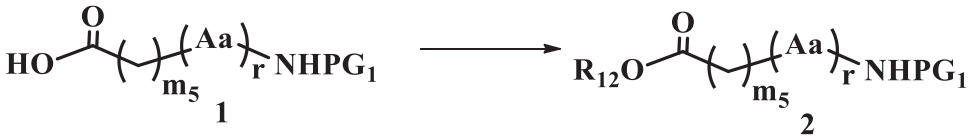
P^1, "〰", R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, m_5, Aa, r, X and Y are defined the same as in **Claim 27**;

R_{12} is definied the same as X above;

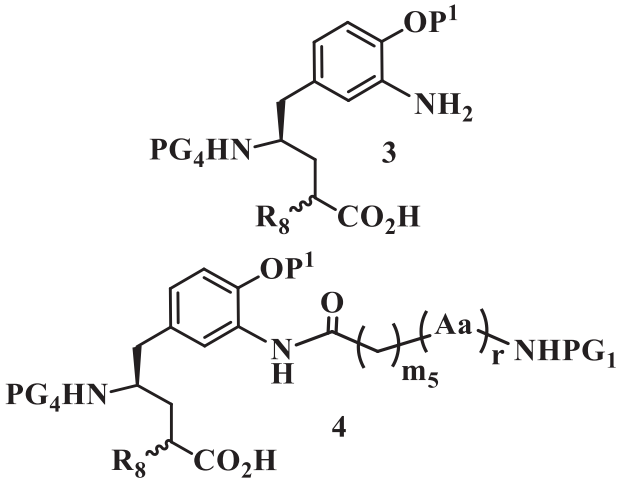
PG_1 and PG_4 are independently a protecting group.

29. The method according to **Claim 28**, wherein the synthesis of the compound of Formula (VI) comprises one or more of the following steps:

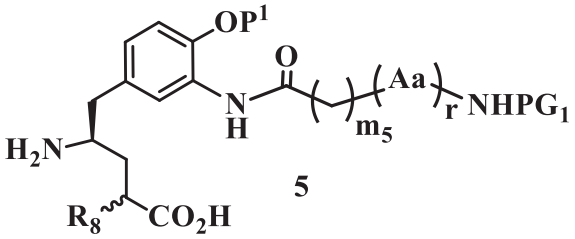
Step 1: Compound **1** reacts with a compound containing a hydroxyl group, in the presence of a condensation reagent, to yield a reactive carboxylic acid derivative compound **2**;



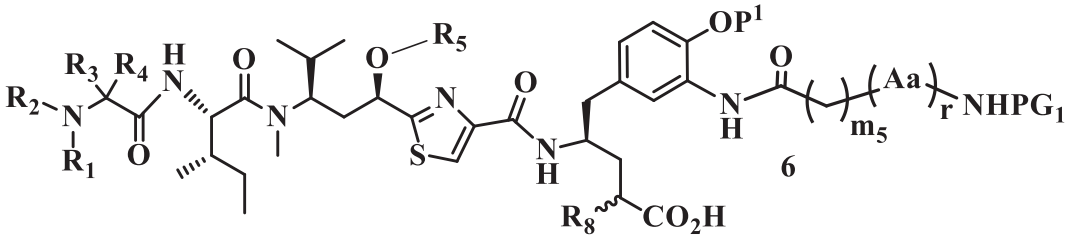
Step 2: Compound **2** and compound **3** condense in an aqueous solution having a pH of 5.0-8.0, or an organic solution, and (i) in the presence of an organic base or an inorganic base, or (ii) in the absence of a base, at a predetermined reaction temperature and reaction time, to yield compound **4**;



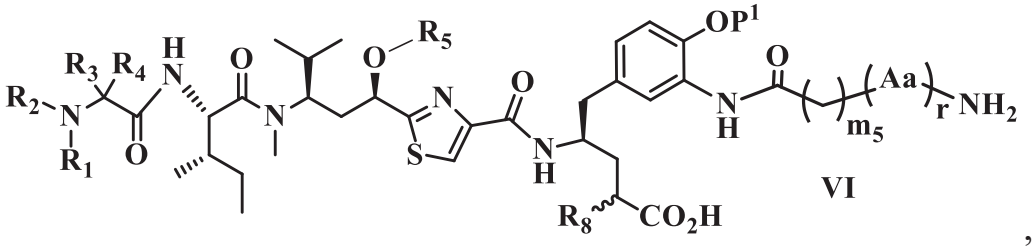
Step 3: The amino protecting group PG_4 of compound **4** is removed selectively under deprotection conditions, to yield compound **5**;



Step 4: Compound **5** and the compound of Formula (IV) condense in an aqueous solution having a pH of 5.0-8.0, or an organic solution, and (i) in the presence of an organic base or an inorganic base, or (ii) in the absence of a base, at a predetermined reaction temperature and reaction time, to yield compound **6**;



Step 5: The amino protecting group PG_1 of compound **6** is removed under deprotection conditions, to yield compound **VI**;



VI

,

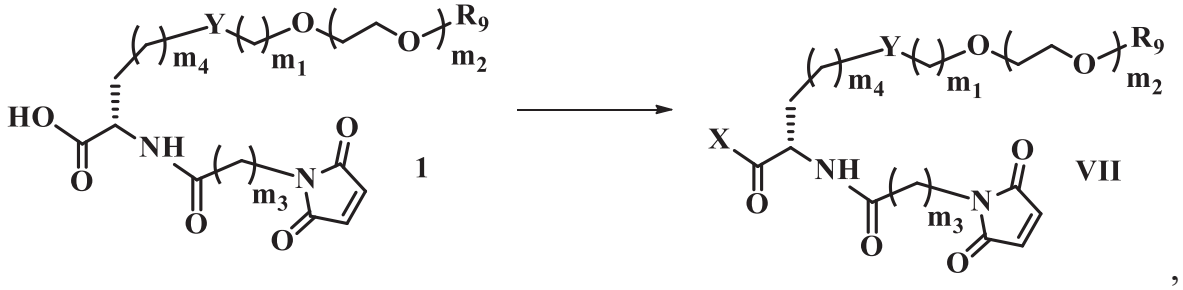
wherein in the above formulae,

P^1, "〰", R_1, R_2, R_3, R_4, R_5, R_8, m_5, Aa, r, X and Y are defined the same as in **Claim 27**;

R_{12} is defined the same as X above;

PG_1 and PG_4 are independently a protecting group.

30. The method according to **Claim 27**, wherein the method further comprises synthesis of compounds of Formula (VII) by one or more of the following steps:



1 VII

,

wherein in the above formulae,

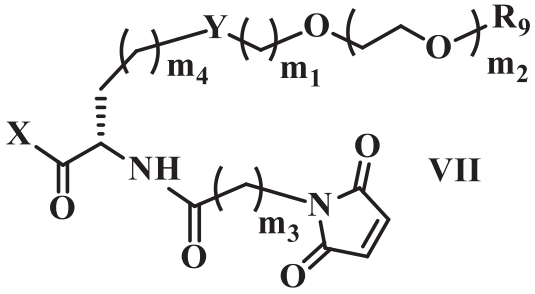
R_9, m_1, m_2, m_3, m_4, X and Y are defined the same as in **Claim 27**.

31. The method according to **Claim 30**, wherein the synthesis of the compounds of Formula (VII) comprises one of the following steps:

Carboxylic acid **1** and a compound with a hydroxyl group condense in the presence of a condensation reagent to yield a reactive ester;

Carboxylic acid **1** reacts with ethyl chloroformate or isobutyl chloroformate, in the presence of an organic base to yield a reactive mixed anhydride;

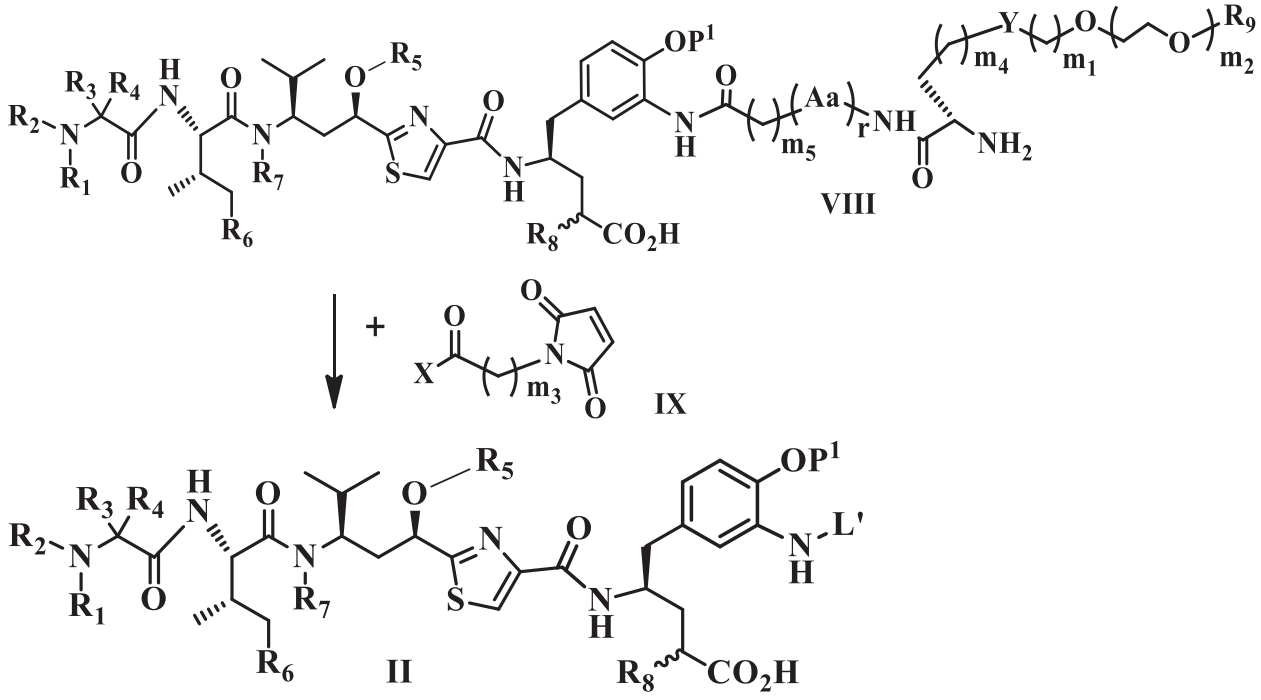
Carboxylic acid **1** reacts with oxalyl chloride, in the presence of an organic base, and a catalytic amount of DMF to yield an acyl chloride:



VII

wherein in the above formula, R_9, m_1, m_2, m_3, m_4, X and Y are defined the same as in **Claim 30**.

32. The method according to **Claim 2**, wherein the method further comprises obtaining the compound of Formula (II) by a condensation reaction of compounds of Formula (VIII) and Formula (IX):



VIII

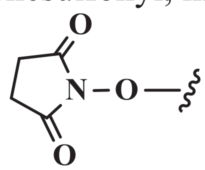
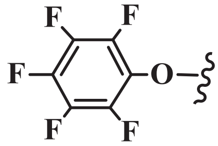
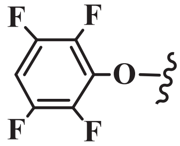
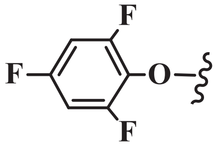
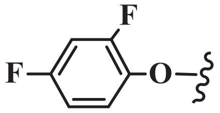
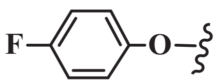
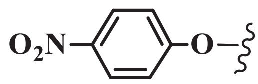
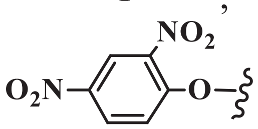
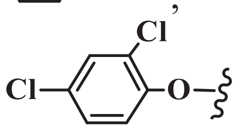
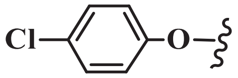
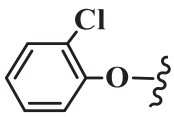
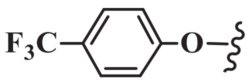
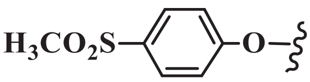
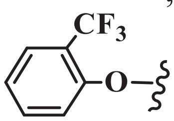
IX

II

wherein in the above formulae,

P^1, "〰", R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_9, m_1, m_2, m_3, m_4, m_5, and Y are defined the same as in **Claim 2**;

X is OH, halogen, phenoxy, pentachlorophenoxy, trifluoromethanesulfonyl, imidazole, dichlorophenoxy, tetrachlorophenoxy, 1-

hydroxybenzotriazole, p-toluenesulfonyl, methanesulfonyl, 2-ethyl-5-phenyl isoxazole -3'- sulfonyl group,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  or  , an anhydride formed by an acid itself or with another anhydride of acetyl anhydride or formic anhydride; or a peptide coupling reaction intermediate or a Mitsunobu reaction intermediate;

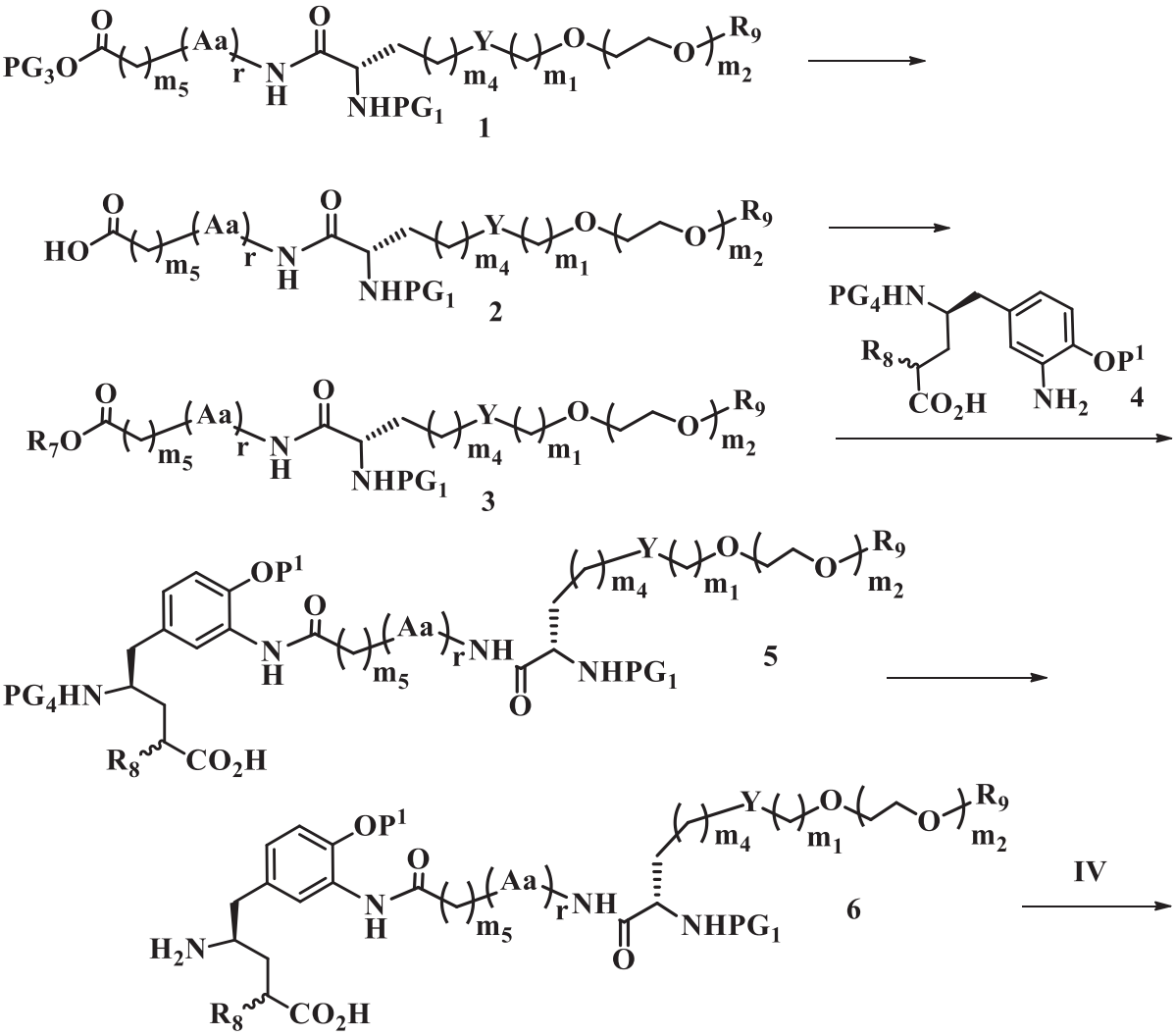
wherein the condensation reaction is carried out in dichloroethane, DMF, DMA, tetrahydrofuran (THF), DMSO, acetone, isopropanol, n-butanol or acetonitrile, or mixed solvents of two or three of the above, containing 1 to 100% pyridine, triethylamine or diisopropylethylamine; with or without an inert gas, at -20 to 150 °C, for 5 minutes to 120 hours;

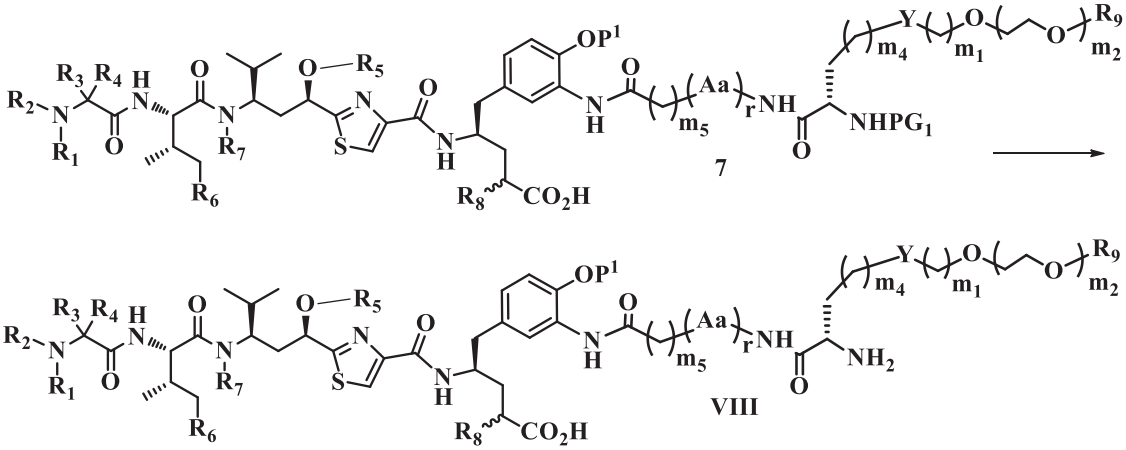
or the condensation reaction is conducted in following buffer system and under following conditions: a buffer system has a pH of 5.0 - 9.5, is 1 mM - 1000 mM phosphoric acid, acetic acid, citric acid, boric acid, carbonic acid, barbituric acid, Tris (Tris-hydroxymethyl aminomethane), benzoic acid or triethanolamine system, or a mixture thereof, containing 0 to 35% a miscible organic solvent of methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, acetonitrile, acetone, DMF, DMA or DMSO; a reaction temperature is 0 to 45 °C and reaction time is from 5 minutes to 96 hours.

33. The method according to **Claim 32**, wherein the NH_2 group of formula (VIII) participates in the conjugation reaction in a form of salt, with

trifluoroacetic acid, hydrochloride acid, formic acid, acetatic acid, sulfuric acid, phosphoric acid, nitric acid, citric acid, succinic acid, benzoic acid or sulfonic acid.

34. The method according to **Claim 32**, wherein the method further comprises synthesis of the compound of Formula (VIII) by one or more of the following steps:

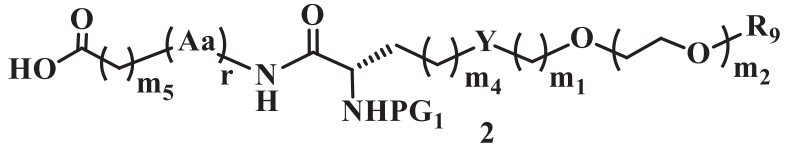




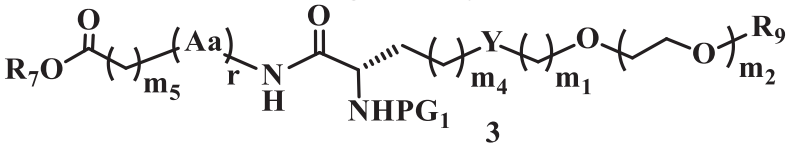
wherein in the above formulae, P^1, "〰", R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_9, m_1, m_2, m_3, m_4, m_5, Aa, r, and Y are defined the same as in **Claim 32**; and PG_1, PG_3 and PG_4 are independently a protecting group.

35. The method according to **Claim 34**, wherein the synthesis of compounds of Formula (VIII) comprises one or more of the following steps:

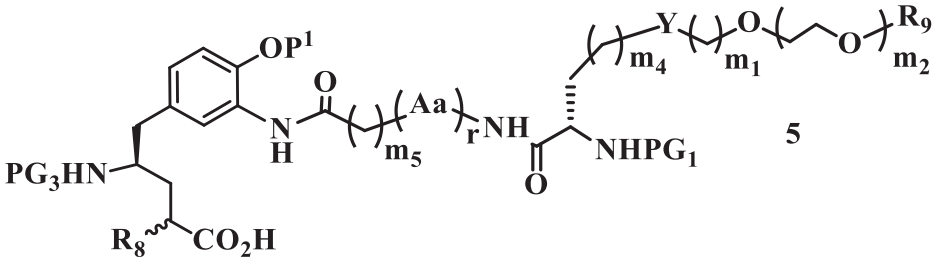
Step 1: The carboxyl protecting group PG_3 of compound **1** is removed under deprotection conditions, to yield compound **2**;



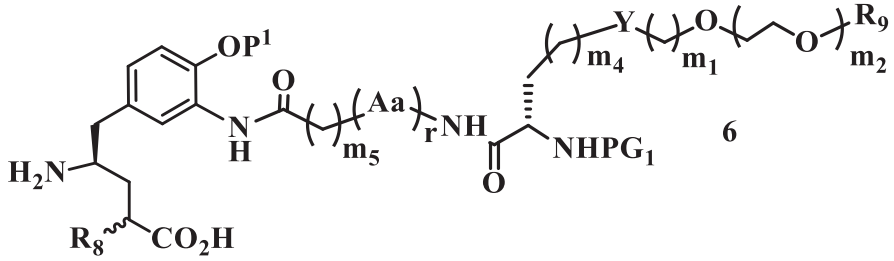
Step 2: Compound **2** reacts with a compound containing a hydroxyl group, in the presence of a condensation reagent, to yield a reactive ester compound **3**;



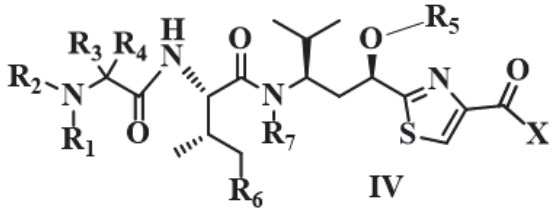
Step 3: Compound **3** and compound **4** condense in an aqueous solution having a pH of 5.0-8.0, or an organic solution, and (i) in the presence of an organic base or an inorganic base, or (ii) in the absence of a base, at a predetermined reaction temperature and reaction time, to yield compound **5**;

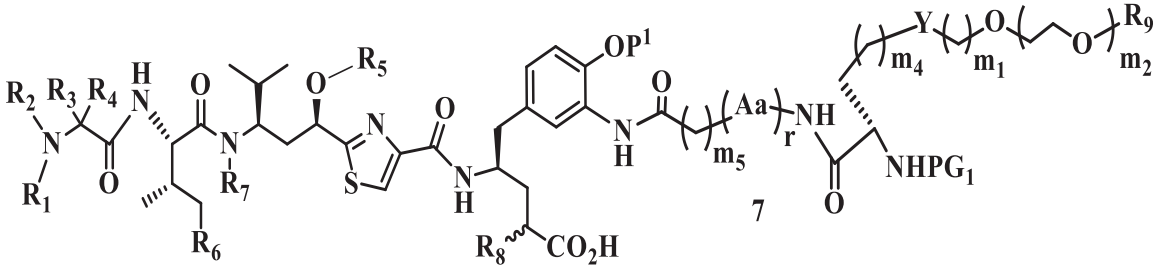


Step 4: The amino protecting group PG_4 of compound **5** is removed under deprotection conditions, to yield compound **6**;

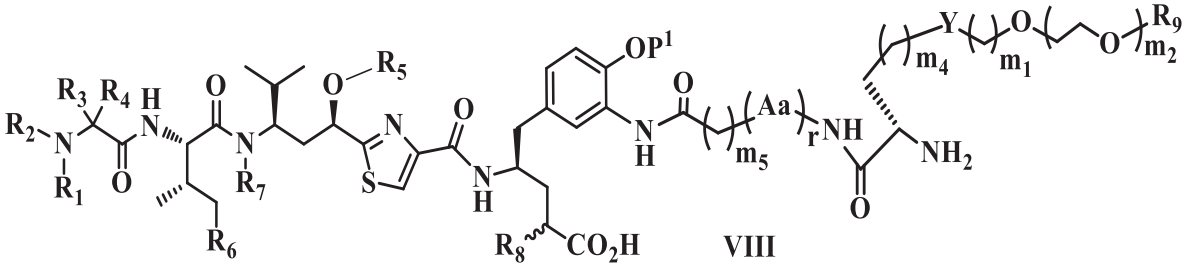


Step 5: Compound **6** and a compound of Formula (IV), condense in an aqueous solution having a pH of 5.0-8.0, or an organic solution, and (i) in the presence of an organic base or an inorganic base, or (ii) in the absence of a base, at a predetermined reaction temperature and reaction time, to yield compound **7**;





Step 6. The amino protecting group PG_1 of compound **7** is removed under deprotection conditions, to yield compound VIII;



,

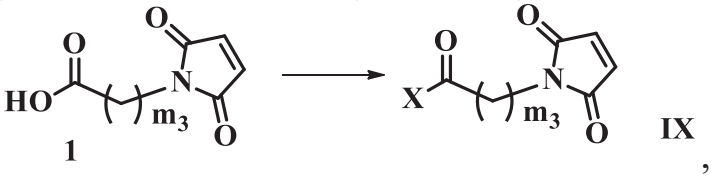
wherein in the above formulae, P^1, "〰", R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_9, m_1, m_2, m_3, m_4, m_5, Aa, r, Y, PG_1, PG_3 and PG_4 are defined the same as in **Claim 34**.

36. The method according to **Claim 32**, wherein the method further comprises synthesis of the compound of Formula (IX) by one of the following steps:

Carboxylic acid **1** and a compound with a hydroxyl group condense in the presence of a condensation reagent to yield a reactive ester IX;

Carboxylic acid **1** reacts with ethyl chloroformate or isobutyl chloroformate, in the presence of an organic base to yield a reactive mixed anhydride IX;

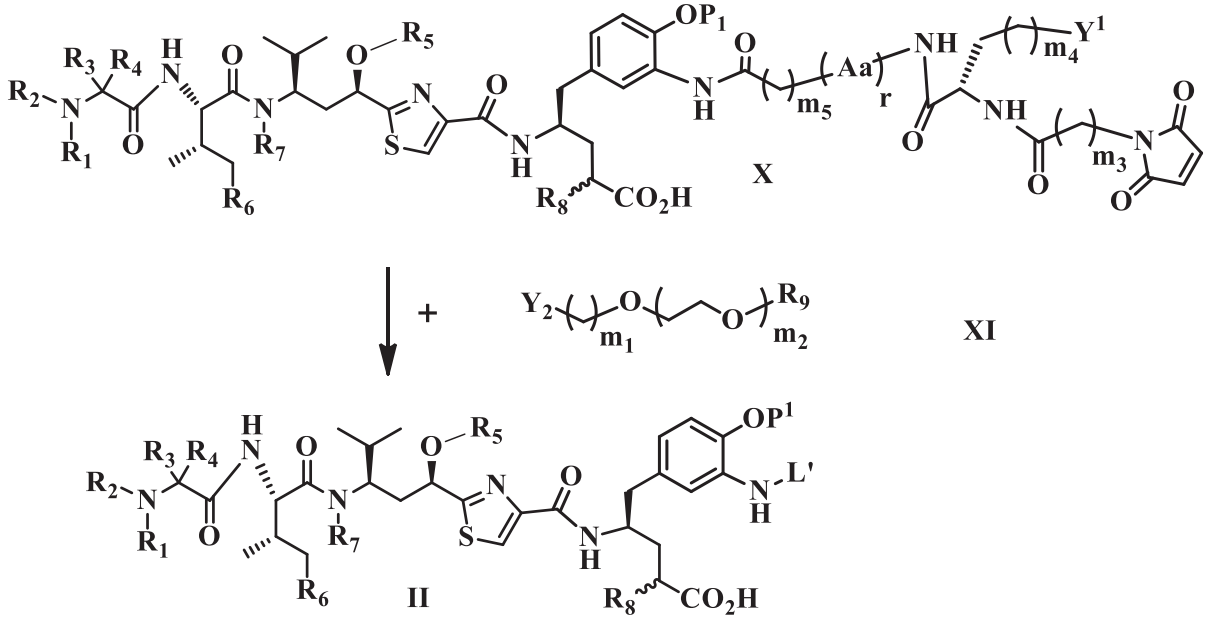
Carboxylic acid **1** reacts with oxalyl chloride, in the presence of an organic base, and a catalytic amount of DMF to yield an acyl chloride IX.



1 IX ,

wherein in the above formulae, m_3, and X are defined the same as in **Claim 32**.

37. The method according to **Claim 2**, wherein the method further comprises obtaining the compound of Formula (II) by a condensation reaction of compounds of Formula (X) and Formula (XI):

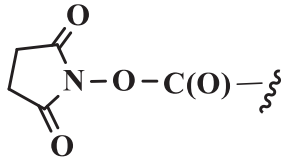
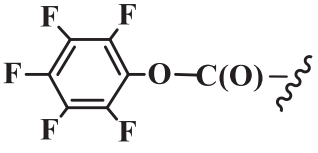
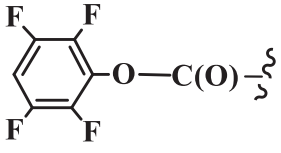
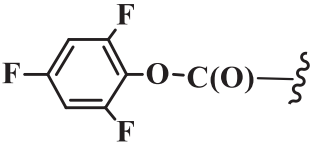
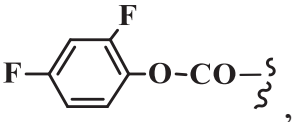
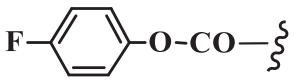
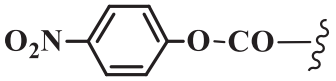
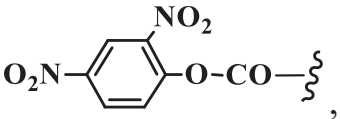
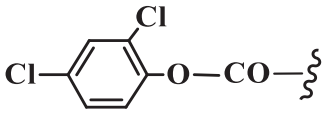
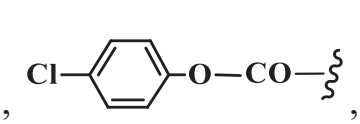
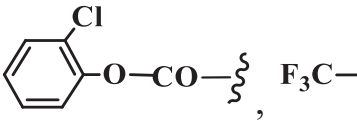
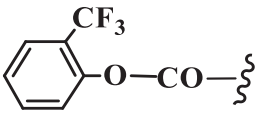


X XI II

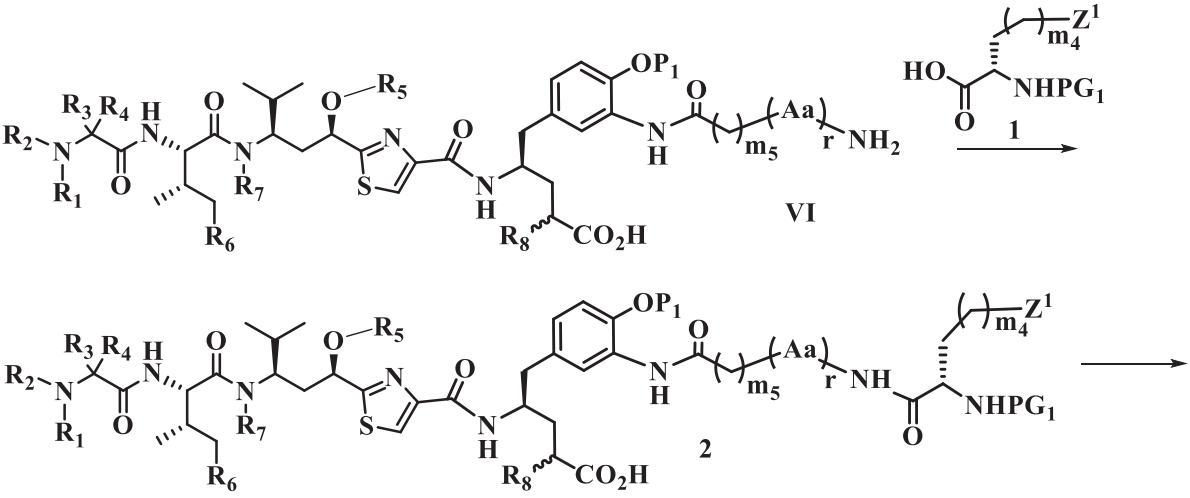
wherein Y^1 and Y^2 condense to form Y group;

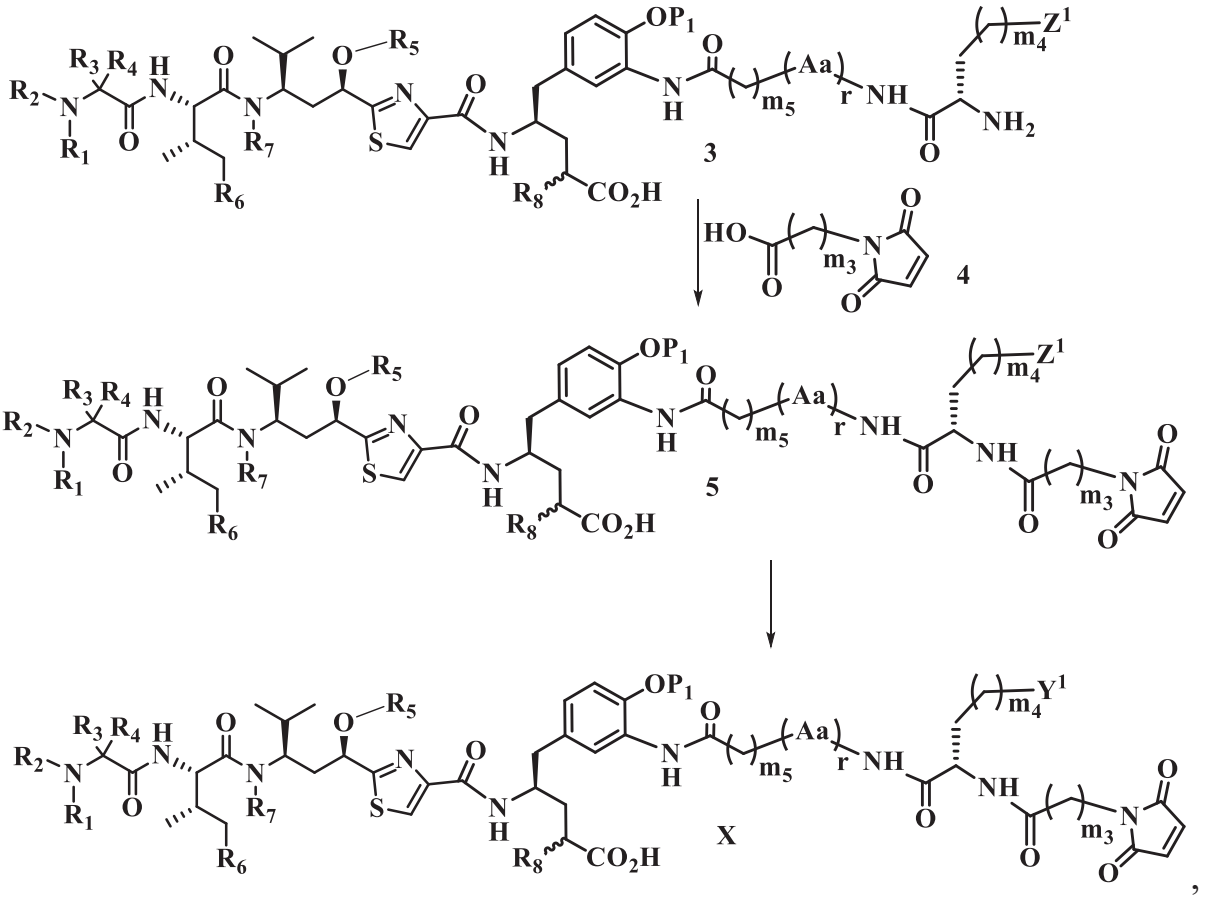
wherein in the above formulae,

P^1, "〰", R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, m_1, m_2, m_3, m_4, m_5, Aa, r and L' are defined the same as in **Claim 2**;

Y^1 and Y^2 are independently NH_2, $-^+NH_3$, COOH, COX, SO_2Cl, $P(O)Cl_2$, NHCOX, $NHSO_2Cl$, $NHP(O)Cl_2$, $NHP(O)(OH)Cl$,  (NHS),  (PFP),  ,  ,  ,  ,  ,  ,  ,  ,  or  .

38. The method of **Claim 37**, wherein the synthesis of compounds of Formula (X) comprises one or more of the following steps:

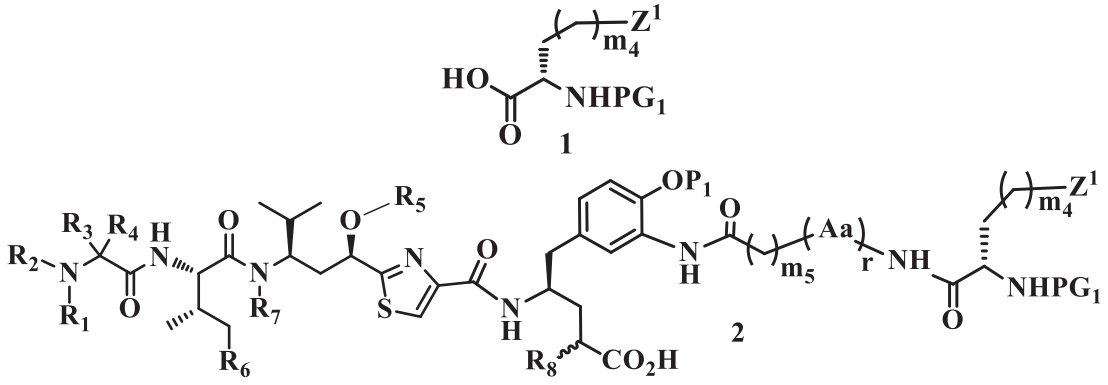




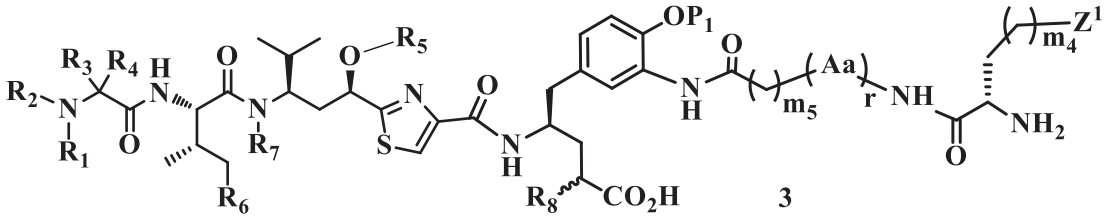
wherein in the above formulae, P^1, "〰", R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, m_3, m_4, m_5, Aa, r, and Y^1 are defined the same as in **Claim 37**; PG_1 is a protecting group; and Z_1 is a precursor of Y^1.

39. The method according to **Claim 38**, wherein the synthesis of compounds of Formula (X) comprises one or more of the following steps:

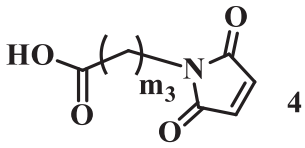
Step 1: Carboxylic acid **1** and compound **VI** condense in the presence of a condensation reagent, or by another indirect condensation reaction routes, to yield compound **2**;

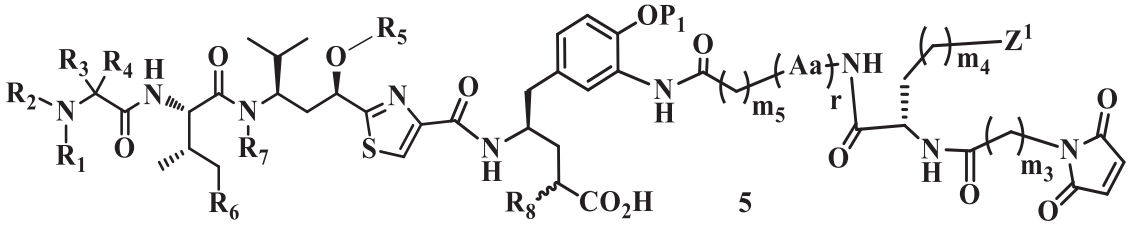


Step 2: The amino protecting group PG_1 on compound **2** is removed under deprotection condition, to yield compound **3**;

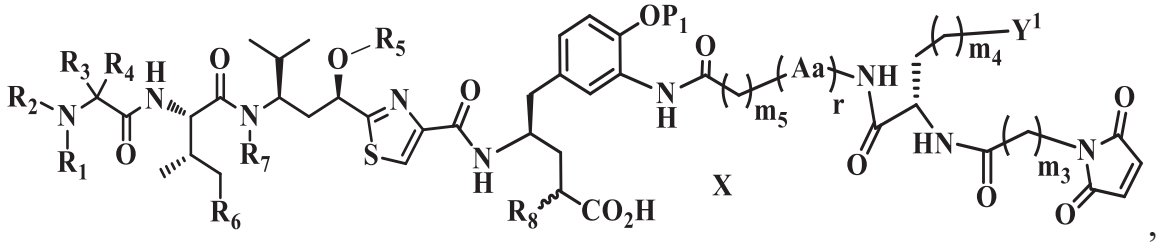


Step 3: Carboxylic acid **4** and compound **3** condense in the presence of a condensation reagent, or by another indirect condensation reaction routes, to yield compound **5**;



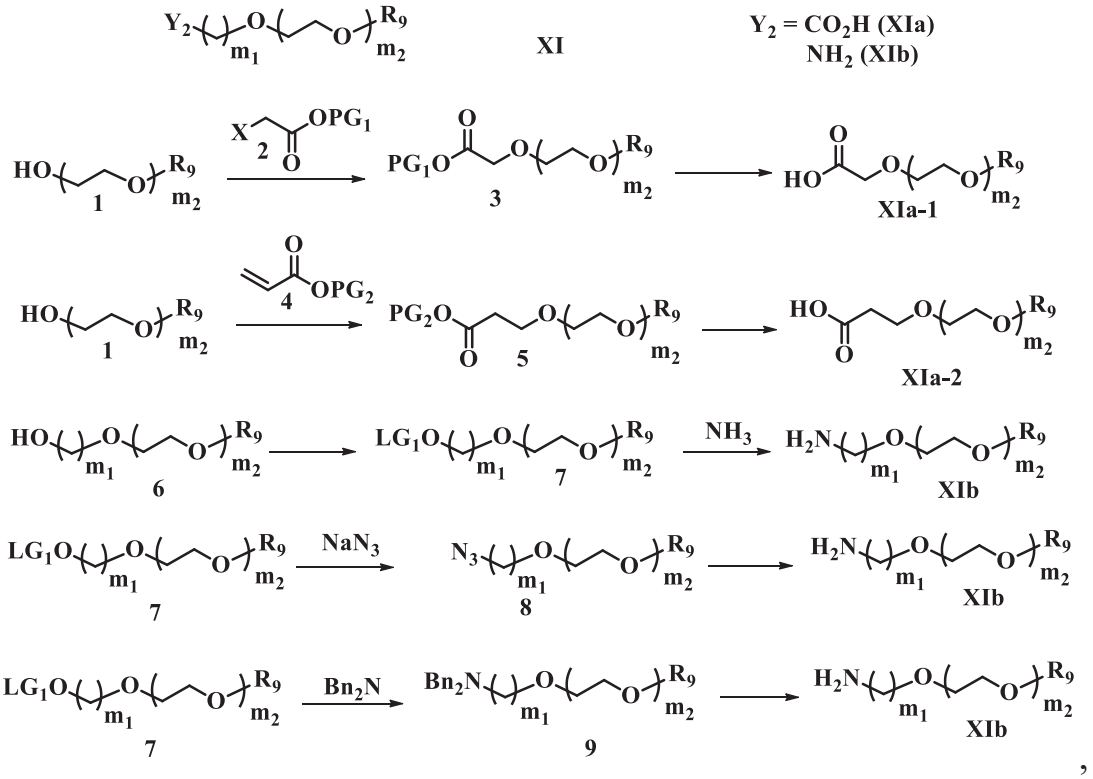


Step 4: The functional group Z^1 of compound **5** is converted to a functional group Y^1, leading to formation of compound X;



wherein in the above formulae, P^1, "〰", R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, m_3, m_4, m_5, Aa, r, PG_1, Y^1 and Z^1 are defined the same as in **Claim 38**.

40. The method according to **Claim 37**, wherein the method further comprises synthesis of the compound of Formula (XI) by one or more of the following steps:



wherein in the above formulae, m_1, m_2, and R_9 are defined the same as in **Claim 37**; PG_1 and PG_2 are independently a protecting group; X is a leaving group; and LG_1 is a leaving group.

41. The method of **Claim 40**, wherein the synthesis of the compound of Formula (XI) comprises one or more of the following steps:

Step 1: Compound **1** is dissolved in an organic solvent, and then deprotonated with a base, and then mixed and stirred with compound **2** at a predetermined temperature to yield compound **3**;

Step 2: The carboxyl protecting group PG_1 of compound **3** is removed under deprotection conditions, to yield compound XIa-1;

Step 3: Compound **1** is dissolved in an organic solvent, and then deprotonated with a base, and then mixed and stirred with compound **4** at a predetermined temperature to yield compound **5**;

Step 4: The carboxyl protecting group PG_1 of compound **5** is removed under deprotection conditions, to yield compound **XIa-2**;

Step 5: Compound **6** is dissolved in an organic solvent, and in the presence

of an organic base reacts with methylsulfonyl chloride or 4-toluenesulfonyl chloride, at 0-5°C to yield compound **7**;

Step 6: Compound **7** and ammonia solution react in water or an organic solvent, optionally under heat, to yield compound **XIb**;

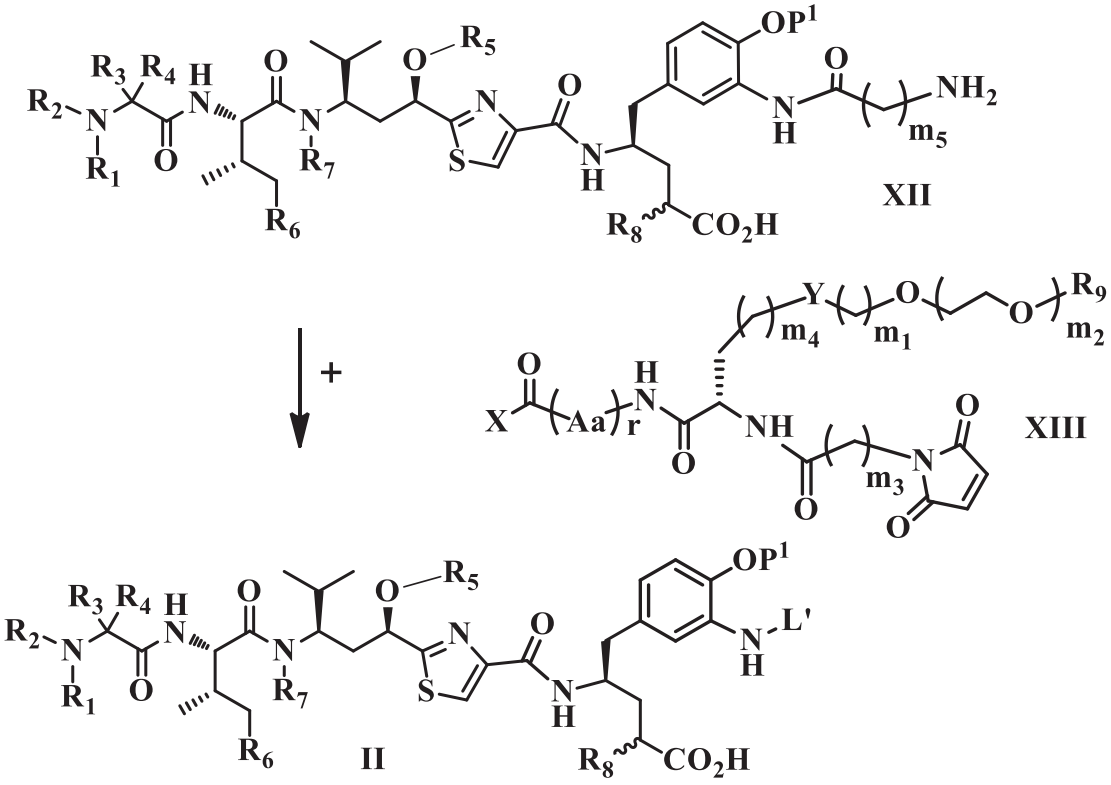
Step 7: Compound **7** and sodium azide react in an organic solvent, to yield compound **8**;

Step 8: Compound **8** is reduced, under hydrogenation condition, to give compound **XIb**;

Step 9: Compound **7** and dibenzylamine in an organic solvent, are heated to 100° C, to yield compound **9**;

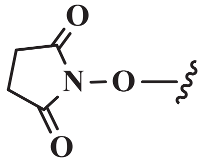
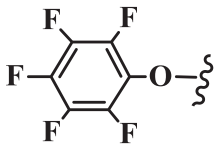
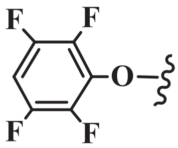
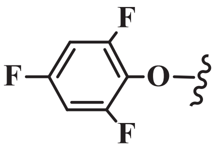
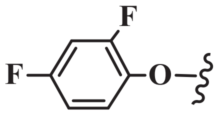
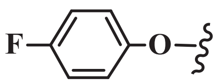
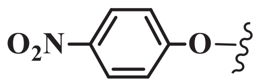
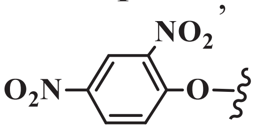
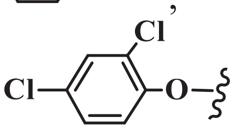
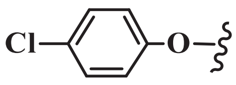
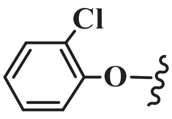
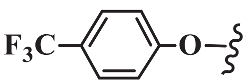
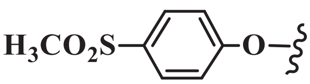
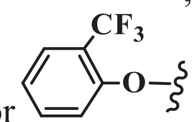
Step 10: Compound **9** is dissolved in an organic solvent, hydrogenated under H_2, in the presence of Pd/C catalyst and optionally the heated to 45°C, to yield the compound **XIb**.

42. The method according to **Claim 2**, wherein the method further comprises obtaining the compound of Formula (II) by a condensation reaction of the compounds of Formula (XII) and Formula (XIII):



wherein in the above formulae,

P^1, "〰", R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, m_1, m_2, m_3, m_4, m_5, Aa, r, Y and L' are defined the same as in **Claim 2**;

X is OH, halogen, phenoxy, pentachlorophenoxy, trifluoromethanesulfonyl, imidazole, dichlorophenoxy, tetrachlorophenoxy, 1-hydroxybenzotriazole, p-toluenesulfonyl, methanesulfonyl, 2-ethyl-5-phenyl isoxazole -3'- sulfonyl group,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  or  , an anhydride formed by an acid itself or with another anhydride of acetyl anhydride or formic anhydride; or a peptide coupling reaction intermediate or a Mitsunobu reaction intermediate;

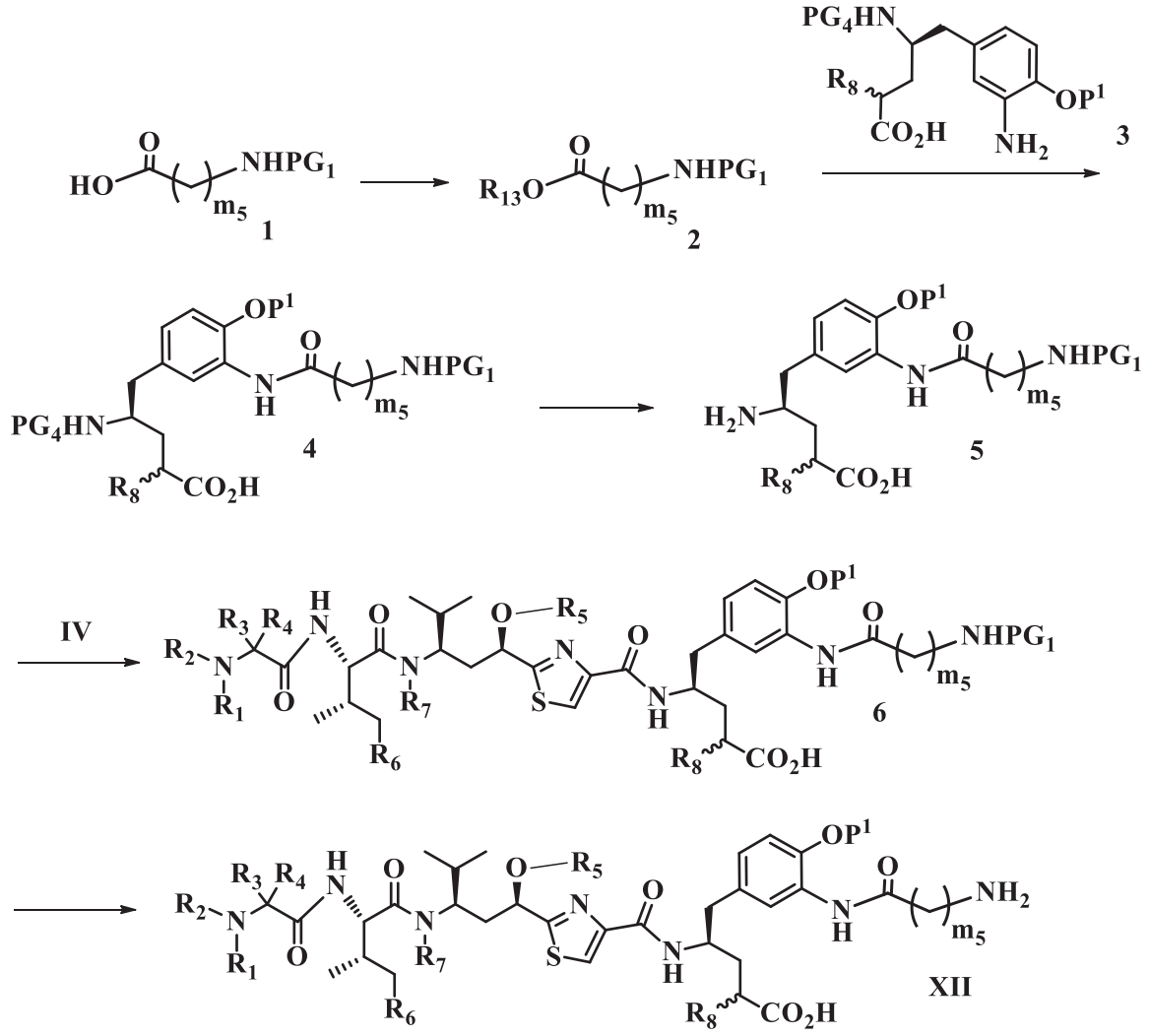
wherein the condensation reaction is carried out in dichloroethane, DMF, DMA, tetrahydrofuran (THF), DMSO, acetone, isopropanol, n-butanol or acetonitrile, or mixed solvents of two or three of the above, containing 1 to 100% pyridine, triethylamine or diisopropylethylamine; with or without an inert gas, at -20 to 150 °C, for 5 minutes to 120 hours;

or the condensation reaction is conducted in following buffer system and under following conditions: a buffer system has a pH of 5.0 - 9.5, is 1 mM - 1000 mM phosphoric acid, acetic acid, citric acid, boric acid, carbonic acid, barbituric acid, Tris (Tris-hydroxymethyl aminomethane), benzoic acid or triethanolamine system, or a mixture thereof, containing 0 to 35% a miscible

organic solvent of methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, acetonitrile, acetone, DMF, DMA or DMSO; a reaction temperature is 0 to 45 °C and reaction time is from 5 minutes to 96 hours.

43. The method of **Claim 42**, wherein the NH_2 group of Formula (XII) participates in the conjugation reaction in a form of salt, with trifluoroacetic acid, hydrochloride acid, formic acid, acetatic acid, sulfuric acid, phosphoric acid, nitric acid, citric acid, succinic acid, benzoic acid or sulfonic acid.

44. The method according to **Claim 42**, wherein the method further comprises synthesis of the compound of Formula (XII) by one or more of the following steps:



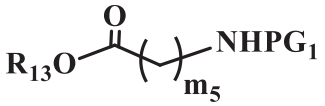
,

wherein in the above formulae, P^1, "〰", R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, and m_5

are defined the same as in **Claim 42**; PG_1 and PG_4 are independently a protecting group; and R_{13} is defined the same as X above.

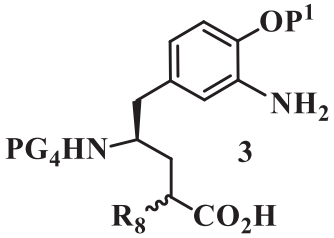
45. The method according to **Claim 44**, wherein the synthesis of the compound of Formula (XII) comprises one or more of the following steps:

Step 1: Compound **1** reacts with a compound containing a hydroxyl group, in the presence of a condensation reagent, to yield a reactive carboxylic acid derivative compound **2**;

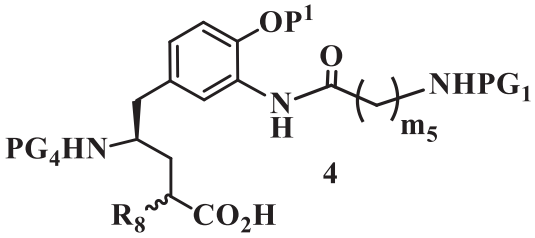


2

Step 2: Compound **2** and compound **3** condense in an aqueous solution having a pH of 5.0-8.0, or an organic solution, and (i) in the presence of an organic base or an inorganic base, to yield compound **4**;

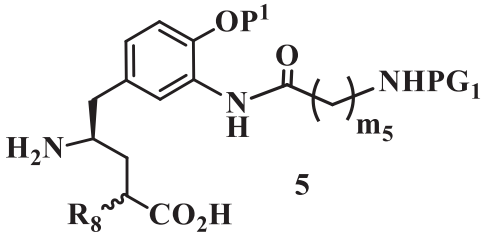


3



4

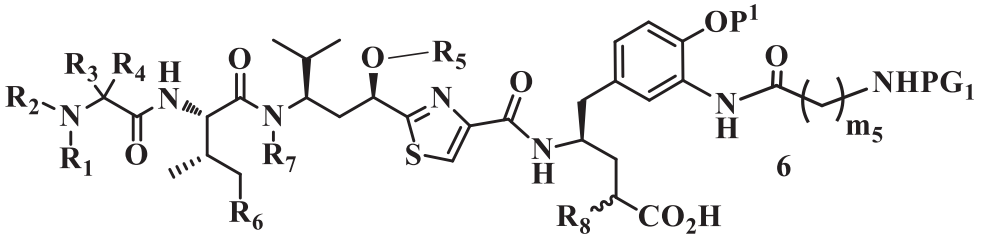
Step 3: The amino protecting group PG_4 of compound **4** is removed selectively under deprotection conditions, to yield compound **5**;



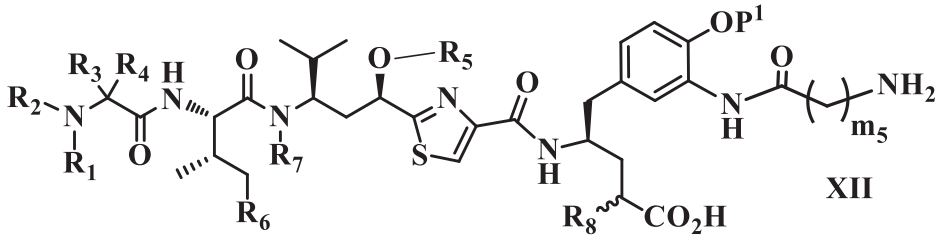
5

Step 4: Compound **5** and a compound of Formula (IV) condense in an aqueous solution having a pH of 5.0-8.0, or an organic solution, and (i) in the presence of an organic base or an inorganic base, or (ii) in the absence of a base,

at a predetermined reaction temperature and reaction time, to yield compound **6**;



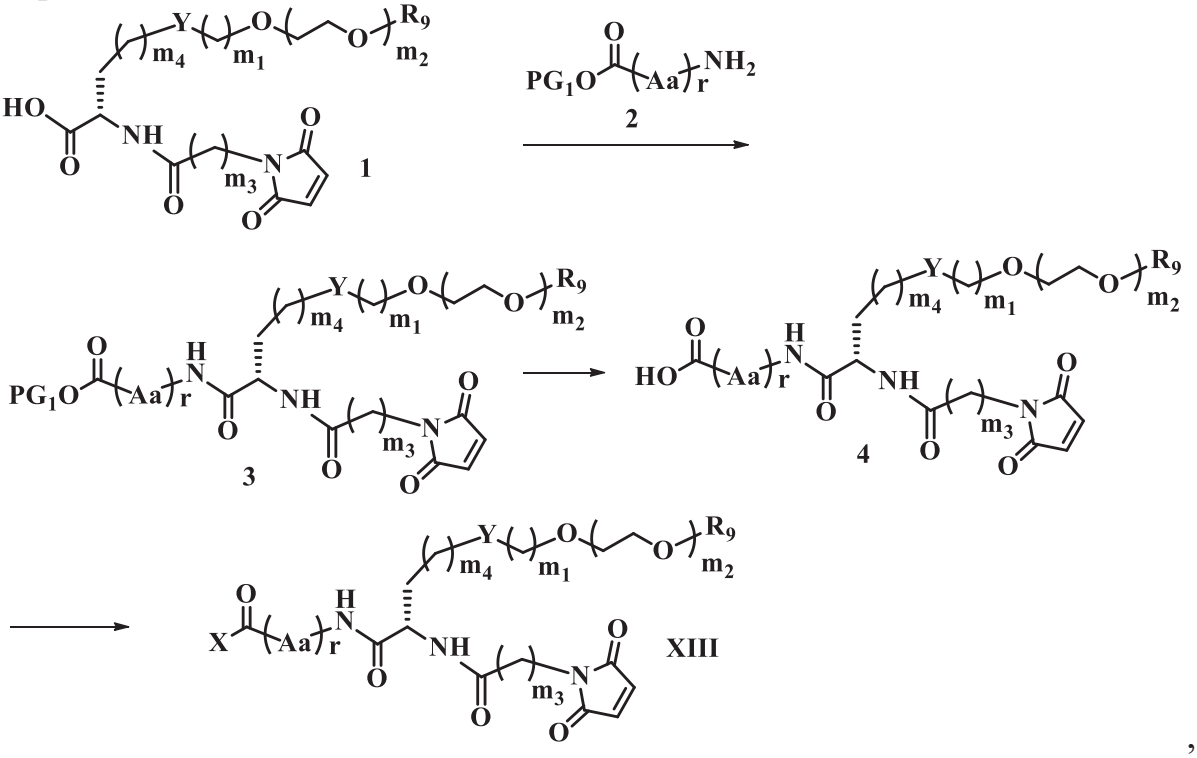
Step 5: The amino protecting group PG_1 of compound 6 is removed under deprotection conditions, to yield compound XIII



,

wherein in the above formulae, P^1, "〰", R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_{13}, m_5, PG_1 and PG_4 are defined the same as in **Claim 44**.

46. The method according to **Claim 42**, wherein the method further comprises synthesis of the compound of Formula (XIII) by one or more of the following steps:



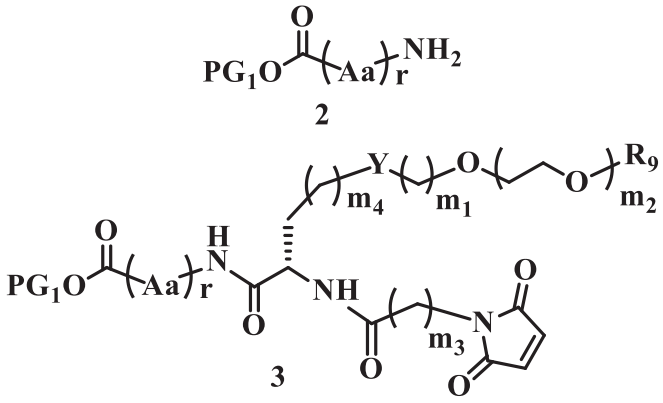
,

wherein in the above formulae, R_9, m_1, m_2, m_3, m_4, m_5, Aa, r and Y are defined

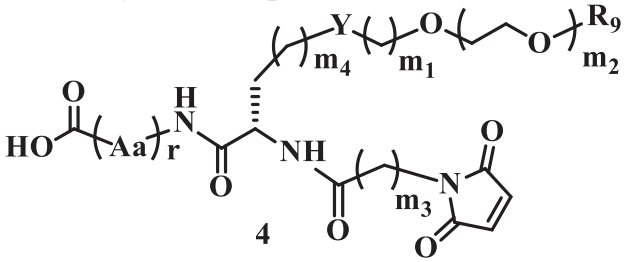
the same as in **Claim 42**; and PG_1 is a protecting group.

47. The method according to **Claim 46**, wherein the synthesis of compounds of Formula (XIII) comprises one or more of the following steps:

Step 1: Carboxylic acid **1** and compound **2** condense in the presence of a condensation reagent, or by another indirect condensation reaction routes, to yield compound **3**;



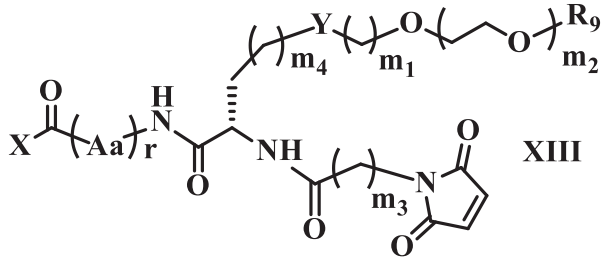
Step 2: The carboxyl protecting group PG_1 of compound **3** is removed under deprotection conditions, to yield compound **4**;



Step 3: Compound **4** reacts with a compound containing a hydroxyl group, in the presence of a condensation reagent, to yield a reactive ester compound **XIII**;

or carboxylic acid **4** reacts with ethyl chloroformate or isobutyl chloroformate, in the presence of an organic base to yield a reactive mixed anhydride **XIII**;

or carboxylic acid **4** reacts with oxalyl chloride, in the presence of an organic base and a catalytic amount of DMF to yield an acyl chloride **XIII**

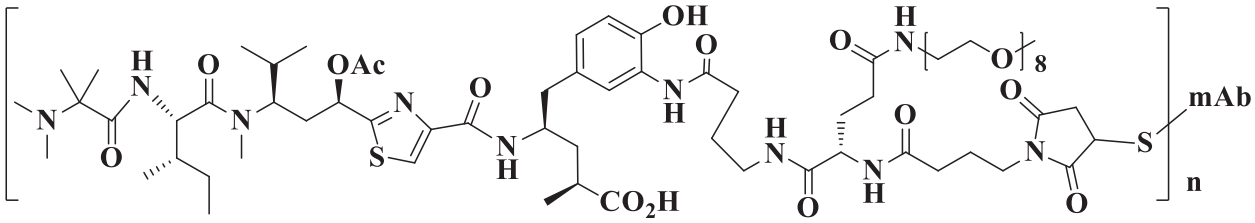


XIII

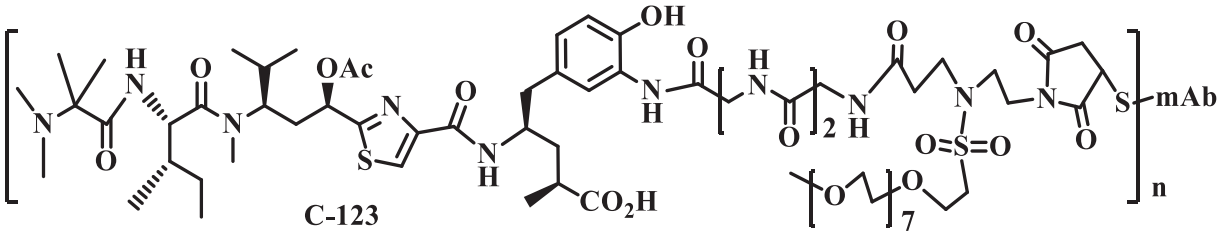
,

wherein in the above formulae, R_9, m_1, m_2, m_3, m_4, m_5, Aa, r, PG_1, X and Y are defined the same as in **Claim 46**.

48. The conjugate according to **Claim 1**, wherein the compounds of Formula (I) has one of the following structures:



C-72,

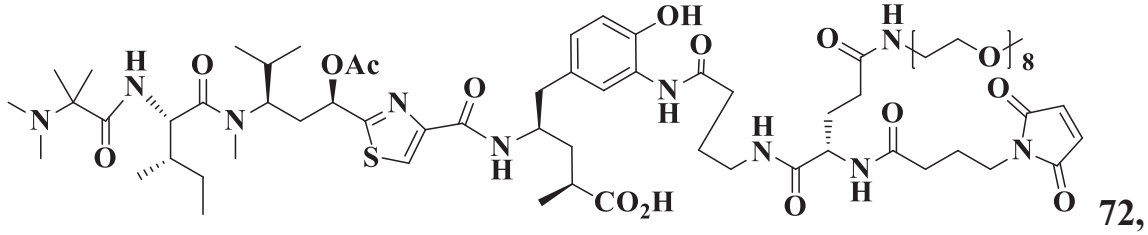


C-123

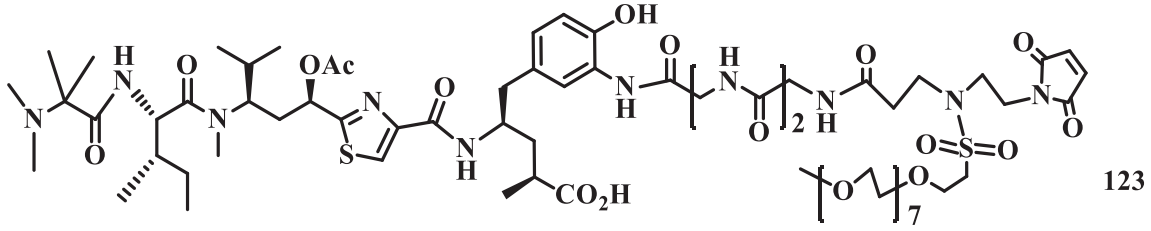
,

wherein in the above formulae, mAB is a monoclonal antibody; and n is defined the same as in **Claim 1**.

49. A compound having one of the following structures:



72,



123

50. A pharmaceutical composition comprising conjugate of **Claim 1**, and a pharmaceutically acceptable excipients therefor.

51. The pharmaceutical composition according to **Claim 50** for use in treating a cancer, infection or autoimmune disease.

52. A pharmaceutical composition comprising the compounds according to **Claim 49**.

53. The pharmaceutical compositions according to **Claim 52** for use in treating cancer, infection or autoimmune disease.